EARN 2 CE CREDITS–Pregnancy and the Eye: What to Do When You're Caring for Two, *p. 76*


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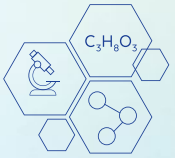


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[1]IRI Artificial tears preservative-free dollar and unite sales by manufacturer, 52 weeks ending 12/22/19.



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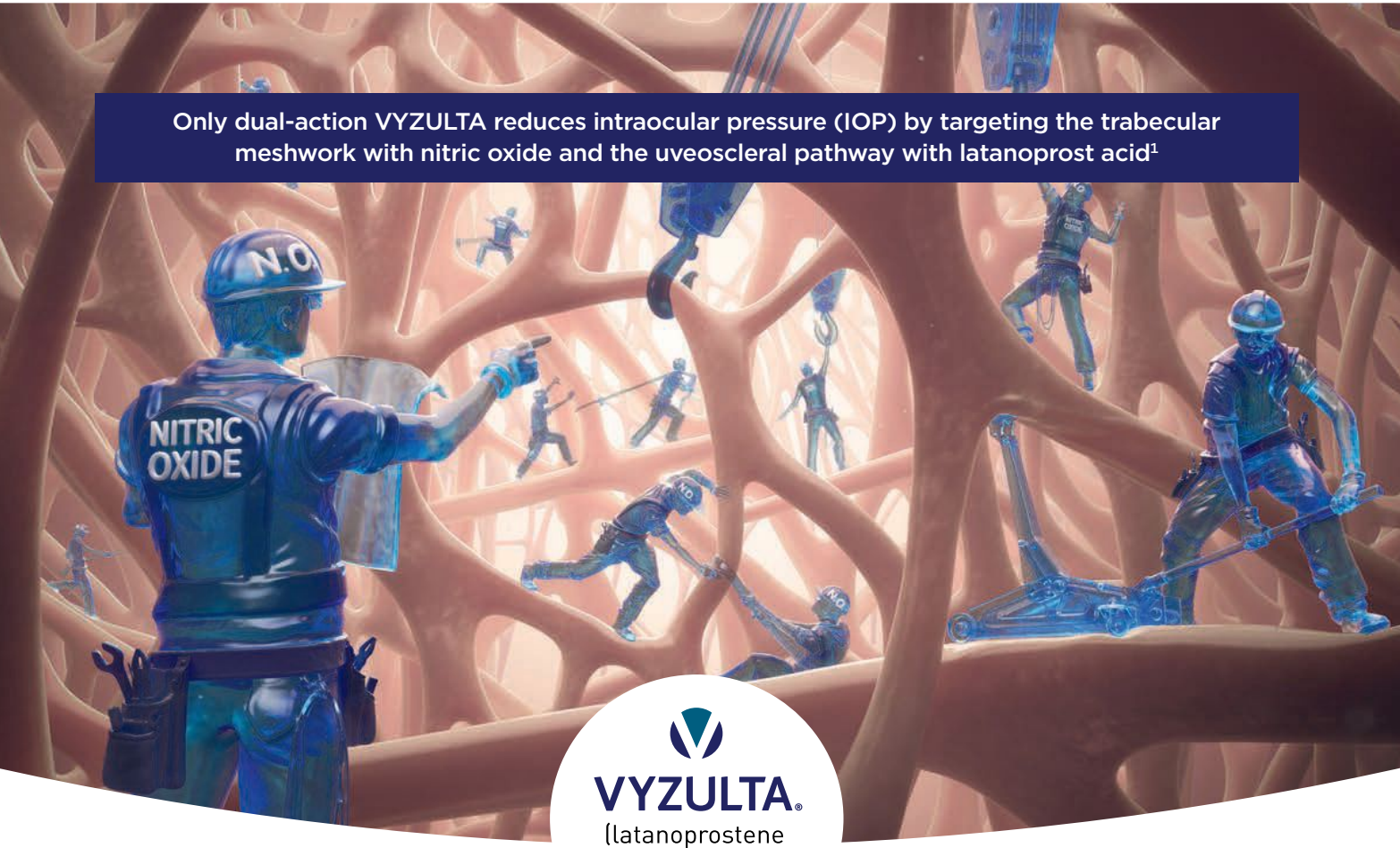
11th Annual Retina Report

# Reconsider Your Approach to DIABETIC RETINOPATHY

*New findings may create protocols that minimize, or even prevent, vision loss. Page 28*



ALSO:




# EXPAND THE TRABECULAR MESHWORK WITH THE POWER OF NITRIC OXIDE[2-6]

**VYZULTA achieved significant and sustained long-term IOP reductions vs Timolol 0.5% in pivotal trials[7]**

*P*<0.001 vs baseline at all pre-specified visits over 12 months in a pooled analysis of APOLLO and LUNAR clinical trials (N=831)

**VYZULTA demonstrated safety profile in clinical trials**

Only 6 out of 811 patients discontinued due to ocular adverse events in APOLLO and LUNAR clinical trials[1,8,9]

**Visit VYZULTANOW.com to see our efficacy results**

## INDICATION

VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

## IMPORTANT SAFETY INFORMATION

- Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent
- Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation
- Use with caution in patients with a history of intraocular inflammation (iritis/uveitis). VYZULTA should generally not be used in patients with active intraocular inflammation
- Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Use with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema

## IMPORTANT SAFETY INFORMATION cont'd

- There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products that were inadvertently contaminated by patients
- Contact lenses should be removed prior to the administration of VYZULTA and may be reinserted 15 minutes after administration
- Most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%)

**For more information, please see Brief Summary of Prescribing Information on next page.**

**References: 1.** VYZULTA Prescribing Information. Bausch & Lomb Incorporated. **2.** Cavet ME. *J Ocul Pharmacol Ther*. 2018;34(1):52-60. DOI:10.1089/jop.2016.0188. **3.** Wareham LK. *Nitric Oxide*. 2018;77:75-87. DOI:10.1016/j.niox.2018.04.010. **4.** Stamer DW. *Curr Opin Ophthalmol*. 2012;23:135-143. DOI:10.1097/ICU.0b013e32834ff23e. **5.** Cavet ME. *Invest Ophthalmol Vis Sci*. 2015;56(6):4108-4116. **6.** Kaufman PL. *Exp Eye Research*. 2008;861:3-17. DOI:10.1016/j.exer.2007.10.007. **7.** Weinreb RN. *J Glaucoma*. 2018;27:7-15. **8.** Weinreb RN. *Ophthalmology*. 2016;123(5):965-973. **9.** Medeiros FA. *Am J Ophthalmol*. 2016;168:250-259.



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**BRIEF SUMMARY OF PRESCRIBING INFORMATION**

**This Brief Summary does not include all the information needed to use VYZULTA safely and effectively. See full Prescribing Information for VYZULTA.**

# VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%, for topical ophthalmic use.

**Initial U.S. Approval: 2017**

## 1 INDICATIONS AND USAGE

VYZULTA® (latanoprostene bunod ophthalmic solution) 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

## 4 CONTRAINDICATIONS

None

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Pigmentation

VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% may cause changes to pigmented tissues. The most frequently reported changes with prostaglandin analogs have been increased pigmentation of the iris and periorbital tissue (eyelid).

Pigmentation is expected to increase as long as latanoprostene bunod ophthalmic solution is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of VYZULTA, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes are likely to be reversible in most patients. Patients who receive prostaglandin analogs, including VYZULTA, should be informed of the possibility of increased pigmentation, including permanent changes. The long-term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly *[see Patient Counseling Information (17) in full Prescribing Information]*.

### 5.2 Eyelash Changes

VYZULTA may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and the number of lashes or hairs. Eyelash changes are usually reversible upon discontinuation of treatment.

### 5.3 Intraocular Inflammation

VYZULTA should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation as it may exacerbate this condition.

### 5.4 Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. VYZULTA should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

### 5.5 Bacterial Keratitis

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

### 5.6 Use with Contact Lens

Contact lenses should be removed prior to the administration of VYZULTA because this product contains benzalkonium chloride. Lenses may be reinserted 15 minutes after administration.

## 6 ADVERSE REACTIONS

The following adverse reactions are described in the Warnings and Precautions section: pigmentation (5.1), eyelash changes (5.2), intraocular inflammation (5.3), macular edema (5.4), bacterial keratitis (5.5), use with contact lens (5.6).

### 6.1 Clinical Trials Experience

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

VYZULTA was evaluated in 811 patients in 2 controlled clinical trials of up to 12 months duration. The most common ocular adverse reactions observed in patients treated with latanoprostene bunod were: conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%). Approximately 0.6% of patients discontinued therapy due to ocular adverse reactions including ocular hyperemia, conjunctival irritation, eye irritation, eye pain, conjunctival edema, vision blurred, punctate keratitis and foreign body sensation.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Risk Summary

There are no available human data for the use of VYZULTA during pregnancy to inform any drug associated risks.

Latanoprostene bunod has caused miscarriages, abortion, and fetal harm in rabbits. Latanoprostene bunod was shown to be abortifacient and teratogenic when administered intravenously (IV) to pregnant rabbits at exposures ≥ 0.28 times the clinical dose. Doses ≥ 20 µg/kg/day (23 times the clinical dose) produced 100% embryofetal lethality. Structural abnormalities observed in rabbit fetuses included anomalies of the great vessels and aortic arch vessels, domed head, sternebral and vertebral skeletal anomalies, limb hyperextension and malrotation, abdominal distension and edema. Latanoprostene bunod was not teratogenic in the rat when administered IV at 150 mcg/kg/day (87 times the clinical dose) *[see Data]*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies.

Data

*Animal Data*

Embryofetal studies were conducted in pregnant rabbits administered latanoprostene bunod daily by intravenous injection on gestation days 7 through 19, to target the period of organogenesis. The doses administered ranged from 0.24 to 80 mcg/kg/day. Abortion occurred at doses ≥ 0.24 mcg/kg/day latanoprostene bunod (0.28 times the clinical dose, on a body surface area basis, assuming 100% absorption). Embryofetal lethality (resorption) was increased in latanoprostene bunod treatment groups, as evidenced by increases in early resorptions at doses ≥ 0.24 mcg/kg/day and late resorptions at doses ≥ 6 mcg/kg/day (approximately 7 times the clinical dose). No fetuses survived in any rabbit pregnancy at doses of 20 mcg/kg/day (23 times the clinical dose) or greater. Latanoprostene bunod produced structural abnormalities at doses ≥ 0.24 mcg/kg/day (0.28 times the clinical dose). Malformations included anomalies of sternum, coarctation of the aorta with pulmonary trunk dilation, retroesophageal subclavian artery with absent brachiocephalic artery, domed head, forepaw hyperextension and hindlimb malrotation, abdominal distention/edema, and missing/fused caudal vertebrae.

An embryofetal study was conducted in pregnant rats administered latanoprostene bunod daily by intravenous injection on gestation days 7 through 17, to target the period of organogenesis. The doses administered ranged from 150 to 1500 mcg/kg/day. Maternal toxicity was produced at 1500 mcg/kg/day (870 times the clinical dose, on a body surface area basis, assuming 100% absorption), as evidenced by reduced maternal weight gain. Embryofetal lethality (resorption and fetal death) and structural anomalies were produced at doses ≥ 300 mcg/kg/day (174 times the clinical dose). Malformations included anomalies of the sternum, domed head, forepaw hyperextension and hindlimb malrotation, vertebral anomalies and delayed ossification of distal limb bones. A no observed adverse effect level (NOAEL) was established at 150 mcg/kg/day (87 times the clinical dose) in this study.

### 8.2 Lactation

Risk Summary

There are no data on the presence of VYZULTA in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for VYZULTA, and any potential adverse effects on the breastfed infant from VYZULTA.

### 8.4 Pediatric Use

Use in pediatric patients aged 16 years and younger is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

### 8.5 Geriatric Use

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

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Latanoprostene bunod was not mutagenic in bacteria and did not induce micronuclei formation in the *in vivo* rat bone marrow micronucleus assay. Chromosomal aberrations were observed *in vitro* with human lymphocytes in the absence of metabolic activation.

Latanoprostene bunod has not been tested for carcinogenic activity in long-term animal studies. Latanoprost acid is a main metabolite of latanoprostene bunod. Exposure of rats and mice to latanoprost acid, resulting from oral dosing with latanoprost in lifetime rodent bioassays, was not carcinogenic.

Fertility studies have not been conducted with latanoprostene bunod. The potential to impact fertility can be partially characterized by exposure to latanoprost acid, a common metabolite of both latanoprostene bunod and latanoprost. Latanoprost acid has not been found to have any effect on male or female fertility in animal studies.

### 13.2 Animal Toxicology and/or Pharmacology

A 9-month toxicology study administered topical ocular doses of latanoprostene bunod to one eye of cynomolgus monkeys: control (vehicle only), one drop of 0.024% bid, one drop of 0.04% bid and two drops of 0.04% per dose, bid. The systemic exposures are equivalent to 4.2-fold, 7.9-fold, and 13.5-fold the clinical dose, respectively, on a body surface area basis (assuming 100% absorption). Microscopic evaluation of the lungs after 9 months observed pleural/subpleural chronic fibrosis/inflammation in the 0.04% dose male groups, with increasing incidence and severity compared to controls. Lung toxicity was not observed at the 0.024% dose.

U.S. Patent Numbers: 7,273,946; 7,629,345; 7,910,767; 8,058,467.



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VOL. 157 NO. 6 ■ JUNE 15, 2020

## IN THE NEWS

Researchers recently discovered that **cosmetic preservatives such as benzalkonium chloride and formaldehyde can be toxic to meibomian gland epithelial cells**; exposure could lead to cellular atrophy and death within hours. The investigators found that 30 minutes of exposure to these preservatives resulted in a significant reduction in cell activity, an effect they confirmed is dose-dependent and occurs at concentrations equal to or less than dosages approved for human use.

Wang J, Liu Y, Kam WR, et al. Toxicity of the cosmetic preservatives parabens, phenoxyethanol and chlorphenesin on human meibomian gland epithelial cells. Exp Eye Resear. May 5, 2020. [Epub ahead of print].

A new study has documented **retinal findings possibly associated with COVID-19 infection**. The researchers believe their findings could be associated with central nervous system manifestations already described. All 12 adults examined after COVID-19 symptom onset showed hyper-reflective lesions at the level of ganglion cell and inner plexiform layers, more prominently at the papillomacular bundle in both eyes. With fundus examination and imaging, they found subtle cotton-wool spots and microhemorrhages along the retinal arcade in four patients.

Marinho PM, Marcos AAA, Romano AC, et al. Retinal findings in patients with COVID-19. Lancet. 2020;395(10237):1610.

Researchers recently found **patients with a history of statin use or dyslipidemia have elevated risk of dry eye disease (DED)**. Of 39,336 patients seen over 10 years, the researchers found DED in 8.6%. The usage was categorized as low in 1.9%, moderate in 6.8% and high in 2.6%. The study identified the odds of a DED diagnosis as 1.39 in low-intensity statin use, 1.47 in moderate-intensity use and 1.46 in high-intensity statin use.

Aldaas K, Ismail O, Hakim J, et al. Association of dry eye disease with dyslipidemia and statin use. Am J Ophthalmol. May 12, 2020. [Epub ahead of print].

# New Insights on LWE Diagnosis: Use Two Drops

Getting the staining protocol right is just the first step in understanding this condition.

**By Bill Kekevian, Senior Editor**

Recently published research on lid wiper epitheliopathy (LWE) concludes that using only a single drop of dye to diagnose the little-understood condition is insufficient.[1] To truly reveal the full extent of LWE through staining, two drops are superior, the data shows. In a number of cases the research team, led by Christopher Lievens, OD, reviewed, patients didn't even show any LWE damage after that first drop. However, after a second drop, Dr. Lievens says, the condition proved to be widespread. "Unlike staining the cornea, it requires two sequential drops—doing it wrong risks a misdiagnosis," he explains.

## Man on a Mission

While that finding has a practical purpose in optometric clinics, Dr. Lievens, a professor and the chief of internal clinics at Southern College of Optometry, has an ulterior motive to evangelize about LWE.

"If you surveyed 100 optometrists, 99 probably wouldn't know what you're talking about," he says about the condition. And those who do know about it "don't know how best to look for it or what to specifically do if they find it." And that's not any doctors' fault. Even the known research on LWE shows variations on how to diagnose, grade and treat it.[2,3] Dr. Lievens is hoping to change that.

Primarily, Dr. Lievens explains, lens wearers are at particular risk due to the device's propensity for collecting debris and physical interaction with various anterior segment structures. A daily disposable might be the best option for avoiding LWE damage, he says, because this lens choice can offer quality lubrication and the least issues with surface deposits.

## Timing is Everything

But the recent publication in *Contact Lens & Anterior Eye* narrows in on diagnostics. It relied on data from 37 participants with LWE. The team applied a single drop of 1% lissamine green (LG) (10µL) to the superior bulbar conjunctiva in the right eye, and took photographs of the lid margin at one, three and five minutes after instillation. Then, they repeated the measurements using two drops of 1% LG instead. The same procedures were followed using 2% sodium fluorescein (NaFl) (2µL) to the left eye.

For both LG and NaFl, the evaluation timing was significant. For ease, the investigators suggest

*Continued on page 6*

NEWS STORIES POST EVERY WEEKDAY MORNING AT www.reviewofoptometry.com/news

# COVID-19's Impact on Uveitis Management

COVID-19 has shifted the way clinicians approach patient care. In the case of uveitis specifically, every step of the process, from diagnosis to management, has been affected. Clinicians recently outlined the changes in an *Ophthalmology* article:

***Diagnosis.*** COVID-19 is changing what tests are considered necessary to diagnose a patient with uveitis. The uveitis specialists noted that, for the most part, only syphilis and tuberculosis testing are to be performed in all cases of uveitis. Unless presenting signs and symptoms are inconsistent with those of classic uveitis, tests that pose a higher risk of infection should be avoided.

***Treatment.*** Although no published reports of COVID-19-associated uveitis exist, findings show a higher risk of infection in immunosuppressed patients and those with infectious uveitis whose treatment regimen includes anti-microbial and anti-inflammatory drugs. At the same time, these patients may experience worse outcomes if their therapy is interrupted.

Eyecare providers, as well as those in other fields, have found that immunomodulatory treatment is not a major risk factor for severe COVID-19 and should not be discontinued unless a patient has been exposed to the virus or has a suspected or confirmed infection.

In the case of infection, locally delivered corticosteroids are an effective option to avoid systemic drug use in non-infectious uveitis.

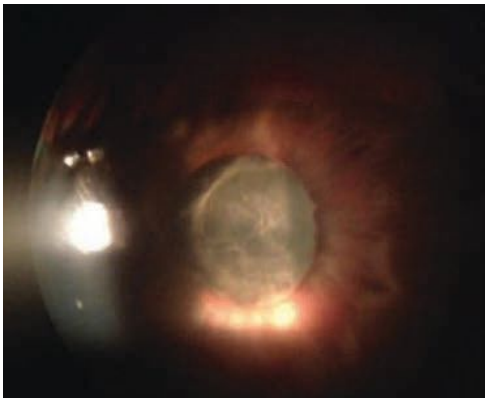


Photo: Michael Trottini, OD, and Candice Tolud, OD

**Managing patients with uveitis, such as this one with HLA-B27 uveitis, may take some extra thought amid COVID-19.**

***Management.*** As with many other ocular conditions, telemedicine has become the standard of care for uveitis consultation in light of COVID-19. However, eyecare providers have indicated they prefer in-person visits that allow for comprehensive eye examinations in the case of patients who have a new presentation, experience recurrent inflammation or adjust their treatment regimen.

If an office-based appointment is deemed appropriate, personal protective equipment and proper hygiene techniques have proved to be more important than ever in lowering the risk of infection in both the patient and the provider.

Despite the need for more hands-on care in certain cases, providers and patients alike have acknowledged the feasibility of telemedicine in managing and comanaging uveitis, a practice that could persist even after the pandemic.

Smith JR, Lai TYY. Managing uveitis during the COVID-19 pandemic. Ophthalmology. May 18, 2020. [Epub ahead of print].

# Not All Breath Shields Are Created Equal

*Size and curvature appear to be key to protection, experiment shows.*

It's a frightening new world optometrists are embarking on as states slowly reopen amid COVID-19. To keep everyone as safe as possible, clinicians are focusing on personal protective equipment (PPE) because social distance isn't really an option in the office. Slit lamp breath shields, for example, have become almost indispensable. Some optometrists have designed their own breath shields, and most manufacturers now offer shields for their own equipment.[1]

However, a Canadian research team took a closer look at various shields and found not all are equally protective.[2]

The investigators filled a spray gun filled with a colored dye and set it on the "mist" setting to simulate a sneeze. They evaluated six commercially available breath shields and one repurposed from a plastic container lid. They sprayed each breath shield in a standardized fashion three times and measured the amount of "overspray," which they then compared with a control test without a shield.[2]

They found that some of the shields allowed up to 54% overspray. Breath shields that attach to the objective lens arm did a better job than those hung by the oculars of comparable size, they said. Additionally, the repurposed plastic lid breath shield had an unexpected advantage over the others. Its slight curve toward the examiner's face allowed only 2% overspray. It was also aided by its size, at 513cm$^2$. The largest breath shield, at 1,254cm$^2$, performed even better, as it hung near the oculars and prevented essentially all the overspray.[3]

The study says that larger breath shields are preferable, but any shield should be combined with masks, gloves and handwashing.[2]

1. Lucas J. How to make your own slit lamp breath shield. Rev Optom. www.reviewofoptometry.com/article/how-to-make-your-own-slit-lamp-breath-shield. April 23, 2020.
2. Liu J, Wang A, Ing E. Efficacy of slit lamp breath shields. Am J Ophthalmol. May 11, 2020. [Epub ahead of print].

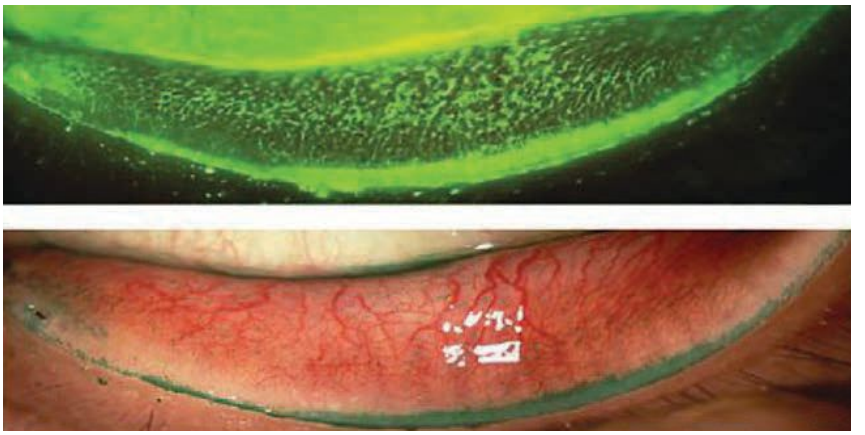
# Updated Staining Protocol for LWE

*Contiued from page 4*

clinical observation take place three minutes after administering the second drop of LG or NaFl. The analysis shows that with two drops of each respective dye, LG could be optimally viewed anywhere between one and five minutes (three minutes had the greatest staining) and NaFl viewed three to five minutes, Dr. Lievens explains.

This study establishes a protocol for diagnosing a patient, but that's just the tip of the iceberg, according to Dr. Lievens. Next on his agenda, he hopes to examine more of the natural course of LWE. Additionally, he would like to restructure the grading scale since "the current model is time consuming," he explains. "Ideally, we should have a picture match system."

Once such a system is in place, clinicians can better target treatment with artificial tears, cyclosporine, refitting contact lenses with more appropriate materials or perhaps even initiating an omega-3 supplement.



Photos: Jalaah Varkooty, Centre for Contact Lens Research.

**To properly diagnose lid wiper epitheliopathy with sodium fluorescein, above, and lissamine green, below, clinicians should instill two drops and wait three minutes, new research suggests.**

1. Lievens C, Norgett Y, Briggs N. Optimal methodology for lid wiper epitheliopathy identification. Contact Lens & Anterior Eye. May 14, 2020. [Epub ahead of print].
2. Efron N, Brennan N, Morgan P, Wilson T. Lid wiper epitheliopathy. Prog Retin Eye Res. 2016;53:140-74.
3. Korb D, Greiner J, Herman J, et al. Lid-wiper epitheliopathy and dry eye symptoms in contact lens wearers. CLAO J. 2002;28(4):211-6.

# Glaucoma Coach May Help with Non-compliance

Glaucoma patients with poor medication compliance may benefit from a personalized coaching program, a study in *Ophthalmology Glaucoma* suggests. The approach could help to improve their lax habits.

Researchers from the University of Michigan created the Support, Educate, Empower (SEE) program that includes automated medication reminders, three in-person counseling sessions with a glaucoma coach trained in motivational interviewing and five additional coaching calls for in-between session support.

Results from the SEE program show promise, as medication adherence improved from 59.9% at baseline to 81.3% by the program's end. Additionally, 95% of participants reported improved compliance while 59% had adherence rates of more than 80% upon completion of the program.

A multi-pronged approach that supports the patient's autonomy and includes personalized education, feedback and a reminder system can have a substantial impact on improving adherence, says researcher Paula Anne Newman-Casey, MD, MS, assistant professor and education director of the Kellogg Eye Center for eHealth. "This type of purposeful, increased attention is best delivered by trained glaucoma health coaches who have the time to form deeper relationships with patients," she says.

Dr. Newman-Casey describes glaucoma health coaches as a new class of para-professional staff who fulfill a role comparable to diabetes educators, where they help to support the patient in improving their glaucoma self-management skills.

She and her team recruited 48 patients with self-reported poor medication compliance. Participants were approximately 64 years old, and the group was 54% male and 46% white. Individuals took at least one medication and had a worse eye mean deviation of approximately -7.9dB. The researchers electronically monitored adherence for a three-month baseline period. Individuals with an average adherence of 80% or less were enrolled in SEE.

Participant adherence was also monitored electronically over the course of the seven-month program. The study calculated adherence as the percentage of prescribed doses taken on time.

During the SEE program, the coach used a web-based tool to generate an education plan tailored to the patient's glaucoma diagnosis, test results and ophthalmologist's recommendations (www.glaucomaeyeguide.org). The coach used the information to help patients identify barriers to adherence and possible solutions.

The 39 individuals who completed the program didn't have significant differences in sex, race, age, mean deviation or baseline adherence compared with the nine dropouts, the researchers noted. ■

Newman-Casey PA, Niziol LM, Lee PP, et al. The impact of the support, educate, empower (SEE) personalized glaucoma coaching pilot study on glaucoma medication adherence. Ophthalmology Glaucoma. April 29, 2020. [Epub ahead of print].

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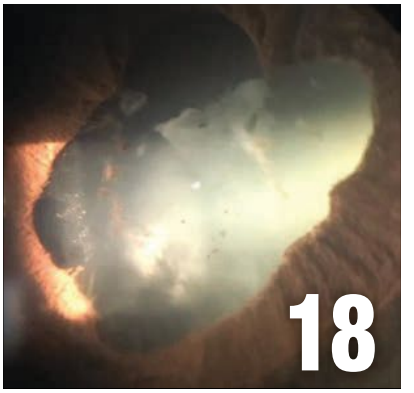



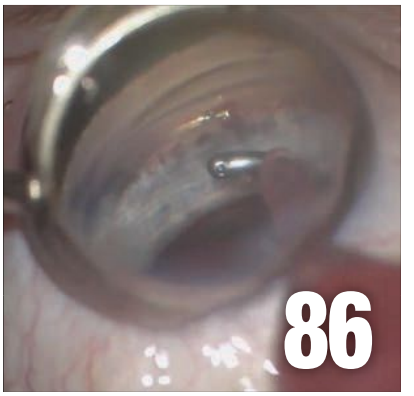


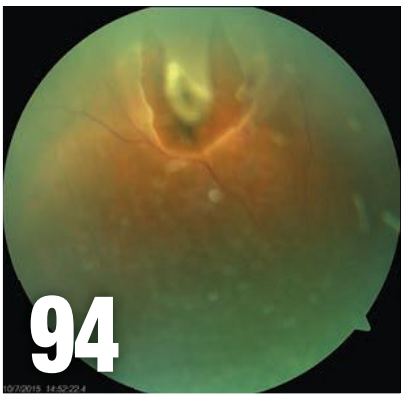



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**Outlook**

**By Jack Persico, Editor-in-Chief**

# Prescription Change

Optometric education has caught up with our annual drug guide, so it's evolving to meet the needs of today.

To an optometrist in the mid-1990s, the prospect of prescribing medications was still somewhat new. Many states had only passed their TPA laws within the last decade, and a few were still fighting the good fight in their legislatures for the privilege. Even many of the ODs empowered to Rx had only sporadic opportunity to do so, as the caseload often just wasn't there. And drug companies were skittish about openly supporting optometry, lest they alienate their core market: ophthalmology.

As has so often been the case in the history of optometry, the profession had to look inward for help. Two ODs from North Carolina—Ron Melton and Randall Thomas—had made names for themselves as ace clinicians and entertaining lecturers, so *Review of Optometry* convinced the two to bring their expertise on ophthalmic drugs to our readers in the form of an annual publication. *The Clinical Guide to Ophthalmic Drugs*, first published in 1996, was a huge success right off the bat, and has been ever since. It's our most anticipated, highest read supplement year in and year out.

And we just did away with it—sort of.

Packaged with this issue comes another compendium of advice from Drs. Melton and Thomas (plus their young protégé Patrick Vollmer, also of North Carolina). But it bears a new name, *Clinical Perspectives on Patient Care*, and a new format throughout. As the authors themselves explain in their introduction, the old format—listing all meds in a category and detailing their pros and cons—suited the needs of 1990s doctors who were still new to the world of prescribing. The medications themselves were exciting, intimidating, even a little exotic.

No longer. All new optometry grads enter practice with a strong grounding in pharmacology and clinical use of drugs, and the more seasoned ODs have a few decades of hands-on experience to rely on.

Even though the therapeutic agents have become more familiar to ODs, your clinical responsibilities have only continued to grow. Optometrists see all manner of eye diseases now, and the top challenge of the day is how to care for them all yourselves, keeping referrals to a bare minimum. Drs. Melton, Thomas and Vollmer have been role models in that regard, arguing strenuously for optometric dominance of eye care and practicing what they preach. To help others get there too, the authors want to share their perspectives on not just meds but also exam techniques, differential diagnosis, patient education, important journal articles, strategic planning for your practice—the whole enchilada. Hence the name and format change.

We all hope you'll consider it a more well-rounded, on-target educational experience suitable for 2020 and beyond. If you slip and still call it "the drug guide" on occasion, don't sweat it. We're sure to do that too. After all, it's still packed with loads of insights on medications, just now with even more advice to put those prescribing decisions in proper context. ■

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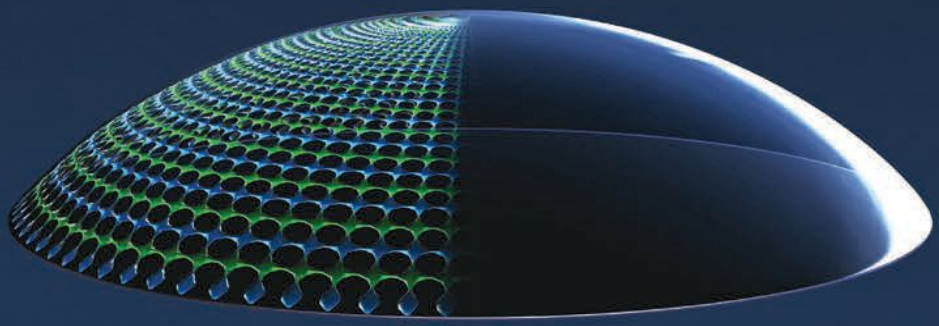

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# Shift Focus to Must-see Patients

Even amid COVID-19 worries, caring for patients with retinal disease is a necessity.

**By Paul M. Karpecki, OD, Chief Clinical Editor**

To rebuild stronger amid the coronavirus pandemic, more optometrists must provide, and be paid for, medical eye care services. However, becoming a medical care provider takes more than just applying to be on an insurance panel provider list, and it's a daunting change for some. Services such as Optometric Medical Solutions can help optometrists navigate through the logistics, billing and insurance verification processes.

Beyond the paperwork, ODs will need to stock up on proper personal protection, including effective but reasonably priced masks (check out The Eye Doctor's Sterileyes antibacterial face masks) and slit lamp shields. Medical eye exams are going to look quite different now:

***Geographic atrophy.*** Currently, most cases of geographic atrophy (GA) require low vision specialists to improve vision. ODs should consider referring to a colleague if they don't offer these services. But if you are looking to help some patients in your office, augmented reality technology (e.g., Eyedaptic) may help the everyday practitioner provide sight to patients who are vision impaired. Therapeutic options are just around the corner with Apellis's Pegcetacoplan in Phase III FDA trials seeking an indication for GA.

***Macular disease.*** This an essential area of focus in the post-COVID era, considering the many vision-threatening etiologies possible. AMD patients, for example, can't afford to miss exams, and optometrists are the ideal clinicians for the job. Tools such as dark adaptometry (AdaptDx Pro) with new augmented-reality technology allow for testing in any room—a big help with social distancing. Hand scanners (Pharmanex) serve as an excellent alternative for recording macular carotid levels. At-home monitoring may be even more paramount.

***Diabetes.*** More than 30 million people in the United States have diabetes—and they are at significantly higher risk of morbidity and mortality with COVID-19.[1] Monitoring any diabetic retinopathy and glucose stability is critical. Whole-body health, ranging from nutritional supplements to maintaining proper weight and avoidance of smoking, is essential.

***Anti-VEGF.*** As frontline eye care providers, we have to properly set our patients' expectations, more so now with COVID-19 than ever before. If a patient you refer for anti-VEGF injections isn't aware of the monthly frequency, they may be surprised and avoid treatment, resulting in permanent vision loss. Fortunately, new knowledge and technology are making things easier. Treat-and-extend protocols are helping, and new therapies require less frequent injections. The Port Delivery System (Genentech) in Phase III clinical testing may reduce follow-up injections to only a couple times per year. Until then, it's up to us to set proper expectations.

***Traumatic brain injury.*** Some technologies may surprise you, but you shouldn't dismiss them. I had a highly symptomatic patient who had a severe concussion following a college soccer game more than two months prior to the examination. The student athlete was unable to continue school or soccer.

Although visual field, OCT and other tests were normal (including MRI and other neurologic testing), she had two striking findings.

First, she had a positive but subtle relevant afferent pupillary defect (0.5D). If it wasn't for the EyeKinetix (Konan Medical) pupil test, I might have missed it.

Second, she reported frequent headaches (three to five per week) since the concussion. Despite trying a number of migraine medications—some with significant side effects—nothing improved. Neurolens (eyeBrain Medical) testing revealed trigeminal dysphoria, esophoria at distance and greater convergence insufficiency at near. Her past vergence testing was normal. After receiving Neurolens glasses, her headaches all but disappeared and she excelled in her December final exams.

Understanding the new normal, new use of technology and adapting to the post-COVID landscape is going to be critical for success. Optometry needs to focus on essential office visits moving forward, and that includes patients with macular disease, diabetes, traumatic brain injury and medical eye care overall. ■

*Note: Dr. Karpecki consults for companies with products and services relevant to this topic.*

1. Peters AL. COVID-19 and diabetes: patterns emerge. Medscape Diabetes & Endocrinology. April 11, 2020. [Epub].

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AMD=age-related macular degeneration; AREDS=Age-Related Eye Disease Study.

**Reference: 1.** Age-Related Eye Disease Study 2 (AREDS2) Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. *JAMA*. 2013;309(19):2005-2015.



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# Masks Up, Shields Up

Keeping everyone safe during COVID-19 might kill some much-needed brain cells in the process. **By Montgomery Vickers, OD**

So, you think you have problems? I know a couple who sold everything and opened a breakfast/lunch place in February. Yeah, they are doing just fine. Sure.

Even if someone has it worse, that doesn't diminish the pain and agony of practicing optometry right now. As I wrote this column, the governor of Texas announced something all optometrists long dreaded: hair salons and barbershops must remain closed until further notice.

How am I supposed to enter society like this? I have to slick my hair back with bear grease (still available online from several essential bear grease factories) just to squeeze my giant bushy head into a T-shirt. Also, I feel like I have gained the COVID 19 pounds but can't be sure since the scale shot springs across the room weeks ago.

It is easy to understand the hair stuff. It just grows. I have friends who wish they had that problem. But how can I be gaining weight? All I do is run… to the liquor store. It's one of the only places we can go to escape the house, and a box from there weighs more than anything I could lift at the gym.

*(Update: Barbers finally opened, and I lost 10 pounds thanks to Michelle and her magic shears; but with nine pounds to go, I have doubled my liquor store runs.)*

## Back to the Grind

Texas's governor has also given the all-clear for optometric practices to reopen! That sounds amazing, but you folks know what a challenge this will be. I think an optometry office is way safer than, for example, a grocery store, but our patients may have a different opinion. As always, the patient runs the show. If patients want to avoid coming in, they probably won't come in.

So, I gave up my temporary career as a garage organizer and trudged back into the office. I was a little rusty, but my colleague kindly reminded me what that white area of the eye is called. He googled it.

I was immediately busy, if seeing 50% of my normal schedule is busy; but, that is required to maintain safe social distancing and give me a chance to remove my N95 and breathe once every 30 minutes.

How can our hero doctors and nurses make intelligent medical decisions when they suit up and reduce their $O_2$ intake by a third? Good thing they were 50% smarter than the rest of us to start with, I guess.

My patients seem comfortable overall. We are all appropriately masked, everything is clean and sanitary, we use automated phoropters and we have cough shields on the slit lamps.

Folks want to get back to whatever normal can be at this point, and we aren't having as many no-shows as I would have thought. Patients want to get their contact lenses and update their glasses. They want us to help them be more comfortable staring at a computer all day and all night under house arrest.

Will this mean a second wave of COVID-19? Probably, and that's not good. However, sitting at home watching our country fade into oblivion is probably not good either. We love our freedom and, despite what you hear on the news every day, Americans are not stupid. We can be as safe as we want to be. It's always been our choice.

But the next outbreak will not, in my opinion, happen because an optometrist took good care of a patient. There's a much greater chance it will happen because you just had to go get a haircut. ■

# COVID Collateral

Digging into an anxious patient's history and medication use often reveals the answer. **Edited by Paul C. Ajamian, OD**

**Q I examined a uveitis patient with a concerning medical history in the early weeks of the COVID-19 crisis. Is there a link, and how aggressively should I be treating him?**

**A** Jeff Gerson, OD, of Grin Eyecare in Kansas City, MO, saw a similar patient. A 40-year-old Asian male called the practice's answering service, noting irritated eyes. He complained of a red left eye and a great deal of light sensitivity. He denied a fever, a cough and recent travel, so Dr. Gerson agreed to see him. Once in the exam room, the patient revealed a history of ankylosing spondylitis and previous bouts of red eye. His medications included vitamin D, albuterol and Cimzia (certolizumab pegol, UCB).

## Clues in the Medicine

While reviewing his patient's medical history, Dr. Gerson learned that the Cimzia his patient was on is a biologic categorized as a tumor necrosis factor–blocker that can lower the immune system's ability to fight infections. "Similar to Humira (adalimumab injection, Abbvie), Cimzia is administered twice a month via injection for ankylosing spondylitis, as well as plaque psoriasis, rheumatoid arthritis and Crohn's disease," Dr. Gerson says. The patient had discontinued the medication on his own because he was afraid of contracting COVID-19 due to a potentially weakened immune system.

"If you are not familiar with a particular medication that your patient is on, look it up!" Dr. Gerson recommends. "A drug that you think may have nothing to do with their presenting signs and symptoms could be the key to unlocking the diagnostic door."

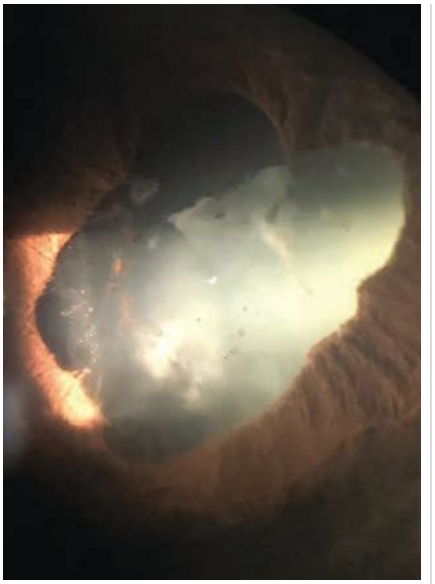

**Fig. 1. Keep atropine and phenylephrine on hand to break synechiae aggressively in an anterior uveitis patient.**

## An Aggressive Approach

Another important point to take note of in this case is that ankylosing spondylitis often causes very severe anterior uveitis. Treat these types of cases extremely aggressively. It didn't help the patient's case that he stopped the medication that had kept the underlying systemic disease in check, even though he had experienced prior episodes on Cimzia.

Dr. Gerson says to start steroids immediately, with a preference for Durezol (difluprednate 0.05%, Novartis), when the iritis is raging. "I prescribed Durezol hourly, along with a steroid ointment at night for around-the-clock coverage," he adds.

The synechiae were a major concern, so Dr. Gerson gave the patient a bottle of atropine 1% and phenylephrine 10% that he keeps in his "stash" for such an occasion. "Pharmacies don't usually stock this, so keep some on hand to give to patients like this," Dr. Gerson notes. He monitored intraocular pressure, which remained in the low teens.

Dr. Gerson saw the patient three days later and many of the synechiae had broken (*Figure 1*). With very slow tapering, and the patient back on Cimzia, this acute episode resolved slowly but steadily in a three- to four-week time frame. "Remember to lag your tapering way behind the improvement, so as not to risk a rebound," advises Dr. Gerson.

Along with ocular treatment, Dr. Gerson had a discussion with the patient regarding his systemic condition. He encouraged the patient to return to the rheumatologist and ensure that he was back on the appropriate dosage of Cimzia, as well as for ongoing monitoring.

"With so many patients on biologics, and knowing that they reduce the immune response, double-checking their dosage is something worth considering in uveitis patients," Dr. Gerson says. "Be curious about the drugs your patients are on, and treat intraocular inflammation with everything in your arsenal." ■

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# A Case of Pediatric Prescribing

Here's an example of how to approach vision care for these young patients.

By Marc B. Taub, OD, MS, and Paul Harris, OD

In our last installment of this column, we presented the evidence base and theoretical foundation for our approach to prescribing for young children. Now, we give an example to illustrate the points we have covered thus far to help you put them into practice.

## The Case

A three-year-old boy presented for his first eye exam. He doesn't seem to enjoy the same detail-oriented activities his two older sisters had actively engaged in when they were his age, so his pediatrician suggested he come in for a complete visual exam.

The patient's visual acuities were 20/40 OD, OS and OU at distance and 20/50 OD, OS and OU at near with Lea symbols, as he didn't know his letters yet. He was squirmy in the chair, and just getting him to hold the paddle over his eye was a challenge. We ended up using an opaque patch, which we held in place with one hand to keep his head pointed forward. We're sure you've all had this type of kid in your chair!

Cover testing showed low exo to ortho at both distance and near. His eye movements were full and comitant in all directions of gaze. We used the new Functional Binocular Assessment Test (FBAT) to assess binocularity.[1] He grabbed for the largest pictures, the hippo and the teddy bear, by reaching his hand out in space away from the cards, showing gross stereo and rudimentary binocularity at the very least. This also confirmed our cover test findings and observations of alignment through eye movement testing.

**We prescribed glasses to begin correcting our patient's high degree of hyperopia.**

As soon as we completed retinoscopy, it hit us that we were dealing with a significant amount of hyperopia. Though one of us prefers the monocular estimation method (MEM) and the other leans toward stress-point retinoscopy (SPR), both tests offer similar insights. With MEM, plus is only applied to one

eye, and often the patient just switches their attention to the other eye and doesn't let the full lag go. With SPR, plus is applied binocularly using flippers, and a target is brought in toward the patient from the plane of the retinoscope.[2] If the reflex remains bright white and balanced and the target can be brought in about four inches closer to the patient before their reflex changes, we keep adding plus. In this case, the MEM was +3.00D and the SPR was +3.50D. We both knew there was more, but not how much more. Houston, we have a problem!

Distance retinoscopy showed +3.50D at distance in both eyes, and damp retinoscopy (tropicamide) showed +4.25D at distance in both eyes. The patient's visual acuity didn't improve significantly with either of these lens options. We attributed this to the fact that he's probably had some degree of blur his whole life and that he isn't very good at precisely pointing his eyes at targets. When a patient has a high degree of hyperopia that has gone uncorrected for a long time, like in this case, we don't always see the desired response as soon as we prescribe some plus. Often, only after the lenses are worn for a period of time do we see the patient begin to calm down, cooperate better with testing, focus more accurately on things and tune into more detail.

**Lea symbols are a good option for patients who don't know their letters yet.**

## How Much is Too Much?

Plus was needed to help this child. Now we ask ourselves how much we should give. We know that at the age of 36 months, we only need to act on hyperopia above +2.50D.[3] Taking into account the most plus we found, +4.25D, the maximum plus we could leave uncorrected is +2.50D. Then we would leave it to emmetropization to help correct the hyperopia over time. The minimum would be +1.75D. However, based on our years of experience with these kinds of cases, we had our suspicions that there was more hyperopia that we had yet to detect, which would only reveal itself as we followed up with the patient.

We also had to factor in the results of the FBAT, cover and eye movement testing. Had any of these tests shown a tendency for an eso shift or had the patient reported seeing double vision during testing, then we would consider giving more plus. Taking all of these findings into consideration, we thought it was best to begin with +2.25D single vision glasses to be worn full-time.

Before finalizing the prescription, we put this lens power on the patient and conducted just-look retinoscopy at near. We had the patient look at certain points as we watched him reach for objects in space. His reflex remained bright throughout the process and got brighter just before he came into contact with each object. This is a nice confirmatory test to help us feel confident in our course of action.

We asked that the patient return in three months, expecting to see more plus that would necessitate new lenses. We are certain that if the glasses are worn as prescribed, future exams will yield more comprehensive and accurate results that we can work with.

Our goal is to not push our patient too far into hyperopia. Based on our clinical experience and the published literature, the best way to do this is to begin with partial plus and add more if needed over time. The opposite approach—prescribing full plus as measured at distance now and continuing to fully correct as more is revealed—seems to leave patients with far more hyperopia as adults. We hope that our patient stabilizes and begins to experience less hyperopia, allowing him to be less dependent on eyewear throughout his life. ■

1. Bernell. Bernell Functional Binocular Assessment Test booklet. www.bernell.com/product/BCFBAT1/Free_Space. Accessed May 4, 2020.
2. Good-Lite. OEP retinoscopy set. www.good-lite.com/Details.cfm?ProdID=892. Accessed May 4, 2020.
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# WELCOME TO THE FUTURE OF AMD CARE

## New technology eliminates virtually every barrier to simple, objective, in-office diagnosis and management of age-related macular degeneration.

The original AdaptDx automated dark adaptometer was introduced in 2014 and has since been used by more than 1,000 eye care professionals to identify and monitor AMD. Since then, dark adaptometry has significantly lessened the profession's reliance on risk assessment by providing a tool that helps clinicians diagnose AMD with 90% accuracy. In addition, the AdaptDx has revolutionized AMD management, leading to a number of publications that discuss in detail new practice guidelines and draw attention to evolving standards of care.

### Leading Optometrists Unite to Develop Practical Guidelines for AMD Diagnosis and Management

The commercialization of dark adaptation sparked intense discussion over the course of several years, especially after a large peer-reviewed study revealed that subjective dilated fundus exam testing and photography are not reliable means to detect AMD—even in patients who have large drusen.[1] Meanwhile, it became increasingly apparent that the AdaptDx removes the guesswork from diagnosing AMD very early

in the disease process. This led to a swift domino effect and, in a few short years, the introduction of dark adaptation in optometric practice was widely recognized as a tipping point, leading to the formation of a group of clinicians devoted to changing AMD care and calling for profession-wide change.

In "Practical Strategies for Preventing Blindness Caused by AMD," the third in a series of annual reports aimed at reducing avoidable vision loss, 27 AMD Ambassadors released the "AMD Manifesto," which includes five essential practice guidelines for modern AMD diagnosis and management:

1. The goal of managing AMD is to preserve visual function—not to wait until vision has already been lost.
2. Dark adaptation testing can overcome the practical challenges associated with diagnosing AMD using only traditional subjective clinical assessment.
3. Optometrists must establish improved practice protocols to proactively identify early disease and monitor it on a regular basis to ensure that CNV is detected as soon as it occurs.
4. Optometrists can, and should, recommend treatments that make a meaningful difference.
5. The treatment of AMD should be initiated at first detection, regardless of the stage.

## Breakthrough Technology Makes It Easy for Everyone

In light of the recently declared need to embrace dark adaptation in optometric settings, MacuLogix was tasked with ensuring that the technology was accessible and that there were no significant obstacles to adoption. As eye care providers were developing best practices, MacuLogix scientists and engineers continued to innovate, solving any practical challenges that could potentially stand in the way of preventing avoidable blindness due to AMD.

In January 2020, the AMD Ambassadors got a first look at a next-generation unit called the AdaptDx Pro™ guided by Theia.™ This revolutionary new device includes all the functionality of the company's tabletop dark adaptometer in a wearable headset that requires no darkroom and features an artificial intelligence-driven onboard technician named Theia.

The self-contained wearable headset was custom-designed and tested for patient comfort and produces the same results as the company's tabletop dark adaptometer. In fact, it creates a comfortable, personal dark room so patients can take the test anywhere in the office, in any light—making it easier than ever to fit dark adaptation testing into any practice workflow. Not only is the entire experience improved for everyone involved, but the addition of Theia's gentle coaching helps ensure accuracy of test results.

After the office technician selects the testing protocol and places the device on the patient, Theia takes over to facilitate a reliable, consistent test by using automated instructions and adaptive feedback spoken directly to the patient.

The AdaptDx Pro is truly a revolutionary way to quickly and effectively measure dark adaptation in virtually any clinical setting, without taking up too much staff or doctor time.

## A Better Future for Your Patients and Your Practice Starts Today

Since 2014, ODs have shared their real-world accounts of how dark adaptation technology has transformed their practices and the lives of countless patients. MacuLogix has used this insight to create the AdaptDx Pro—a one-of-a-kind medical device that improves the testing experience and makes modern AMD diagnosis and management practical in almost any eye care practice. **Are you ready to join your colleagues in embracing progress and improving AMD care by welcoming Theia and the AdaptDx Pro into your practice?**


[1] Neely DC, Bray KJ, Huisingh CE, Clark ME, McGwin G, Owsley C. Prevalence of undiagnosed age-related macular degeneration in primary eye care. *JAMA Ophthalmol.* 2017;135(6):570-5.

# Don't Run Afoul of Imaging Rules

Here's why the CCI edits matter when coding for your high-tech retinal exam.

By John Rumpakis, OD, MBA, Clinical Coding Editor

As technology for retinal imaging improves, the very nature of the retinal exam continues to change. While the standard of care remains the dilated eye examination to assess retinal health, better image capture technology and even the advent of artificial and augmented intelligence are changing the way optometrists approach diagnostic testing for retinal conditions.

## Out With the Old

New CPT codes for the manual retinal exam went into place in January 2020, which redefine the extended ophthalmoscopy codes. The old codes allowed for a new (92225) or subsequent (92226) examination and were unilateral in nature; the new CPT codes 92201 and 92202 are now specific to the area and method of examination:

- *92201:* Ophthalmoscopy, extended, with retinal drawing and scleral depression of peripheral retinal disease (e.g., for retinal tear, retinal detachment, retinal tumor) with interpretation and report, unilateral or bilateral.
- *92202:* Ophthalmoscopy, extended, with drawing of optic nerve or macula (e.g., for glaucoma, macular pathology, tumor) with interpretation and report, unilateral or bilateral.

Additionally, new technology can simultaneously capture a widefield or ultra-widefield image of the retina in color, image with autofluorescence and perform an OCT variant. Practitioners may be tempted to abandon the traditional manual retinal exam in favor of simply capturing a retinal image and making a clinical judgement from that—and therein lies a host of challenges.

## A Medicolegal Challenge

Many may feel the image capture of an ultra-widefield image is less traumatic on a patient, is more convenient, takes less time and does a better job than they can do manually; however, this is not the current medicolegal standard. Manufacturer websites clearly state that the technology is complementary to the doctor's examination and allows for additional diagnostic capabilities.

## A Coding Challenge

The NCCI, or CCI, edits are a set of federal rules that stipulate what CPT codes can be coded for on the same date of service. These rules exist to preserve standards of care and to help with national coding consistency for specific disease states. Carriers follow these rules when they are approving or denying claim submissions.

When using devices that capture many images simultaneously, it is the clinician's responsibility to determine which image is going to be used, coded for and billed for prior to capturing the image, because the CCI edits don't allow for many of these procedures to be performed on the same date of service (*Figure 1*).

Yet I continually see practitioners not respecting these rules or using a modifier to get around them. Be forewarned: if you are going to violate a rule, your medical record should demonstrate that it was imperative, and you must follow the guidelines when using appropriate CPT modifiers to further define the clinical situation you were facing that forced you to violate a rule.

Also of note: none of these codes are approved for telehealth.

The CCI edits don't always make sense because technology is quickly outpacing the coding rules, but they are the rules, for now. Understanding and respecting them is crucial for clinical practice. ■

*Send your coding questions to rocodingconnection@gmail.com.*


**Fig. 1. As this analysis by www.codesafeplus.com shows, myriad CCI conflicts exist when attempting to code for extended ophthalmoscopy on the same day as an OCT and fundus photography.**

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# Work-up and Wait

Although generally not treated, NAION requires close visual field monitoring.

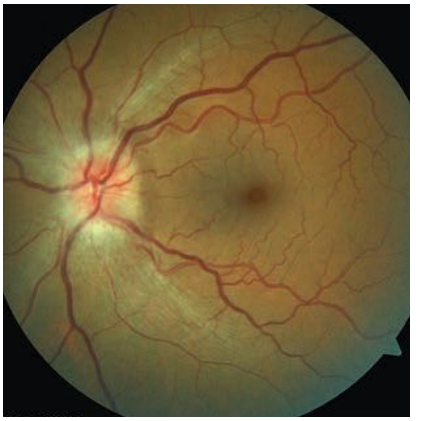
By Michael Trottini, OD, and Michael DelGiodice, OD, PhD

A 54-year-old female presented to the emergency room with a new onset of painless vision loss in her left eye. She stated that she noticed a shadow in the upper left quadrant of her left eye about one week ago. She has a history of an overactive bladder and three months prior was started on Myrbetriq (mirbegron, Astellas Pharma); however, she was then switched to Vesicare (solifenacin succinate, Stellas Pharma) as the Myrbetriq caused headaches.

Her initial blood pressure at triage was elevated at 155/70mm Hg; however, this normalized shortly after and stayed less than 120/80mm Hg for the remainder of her hospitalization. She attributed the blood pressure elevation to stress upon arrival at the emergency department. She was afebrile with normal respiratory rate and pule oxygen.

The patient's visual acuity was 20/20 OD and 20/40 OS. There was a trace afferent pupillary defect in the left eye. Extraocular motilities were full and smooth. Intraocular pressures were 18mm Hg OD and 17mm Hg OS. She reported about 10% decreased brightness and red desaturation in the left eye. Anterior segment exam was unremarkable. Dilated retinal exam revealed significant optic nerve edema in the left eye (*Figure 1*).

Differentials for her disc edema included non-arteritic ischemic optic neuropathy (NAION), arteritic ischemic optic neuropathy (AION), optic neuritis, a compressive lesion and neuroretinitis. After the patient was admitted, I (Dr. Trottini) ordered an MRI of her brain and orbits, as well as a complete blood count and other blood tests, including antinuclear antibody and lipid profile. I also recommended blood pressure monitoring.



**This NAION patient presented with significant optic nerve edema.**

At the follow-up 24 hours later, her clinical exam was stable. MRI was unremarkable, most serology testing was normal and her blood pressure was monitored and normal. She was discharged with a likely diagnosis of NAION and was instructed to see me in the office the following day for a visual field examination.

## Constant Monitoring

The patient's visual field tests showed a minimal superior temporal defect. No treatment was indicated and, given her normal work-up thus far, I recommended to follow-up again in a month to repeat the visual field. I also asked to her to follow-up with her medical doctor to continue monitoring for any possible microvascular issues as well as a hypercoagulopathy work up.

On follow-up one month later, her visual field did show some progression. Her visual acuity was stable at 20/40, her disc edema was resolved and the optic disc was diffusely pale. Her serology testing from her hospitalization was now finalized and normal.

Although the field did look slightly worse from baseline, given her clinical picture, normal testing, stable visual acuity and resolved disc edema, I continued to follow her without any treatment recommendations. She did see her internist for a coagulopathy work-up which was unremarkable.

I recommended she start a daily 81mg aspirin and continue to see her medical doctor as directed. As of our last visit, approximately four months from the onset of her NAION, her visual field showed spontaneous recovery of most of her defect. She had also noticed this improvement subjectively and was pleased to regain most of her vision.

## Discussion

NAION is caused by an infarction of the short posterior ciliary arteries, which supplies the anterior portion of the optic nerve.[1] Vision loss is sudden, painless and usually presents upon awakening as some

authors contribute NAION to nocturnal hypotension.[1]

NAION is typically seen in individuals younger than 50 and in patients with a small cup-to-disc ratio "disc at risk."[1,2] Clinical findings include unilateral disc edema, decreased vision and visual field loss. NAION patients often present with visual field defects, most commonly inferior nasal and inferior altitudinal defects.[3]

Major risk factors include microvascular disease such as diabetes, hypertension and hypercholesterolemia. Additional risk factors include optic disc drusen, smoking, anemia, hypercoagulopathies and obstructive sleep apnea.[1,2]

NAION, AION and optic neuritis can share similar symptoms and clinical findings; however, they are all different entities. So, it's important to differentiate between each one.

AION is ischemia to the short posterior ciliary arteries and optic nerve secondary to inflammation. This is commonly seen in patients older than 65, with unilateral disc edema, significantly greater visual acuity and field defects. Symptoms of giant cell arteritis such as headache, fatigue and scalp tenderness are typical in AION. Elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and platelets levels also raise additional suspicion for AION. If not diagnosed and treated, the fellow eye can become affected and vision loss is typically permanent.

Optic neuritis is typically seen in younger individuals (between the ages of 20 and 40), can occur as unilateral vision loss with or without pain and will most commonly affect the retrobulbar portion of the optic nerve. The disc is usually normal in appearance or mildly edematous in a third of cases.[4] High T2 signal and contrast enhancement of the optic nerve is generally seen on MRI.

Optic neuritis can present idiopathically or as a result of disorders such as multiple sclerosis, lyme, syphilis or sarcoidosis.

## Treatment

Serial visual field testing helps determine improvement or progression of the field defects. Repeated clinical examination should show resolution of the disc edema, with optic nerve pallor forming shortly after. NAION treatment from an optometric standpoint is largely observational. There is no generally accepted, definitive treatment for NAION presently.[2]

Data on treating NAION with anticoagulation, steroids, pressor agents, vasodilators or optic nerve decompression have not shown significant advantages.[2] Some studies show that steroids can help improve visual function; however, the design of these studies as well as the side effects of higher doses of steroids in older patients with vascular disease weaken those findings.[1,5]

While aspirin hasn't been confirmed to be beneficial for treating acute NAION or prevention of NAION in the fellow eye, I recommend patients take an 81mg daily aspirin if they aren't already taking any anticoagulation. This will possibly reduce the risk of stroke or myocardial infarction.[2]

NAION will generally stabilize after two to three months with a guarded visual prognosis, and acuity can improve up to three lines in 43% of patients. There is a less than 5% chance of recurrence in the same eye and a 15% chance of the fellow eye's involvement at five years.[1,2]

Issues such as diabetes, hypertension, hypercholesterolemia and sleep apnea as well as possible nocturnal hypotension need to be tightly controlled by the internist. Identifying and controlling these underlying causes takes careful communication between specialties. Discuss with the patient's primary doctor over the phone instead of just e-mail correspondence to ensure the appropriate management plan.

This patient was interesting because she didn't have any risk factors associated with NAION. She was taking Myrbetriq and discontinued it a few weeks prior to onset of her NAION. Myrbetriq can cause hypertension, but our patient's internist discontinued the medication for her because she was reporting headache but did not check her blood pressure prior to discontinuation. Her medical history was unremarkable otherwise, and her work up was extensive and unrevealing.

Additionally, her visual field defect was not one most commonly seen with NAION. Although not the classical presentation of NAION, her marked disc edema, painless vision loss, relatively good visual acuity, mild visual field defect and normal imaging/work-up made it the most likely diagnosis.

Although no universally accepted treatment for NAION exists, a thorough work-up is necessary to identify any underlying causes and ensure those issues are managed appropriately. It is also of the utmost importance to rule out AION, optic neuritis and other etiologies, as they each require a much different treatment. ■

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11th Annual Retina Report

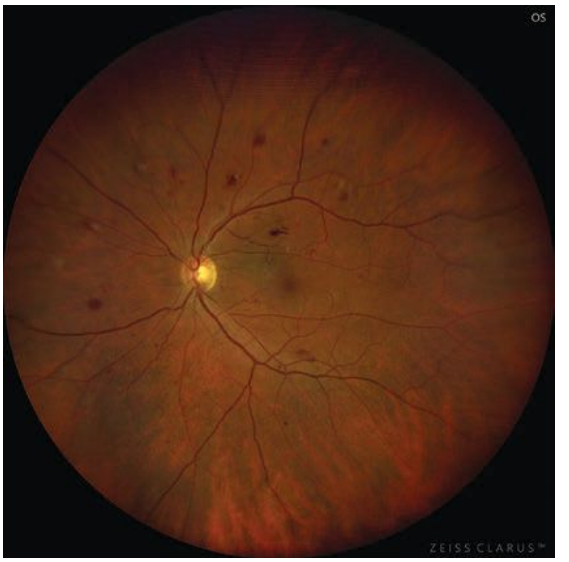
# Reconsider Your Approach to Diabetic Retinopathy

New findings may create protocols that minimize, or even prevent, vision loss.

By Josh Z. Yuen, OD, PhD

The American Optometric Association (AOA) published its most recent evidence-based guidelines on how to care for patients with diabetes in October 2019.[1] These guidelines suggest referring patients with diabetes who present with severe or very severe nonproliferative diabetic retinopathy (NPDR), early proliferative diabetic retinopathy (PDR) with risk of progression or high-risk PDR.[1]

In an effort to prevent diabetic retinopathy (DR) from progressing to the point of referral, current and recent clinical trials have been exploring a new, earlier treatment strategy relying on anti-VEGF injections. This article provides an overview of ocular conditions associated with diabetes, discusses the success anti-VEGF treatment is achieving and offers a protocol for optometrists who work closely with these patients.




**Moderate NPDR care consists of several management techniques, as there is currently no treatment.**

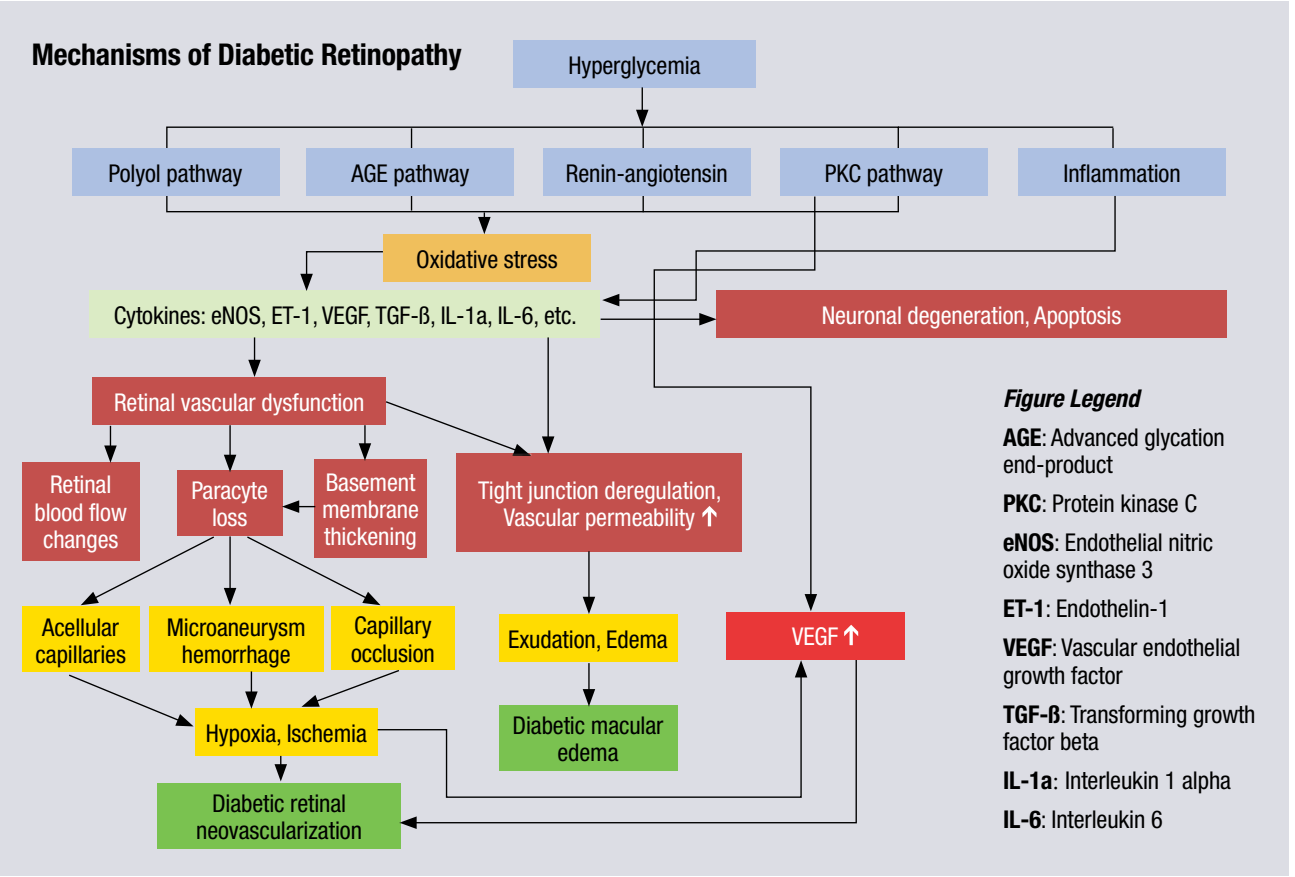
## The Basics

Globally, 35% of patients with diabetes have DR, and 10% have a vision-threatening form, such as PDR, severe NPDR or diabetic macular edema (DME).[1] In the United States alone, 40% of adults older than 40 with diabetes have DR, and 8% have vision-threatening DR.[1]

The early physiological change indicative of DR is decreasing retinal blood flow, or macular ischemia. The imbalance of nitric oxide and endothelin-1 levels induces retinal vessel spasm, leading to blood flow reduction and tissue ischemia in the retina.[2] Visible leaking retinal capillaries are a sign the inner and outer blood-retinal barriers are breaking down.

Macular ischemia is associated with a poor visual prognosis and an even poorer response to treatment.[3] It is defined as widening of the foveal avascular zone, disruption of the perifoveal capillary net and capillary non-perfusion in the central macula (within one disc-diameter of the foveal center).[4] Areas of capillary non-perfusion indicate the severity of retinopathy and the risk of neovascularization. RECOVERY, an ongoing Phase II trial, aims to assess the effect of anti-VEGF injections every one or three months on retinal capillary non-perfusion in PDR over a one-year period.[5]

DME is diagnosable if retinal thickening is present or hard exudates exist within one disc-diameter of the center of the macula. The Early Treatment Diabetic Retinopathy Study (ETDRS) defines clinically significant macular edema (CSME) as DME with at least one of three criteria: thickening of the retina at or within 500µm of the




**This chart illustrates the complex pathophysiology of DR. Note that VEGF elevation happens fairly late in the cascade and directly before neovascularization, which partly explains why anti-VEGF therapy must be maintained indefinitely. Other interventions, especially those that might blunt activity further upstream from VEGF, could have more long-lasting impact.**

center of the macula, hard exudates at or within 500µm of the center of the macula associated with thickening of the adjacent retina or an area of retinal thickening one disc-diameter or larger, part of which is within one disc-diameter of the center of the macula.[6]

There are two kinds of edema: focal and diffuse. Focal edema is induced by a focal leakage from microaneurysms, while diffuse edema is caused by retinal capillary leakage (abnormal permeability).[7]

DME is classified as center involved (CI) DME if retinal thickening greater than 250µm is present in the central subfield zone of the macula or non-CI DME if retinal thickening exists inside the macula but outside the central subfield zone. This classification strategy is becoming the more accepted way of diagnosing DME in a clinical setting. ETDRS showed that CI DME is 10 times more likely than non-CI DME to cause vision loss.[6]

The pathological changes of DR and DME include both angiogenic and inflammatory processes. The molecular mechanisms of DR and DME consist of hyperglycemia-induced oxidative stress, the sorbitol pathway, advanced glycation end-products, the renin-angiotensin system, diacylglycerol-protein kinase C pathway activation, inflammatory markers and raised VEGF levels.[8] Chronic hyperglycemia and hypertension lead to oxidative injury, microthrombi formation, cell adhesion, molecule activation, leukostasis and cytokine activation, causing further retinal damage.[9]

## Treatment Outlook

Ischemia can induce VEGF production. VEGF causes angiogenesis and induces retinal neovascularization in diabetes and choroidal neovascularization in age-related macular degeneration (AMD). It also increases the permeability of the blood-retinal barrier by down-regulating the tight junctions of the endothelium of the retinal vessels.

Intravitreal injections of anti-VEGF agents reduce neovascularization and vessel leakage.[10] The

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## INDICATIONS AND USAGE

CEQUA™ (cyclosporine ophthalmic solution) 0.09% is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

**Potential for Eye Injury and Contamination:** To avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces.

**Use with Contact Lenses:** CEQUA should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution.

## ADVERSE REACTIONS

The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%). Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection.

**Please see brief summary of Full Prescribing Information on the adjacent page.**

**References: 1.** CEQUA [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; 2018. **2.** Data on file. Cranbury, NJ: Sun Pharmaceutical Industries, Inc. **3.** US Patent 9,937,225 B2. **4.** Tauber J, Schechter BA, Bacharach J, et al. A Phase II/III, randomized, double-masked, vehicle-controlled, dose-ranging study of the safety and efficacy of OTX-101 in the treatment of dry eye disease. *Clin Ophthalmol*. 2018;12:1921-1929.


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## INDICATIONS AND USAGE

CEQUA ophthalmic solution is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

## CONTRAINDICATIONS

None.

## WARNINGS AND PRECAUTIONS

### Potential for Eye Injury and Contamination

To avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces.

### Use with Contact Lenses

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## ADVERSE REACTIONS

### Clinical Trials Experience

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

In clinical trials, 769 patients received at least 1 dose of cyclosporine ophthalmic solution. The majority of the treated patients were female (83%).

The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%). Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection.

## USE IN SPECIFIC POPULATIONS

### Pregnancy

Risk Summary

There are no adequate and well-controlled studies of CEQUA administration in pregnant women to inform a drug-associated risk. Oral administration of cyclosporine to pregnant rats or rabbits did not produce teratogenicity at clinically relevant doses.

Data

*Animal Data*

Oral administration of cyclosporine oral solution (USP) to pregnant rats or rabbits was teratogenic at maternally toxic doses of 30 mg/kg/day in rats and 100 mg/kg/day in rabbits, as indicated by increased pre- and postnatal mortality, reduced fetal weight, and skeletal retardations. These doses (normalized to body weight) were approximately 3200 and 21,000 times higher than the maximum recommended human ophthalmic dose (MRHOD) of 1.5 mcg/kg/day, respectively. No adverse embryofetal effects were observed in rats or rabbits receiving cyclosporine during organogenesis at oral doses up to 17 mg/kg/day or 30 mg/kg/day, respectively (approximately 1800 and 6400 times higher than the MRHOD, respectively).

An oral dose of 45 mg/kg/day cyclosporine (approximately 4800 times higher than MRHOD) administered to rats from Day 15 of pregnancy until Day 21 postpartum produced maternal toxicity and an increase in postnatal mortality in offspring. No adverse effects in dams or offspring were observed at oral doses up to 15 mg/kg/day (approximately 1600 times greater than the MRHOD).

### Lactation

Risk Summary

Cyclosporine blood concentrations are low following topical ocular administration of CEQUA. There is no information regarding the presence of cyclosporine in human milk following topical administration or on the effects of CEQUA on breastfed infants and milk production. Administration of oral cyclosporine to rats during lactation did not produce adverse effects in offspring at clinically relevant doses. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CEQUA and any potential adverse effects on the breastfed child from cyclosporine.

### Pediatric Use

The safety and efficacy of CEQUA ophthalmic solution have not been established in pediatric patients below the age of 18.

### Geriatric Use

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

## PATIENT COUNSELING INFORMATION

### Handling the Vial

Advise patients to not allow the tip of the vial to touch the eye or any surface, as this may contaminate the solution. Advise patients also not to touch the vial tip to their eye to avoid the potential for injury to the eye.

### Use with Contact Lenses

CEQUA should not be administered while wearing contact lenses. Patients with decreased tear production typically should not wear contact lenses. Advise patients that if contact lenses are worn, they should be removed prior to the administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution.

### Administration

Advise patients that the solution from one individual single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after administration.

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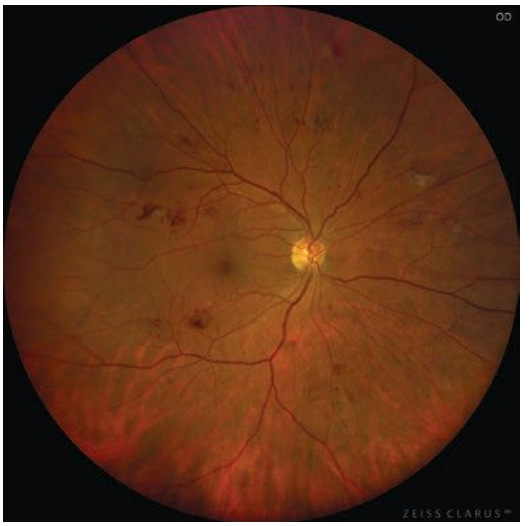



**Anti-VEGF may help improve visual outcomes for cases of moderate to severe NPDR.**

efficacy of injection-only treatment (success rate of 30% to 50%) surpasses that of laser treatment in patients with DME.[11,12]

Four anti-VEGF agents are currently available. Avastin (bevacizumab, Genentech) is FDA-approved for cancer treatment and has been used off-label for several retinal diseases, including DME. Lucentis (ranibizumab, Genentech) is FDA-approved for treating wet AMD, retinal vein occlusion and DR with or without DME. Eylea (aflibercept, Regeneron) is FDA-approved for the treatment of wet AMD, central retinal vein occlusion, DME and DR without DME. Beovu (brolucizumab-dbll, Novartis) is approved to treat wet AMD.

While some retina specialists may consider surgical treatment with lasers if a pre-CSME case meets certain criteria, recently more of an emphasis is being placed on proactively treating these patients with anti-VEGF. Earlier treatment with these intravitreal injections could prevent vision-threatening complications from developing later on, reduce the need for potential future treatment and promote better visual acuity.

Anti-VEGF may also be an effective treatment option for vitreous hemorrhage (VH) secondary to DR, which can induce vision loss. Anti-VEGF and vitrectomy combined with panretinal photocoagulation (PRP) can stabilize or reverse neovascularization in the retina. A two-year trial is currently evaluating the safety and efficacy of prompt vitrectomy plus PRP vs. aflibercept injections in the treatment of eyes with VH from PDR.[13]

Keep in mind that intravitreal injections of anti-VEGF do not come without complications, which must be taken into account before pursuing this option as your treatment of choice.[14]

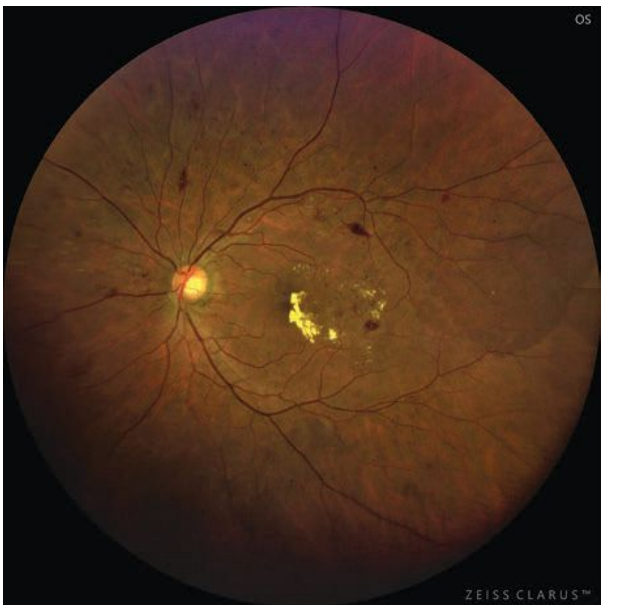
## Managing NPDR

Between 12% and 27% of patients with moderate NPDR without DME progress to PDR in one year.[1] Moderate NPDR care consists of managing blood pressure, blood glucose level and other risk factors (blood lipids, cardiovascular risk, physical health, weight) and following up every six to nine months. Currently, there is no treatment for moderate NPDR.

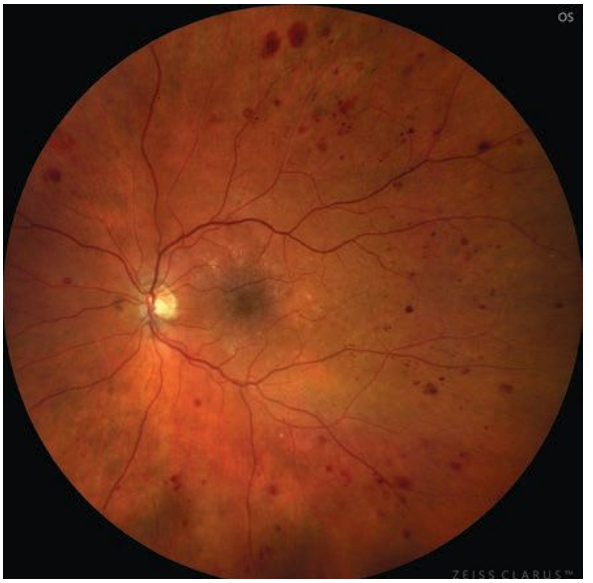
PANORAMA, a Phase III trial, evaluated whether aflibercept can prevent the progression of moderate to severe NPDR—as determined by the Diabetic Retinopathy Severity Scale (DRSS) score—thereby helping reduce the incidence of DME.[15,16] The randomized, double-masked trial included one control group and two aflibercept treatment groups—134 patients received aflibercept every eight weeks and 135 received it every 16 weeks.[15]

After two years, 61.5% of participants treated every 16 weeks and 55.2% of participants treated every eight weeks experienced at least a two-step improvement from baseline in DRSS score.[15] In the control group, on the other hand, only 6.0% of the 133 participants experienced a two-step or greater improvement.[15]

Regarding adverse events, 3.7% of patients treated every 16 weeks and 5.2% of patients treated every eight weeks experienced a vision-threatening complication or CI DME compared with 25.6% of controls.[15] The trial indicated that "consistent aflibercept treatment significantly prevented vision-threatening complications and improved DRSS score on moderately severe to severe NPDR."[17]




**This patient with moderate to severe NPDR developed CSME.**




**Severe NPDR based on hemorrhages and microaneurysms in four retinal quadrants.**

## Managing PDR

PRP, first proposed in the 1960s, has been the standard of care for treating PDR by coagulation of areas of capillary non-perfusion marked by fluorescein angiography, thereby preventing the retinal blood vessels from leaking. However, PRP can sometimes be limited in its ability to reduce neovascularization, and it destroys photoreceptors—especially rods—so vision and peripheral fields rarely improve after PRP treatment. VEGF is a major causative factor in the neovascularization seen in PDR and the vascular permeability in DME, raising the question of whether anti-VEGF can prevent PDR progression and DME.[10]

A pair of studies—DRCR's Protocol S—showed that ranibizumab therapy was non-inferior to PRP on visual acuity measurement at two and five years for PDR treatment.[18,19] Fewer patients treated with ranibizumab developed DME and needed vitrectomy surgery, and there was less visual field loss in the group receiving therapy.[18,19] Unfortunately, it is unclear how long the retinal neovascularization regression will last after the cessation of anti-VEGF treatment.

An ongoing trial is currently evaluating whether aflibercept injections prevent PDR progression or DME in high-risk patients.[20] The team is monitoring visual acuity measurements, OCT findings and the ratio of eyes with at least a two-step worsening to those with at least a two-step improvement in DRSS score over a period of two years.[20] It is possible that anti-VEGF treatment can delay or prevent the need for PRP and reduce the frequency of intravitreal injections for DME.

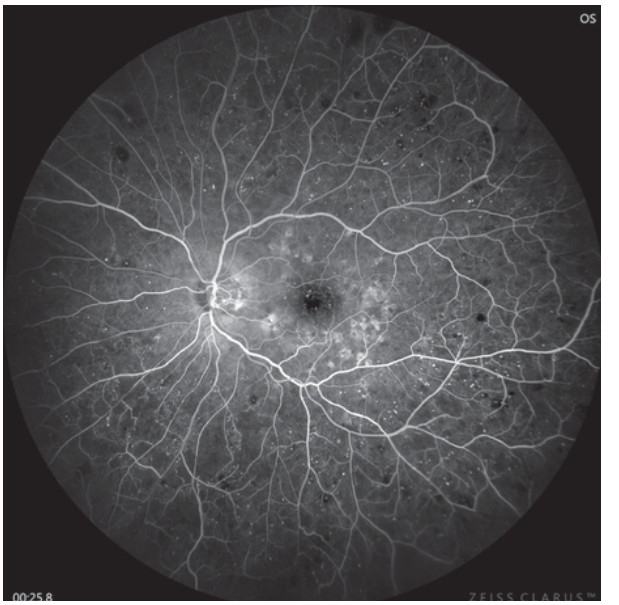
## Step-by-step Approach

Diabetes management differs from office to office, with no consistent standard of care, and is constantly evolving with advances in treatment. Taking into account findings that have emerged from recent studies and my experience as an optometrist, I recommend the following when caring for patients with this condition:

*1. Screen.* Testing for DR is the primary task of an ophthalmic examination for patients with diabetes and the first step toward early detection. Many primary care providers (PCPs) refer their patients with diabetes to an optometrist for a dilated fundus exam. Regardless of the diagnosis, this presents a good opportunity for the optometrist to build a relationship with the PCP, as it is likely that they will be working alongside each other to provide the best joint care for the patient.

*2. Document.* Upon detecting DR, the optometrist should record disease severity and whether DME or CSME is present. Keep a schedule of your treatment or referral and follow-up plans with a clearly-marked timeframe. Detailed charting provides a clear picture of the patient's journey, a consistent means of reporting and protection from potential malpractice lawsuits.

*3. Educate.* Keeping patients informed may be a lot of work upfront but pays off later on. Topics should include risk factors of DR, what effects they can have and how to manage them. Management




**Fluorescein angiography confirms early PDR with significant non-perfusion and neovascularization of the disc.**

## Telehealth and DR

One of the most popular telemedicine applications for DR screening is teleretinal imaging. The program currently assesses veterans with diabetes and is especially useful in rural parts of the country where fewer eye doctors are available.

The teleretinal imaging process is simple and convenient. A nurse or technician takes retinal photos of a diabetes patient with a fundus camera. The photos are then sent to the teleretinal imaging reading center, where an optometrist reviews them. The diagnosis and, if positive for DR, severity of DR and recommendation are saved and sent back to the nurse or technician. The program has specificity and sensitivity values of 95% and 86%, respectively.

Exclusion criteria include patients who have had retinal laser treatment, retinal surgery or intravitreal injection and those who are monocular.

The follow-up schedule looks very similar to that associated with a dilated fundus exam for DR. If retinal photos show PDR, severe NPDR or probable CSME, a face-to-face appointment with an eye care provider is required. In-person evaluations are recommended if retinal photos are blurry, DME, AMD or glaucoma is suspected or a choroidal scar is detected.

Most patients' attitudes toward teleretinal screening are positive, as this process is faster, easier, more accessible and more convenient than traditional in-office screening. It also reduces travel time and cost. On the other hand, the equipment and necessary training is expensive and images may not always be gradable due to poor visual fields, media opacities or small pupil sizes. Dilated pupils also increase the risk of acute angle-closure glaucoma.

All in all, teleretinal imaging represents a substantial step forward for optometry and the care we're able to offer our patients with diabetes.

Shi L, Wu H, Dong J, et al. Telemedicine for detecting diabetic retinopathy: a systematic review and meta-analysis. Br J Ophthalmol. 2015;99(6):823-31.

includes glycemic control, smoking cessation, blood pressure monitoring, lipid-lowering treatment, cardiovascular risk reduction, physical exercise and weight management.[1] Have pamphlets on diabetes and DR available in your office, and be ready to show your patients their scan results so they can better visualize their condition. Patient education has mutual benefits, as it facilitates understanding and promotes compliance in addition to reducing the chance of DR progression and establishing a long-term doctor-patient relationship.

***4. Refer.*** Following the published guidelines from the AOA, refer patients with severe NPDR, PDR or DME to an ophthalmologist.[1] These patients stand to benefit from anti-VEGF treatment, as supported by recent findings. In addition, I recommend referring cases of moderate NPDR without DME but with high A1c levels. Low vision specialists can also help improve the quality of vision and life for severe PDR and DME patients.

***5. Monitor.*** Whether you choose to refer or not, it is important to follow up with your DR patients so you can manage their condition and intervene if necessary. In the event of a referral, the patient is still your responsibility. Research shows that comanagement between local optometrists and hospital-based ophthalmologists improves care for patients with DR.[21]

Recent clinical trials have introduced the idea of proactive anti-VEGF treatment for DR to prevent vision-threatening complications and progression from moderate to severe cases. Armed with this new knowledge, optometrists can now play a more important role than ever in providing the most comprehensive care for patients with diabetes. ■

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11th Annual Retina Report

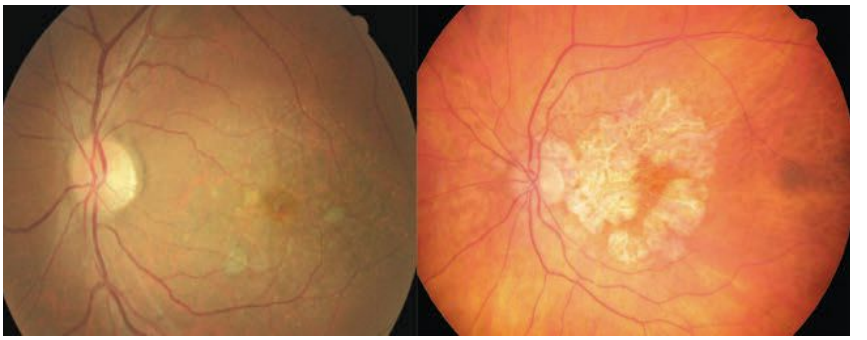
# Sizing Up Geographic Atrophy

Here's how you can assist patients who have progressed to this stage of macular degeneration. By Wendy Harrison, OD, PhD, and Joe Wheat, OD, PhD

Geographic atrophy (GA) represents a late stage of age-related macular degeneration (AMD) where there is loss of the photoreceptors, the retinal pigment epithelium (RPE) and the underlying choriocapillaris.

Clinically, this often appears as well-defined regions with greater visibility of the choroidal vasculature in the macula. Atrophic regions may be small and multifocal early in the disease course, and can spare the fovea. As these regions progress, they can expand, taking any shape as they coalesce over time. The presence of extensive drusen or exudative changes may mask smaller atrophic areas, particularly with a light or blond colored fundus. Visual decline from GA typically occurs once these regions are adjacent to or encompass the fovea. However, the atrophy itself need not impact visual acuity directly to impact quality of life issues such as reading and driving.

The prevalence of GA goes up with age and it is slightly less than that of neovascular AMD.[1] In the United States, researchers estimate GA's prevalence is approximately 0.81% having the atrophic form in at least one eye, but increases to 3.5% in patients older than 75.[1] Severe vision loss from GA is less common than from neovascular AMD, but researchers say it accounts for between 10% and 20% of all cases of legal blindness from AMD.[2] As with all forms of AMD, GA is highest in Caucasians, then followed, in order, by Asian, Hispanic and African populations.[3] Researchers believe approximately four million Americans and Europeans have late-stage dry AMD. This number is projected to increase as the population ages and the number of people worldwide with AMD may grow to 288 million or more by 2040.[4]



**These fundus images show early (left) and advanced geographic atrophy (right). The early patient shows multifocal small extrafoveal regions of GA. In the advanced patient, the lesion has formed an inverted "U" shape almost completely encompassing the fovea, but with apparent foveal sparing.**

Clinically, AMD is generally subdivided into four catagories, defined initially by the Age-Related Eye Disease Study (AREDS).[5] This scale helps to define where AMD changes from early to late stages (*Table 1*). Since that was published, other scales have been developed, including the Beckman

and Three Continent AMD Consortium scales. Whichever one you use, they all rely on the number and size of drusen as key elements.

## Pathophysiology and Progression

GA can be classified into *drusen-associated* (resulting from non-exudative AMD) and *neovascular-associated* (resulting from exudative AMD). Although both of these forms of atrophy result in loss of photoreceptors and RPE, the manner by which they do this may differ. Drusen-associated GA refers to the more classically known late stage of dry AMD. Neovascular GA may represent a relatively new form of atrophy. Researchers have only recently recognized it in long-term studies evaluating the treatment of exudative AMD with anti-VEGF injections.[6,7]

Unlike neovascular AMD, vision loss from drusen-associated GA tends to be more insidious and may go unnoticed until the lesions grow to substantial size, or if the lesion involves the fovea. Rates of GA progression are much slower than rates of exudative AMD. Studies estimate GA progresses anywhere from 0.53mm$^2$ to 2.6mm$^2$ per year, with a median of 1.78mm$^2$.[8]

Research shows several clinical factors are associated with the progression of GA. These include multifocal lesions at baseline, presence of GA in the fellow eye and the presence of drusen-like deposits interior to the RPE called pseudodrusen.[9-11] Patients with GA may still develop choroidal neovascular membranes (CNVM) in other regions, but once the GA has encompassed the majority of macula, risk of CNVM is low.[9-11]

GA may develop as a result of oxidative stress and accumulation of lipofuscin, structural changes in the retina, RPE and choriocapillaris, and dysregulation in the complement cascade.[9-12] It is unknown if these mechanisms are synergistic or if they act independently to lead to the structural and functional changes of this disease.

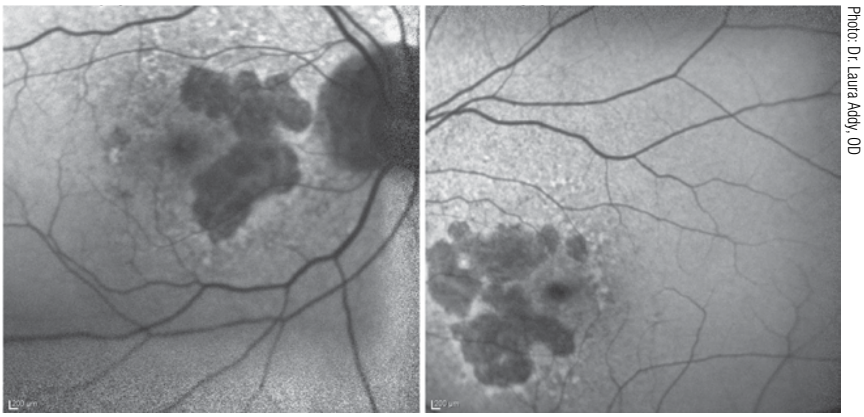


Photo: Dr. Laura Addy, OD

**In this fundus autofluorescence image of geographic atrophy, you can see darkened regions of atrophy in both the patient's eyes.**

Oxidative stress on the RPE from accumulation of byproducts, and the aging of the RPE itself is thought to be an important factor in both the development of drusen and in GA.[12] The photoreceptors cells are highly metabolic and produce numerous oxidative byproducts which can accumulate in the region where they contact the RPE, futher stressing an already compromised RPE.[12]

Lipofuscin—another waste product of oxidation—coming from the outer photoreceptors may also play a role in GA by disturbing normal RPE functionality and aiding in the formation of drusen.[13] When AMD is present in the eye, the individual RPE cells can migrate out of place, which may also be involved in the progression of the disease to more advanced stages.[13]

Defects within the complement pathway and alternative complement cascade are also believed to play a role in the in the progression of AMD to GA.[14] Genome-wide association studies first brought this link to the attention of the eye research community and it is an emerging area for treatments for AMD.[15]

The complement system normally manages inflammation and cell death and it is responsible for clearing apoptotic cells and protection against infection. Dysregulation of this pathway in the presence of inflammatory proteins found in AMD may contribute to the cell death in GA.[16] The abnormalities can be found in many of the complement factors in the complement pathway, and thus provide multiple therapeutic targets for interruption to prevent worsening of GA.[16] Lastly, genetic factors play a role in the development and progression of AMD.[17] Known polymorphisms in some genes, including the CFH gene (a complement factor), can be passed down in families, which can increase the susceptibility of patients to develop GA.[17]

## Examination

In monitoring GA patients, optometrists need to establish a baseline

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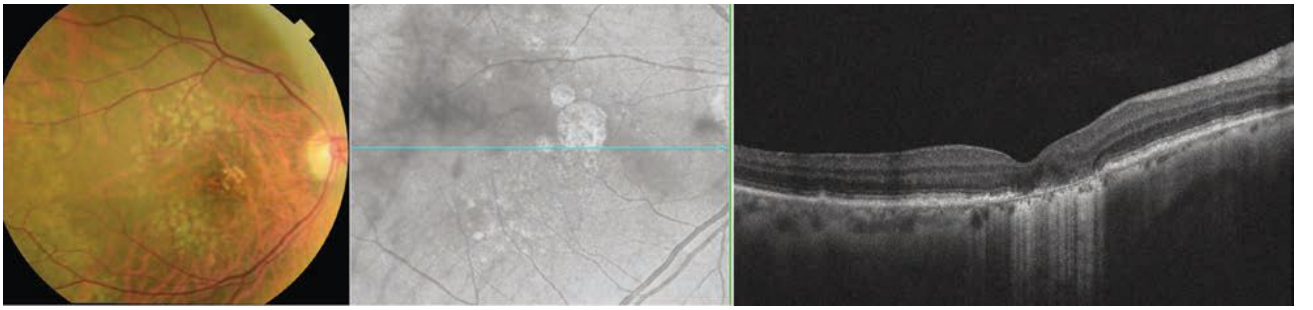


**Here are three types of images of the same patient with subtle juxtafoveal GA. The color fundus photo (left) shows multiple soft drusen but no sharply defined GA lesion. The *en face* OCT image (center) shows well-defined GA borders. The OCT of the macula (right) reveals a juxtafoveal region of GA showing collapse of the retinal tissue just nasal to the fovea, with loss of the photoreceptors and RPE and revealing an increased signal of the underlying layers.**

and regularly monitor for both changes to the patient's biological structures and their visual functioning.

For GA specifically, our clinic performs structural imaging with OCT every six months, or in any case of subjective visual changes. Functional tests can be added with patient reported changes in vision as needed. Since GA progresses at different rates for each patient, and even in each eye in each patient, no set protocol exists.

***Structual imaging.*** GA can be imaged using a variety of methods. Color fundus photography is one of the more accessible modes of imaging but newer technologies allow for the capture of even more subtle changes.

Fundus autofluorescence (FAF) relies on short wavelength excitation of lipofuscin found in the RPE. In the case of GA, FAF shows large areas of hyporeflectance in the regions of RPE loss, often with a perilesional region of hyperreflectance around the atrophy representing regions of the retina with accumulation of lipofuscin and other autofluorescent byproducts whch are in regions that are progressing. Take these photos early to establish a baseline for reference going forward. Photos with FAF can be repeated yearly.

OCT is also commonly employed to observe areas of GA. OCT angiography (OCT-A) is an even more advanced option. OCT reveals the loss of the outer retinal layers and the collapse of overlying layers in the region of the GA. These often exhibit an increased reflectance of the underlying choriocapillaris and choroid in the absence of the RPE and photoreceptors (i.e., the "waterfall" artifact). This is the easiest way to follow GA patients and it should be repeated at least every six months along with OCT-A to evaluate for neovascularization if available.

Fluorescein angiography has also been used to evaluate GA size and other characteristics, but it is typically more beneficial for detecting neovascularization in AMD. More recent imaging capture techniques, which include near-infrared reflectance and multicolor imaging, offer alternative means of imaging GA that highlight lesion borders markedly in comparison with color fundus photography. As imaging continues to move forward, adaptive optics scanning laser opthalmoscopes are allowing researchers to image individual cells, drusen byproducts and cellular microstructure.[18]

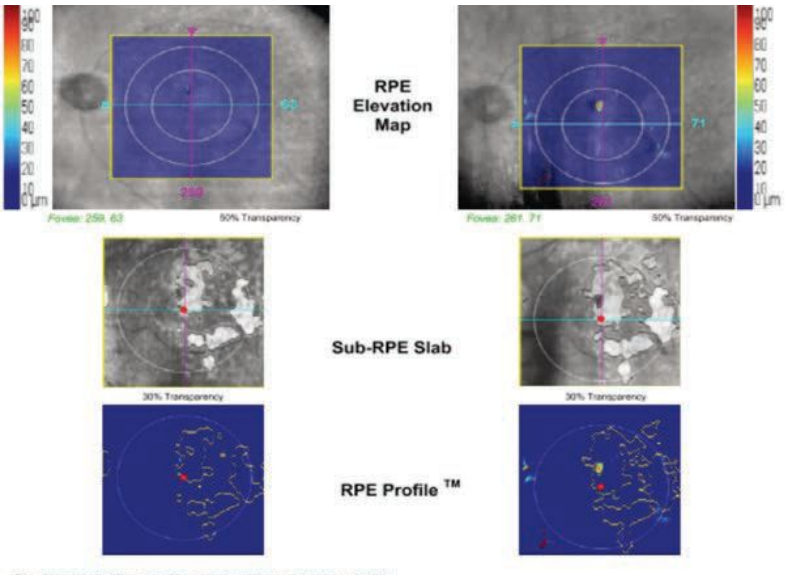
***Functional testing.*** Standard automated perimetry (SAP) is not typically of benefit to measure visual dysfunction due to GA alone. However, it may provide a qualitative measure of functional vision if the right strategy is employed for the location of the atrophy. To achieve this, be sure to set the target at the correct size so the patient can view it and, if possible, choose a testing strategy where as many targets are in the testing area as possible. Kinetic targets may be the best option for these cases.

Microperimetry may offer a more appropriate means of monitoring for progression because the regions tested are smaller and more directed, but such instrumentation is not as readily available and would likely require more advanced techniques during testing than is commonly performed with SAP.

It is typical to run a field—such as a Humphrey visual field (HVF) 10-2 or a kinetic strategy—when GA is noted to determine proximity of vision loss to central vision and overall size of any scotoma.

Amsler grid testing is also common, as it can be done by the patient at home with no other special equipment, but it lacks the sensitivity needed to detect small changes in the size of the atrophy.

Multifocal electroretinography (mfERG) also tests retinal func-




*The calculated difference does not consider test-retest variability.

| RPE Elevations | Prior | Current | Difference* | % Change |
|---|---|---|---|---|
| Area in 3 mm Circle (mm²) | 0.0 | 0.1 | 0.1 | xxx |
| Area in 5 mm Circle (mm²) | 0.0 | 0.2 | 0.2 | xxx |
| Volume in 3 mm Circle (mm³) | 0.00 | 0.01 | 0.01 | xxx |
| Volume in 5 mm Circle (mm³) | 0.00 | 0.01 | 0.01 | xxx |
| **Sub-RPE Illumination** | **Prior** | **Current** | **Difference*** | **% Change** |
| Area in 5 mm Circle (mm²) | 4.7 | 6.8 | 2.1 | 44.7% |
| Closest distance to Fovea (mm) | 0.0 | 0.0 | 0.0 | xxx |

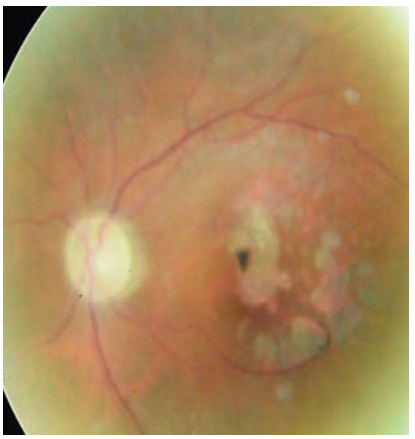
tioning. Its use in GA is largely for evaluating retinal function when there is a discrepancy between what clinicians observe structurally and what patients report functionally. For example, a case where the practitioner views the retina as having only a couple small drusen and pigment changes in a patient who is 20/100 or 20/200 could benefit from an mfERG and OCT-A to view changes that are not funduscopically obvious.

At baseline, for a patient with GA, the following tests are typically done in two visits close in time, a field (10-2 or kinetic, sometimes both), an OCT or OCT-A and a photo series with FAF. The patient should be given an Amsler grid to self monitor changes at home. If progression is discovered, or vision is lost, mfERG, microperimetry and FA referrals may be useful for the patient. Otherwise, following with OCT or OCT-A at three-to-six month intervals is sufficient.

## Treatments

Currently, the FDA has approved no treatments specifically for GA. As with all forms of AMD, the use of high-dose vitamin supplements are recommended for patients with category 3 or 4 level AMD, but research shows supplements make no difference in the progression of existing GA.[5]

For the most part, management of patients with GA should be aimed at identifying modifiable risk factors (e.g., smoking cessation, nutrition) and monitoring for progression to exudative AMD and/or enlargement of the existing atrophic regions. The patient's visual demands and limitations should also be considered by the optometrist and visual rehabilitation should be encouraged in advanced cases. Low vision aids can augment visual function for those in need of assistance with everyday life tasks including reading and driving. In cases of larger areas of atrophy outside the fovea, the location of the scotoma caused by the atrophic areas should be considered in association to the patient's visual demands.



**At left, OCT analysis reveals the advancement of GA over time (2014 to 2019) with an increase in area of 44.7% as illustrated in the table. The fundus photo above shows this patient in 2018.**

Clinical trials are currently underway for several investigational biological interventions. One of these treatments is APL-2, a factor that inhibits the complement cascade at C3.[19,20] In the early research, APL-2 has reduced the growth of GA lesions (compared with sham).

Zimura (avacincaptad pegol, Iveric Bio) is another drug that may be available for use in the near future. It is a complement factor 5 inhibitor. Its Phase IIb results found a mean reduction in atrophy of 27%.[21]

Additional clinical trials for GA drugs include ongoing evaluation of 40mg Oracea (doxycycline, Galderma) for GA.[22] This 31-month study, with observation and treatment phases, is ongoing.[22]

With the introduction of Luxturna (voretigene neparvovec-rzyl, Spark Therapeutics) RPE-65 gene therapy for retinitis pigmentosa, as well as Leber congenital amaurosis, research has turned its

attention to gene therapy for other retinal pathologies, including GA.

For instance, Gyroscope Therapeutics, a UK-based company, is developing a formulation called GT005 to stimulate the production of complement factor I (CFI) with the hope that it can restore balance to the complement system and slow the progression of GA.[23] A reduction of CFI in the serum is a factor that can contribute to GA.[23] Patients in the ongoing Phase I/II clinical trial, known as the FOCUS study, receive a single dose of GT005 that is surgically delivered to the suprachoroidal space.[23] The company is preparing to move into its proof of concept Phase II clinical program later this year.[23]

## Patient Education

Given the information above, when an optometrist examines a patient who shows early signs of AMD or AMD that has progressed toward GA, it's time for an important conversation. This conversation should have three parts. First, the optometrist must explain the data. Second, the modifiable risk factors and low vision need to be discussed. Lastly, the importance of follow-up should be emphasized.

Specifically, the patient should be shown their fundus photograph and areas of atrophy, and drusen and pigment changes should be explained if possible. The OCT can also aid in this discussion as it shows the drusen as areas of buildup that affect vision. Areas of atrophy can be explained as scars.

Most patients have heard of AMD and many will be frightened by the diagnosis. It is important to share data with the patient so they understand where they are in the disease process. If FAF is available, those images can be easy enough for the patient to understand.

**Table 1. Stages of AMD from the AREDS Study**

| Category | Drusen | Other Features |
|---|---|---|
| Grade 1 – No AMD | 5-15 small drusen (<63 microns) | No real pigment changes |
| Grade 2 – Early AMD | Several small drusen, a few intermediate sized (63-124 microns) | Pigmentary changes in one or both eyes |
| Grade 3 – Intermediate AMD | extensive (20 soft or 65 hard without any soft) intermediate-sized drusen, one large (>125µm) druse | Can have geographic atrophy not affecting the macula |
| Grade 4 – Advanced AMD | | Macula-involving geographic atrophy or exudative form with choroidal neovascularization in one eye |
| Grade 4a | | Advanced AMD in one eye with category 1, 2, or 3 AMD in the fellow eye |
| Grade 4b | | Advanced AMD in one eye and decreased visual acuity (<20/32) secondary to AMD in the fellow eye; however, advanced AMD is not present in both eyes |

Most patients ask if they are going to lose all their vision during this conversation, and even if they don't ask, they are likely worried about this possibility, so include this element in the conversation. The response should be honest and compassionate. AMD only affects central vision, so *all* vision will not be lost, but this could affect elements of their life if it progresses.

We tell patients that we don't know what the future will hold, but there are things they can do to help their eyes. It is better for them to hear the truth from their doctor than to search the internet and potentially find unreliable sources. The discussion should then turn to what the patient needs to do. As there are no FDA-approved treatments for GA, this discussion will involve reducing risk for progression as much as possible. No studies indicate how to do this, but for GA most clinicians believe that reducing the risk factors for AMD could reduce risk of progression. Helpful steps can include smoking cessation, if needed, a diet filled with green leafy vegetables, AREDS2 vitamins, sunglasses to reduce UV exposure to an already fragile retina and monitoring for changes to neovascular AMD, which can be treated. Also, explain that AMD runs in families, so they should tell their loved ones about their diagnosis.

Low vision aids may also be of use to these patients. In fact, any GA case should be referred to a low vision provider, even if acuity is still adequate, to offer them specialized support. It is an error to wait until the patient is 20/200 to consider a referral to a low vision specialist for these patients. Patients in the 20/50 range can learn how to use devices which will continue to aid them if they progress and early referral for GA

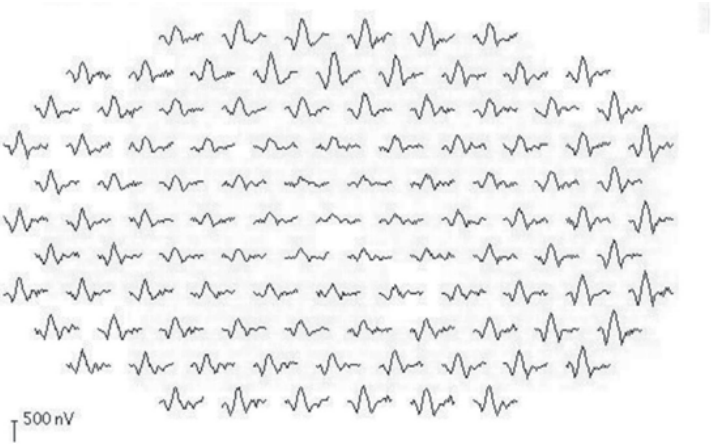
patients to low vision can be beneficial.

Lastly, the doctor should discuss how to use an Amsler grid with the patient. While the grid is not sensitive to small changes, it is a marker for larger change in vision and gives the patient some part of their own care. Patients are told if they see a difference in the grid or while reading to please call the office. Patients are typically seen every three to six months otherwise for dilated examination with OCT and OCT-A and occasional HVF. The other tests can be added as needed to monitor changes carefully. If the patient develops neovascularization, they need prompt referral for treatment. It is important for the patient to know that neovascular AMD does have treatments which would need to be initiated as quickly as possible.

Overall, your management of GA should include identifying modifiable risk factors for progression and monitoring visual function and structural changes that may alter the patient's quality of life, along with a combination of careful examination, regular follow-up and visual aids. The clinician should determine exam intervals based on progressive risk factors, such as the level of vision in the fellow eye, confluent or soft drusen, presence of pseudodrusen, or development of CNV in the fellow eye.

A maximum of six-month intervals is ideal for most patients who are already experiencing evidence of GA, and you can shorten these intervals if patients note any progression or have extensive vision loss.

With any luck, future treatment options will alter the progressive course of this disease and spare visual morbidity. If any of them do pan out, the improved detection techniques optometry has developed—both structural and functional—are likely to remain valuable and perhaps play an even more vital role in AMD management. ■




**This mfERG shows a patient with central atrophy. Note the reduction in the size of the peaks for the central waveforms.**

*Drs. Harrison and Wheat are associate professors at the University of Houston College of Optometry.*

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11th Annual Retina Report

# Macula Exam Tips and Tricks

This small structure plays an important role in patients' vision. Here's how you can assess its health. By Juan Canizales, OD, and Christopher Suhr, OD, MPH

Decreased vision is one of the cardinal concerns that sends patients to our offices. Myriad conditions can be behind reports of failing vision, including numerous macular pathologies. Optometrists must be proficient in recognizing macular disease during the ocular examination and in using the latest diagnostic technology to do so.

Although of great visual importance, the macula only encompasses approximately 5.5mm of the central retina.[1] A thorough macular assessment is an essential part of a comprehensive or problem-oriented eye exam and can often reveal the underlying etiology of patient's vision loss. This article addresses several exam elements that may be crucial in the diagnosis of macular pathology, beginning with a targeted history, the use of everyday slit lamp techniques, the benefits of various condensing lenses options and, finally, the use of diagnostic imaging, including photographic techniques and OCT.

**Fig. 1. The WASBT is a good low-tech tool to help distinguish between full-thickness macular holes and pseudo-holes. Patients can describe one of these slit beam options after testing.[16]**

## Ask Better Questions

A chief complaint and thorough history are integral to an optometric examination and can go a long way toward revealing a macular problem. Symptoms associated with macular disease include blurred vision, loss of central vision or central scotomas, distorted vision or metamorphopsia, loss of color vision, perception of shadows and images that could be fixed or floating, and alteration of image size. Each of these symptoms may suggest a specific form of macular pathology; however, these same symptoms may be caused by other posterior segment pathology such as optic nerve involvement. Asking specific questions about the quality of vision loss may lead us to a better physical examination in search of the actual cause.

Clinicians must ask the right questions to understand, for example, whether the patient is trying to describe a relative scotoma (decreased detail) or absolute scotoma (blacked out or loss of detail). A visual distortion described as an alteration of the image shape is likely a metamorphopsia, while decreased image size is more likely micropsia (caused by foveal cone spreading) and increased image size often indicates macropsia (caused by foveal cone crowding).[1]

Another important history element is the patient's systemic diseases and treatment therapies. Many systemic medications are linked with macular complications (*Table 1*). A history of past ocular surgeries or injuries is important as well. For example, a patient who reports

reduced vision after undergoing a recent cataract extraction should prompt the clinician to rule out cystoid macular edema, as it may occur in 1% to 3% of uncomplicated cataract surgeries.[2] Additionally, trauma to the head, eyes or body can yield macular manifestations, such as in cases of Purtscher retinopathy, commotio retinae, choroidal rupture, valsalva maculopathy or other posterior pathologies.[1,3,4] A history of laser exposure, welding and sun gazing, for example, can cause macula lesions and holes.[5-7]

Several comorbidities are associated with macular findings, and they should prompt clinicians to take a closer look at the macula. For example, serous detachments develop in about 45% of patients with non-central disc pits.[1] Myopic degeneration can manifest as a macular hole, Förster-Fuchs spot, choroidal neovascular membrane, subretinal 'coin' hemorrhages and geographic atrophy.[1]

Diabetes as well as vascular, infectious, retinal and inflammatory diseases can present in the macula. In addition, many systemic conditions can have similar macular findings. For example, non-ischemic central retinal vein occlusion and diabetic retinopathy can each present with "dot-blot" hemorrhages in all four quadrants by the macula and macular edema, so looking at the bigger picture is important.[8,9] Macular star is another example of a finding that can have several causes, such as syphilis, cat-scratch disease, severe hypertension retinopathy, cytomegalovirus retinitis posterior hyaloid detachment, non-arteritic anterior ischemic optic neuropathy (incomplete macular star) and Lyme disease.[1,10-12]

Careful questioning of hereditary fundus dystrophies, such as age-related macular degeneration, can direct your attention to examine the macula closely as well.

**Table 1. Medications and the Macula**

These drugs are known to cause damage to the RPE and photoreceptor complex:[1]

- Chloroquine and hydroxychloroquine
- Phenothiazines
- Clofazimine
- Deferoxamine
- Dideoxyinosine
- MEK inhibitors
- Sildenafil
- Corticosteroids
- Poppers/Alkyl nitrates (recreational drugs)
- Cisplatin and carmustine

Myriad other drugs are associated with macular damage, including the following reports:

- Intraocular gentamicin/tobramycin/amikacin can cause macular ischemia.[1]
- Recreational intravenous drug use may lead to talc retinopathy that can present with perifoveal yellow-white glistening crystals, ultimately causing ischemic retinopathy.[1]
- Methanol can cause macular edema.[1]
- Topiramate is known to cause macular striae, suprachoroidal effusions and retinal hemorrhages.[2]
- Quinine sulfate can damage the ganglion cell layer.[1]
- Topical epinephrine, high-dose nicotinic acid/niacin, paclitaxel/docetaxel, deferoxamine and topical latanoprost can cause cystoid macular edema, as can hypoglycemics such as glitozones, rosiglitazone and pioglitazone.[1]
- Tamoxifen and canthaxanthin are associated with crystalline retinopathy.[1]

Other medications that have macular manifestations are not available in the United States or present with findings (i.e., cotton-wool spots, hemes) similar to other retinopathies.

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## Lenses: Choose Your Weapon

An extensive examination and detection of macular abnormalities requires good magnification and resolution with a condensing lens. Clinicians can have a macula and optic nerve lens for specific evaluations. Though 90D and 78D lenses remain the standard for examining the macula and posterior segment with a slit lamp, a variety of other lenses may also be useful, each with their own benefits (*Table 2*). Some important things to consider are magnification, dioptric power, field of view, working distance and lens size.

When choosing a lens with higher magnification, remember that as the image size is larger, the field of view is reduced. As such, it may be beneficial to initially perform a gross examination with a lens of lower magnification and then use a higher-powered lens to better see a specific area. In addition, increasing the magnification will decrease the image resolution. The lower the dioptric power of a lenses, the higher the magnification. The higher the dioptric power, the more it converges light. Thus, higher dioptric-powered lenses also require a closer working distance because of the convergence, and closer working distances can induce fogging from

patient's eyes or oil from their lashes.

Because higher-powered lenses are easier to use with small pupils, the 90D is a great choice for undilated exams or for patients with poor pupillary dilation, though the view may be limited based on the aperture size of the pupil, hence the significant benefit of a dilated exam.

Some of the newer lenses can offer the best of both worlds; for instance, an enhanced 78D lens has a wider field of view, higher magnification and larger working distance, and other lenses can provide high resolution, such as the Ocular Maxfield High Mag 78D, and high magnification, such as the Volk Digital 1.0x.

Another non-contact slit lamp lens to consider is the Volk Digital High Mag, which provides high resolution and highest magnification for detailed views of the macula and optic nerve. Macular contact lenses, such as Haag Streit's 901 fundus contact lens, can provide direct views of the macula and vitreous cavity as far out as 30˚, with fewer issues such as fogging and makeup or oil from the patient's eye lashes smearing the posterior part of the lens. However, the patient will require topical anesthetic for this procedure. A standard gonioscopy lens can also provide a great view of the posterior pole without an inverted image, all while checking for neovascularization of the angle in diabetes patients.

## Red Free Filter: Seeing Green

Originally, red-free illumination was used to evaluate the peripapillary retinal nerve fiber layer (RNFL) for suspected optic neuropathies.[13] The red-free filter (RFF) comes with most slit lamps, ophthalmoscopes and binocular indirect ophthalmoscopes. RFF is also used with fluorescein angiography and fundus photography. The green light is absorbed by the RPE, which can distinguish between the location of a lesion within certain retinal layers.[14]

**Table 2. Condensing Lens Comparison**

| Lens | Field of View (static/dynamic) | Image Magnification | Working Distance | Additional Infomation |
|---|---|---|---|---|
| *High Power/Low Magnification* | | | | |
| Ocular Maxfield 84D | 105/158° | 0.71x | 5mm | High resolution, widefield 90D |
| Ocular Maxfield Standard 90 | 94/153° | 0.75x | 5mm | Also comes in standard 90D with large ring |
| Volk 90D | 74/89° | 0.76x | 7mm | General use; good for small pupils and dynamic funduscopy |
| Volk Super Field NC | 95/116° | 0.76x | 7mm | Enhanced 90D, same magnification with wider field of view |
| Ocular Maxfield 100D | 110/146° | 0.6x | 4mm | General screening lens; large field of view; good for small pupils |
| Volk Super Pupil XL | 103/124° | 0.45x | 4mm | Small (1mm to 2mm) pupil capability but low magnification |
| Volk Digital Wide Field | 103/124° | 0.72x | 4mm to 5mm | Similar 90D magnification with widest field of view; high resolution; good for small pupils |
| Ocular Maxfield 120D | 120/173° | 0.5x | 4mm | Wide field of view, 80° with 2mm pupil |
| *Low Power/High Magnification* | | | | |
| Ocular Maxfield 54D | 86/137° | 1.10x | 10mm | High magnification and resolution for macula and disc |
| Ocular Maxfield 60D | 85/154° | 1.00x | 10mm | High resolution, one to one image of fundus |
| Volk 60D | 68/81° | 1.15x | 13mm | High magnification for macula and optic nerve detail |
| Ocular Maxfield 66D | 91/144° | 0.91x | 8mm | Static field of view to arcades |
| Ocular Maxfield 72D | 102/155° | 0.83x | 7mm | Similar to 78D with a little more magnification |
| Ocular Osher Maxfield 78D | 98/155° | 0.77x | 7mm | Formerly the Osher Panfundus |
| Ocular Maxfield High Mag 78D | 88/154° | 0.98x | 10mm | Wide field and sharp image |
| Volk 78D | 81/97° | 0.93x | 8mm | General use; balance of magnification and field of view |
| Volk Super 66 | 80/96° | 1.0x | 11mm | High magnification, more detailed evaluation of macula and disc |
| Volk Digital 1.0x | 60/72° | 1.0x | 12mm | High magnification; high resolution of posterior pole |
| Volk Digital High Mag | 57/70° | 1.30x | 13mm | High magnification; high resolution of posterior pole |

Findings deeper than the RPE tend to disappear, while those in front of the RPE tend to stay.

Blood appears darker with RFF, creating enhanced contrast between blood vessels and hemorrhages, and the retinal background.[14] For example, the RFF can make hemorrhages appear darker, which can give a clinician more confidence identifying intraretinal microvascular abnormalities or questionable small hemorrhages. RFF can be a great tool to screen for subtle retinopathy in diabetics.

Other uses of RFF include cystoid macular edema, in which the fluid-filled area in the macula appears light gray. Epiretinal membrane striae appear more noticeable since the RPE disappears with RFF and can take away some glare from white light. In addition, central serous choroidopathy and pigment epithelial detachment borders can look more defined.

The filter can be used to look for a cuff of subretinal fluid around a macular hole. Retinal nevi will disappear or become lighter/gray with RFF, while choroidal hypertrophy of the RPE will remain visible. Drusen, exudates and cotton-wool spots in the macula all show as increased contrast with RFF.

However, the tool isn't perfect, and the overall views of the macula and retina are darker because of the green light compared with white light. Luckily, increasing the illumination helps and does not seem to bother patients much.

## The Poor Person's OCT

The Watzke-Allen Slit Beam Test (WASBT) is a subjective visual function assessment that can determine the loss or distortion of foveal photoreceptors.[13] Historically, the WASBT was used for evaluation of macular disease.[14] We now use this test for distinguishing between full-thickness macular holes and pseudo-holes. The advantages of the WASBT is its availability, affordability, and the ability to use it through relatively hazy media, which can help make up for the limitations of spectral-domain OCT.[15] One study found that WASBT was more useful than SD-OCT initially following macular hole closure of a gas-filled eye due to light reflex and media opacity.[15]

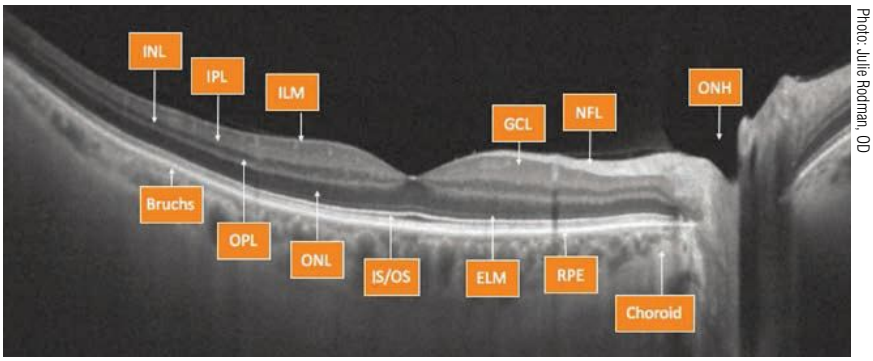

Photo: Julie Rodman, OD

**Fig. 2. OCT can help clinicians evaluate the retina, layer by layer.**

The WASBT is best performed on a dilated eye with the slit lamp. A slit beam of approximately 100µm is placed on the center of the macula with a non-contact slit lamp (or macula contact) lens.[16] The beam is tested in the vertical and then horizontal orientations. The patient is asked to look at the middle of the beam and remember any details regarding the slit beam, such as whether the beam is regular in outline or if it is distorted. Often, patients are asked to draw a representation of the slit beam after the exam.[17] The patient could also identify the slit beam characteristics on a diagram (*Figure 1*).[14]

A broken light beam is considered a positive Watzke sign. One study suggests that thinning of the slit beam can also be a sign of a full-thickness macular hole and a positive Watzke sign.[16] Other researchers found a positive Watzke signs in 91% of patients with medium and large full-thickness macular holes and 67% of patients with a small full-thickness macular hole, vitreomacular traction and lamellar macular holes.[18] Indication for treatment sensitivity was 93%, but 33% for specificity with the WASBT.[18]

Any negative sign, however, with a presumed macular hole would still warrant further evaluation by OCT, if available. Regardless, the WASBT remains a useful tool in practice, as not all clinicians have access to advanced technology in their office. Even as a simple screening tool, WASBT can help lead the clinician to a presumed diagnosis.

## High-tech Evaluation

Evaluating the different macular layers can be challenging during a fundus examination, as the tissue may appear normal. Though other noted techniques may help the clinician, a more in-depth analysis is often warranted. OCT is one of the most useful devices that have come to market to assist the evaluation of these patients.

As many macular conditions affect specific layers of the retina, the ability to image these layers individually is crucial (*Figure 2*). The ability to differentiate layers can help clinicians determine between various edematous conditions that may appear similar, but have different

etiologies revealed by the location of the changes—warranting individualized treatment approaches.[19]

OCT can also assist the clinician in assessing the vitreoretinal interface. This becomes beneficial when evaluating for epiretinal membranes and vitreomacular traction (VMT), as even subtle changes can cause visual symptoms. Clinicians should consider imaging with OCT to evaluate for VMT when there is an ERM with striations radiating into the macula or a macula with non-uniform pigmentation, noted funduscopically, often associated with an adjacent ERM.

The advent of OCT has the additional purpose of patient education. The images are excellent tools to help patients understand their ocular status. It also allows for collaboration with other providers, such as retina specialists.

OCT is also a means to measure the RNFL to assist in the diagnosis and management of glaucoma. Studies show that there is also benefit in evaluating the macula to gain information regarding glaucoma. Thinning in the three most inner layers (macular RNFL, macular ganglion cell layer and macular inner plexiform layer) can be indicative of glaucomatous changes and may be beneficial in glaucoma diagnosis and management.[20]

More recent OCT advancements, such as OCT angiography, can capture blood movement through the vasculature, allowing for computer assessment that results in a simulated angiography, without the complications associated with more invasive fluorescein angiography.[21]

OCT is not the only imaging tool proven beneficial in macular evaluations. Fundus autofluorescence (FAF) can help clinicians evaluate the macula for possible defects. This technology is readily available on many imaging devices, including posterior segment cameras and OCT. FAF emits a blue light that is absorbed in molecules found within retinal tissue. The excited molecules emit return light the device then evaluates for certain compounds in varying levels. As an example, FAF can reveal lipofuscin density changes often found in certain inherited retinal conditions, macular degeneration and choroidal melanomas.

Clinicians can also use FAF to evaluate the macular region in patients taking hydroxychloroquine, and, in severe disease, the macula may develop the classic bull's eye changes and continue to lose reflectivity, resulting in a dark macula.[22]

Scanning laser ophthalmoscopy is another effective tool for evaluating the macula. As with FAF, this technology is often integrated into other devices, mainly OCTs, but may also be stand-alone. It can be enhanced with adaptive optics that provide more in-depth scanning capabilities. In essence this technology uses a scanning laser and software to create high-resolution images.[23] These images can help the clinician assess changes in the tissue appearances.

Several examination techniques, some of which have been in the clinician's toolbox for years, are key to a good macular exam. These techniques can be augmented by the use of diagnostic lenses. With the advent of imaging devices, the macular exam can be more extensive and thorough. OCT is a great tool that can yield a closer look at each layer involved. OCT-A, FAF and SLO are also helpful technologies when evaluating the macula. By meshing these techniques and technology, clinicians have more at their disposal than ever before to appropriately evaluate the macula and choose the best course of action. ■

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*Dr. Suhr is the chief of optometry at the Corporal Michael J. Crescenz Vetereans Affairs Center in Philadelphia, Pa. He is a Fellow of the Optometric Retina Society.*

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11th Annual Retina Report

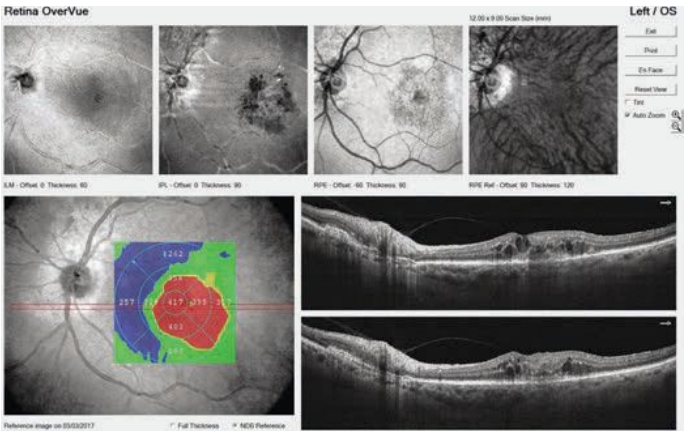
# Setting Patient Expectations for Anti-VEGF Therapy

Here's how the primary care optometrist can make sure patients are ready for intravitreal injections. By Steven Ferrucci, OD, and Brenda Yeh, OD

Intravitreal injections are the most commonly performed ophthalmologic procedure—more so even than cataract surgery—with over three million injections performed in 2016.[1] With an aging population and an expected coinciding rise in retinal disease, studies suggest these numbers will only grow.[2] One particular class, anti–vascular endothelial growth factor (VEGF) medications, can treat patients with various retinal conditions.

While optometrists don't perform the procedure, patients value guidance from their ODs, and providing that guidance requires knowledge of how the procedure is performed, any complications that can arise and what types of patients benefit from these treatments. This helps to make appropriate referrals, manage co-existing ocular conditions, set patient expectations and identify potential side effects.

This article explains the procedure, changes its seen over the years and the academic literature that can help you communicate the key points to your patients.




**OCT imaging shows the left eye of an 81-year-old CNVM patient with intraretinal fluid. He'll be treated with intravitreal anti-VEGF injections.**

## Yes, a Needle In Your Eye

To patients who've never received an intravitreal injection, a needle to the eye can sound unnerving. They need reassurance that this is a common and low-risk procedure with a significantly positive outcome. Explain that, when they arrive at their ophthalmologist's office, they will be asked to sign a consent form that discusses the risks, benefits and alternatives of intravitreal injection. Assure them their doctor will follow established protocols and explain that the majority of endophthalmitis complications stem from the practitioner's or even the patient's own oral flora—so, they should refrain from speaking during the procedure.[3,4] Research shows a clean room in an office setting is adequate to reduce the risk of infection.[5]

Due to the increasing incidence of bilateral macular edema as well as bilateral choroidal neovascular membranes (CNVM), many patients now require bilateral injections.[6] This can reduce the treatment burden, and it's generally well tolerated, preferred by patients and appears safe, as no evidence shows bilateral injections increase the endophthalmitis risk.[6]

Assuage your patients' fears by explaining that they will be given adequate anesthesia to minimize discomfort. While a number of studies compare various techniques, the literature shows no consistently preferred approach. Researchers looked at proparacaine, tetracaine, lidocaine pledgets or gel and subconjunctival injection of 2% lidocaine and found patients reported mild pain only, regardless of anesthesia used.[7] Most clinicians opt for localized application of topical anesthetic with cotton pledgets, as it is easy and seems to work as well as other methods.[7]

Injections are commonly made 3.5mm from the limbus in pseudophakic eyes and 4.0mm in phakic eyes. Theoretically, the injection can be performed in any quadrant of eye, but is typically done in the superotemporal or inferotemporal quadrant due to ease of access.

## Intimidating Equipment

Another aspect that might spook patients is the use of a lid speculum. The use of this device is not essential, but patients may be interested to know that some research shows patients for whom a speculum was not used had higher rates of endophthalmitis than those in whom the speculum was used.[8] However, that research dates back to 2004—early days in regards to intravitreal injections—so things may have changed.

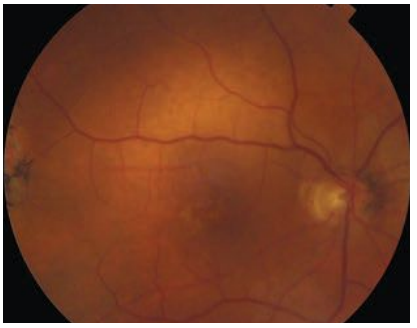
However, the lids and lashes must be kept away from the needle as they can serve as a potential source of contamination.[9] A recent survey of retina specialists revealed that 92% still use a speculum, so chances are patients will have to get comfortable with it.[10]

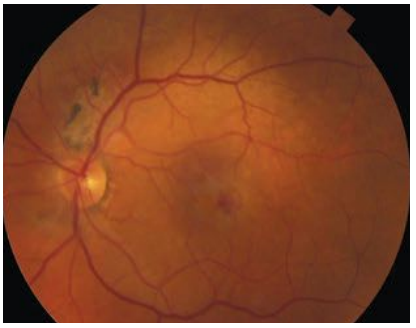
## Reducing Risks

Cleaning the eye thoroughly, including the lids and lashes, with 5% to 10% povidone-iodine is probably the single best precaution for endophthalmitis, and has emerged as the standard of care for intravitreal injections.[11] Research shows that the omission of povidone-iodine is associated with much higher rates of endophthalmitis and, in general, should be the last agent applied to the eye immediately before an injection.[11] While povidone-iodine is a necessity, repeated exposure to it does seem to lead to increasing reports of dry eye, which should be managed by the referring optometrist accordingly.[12]

Any active infection, such as blepharitis, should be treated prior to injection. Eyelid abnormalities, such as ectropion, can increase the risk for endophthalmitis and may need to be addressed as well.[13]

Also, in the early days of injections, patients were treated with pre- and post-procedural topical antibiotics, typically a fluoroquinolone. However, the literature has not demonstrated that topical prophylactic antibiotics reduce the risk of post-injection endophthalmitis. Further, some researchers believe antibiotic overuse may contribute to antibiotic-resistant bacteria, or have other detrimental effects on ocular surface health.[14] For this reason, doctors have mostly abandoned prophylactic antibiotics in these cases.





**These fundus photos show the same patient from page 50. He had a decreased VA in the left eye. Note the heme still visible in the macula, even after treatment. Anti-VEGF injections helped him maintain best-corrected visual acuities of 20/30 OD, 20/70 OS.**

## Drugs in the Literature

Currently, several anti-VEGF agents are available and each have pros and cons. While optometrists don't make the decision about which agent to inject, a robust understanding of the various agents available may help illuminate the patient's experience.

Intravitreal anti-VEGF has largely replaced grid or focal lasers for macular edema treatment, both in diabetic retinopathy (DR) and retinal vein occlusions (RVO), and has almost completely replaced the laser treatments for choroidal neovascularization (CNV) of any etiology.

Macugen (pegaptanib, Bausch + Lomb) was the first intravitreal anti-VEGF approved for the treatment of wet age-related macular degeneration (AMD), but has since been supplanted by newer agents.

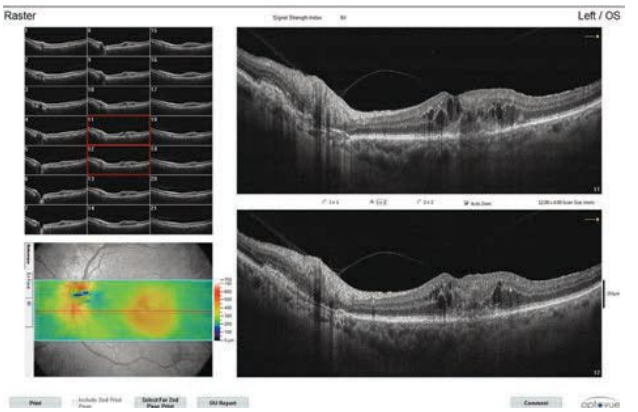
Lucentis (ranibizumab, Genentech) was first approved for the treatment of wet AMD and has since received approval to treat macular edema following RVO, the treatment of DME, all forms of DR and myopic (CNV). Avastin (bevacizumab, Genentech) is also widely used off label for retinal diseases, but is not FDA approved for the use in the eye. Investigators originally believed the molecule at the heart of it was too large to penetrate the retina, so it was redesigned as Lucentis. However, doctors widely use it

off-label, after having a compounding pharmacy reformulate it for intraocular use, in myriad eye diseases, including CNV of any etiology, DME and RVO. Studies conducted worldwide show Avastin injections are comparable to Lucentis in safety and efficacy at less cost.[15-17]

Eylea (aflibercept, Regeneron) was first FDA approved for wet AMD and has since gained approval for DME and all forms of DR.[18-20] In 2018, Eylea received FDA clearance to inject every 12 weeks.[18,19] The major advantage, research shows, is that it has longer action than Lucentis, and perhaps requires less frequent injections, decreasing the treatment burden.[20]

The most recent FDA-approved agent for the treatment of wet AMD is Beovu (brolucizumab-dbll, Novartis). It was FDA approved in October 2019 for the treatment of wet AMD based on the Phase III trials HAWK and HARRIER—which showed non-inferiority to Eylea in best-corrected visual acuity at one year (48 weeks) when injected every three months.[21] Approximately 30% of patients gained at least 15 letters by end of one year.[21] It also demonstrated greater reduction in central retinal thickness as early as week 16 and at one year vs. Eylea.[21] Also, the data showed more than half the patients were maintained on the three months-dosing schedule (56% in HAWK, 51% in HARRIER), with the remaining patients receiving injections every eight weeks.[21]

However, recent reports have emerged regarding potential adverse effects of Beovu.[22] In late February, the American Society of Retina Specialists issued a letter warning its members of 14 cases of vasculitis, 11 of which were reported as retinal arterial occlusive disease.[22]




**These images show additional findings from the CNVM patient with intraretinal fluid in the left eye. Monitoring is a key part of the OD's role in managing patients undergoing anti-VEGF shots.**

Intravitreal steroids, most notably triamcinolone acetate (TA), are also used to treat retinal disorders such as DME, macular edema from RVO and posterior uveitis due to their anti-inflammatory, antiangiogenic and anti-permeability properties. Intravitreal TA was previously widely used for the treatment of DME, until a study showed that laser photocoagulation for DME is more effective over time and has fewer side effects than TA.[23] Similar studies with both central and branch RVO show intravitreal triamcinolone are not as effective as anti-VEGF treatment, with more side effects.[24]

Intravitreal steroids have also been used to treat wet AMD either alone or with anti-VEGF. However, due their side effects, such as cataract formation and increased IOP, intravitreal steroids are generally not first line for the treatment of retinal disease. They are still an option for patients who do not respond to traditional anti-VEGF injections, and as such, are rarely if ever used for AMD.[25]

## Monitor IOP

Acute IOP rise after intravitreal injection is common, and typically lasts for a few hours at the most.[26] Specialists may check the patient's IOP after injection, as an acute, severely elevated IOP may lead to central retinal artery occlusion.

Some studies, however, have reported that increased number of injections may be associated with an increased risk for IOP elevation.[26] Further, IOP elevation rates are higher in patients with preexisting glaucoma than in those without. While preexisting glaucoma is not a contraindication for intravitreal injection, clinicians must use caution in treating glaucoma patients, and all patients should have their IOP routinely monitored, and treated with either drops or surgery should the IOP become a concern.[26]

## Complication Coaching

The patient should be counseled regarding common complications, such as discomfort, pain and subconjunctival hemorrhage, as well as uncommon but important post-op complications, such as retinal detachment and endophthalmitis. The patient should be advised they may experience slight discomfort for the rest of the day, but significant pain, redness or acute vision loss should warrant a call or office visit.

Reports show subconjunctival hemorrhages occur in nearly 10% of all injections, with higher frequency in patents on aspirin or other blood thinners. Like most subconjunctival hemorrhages, they are self-limiting but can be concerning for the patient, so reassurance is advised.[27] However, clinicians should not advise patients to discontinue their

blood thinners for the procedure.

Perhaps the most serious complication of intravitreal injections is endophthalmitis. Infectious endophthalmitis following intavitreal injection can be recognized by the presence of pain, redness and a severe anterior reaction consisting of keratic precipitates, hypopyon, fibrin or anterior synechia.[28] In clinical trials, the rate of endophthalmitis with anti-VEGF agents was reported to range from 0.019% to 1.6%.[29]

However, the rate appears lower in more recent studies. In one study, among the 4.3 million injections reviewed, the rate of endophthalmitis was one in 2,771 (0.036%).[30] Unlike other studies that seemed to show similar rates among different agents, this study showed aflibercept had a statistically higher rate of suspected endophthalmitis vs. the other agents, at 0.049%.[31] A higher rate was found in steroids vs. anti-VEGF agents, with triamcinolone injections having a rate of 0.147%.[32] The mean time it took for endophthalmitis to set in was 4.7 days after the injection, with an average visual acuity reduction of 74 letters on presentation.[32]

Furthermore, approximately 50% of patients who develop endophthalmitis after injection will not return to their pre-injection level of acuity, despite appropriate treatment.[32] For this reason, some retina specialists institute a follow-up phone call three to seven days after the injection and inquire about symptoms suggestive of endophthalmitis, such as reduced vision, severe redness or pain.[29]

Other uncommon side effects include retinal detachments (up to 0.67%) traumatic cataract (<0.1%) and other rare ocular events such as anterior ischemic optic atrophy, RVO, retinal artery occlusions, hemorrhagic macular infarction and sixth nerve palsy.[33] Further, corneal abrasions, most likely due to the lid speculum, as well as dry eye from repeated povodine-iodine use, may also be infrequently encountered.[34]

No clinical evidence shows what patients should avoid after injections, but in theory, attempts to limit the exposure of microorganisms near the site of injection is practical. Many physicians tell patients to avoid swimming, rubbing eyes, gardening, wearing makeup or performing dusty work for 24 hours.[34]

## On the Horizon

Treatment with intravitreal anti-VEGF agents is not curative for any disease. Many patients require long-term therapy, with some requiring monthly injections. This presents a high burden of treatment to patients, caregivers and physicians. Patients may become discouraged by their need for ongoing treatment. There is significant effort being put into the development of medications that work better and last longer, in addition to delivery systems that would allow less frequent dosing. While the following treatment options are still in clinical trials, this type of information may be encouraging to share with patients who are dismayed by the idea of needing regular injections long-term.

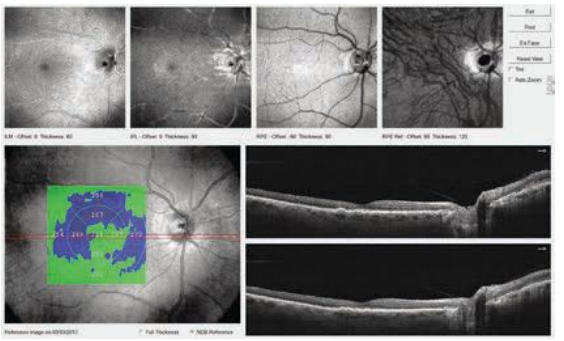
One of these promising new agents, faricimab (Genentech/Roche), is the first bispecific antibody designed for intravitreal use.[35,36] Essentially, it is one molecule with two agents on two separate arms; one arm binds to and inactivates VEGF, similar to the current anti-VEGF agents.[35,36] The second arm binds to and inactivates angiopoietin-2.[36] Research shows angiopoietin-2 levels are elevated in retinal vascular diseases, such as wet AMD, DR and vein occlusions.[35,36] It also appears to play a role in angiogenesis, vascular instability and inflammation in the retina, which makes it an attractive target for treatment.[35,36]

The Phase II BOULEVARD study evaluated patients with DME treated with faricimab vs. Lucentis.[35] The study showed that faricimab had gains in best-corrected visual acuity at six months, with a mean of 13.9 letters gained from baseline.[35] The decrease in central retinal thickness was actually better than Lucentis, with no safety concerns.[35]

YOSEMITE and RHINE Phase III studies are currently underway comparing faricimab with Eylea for DME, and represent the largest DME studies to date.[37,38]

The AVENUE and STAIRWAY Phase II studies evaluated faricimab in wet AMD.[39] In the studies, patients were treated with faricimab either every four weeks or every eight weeks and compared with Lucentis every four weeks. The STAIRWAY study evaluated faricimab every 16 or 12 weeks.[39] The results show that 65% of faricimab patients had no disease activity at 12 weeks and visual acuity was comparable to that of Lucentis every four weeks. Further central retinal thickness was reduced and a decrease in size of CNVM lesions was noted.[39] Phase III studies comparing faricimab every 16 weeks to Eylea every eight are currently underway.[40,41]

Other research is looking at alternative methods. One of these, the Port Delivery System (Genentech/Roche) with ranibizumab is a reusable, surgically implanted drug reservoir placed through a scleral incision in the pars plana.[42-44] It can hold approximately 20 microliters of ranibizumab (of a slightly different formulation than Lucentis), which it diffuses continuously into the vitreous.[42-44] When empty, the



**OCT identified a few small drusen in our patient's right eye. Increasingly, patients who undergo anti-VEGF injections are now being treated bilaterally to reduce the logistical elements of the treatment burden.**

device can be refilled in-office using a specialized refill needle, eliminating the need for monthly intravitreal injections.[42-44] The Phase II LADDER study evaluated more than 200 patients with exudative AMD with three different concentrations of ranibizumab in the reservoir vs. monthly injections of Lucentis.[42,43] Overall, the vision was similar across all treatment arms, with an average best-corrected vision of 20/40.[42,43] The procedure was relatively safe, with few cases of endophthalmitis and retinal detachment.[42-44] The refill procedure, done under local anesthesia, is also well tolerated.[42-44]

By developing a better understanding of the procedure of intravitreal injections—and providing proper comanagement of concomitant disease such as dry eye, blepharitis and glaucoma—the primary care optometrist can better counsel their patient on what to expect when referred to a retina specialist for treatment. New advancements in injections, such as longer acting agents and alternate delivery systems, may hold hope for optometric patients as well as the profession's future. ■

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# Tracing Clues Back to Retinitis Pigmentosa

Evaluating this condition can prove to be a genetic mystery.

By Michael DelGiodice, OD, PhD, and Allison Viray, BS

Retinitis pigmentosa (RP) is a group of inherited diseases involving progressive retinal degeneration of retinal pigmented epithelial cells and photoreceptors. The disease affects approximately one in 3,000 to 5,000 people without sex predilection and requires frequent examination.[1] Inheritance patterns of RP are most often autosomal recessive (AR), autosomal dominant (AD) and X-linked.

Because there is variability between the genotype and its phenotypic expression, the prognosis cannot be determined by the inheritance pattern alone. However, there is a general correlation between age-related visual acuity and mode of inheritance.[2] In cases where only one person in a family is affected, the disorder is described as *simplex*, which may occur through a new gene mutation. As it stands, researchers believe approximately 60 genes cause RP with variable inheritance patterns.[3] Primary RP is the predominant form of the disease restricted to ocular manifestations. Secondary RP occurs as a manifestation of systemic syndromes, most notably Usher syndrome.

## Presentation

Clinical manifestations of RP are generally characterized by bilateral nyctalopia, constricted visual fields, pigment atrophy, pigment clumping in a bone-spicule configuration and rod-cone dysfunction.[4] Symptoms of decreased peripheral vision and nyctalopia typically begin in the first and second decades of life and steadily worsen.[4]

Nevertheless, genotypic variability often gives rise to variable phenotypic observations. As such, two individuals with AR-RP may produce variable expression patterns.[4] Less common forms of the disease include unilateral RP and RP sine pigmento, the latter of which is characterized by a normal-appearing fundus with an abnormal electroretinogram (ERG).

Early funduscopic signs of RP include mild arteriole attenuation, pigment dusting in the vitreous, and retinal pigment dispersion of the anterior and mid-peripheral retina.[5] At this stage, an ERG may show flattening of both a-waves (photoreceptor) and b-waves (inner retinal cells).[5] Generally, formal visual field testing will display a mid-peripheral scotoma. Early fundus autofluorescence (FAF) may demonstrate both hyper- and hypofluorescence of the anterior and mid-periphery signaling retinal pigment epithelial (RPE) distress. With time, melanin will migrate anteriorly within the intraretinal space in a bone-spicula configuration.

Patients with advanced RP typically exhibit marked vessel attenuation, severely constricted visual fields, optic atrophy, posterior subcapsular cataracts, cystoid macular edema (CME), central vision loss, dyschromatopsia and photophobia.[5] In advanced-stage RP, FAF will usually display a hyperfluorescent parafoveal ring, signaling preservation of the ellipsoid zone (EZ) as visualized on OCT.[6]

## Examination

The American Academy of Ophthalmology recommends that the clinical assessment of suspected

inherited retinal dystrophies include a comprehensive examination along with imaging (color fundus photos, fundus autofluorescence and SD-OCT), formal visual fields, full field ERG and molecular genetic testing.[7]

A clinical exam should begin with a thorough evaluation of the patient's ocular, medical, social and family histories, including identifying any past history of retinotoxic medications that may help differentiate RP from alternative etiologies.

Annual comprehensive exams are required to identify progression as well as potential secondary complications, such as posterior subcapsular cataracts, optic atrophy, optic disc drusen and CME.[7] We prefer the widefield FAF over the standard color photograph, as it can demonstrate photoreceptor degeneration (hypofluorescence), as well as accumulation of lipofuscin (hyperfluorescence). In addition, a large number of patients will exhibit a hyperfluorescent Robson-Holder ring. The diameter of the ring on FAF corresponds well with retinal sensitivity and constriction, as demonstrated by formal visual field testing.[8] While the ERG remains the standard of care for diagnosis, FAF can be used in lieu of ERG to monitor progression, especially in later stages of the disease when ERG is less reliable.[9]

As the disease progresses, OCT is sensitive at identifying early changes in the macula responsible for central vision loss. Close inspection of the EZ can help identify early structural abnormalities.[10] Discontinuity of the EZ is followed by shortening of the ELM and RPE.[11] To quantify the extent and degree of peripheral vision, perform visual field testing (HVF 30-2).

Early changes usually begin with isolated, mid-peripheral scotomas that gradually coalesce to form a partial ring scotoma. As the disease progresses, the outer edge of the ring expands to the periphery, while the inner edge constricts centrally. Examine patients who lack central fixation with the full-field stimulus test.[7]

ERG measures the electrical potential of the photoreceptors and can establish the diagnosis. In early stages of the disease, the amplitudes of the a- and b-waves are diminished. With progression, the amplitudes may become extinguished. At this stage, multifocal ERG and microperimetry are effective at objectively measuring functional vision.[12,13]

## Treatments

Since RP has no cure, most therapies are limited. Studies show that vitamin A, lutein and docosahexaenoic acid (DHA) supplements may reduce the risk of progression.[14-19] Counsel patients with primary RP and those with Usher syndrome on the potential therapeutic benefits of daily intake of vitamin A palmitate 15,000 IU, lutein (12mg), two ounces of omega-3 rich foods or a DHA supplement (200mg), and to avoid supplemental vitamin E as it hastens the progression of the disease.[18-20]

Prior to initiating therapy, we recommend that patients undergo medical evaluation to assess fasting serum vitamin A, red blood cell DHA levels and liver enzymes. Following a normal baseline, perform blood tests annually. Aside from supplementation, a number of studies are exploring new treatment options. Novel therapies are aimed at preserving and restoring vision in patients with RP. Some of these methods include gene therapy, autoserum, stem cell therapy and visual prostheses.[21-23] Most notably, Luxturna (voretigene neparvovec, Spark Therapeutics) has received FDA approval for treating patients with biallelic RPE65-mediated retinal dystrophy.[24]

Low vision aids can improve visual performance in patients with RP. Traditional optical aids include telescopes, reverse telescopes, widefield and high-intensity flashlights, CPF 550 lenses (Corning), handheld magnifiers, stand magnifiers, half-eye base-in prism lenses and electronic devices. Additionally, the Argus II retinal prosthesis has received FDA-approval for a limited number of patients with vision of light perception or worse.[25]

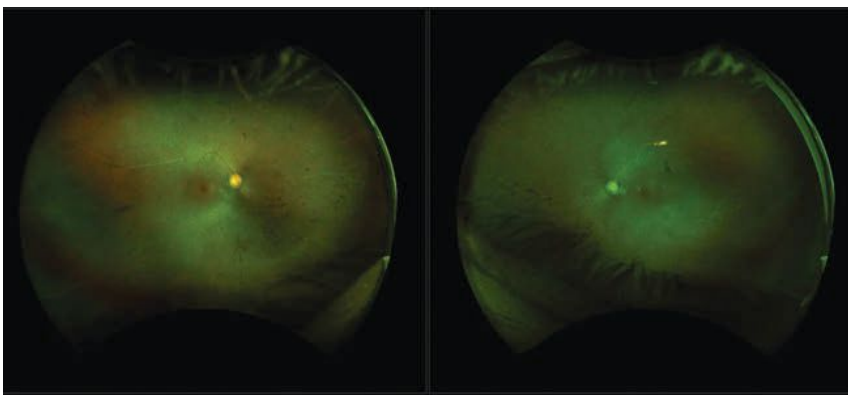

**Fig. 1. FAF that displays a hyperfluorescent ring and hypopigmentation in the mid-periphery can be related to late-stage RP.**

# Retinitis Pigmentosa

## Case Presentation

A 59-year-old Hispanic female presented with progressive vision loss and night blindness since childhood. She was first seen 10 years ago in Puerto Rico for a gradual decrease in vision and difficulty driving at night attributed to cataracts. Shortly after cataract surgery, she was lost to follow-up,with no records to review. During this period, the patient began to notice a gradual decline of peripheral vision in both eyes and significant loss of central vision in the left eye. Her ocular history was positive for cataract surgery, mild hyperopia and presbyopia OU. She had no history of ocular inflammation or eye trauma. Her medical history was positive for hypothyroidism, which she treated with levothyroxine. A complete review of systems was unremarkable for inflammatory disease, prior infection, infantile illness or sexually transmitted disease. Her family and social histories were unremarkable.

Best-corrected visual acuity was 20/50 OD and light perception OS. Pupils were round and slowly reactive to light with a relative afferent defect OS. Confrontation visual fields were severely constricted OU. Color vision, measured with Ishihara plates, was reduced to 8/10 OD and 0/10 OS. The posterior vitreous was detached OU. The estimated cup-to-disc ratio was 0.50 OD and 0.70 OS. The color of the disc was normal OD and diffusely pale OS. A dilated fundus exam revealed diffuse atrophy and clumping of the RPE OU. Examination of the macula revealed cystic elevation and granular pigmentary changes in both eyes. Retinal arterioles were moderately attenuated OD and severely attenuated OS. Retinal photography was performed to document the findings.

Fundus autofluorescence revealed a parafoveal hyperfluorescent ring and hypopigmentation in the midperiphery (*Figure 1*). SD-OCT demonstrated CME as well as significant disruption of the EZ, external limiting membrane (ELM) and RPE (*Figure 2*). Automated Humphrey 30-2 standard visual field showed severe defects in all four quadrants OU with sparing of central fixation OD.

Based on the patient's history and clinical presentation, we established a tentative RP diagnosis OU with secondary optic nerve cupping and pallor OS. Since we could not discount glaucoma, we recommended a full glaucoma work-up to include disc OCT, gonioscopy and pachymetry. To confirm the diagnosis of RP, we ordered a full-field electroretinogram (ERG) and genetic testing. We used Invitae's (Spark Therapeutics) inherited retinal disease genetic testing program that tests approximately 250 genes for variants known to cause inherited retinal disease.[26]

The ERG revealed diminished a- and b-waves in the both eyes. Genetic testing confirmed phosphodiesterase 6A (PDE6A) gene mutation. PDE6A is a critical component of the visual cycle involved in regulating levels of intracellular cyclic guanosine monophosphate (cGMP) during phototransduction; in RP, low levels of this gene are implicated as the cause of rod apoptosis.[3]

Results of the ERG and genetic testing established the diagnosis of autosomal recessive RP. We began treatment with oral acetazolamide 250mg BID to treat the CME, as well as brimonidine 0.2% BID OU to lower IOP.

## Genetic Testing

Once a tentative diagnosis is established, genetic testing can help confirm the diagnosis, determine

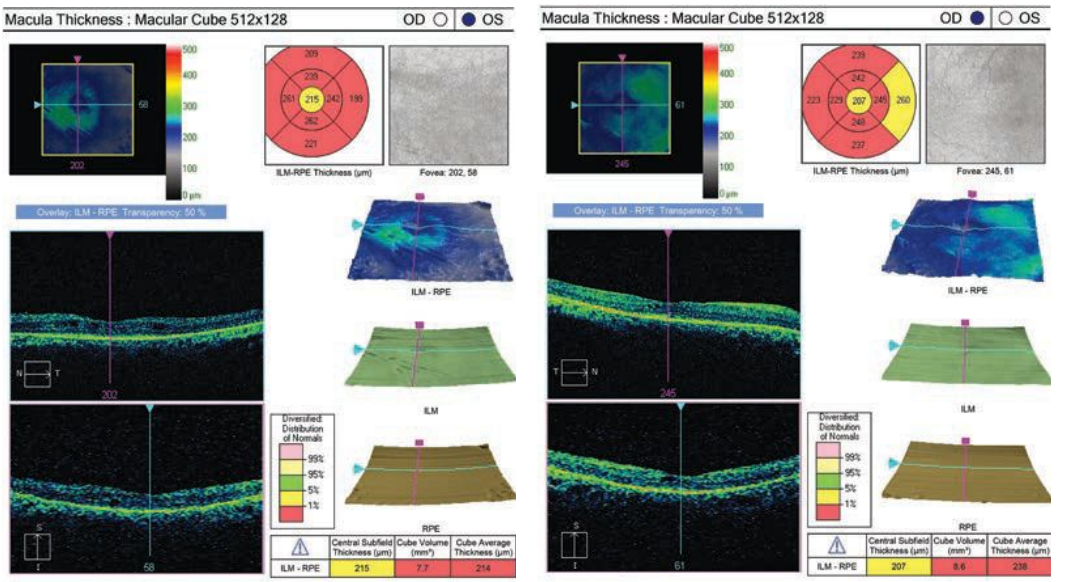


**Fig. 2. OCT is sensitive at identifying CME responsible for central vision loss. Close inspection of the EZ can also help identify structural abnormalities suggestive of RP.**

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the inheritance pattern, and identify at-risk family members. Multi-gene testing is preferred, as it covers a wide-range of gene mutations.[7] Several commercial laboratories offer comprehensive retinal dystrophy panels including: Spark Therapeutics, Blueprint Genetics, Molecular Vision Laboratory and Prevention Genetics. Using Spark Therapeutics, we identified our patient as having the PDE6a mutation causing AR-RP.

Patients who have undergone genetic testing should then be referred for genetic counseling. In addition, we recommended the My Retina Tracker Registry—a research database of the Foundation Fighting Blindness. The registry provides more than 20 retinal degenerative diseases, including RP.[27] The registry is designed to share information of rare retinal diseases in order to identify individuals who might be interested in participating in research studies and clinical trials.

While we have yet to discover a cure for RP, the field of restorative vision therapy is dynamic. Progress is being made in retinal prostheses as well as in optogenetics, stems cells and gene therapy. We look forward to advances in technology and offering our patients new therapeutic options in the future. ■

*Dr. DelGiodice practices at Associated Eye Physicians in Clifton, NJ.*

*Ms. Viray is a fourth-year student at Salus University.*

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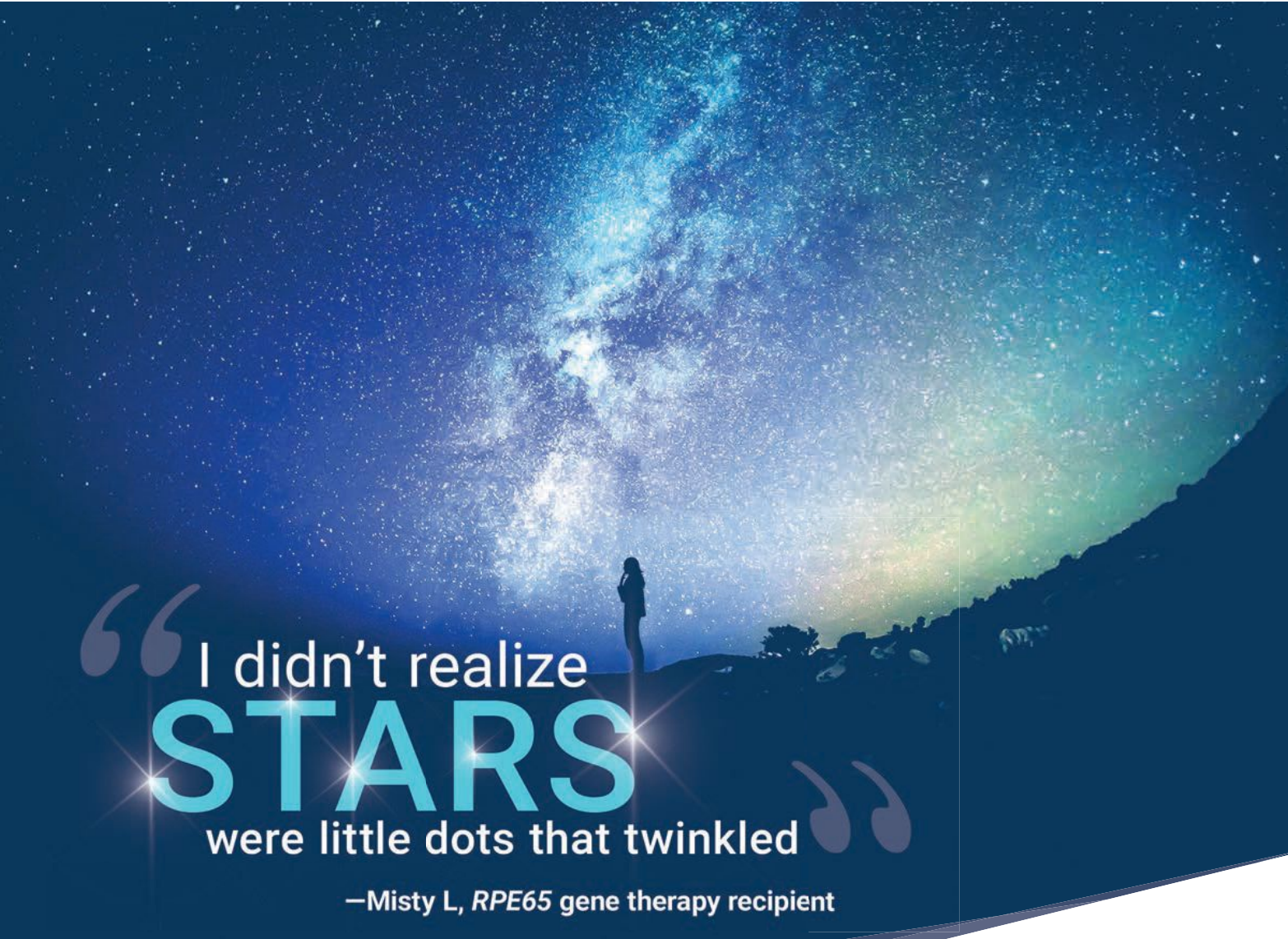


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# How to Calm Patients' Nerves About COVID

Most practices are now open for routine care. Here's how to prepare your patients for your new safety protocols. **By Jane Cole, Contributing Editor**

As practices across the country are reopening for routine care amid COVID-19, the process isn't business as usual. For instance, when patients enter optometrist Bradley Richlin's practice in Beverly Hills, they are now greeted with a sign that reads, "Welcome to Our Sterile Office," followed by a masked staff member who reinforces the message: "Welcome to our office. Things have changed for your safety and ours."

With the addition of personal protective equipment (PPE), slit lamp breath shields and routine disinfection, ODs are going to great lengths to protect their patients, staff and themselves. Communicating these efforts can be paramount in allaying patient fears. "The number one question we get from patients is, 'What are you doing to keep me safe?'" Dr. Richlin says.

In the 10th wave of Jobson's weekly Coronavirus ECP Survey, a majority of respondents (52%) said patients were willing to reschedule appointments if they were comfortable with the safety precautions.

Still, patient education in the time of COVID-19 encompasses far more than simply touting new office cleaning protocols. Doctors also find themselves fielding questions on how to safely wear contact lenses and whether they can contract the virus through their eyes.

Photo: Ian Whipple, OD


**Dr. Whipple's office has a screening area set up before patients even enter the office.**

## It Starts With a Call

The initial scheduling call is the first opportunity to educate patients on the office changes. When patients call optometrist Glenn Corbin's practice in Wyomissing, Pa., staff let them know everyone is required to wear a mask—something most patients appreciate, Dr. Corbin says.

Not only that, if patients take their mask off during the visit, staff ask them to either put their mask back on or leave.

During that initial phone call, staff also advise patients that they will take their temperature when they arrive, and the individual should plan to come alone. "We don't want additional family members or others in the practice unless it's medically appropriate or the additional person is a parent of a child," Dr. Corbin says.

For Ian Whipple, OD, of Farr West, Utah, his staff reassure patients that they will be given a mask and gloves when they arrive. They also outline the new check-in protocols and extended appointment time to allow for cleaning.

## In-office Precautions

Often, the best defense is a good offense, and many ODs are getting ahead of any concerns with extended patient intake forms. All of Dr. Whipple's patients complete a risk assessment to determine if anyone in their household is ill; the form not only gathers information but also conveys to patients a strong message: the office isn't taking any

risks if patients feel ill. If they are, the individual is rescheduled.

Recently, two patients had to reschedule due to red flags, the latter being a teething infant. The child returned to the practice 10 days later with her father, and the mother joined the appointment via Skype since the practice only allows one individual to accompany a patient, when necessary. Dr. Whipple says both parents were appreciative that his practice took precautionary methods to keep their family safe.

If a patient enters Dr. Richlin's practice already wearing gloves, staff ask the individual to remove them. "Some patients think the gloves are protecting them, but we let them know their gloves are dirty, and gloves are just like your hands, but you don't wash your gloves."

Patients are instructed to clean their hands with the touchless hand sanitizer and don a clean surgical mask (even if they are already wearing a cloth mask). Staff then take their temperature with a no-touch thermometer and place a bright neon sticker on their shoulder, indicating they've passed the checkpoint.

During the visit, staff educate patients on the rigorous precautions the office is taking to ensure everyone's safety. When staff arrive at work, everyone is required to log in and record their temperatures and any symptoms. Anything suspicions prompts a pop-up alert instructing them to go home and contact their primary care physician.

## Exam Lane Changes

The eye exam requires the doctor to work in close proximity to the patient, less than the six-foot guidance—perhaps not as close as a dental hygienist or dentist, but close nonetheless, and especially with contact lens services, says Brian Chou, OD, who practices in San Diego.

"I believe that the close nature of examinations is implicit for patients that have previously had an eye exam," he says.

Still patients should expect increased disinfection, more hand washing and the use of masks and gloves. When entering the exam room, patients' worries may be eased just by seeing disinfection taking place before they sit in the chair.

Dr. Richlin's staff cleans every surface before and after each patient. Because patients want to see the room cleaned in front of them, staff will clean the arm rests, microscope, eye drop bottles and other surfaces in their presence, he adds.

"Aside from conspicuous and regular hand washing, I'm not doing much different compared to before COVID-19 with instilling eye drops, contact lens application and expressing meibomian glands," says Dr. Chou. "With instilling topical anesthetic and dilating drops, as before, I take care not to contact the bottle tip with the patient's ocular tissue."

But some ODs have implemented changes for each of these instances:

***Eye drops.*** Dr. Whipple's practice is trying to eliminate eye drops as much as possible and is encouraging ultra-widefield imaging as an alternative to dilation whenever possible.

***Contact lenses.*** While Dr. Whipple now wears gloves during contact lens insertion and removal, ODs at Dr. Richlin's practice are still doing contact lens appointments with

### Sanitation Products Abound

Most optometric practices have set strict cleaning protocols upon reopening for routine care. In addition to wiping down surfaces between patients, some ODs are adding extra steps in an effort to sanitize and better reassure patients:

- **COVID-19 disinfectants:** While many household cleaning products claim to kill COVID-19, the EPA offers a list of approved disinfectants: ww.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2. On this list is hypochlorous acid, which is often used to manage a number of ocular conditions. Dr. Whipple now uses hypochlorous acid to disinfect surfaces in his practice and explains its benefits to patients when they enter the exam room. He chose this cleaning product in particular because it is gentle enough that he doesn't need to glove up as is often the case with harsher products, he adds.
- **Electrostatic disinfection:** Dr. Corbin recently committed to an electrostatic system for disinfecting his practice. The new misting sprayer, eMist from Eye Designs, is said by its manufacturer to adhere to surfaces more readily because electrostatic attraction allows it to coat a larger surface area than spray-and-wipe techniques that may leave large areas untouched. For some, this could mean a faster, more efficient sterilization process for frames, equipment, chairs and doors. The active ingredient here is also hypochlorous acid.
- **Air purifiers with HEPA filters:** Dr. Richlin purchased three medical-grade HEPA air filters for his practice. Each has a charcoal filter for smell and uses UV light to kill viruses, mold, fungi and bacteria. On top of each air filter he added signs reading, "Hi. Don't mind me. I'm an air filter, I'm here to clean your air, kill viruses and bacteria and keep you safe."
- **UV boxes to sanitize frames:** Ultraviolet LED sterilizer boxes are designed to clean objects during a quick two-to-three minute light cycle. Most are easy to use with just a push of a button. Reseach shows UV sanitizing makes viruses non-viable, and as such, hospitals routinely use this technology, Dr. Richlin says. In Dr. Richlin's dispensary, used frames get a double cleaning, first with soap and water followed by a turn in a UV box.
- **Touch-free hand sanitizers:** Upon reopening, Dr. Richlin added 15 touchless hand sanitizers throughout the office, which he says are meant to eliminate a common contact point where germs can be transferred—a traditional sanitizer bottle's pump.

clean hands that are washed again immediately after the process is complete.

With contact lens application, and particularly with new wearers, Dr. Chou generally takes charge of the lens handling in the exam room, since he says he is usually faster, more hygienic and less prone to time-consuming complications.

*Gland expression.* For meibomian gland expression, Dr. Richlin now relies heavily on the LipiFlow (Johnson & Johnson Vision) and wears gloves during the procedure.

Photo: Glenn Corbin, OD

**Dr. Corbin and his patients wear masks and gloves throughout the exam.**

## Allay CL Fears

While many people are hungry for information regarding how to stay safe during the pandemic, misinformation is rampant about contact lens wear, according to the Centre for Ocular Research and Education (CORE).[1] Despite the myths and misinformation, contact lens wear remains safe—something clinicians need to stress to their patients who may be uncertain.[1]

Optometrists can reassure patients that no scientific evidence suggests lens wear increases their risk of contracting COVID-19 compared with spectacle wear.[2,3]

In addition, good hygiene, and specifically hand washing, is widely accepted as a critical preventative measure against COVID-19. For contact lens wearers, hand washing has always been important, but more so now than ever. Clinicians must re-educate contact lens wearers on the need for thorough hand washing and drying before inserting and removing lenses and proper lens wear and care, including replacing contact lens cases regularly.[2,3] Spectacle wearers should regularly clean their glasses with soap and water.[2,3] CORE also offer these additional pearls:[2,3]

- Regular eyeglasses don't provide protection from COVID-19.
- Keep unwashed hands away from your face.
- If you become sick, temporarily stop wearing your lenses and switch to glasses.[2,3]

Still, conflicting reports that suggest patients shouldn't wear contact lenses during the pandemic may be influencing patients' lens wearing habits.[4] An early April poll of 89 patients on lockdown found 72% were wearing their lenses less than normal. The most common reason was "less need" for contact lenses while at home. Another reason for reduced contact lens wear during the lockdown included concern about infection due to lens use (8%).[4]

Dr. Richlin reminds his patients that if they keep their fingertips clean—as they should rgardless of COVID-19—they shouldn't have any issues, as contact lenses are rarely the source of infection; rather, unclean cases, dirty fingers and dirty eyelids are often the culprits.

## No-touch Dispensing

The dispensary, perhaps more so than the waiting area or exam room, is likely to be a patient's biggest source of anxiety in a newly reopened practice. It's also a concern

### ODs Do Double-Duty as Mask Enforcers

Masks have become a flashpoint in some areas of the country during the pandemic. Upon reopening, many doctors have enforced strict mask policies. According to Jobson's 10th wave Coronavirus ECP Survey, 64% of clinicians are offering free masks and 14% are providing one for a fee. Another 13% are barring unmasked patients from entering the practice, while only 3% are willing to see them without a mask.

If a patient is uncomfortable wearing a mask in Dr. Corbin's practice, the individual is rescheduled in one to two months when the requirement may be lifted. "My attitude is, if you don't want to wear a mask, you won't have access to my practice. I'm not going to put my patients, my staff and myself at elevated risk because someone doesn't want to wear a mask," Dr. Corbin says.

In the first week of his practice's reopening, Dr. Whipple had to turn away a patient for refusing to wear a mask and gloves. "It wasn't worth the risk to our employees," he says. "I was really proud of my staff members for sticking to their guns."

Some patients may come armed with a letter outlining their rights to not wear a mask based on the Americans with Disabilities Act (ADA)—a sticky situation for ODs trying to keep everyone safe. Recently, the Department of Justice released a warning that it has not issued any formal letter, so any patient claiming to have one may not realize it's not official.[1]

In addition, the ADA does allow medical offices to refuse care if the patient "poses a direct threat to the health or safety of others."[2]

1. United States Department of Justice. *COVID-19 ALERT: Fraudulent Facemask Flyers*. www.ada.gov/covid-19_flyer_alert.html. Accessed May 28, 2020.
2. Americans With Disabilities Act of 1990. Equal Opportunity For Individuals With Disabilities. www.ada.gov/pubs/adastatute08.htm. Accessed May 28, 2020.

for practitioners, as 46% of Jobson's Coronavirus ECP Survey respondents are looking for information on how to handle patients and frame selection in the optical/dispensary.

Long gone are the days when patients can browse freely and take various frames from the board for a test drive. This is sure to cause both relief and frustration. Everyone wants to feel insulated from exposure, but the "customer first" environment of the dispensary may compel patients to still do as they please. Plan to invest time reorienting patients to a new experience.

Dr. Whipple's practice launched a mandatory guided frame selection process following reopening. His opticians were already well-trained to offer patients frame recommendations; now, staff stay by the patient's side in the dispensary, make suggestions, take the frames from the board and immediately place the unwanted frames in a separate bin for disinfection—a process Dr. Richlin's practice is following as well.

Dr. Richlin added an extra ultraviolet (UV) light sanitation step for already cleaned frames.

## Limited Bathroom Access

These days, you can never be too careful about safety, and now that means stricter bathroom protocols as well. Dr. Whipple only opens the office bathroom upon request. "It might be a bit overboard, but we weren't sure if people were using it, so we decided to lock the door and if someone does need it, we give them the key and know to wipe it down afterward."

## COVID-19 and the Eye

Researchers are working overtime to better understand this novel coronavirus, yet much remains uncertain. Patients are bound to ask if COVID-19 can manifest in the eye, and even well-read doctors will likely say the answer isn't clear.

However, some preliminary investigations can help clinicians educate patients on the current understanding. Some studies suggest the virus is capable of causing ocular complications such as viral conjunctivitis in the middle phase of illness.[5]

One case study highlights a patient diagnosed with viral conjunctivitis two days before classic symptoms of COVID-19 presented.[6]

A recent non–peer reviewed investigation from Johns Hopkins University suggests the ocular surface is susceptible to infection and could serve as a portal of entry through exposure to aerosolized droplets or hand-eye contact.[7]

Still, a comprehensive review as of April 15 noted that coronaviruses are unlikely to bind to ocular surface cells to initiate infection. The review also found only occasional cases of conjunctivitis reported in patients with COVID-19.[9]

Dr. Whipple admits everything he's doing at his practice might not be a one-size-fits all for other doctors. "I feel every small thing we do hopefully shows patients we really do care about keeping them safe and we're taking this seriously. Hopefully, it's giving patients a little more trust in what we do." ■

*The content contained in this article is for informational purposes only. The content is not intended to be a substitute for professional advice. Reliance on any information provided in this article is solely at your own risk.*


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Photo: Glenn Corbin, OD

**In many offices, the COVID-19 optical experience looks a lot different now, with masks, face shields, a personalized frame selection process and sanitizing between patients.**

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**Preexisting Inflammatory Bowel Disease:** TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

**References: 1.** TEPEZZA (teprotumumab-trbw) [prescribing information] Horizon. **2.** Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Engl J Med*. 2020;382(4):341-352. **3.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18):1748-1761. **4.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18)(suppl):1748-1761. https://www.nejm.org/doi/suppl/10.1056/NEJMoa1614949/suppl_file/nejmoa1614949_appendix.pdf.

TEPEZZA™
teprotumumab-trbw

## Significantly greater proptosis responder rate* (Study 2)[1,2]

| TEPEZZA | | Placebo |
|---|---|---|
| **83%** | vs | **10%** |
| **TEPEZZA (n=41)** | | **Placebo (n=42)** |

*P*<0.001 at Week 24

*Both the safety and efficacy of TEPEZZA were evaluated in 2 randomized, double-masked, placebo-controlled clinical trials (Studies 1 and 2) consisting of 171 patients with TED (84 were randomized to TEPEZZA and 87 to placebo). The primary endpoint in Studies 1 and 2 was proptosis responder rate, defined as having a ≥2-mm reduction from baseline in proptosis in the study eye at Week 24 without deterioration (≥2-mm increase in proptosis) in the non-study eye.[1]

**Hyperglycemia:** Increased blood glucose or hyperglycemia may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be managed with medications for glycemic control, if necessary. Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

### Adverse Reactions

The most common adverse reactions (incidence ≥5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, and dry skin.

**Please see Brief Summary of Prescribing Information for TEPEZZA on following page.**

HORIZON

# TEPEZZA™
## teprotumumab-trbw

**For injection, for intravenous use**

**Brief Summary - Please see the TEPEZZA package insert for full prescribing information.**

### INDICATIONS AND USAGE

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

### WARNINGS AND PRECAUTIONS

#### Infusion Reactions

TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Signs and symptoms of infusion-related reactions include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain. Infusion reactions may occur during any of the infusions or within 1.5 hours after an infusion. Reported infusion reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

#### Exacerbation of Preexisting Inflammatory Bowel Disease

TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

#### Hyperglycemia

Hyperglycemia or increased blood glucose may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be controlled with medications for glycemic control, if necessary.

Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

### ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Infusion Reactions [see Warnings and Precautions]
- Exacerbation of Inflammatory Bowel Disease [see Warnings and Precautions]
- Hyperglycemia [see Warnings and Precautions]

#### Clinical Trials Experience

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

The safety of TEPEZZA was evaluated in two randomized, double-masked, placebo-controlled clinical studies (Study 1 [NCT:01868997] and Study 2 [NCT:03298867]) consisting of 170 patients with Thyroid Eye Disease (84 received TEPEZZA and 86 received placebo). Patients were treated with TEPEZZA (10 mg/kg for first infusion and 20 mg/kg for the remaining 7 infusions) or placebo given as an intravenous infusion every 3 weeks for a total of 8 infusions. The majority of patients completed 8 infusions (89% of TEPEZZA patients and 93% of placebo patients).

The most common adverse reactions (≥5%) that occurred at greater incidence in the TEPEZZA group than in the control group during the treatment period of Studies 1 and 2 are summarized in Table 1.

**Table 1. Adverse Reactions Occurring in 5% or More of Patients Treated with TEPEZZA and Greater Incidence than Placebo**

| Adverse Reactions | TEPEZZA N=84 N (%) | Placebo N=86 N (%) |
|---|---|---|
| Muscle spasms | 21 (25%) | 6 (7%) |
| Nausea | 14 (17%) | 8 (9%) |
| Alopecia | 11 (13%) | 7 (8%) |
| Diarrhea | 10 (12%) | 7 (8%) |
| Fatigue[a] | 10 (12%) | 6 (7%) |
| Hyperglycemia[b] | 8 (10%) | 1 (1%) |
| Hearing impairment[c] | 8 (10%) | 0 |
| Dysgeusia | 7 (8%) | 0 |
| Headache | 7 (8%) | 6 (7%) |
| Dry skin | 7 (8%) | 0 |

a - Fatigue includes asthenia
b - Hyperglycemia includes blood glucose increase
c - Hearing impairment (includes deafness, eustachian tube dysfunction, hyperacusis, hypoacusis and autophony)

#### Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

In a placebo-controlled study with TEPEZZA, 1 of 42 patients treated with placebo had detectable levels of antidrug antibodies in serum. In the same study, none of the 41 patients treated with TEPEZZA had detectable levels of antidrug antibodies in serum.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action inhibiting insulin-like growth factor-1 receptor (IGF-1R), TEPEZZA may cause fetal harm when administered to a pregnant woman. Adequate and well-controlled studies with TEPEZZA have not been conducted in pregnant women. There is insufficient data with TEPEZZA use in pregnant women to inform any drug associated risks for adverse developmental outcomes. In utero teprotumumab exposure in cynomolgus monkeys dosed once weekly with teprotumumab throughout pregnancy resulted in external and skeletal abnormalities. Teprotumumab exposure may lead to an increase in fetal loss [see Data]. Therefore, TEPEZZA should not be used in pregnancy, and appropriate forms of contraception should be implemented prior to initiation, during treatment and for 6 months following the last dose of TEPEZZA.

If the patient becomes pregnant during treatment, TEPEZZA should be discontinued and the patient advised of the potential risk to the fetus.

The background rate of major birth defects and miscarriage is unknown for the indicated population. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.

Data

*Animal Data*

In an abridged pilot embryofetal development study, seven pregnant cynomolgus monkeys were dosed intravenously at one dose level of teprotumumab, 75 mg/kg (2.8-fold the maximum recommended human dose [MRHD] based on AUC) once weekly from gestation day 20 through the end of gestation. The incidence of abortion was higher for the teprotumumab treated group compared to the control group. Teprotumumab caused decreased fetal growth during pregnancy, decreased fetal size and weight at caesarean section, decreased placental weight and size, and decreased amniotic fluid volume. Multiple external and skeletal abnormalities were observed in each exposed fetus, including: misshapen cranium, closely set eyes, micrognathia, pointing and narrowing of the nose, and ossification abnormalities of skull bones, sternebrae, carpals, tarsals and teeth. The test dose, 75 mg/kg of teprotumumab, was the maternal no observed adverse effect level (NOAEL).

Based on mechanism of action inhibiting IGF-1R, postnatal exposure to teprotumumab may cause harm.

#### Lactation

Risk Summary

There is no information regarding the presence of TEPEZZA in human milk, the effects on the breastfed infant or the effects on milk production.

#### Females and Males of Reproductive Potential

Contraception

*Females*

Based on its mechanism of action inhibiting IGF-1R, TEPEZZA may cause fetal harm when administered to a pregnant woman (see Use in Specific Populations). Advise females of reproductive potential to use effective contraception prior to initiation, during treatment with TEPEZZA and for 6 months after the last dose of TEPEZZA.

#### Pediatric Use

Safety and effectiveness have not been established in pediatric patients.

#### Geriatric Use

Of the 171 patients in the two randomized trials, 15% were 65 years of age or older; the number of patients 65 years or older was similar between treatment groups. No overall differences in efficacy or safety were observed between patients 65 years or older and younger patients (less than 65 years of age).

### OVERDOSAGE

No information is available for patients who have received an overdosage.

### PATIENT COUNSELING INFORMATION

Embryo-Fetal Toxicity

Advise females of reproductive potential that TEPEZZA can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy.

Educate and counsel females of reproductive potential about the need to use effective contraception prior to initiation, during treatment with TEPEZZA and for 6 months after the last dose of TEPEZZA.

Infusion-Related Reactions

Advise patients that TEPEZZA may cause infusion reactions that can occur at any time. Instruct patients to recognize the signs and symptoms of infusion reaction and to contact their healthcare provider immediately for signs or symptoms of potential infusion-related reactions.

Exacerbation of Inflammatory Bowel Disease

Advise patients on the risk of inflammatory bowel disease (IBD) and to seek medical advice immediately if they experience diarrhea, with or without blood or rectal bleeding, associated with abdominal pain or cramping/colic, urgency, tenesmus or incontinence.

Hyperglycemia

Advise patients on the risk of hyperglycemia and, if diabetic, discuss with healthcare provider to adjust glycemic control medications as appropriate. Encourage compliance with glycemic control.

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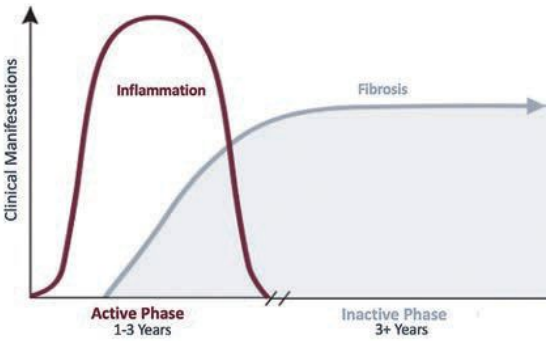
HORIZON

# Racing the Rundle Against Thyroid Eye Disease

A new clinical approach to this condition may give patients a fighting chance at recovery. **By Jacob Lang, OD, Nicole Harris, OD, and Sara Tullis Wester, MD**

Thyroid eye disease (TED) is the most common orbital disease in North America and is frequently associated with Graves' disease.[1] Although TED often occurs in patients with hyperthyroidism, it is a distinct disease, and treating the underlying systemic thyroid dysfunction often does not resolve the ocular signs and symptoms. At the root of this condition's pathophysiology is the activation of orbital fibroblasts by autoantibodies, which leads to orbital inflammation early in the disease and subsequent fibrosis.

TED has long been a disease of "watching and waiting," as traditional treatments are fraught with poor response rates and significant side effects. Early surgical intervention, reserved for severe cases involving vision loss, focuses on controlling inflammation, but patients often still require surgical rehabilitation after reaching the fibrotic phase. Recent new advances in therapeutic options, however, provide promising options to treat the proptosis, inflammation and diplopia that can cause significant patient morbidity in TED.




**The disease process of TED usually follows the trajectory of Rundle's curve.**

## The Phases of TED

The ophthalmic manifestations of TED begin with an active, inflammatory phase that worsens until reaching a point of maximum severity before leveling off at a static plateau. This disease process typically follows a curve commonly known as Rundle's curve, which demonstrates the significance of early initiation of therapy in the active phase to diminish overall disease severity.

Unfortunately, patients often have orbital and eyelid changes that persist after the inflammation resolves due to tissue expansion, which occurs in a confined bony orbit, and fibrotic changes, which occur in the orbit and eyelid during the inflammatory phase. Initiating therapy earlier could decrease the potential for long-term damage resulting from this process.

The active phase is typically a self-limited process that lasts an average of one year in nonsmokers and two to three years in smokers. Although physicians view TED as a self-limiting disease, only 2% of patients consider themselves recovered at the end of this phase.[2] This disconnect between the physician and patient demonstrates the need for better treatment options that yield clearer results.

## Treatment Shortcomings

Current treatment for TED focuses primarily on supportive and palliative care and includes ocular lubrication, prism glasses for diplopia and lifestyle modifications, such as smoking cessation, selenium and vitamin D supplementation and systemic thyroid disease control.

Once a patient is in the stable phase, some undergo surgical intervention, including orbital

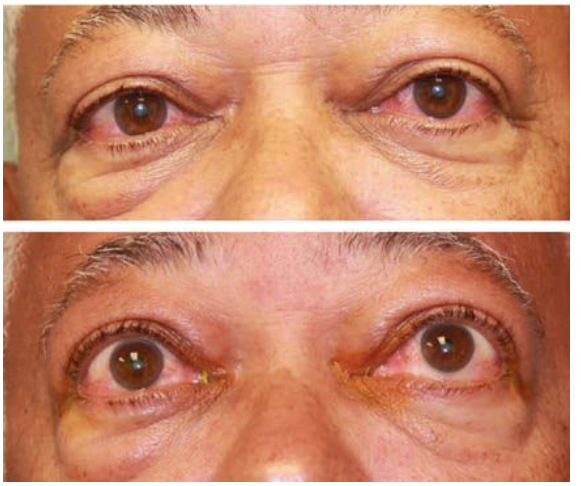


Fig. 1. This patient was diagnosed with TED.

decompression, strabismus surgery and eyelid reconstruction. Urgent surgery is reserved for severe situations involving compressive optic neuropathy or extensive corneal exposure.

Oftentimes, overlooked or underacknowledged in treatment is the chronic ocular discomfort, visual impairment and morbidity rate commonly associated with TED. This disease also severely impacts patients emotionally and psychologically—another area that is usually under-treated.

## Another Option in the Mix

Historically, there has been little practitioners could do to alter the disease process until research revealed a signaling pathway that involves activation of insulin-like growth factor 1 receptors (IGF-1Rs) in patients with Graves' disease. This pathway acts synergistically with thyroid-stimulating hormone receptors and enhances their mechanism of action, increasing orbital tissue inflammation.[3] Blocking and inhibiting IGF-1Rs can diminish the inflammatory and proliferative process associated with Graves' ophthalmopathy.

This knowledge led to the recent FDA approval of Tepezza (teprotumumab, Horizon Therapeutics), an antigen-specific therapy designed to block IGF-1Rs and halt the signaling pathway. The medication is "indicated for the treatment of TED."[4] This broad indication offers an advantage, considering the extensive breadth and scope of the disease, and gives providers an option for complex, multifaceted cases.

A Phase III trial found that teprotumumab could significantly reduce both proptosis and diplopia in patients with active, moderate-to-severe TED.[5,6] Participants underwent standardized infusions every three weeks for a total of eight treatments, receiving 10mg per kilogram of body weight for the first infusion and 20mg per kilogram for the remaining seven.[5,6] At week 24, 83% of patients—compared with 10% of controls—experienced a reduction in proptosis.[5,6] Each secondary outcome (overall response, inflammation reduction, proptosis change, diplopia reduction and quality of life score) also faced a more significant improvement with teprotumumab than with placebo.[5,6]

## Additional Considerations

The majority of TED patients are female and in their childbearing years. Given the potential for growth retardation and developmental anomalies, discussing proper contraceptive measures as well as possible pregnancy and fetal development complications with Tepezza is warranted. This medication should not be used in pregnant or lactating women. Contraception is recommended prior to initiating therapy, during treatment and for six months after the last dose of Tepezza.[4]

While not a contraindication, be sure to warn patients with inflammatory bowel disease (IBD) that there is a risk Tepezza may worsen or cause a flare-up of this condition and counsel them accordingly. A discussion with their gastroenterologist is recommended to assess the severity of their underlying IBD prior to consideration of Tepezza.[4]

Although there are few adverse events associated with this medication, the most common side effects that providers should be aware of include muscle spasm, alopecia, nausea and fatigue, the majority of which tend to be mild in severity and resolve after treatment.[5,6]

An adverse effect of special interest documented in the Phase III trial was hearing impairment in five patients (two had hypoacusis, one had deafness, one had autophony and one had mild patulous eustachian tube), which resolved without treatment.[5,6] Also during the trial, 10% of patients (two-thirds of who had pre-existing diabetes or impaired glucose tolerance) experienced hyperglycemia, so don't skimp on monitoring blood sugar levels during the infusion period.[4-6] It is

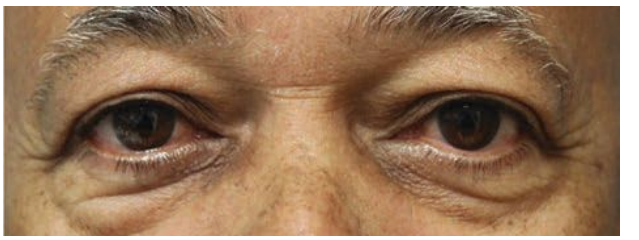


Fig. 2. Visible improvements can be seen in the patient's eyes after the first Tepezza infusion.

### The Many Faces of TED

In some cases, TED can be challenging to diagnose. These masquerading signs and symptoms should heighten the clinician's suspicion that there may be an underlying thyroid basis to a patient's ocular condition, warranting further history and workup:

a. Orbital congestion (not to be mistaken for conjunctivitis)

b. Allergic conjunctivitis without any papillary reaction that doesn't improve with allergy drops

c. Unexplained changes in vision that are inconsistent with corneal changes from dryness or other pathologies, which can actually be caused by low-grade chronic compressive optic neuropathy

i. Resistance to retropulsion, an unsatisfactory response to a careful motility check and lid lag on downgaze can help with this diagnosis

ii. Optic nerve imaging with OCT and visual field testing can be helpful in these cases

d. Temporal chemosis with injection overlying the extraocular muscles

e. Chronic ocular ache and pain as opposed to the more common sharp pains associated with dry eye and other corneal disorders

also suggested that these patients undergo baseline hemoglobin A1c and fasting blood glucose testing.

As with any infused medication, infusion reactions are rare but possible and affect approximately 4% of Tepezza patients.[4] They may occur during or within 1.5 hours after an infusion and range in severity from mild to moderate.[4] Signs and symptoms of infusion-related reactions include transient increases in blood pressure, hot flashes, tachycardia, dyspnea, headache and muscular pain. They are usually successfully managed with corticosteroids and antihistamines.[4]

## Patient Management

As TED is a multisystem disease, these patients are best managed through integrated care provided by a team of medical professionals from various fields, including endocrinology, oculoplastics, primary care, optometry and infusion clinic staff. Optometrists specifically are well positioned and able to play a key role in the detection, management and ongoing visual care of these patients, as TED is, at its roots, an eye disease.

Monitoring ocular inflammation, proptosis, binocular function and optic nerve integrity is extremely feasible in the optometric setting, offering a clearer clinical picture and placing optometrists at the heart of the equation to serve as the link between other subspecialties.

By intercepting Rundle's curve early in its surge, we have the chance to prevent severe manifestations that could arise when TED is left untreated. With its FDA approval, Tepezza is in a position to become the standard of care in treating patients with this cosmetically disabling condition. Given the medication's effectiveness and associated improvements, it is critical that TED patients be offered it as an option.

At a bare minimum, Tepezza has changed how we should look at and think about TED. It shatters the "watch and wait" mentality and challenges practitioners to be on the lookout for the initial signs of this debilitating disease so we can treat it earlier and more effectively than ever before. It's also encouraging to know there is now something we can offer patients to help modify the course of their disease and improve their quality of life, something these patients—and their doctors—have long been hoping for. ■

*Dr. Lang is an adjunct clinical faculty member at the Illinois College of Optometry and Salus University, the residency coordinator for Associated Eye Care's optometric residency program in Stillwater, MN, a diplomate of the American Board of Optometry and a fellow of the American Academy of Optometry. He participates in clinical research and FDA trials, writes articles for several publications and lectures at various meetings, with a focus on dry eye and external disease.*

*Dr. Harris graduated from the Illinois College of Optometry in 2019. She is currently pursuing her residency in ocular disease at Associated Eye Care.*

*Dr. Wester is an associate clinical professor at the University of Miami Bascom Palmer Eye Institute. She specializes in TED and reconstructive and cosmetic surgery of the eyelids and orbit. She conducts clinical research and trials, has authored many publications, is a consultant for Horizon Therapeutics and speaks at conventions around the world.*

*The authors wish to thank Aaron Bronner, OD, for his assistance in preparing this manuscript.*

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# Bring Concussion Care Into Your Practice

Adapt to the problems these patients present during treatment, and be an advocate for preventative measures. By Maria Richman, OD

Millions of Americans suffer from a traumatic brain injury (TBI) each year, with nearly 75 percent of all those with TBI suffering from some form of visual dysfunction.[1] Patients may come into the primary care optometrist's office complaining about double vision, blurred vision, closing one eye, dizziness, headaches, sensitivity to lights, bumping into things and/or poor coordination.

**TBI patients can use a saccadic fixator for oculomotor therapy.**

Visual symptoms of a concussion include visual acuity problems, visual field loss, oculomotor dysfunction, convergence and accommodative disorders, photophobia and reduced visual attention.[1] A brain insult can also affect a person's posture, balance, gross motor and fine motor skills, cognition, attention, concentration, learning, productivity and daily activities.

Although sight may begin with the eyes, it actually occurs in the brain. Over half of the brain is dedicated to vision and visual processing. There are many pathways in the brain that carry visual input from the eyes to the back of the brain where the visual cortex is located. Since vision involves so much of the brain, even a mild injury to almost any part of the brain can significantly impact the multiple processes involved in vision.

Patients with a mild TBI (mTBI), also known as a concussion, should be seen by their optometrist for an evaluation and appropriate vision rehabilitation treatment, as optometrists are essential in the rehabilitation process.

## At-risk Patients

The top two reasons for TBI are unintentional falls, which accounted for almost 50% of all TBI-related emergency room visits in 2014, and being struck by an object, which accounted for nearly 20%.[2] Motor vehicle accidents, assaults, explosions and sports injuries can also cause a TBI. While many of these are not preventable injuries, it is well within the purview of the primary care optometrist to talk about them with susceptible populations.

Besides the high-risk populations of athletes, first responders and military personnel, consider collecting baseline tests on all patients for a comparison if an injury does occur.

For the elderly, optometrists can address their maturing visual function and suggest environmental adaptations, such as lighting and contrast changes.

Provide parents of small children with additional guidance, and educate them of the safety precautions for cribs that children can climb out and the value of placing gates at stairwells.

Remind older children of the increased risk ofTBI when they fall and are not wearing a helmet on bikes, scooters and skateboards, as well as the importance of wearing helmets in all sports that offer them.

All age groups should wear seat belts in moving vehicles, and first responders and military personnel should always wear their protective equipment.

## In-office Exam and Care

Unfortunately, many optometric interactions with patients often come well after the injury. Fortunately, there's a growing body of evidence that shows optometrists can play a key role in helping identify if a concussion has occurred, providing treatment and monitoring how well the patient is progressing in their recovery.[3]

When caring for a concussion patient, observe the effects of vision deficits possibly related to the head injury. Allot extra time when scheduling patients with concussions, as they may have difficulties during the examination due to fatigue, dizziness, light sensitivity or attentional issues. When these occur, frequent breaks can help make the patient more comfortable and may lead to more accurate and productive testing. Be aware that, sometimes, the examination needs to be done in a dark or dim environment, while other times, normal room lighting is acceptable.

A comprehensive eye exam provides baseline measurements for a concussion and also serves as an entry point for a more formal concussion workup by a primary care optometrist if ever needed. During the initial comprehensive eye exam, take a detailed history and evaluate visual acuity, visual fields, pupils, stereopsis, color vision, cover test and eye movements (saccades, pursuits, near point of convergence, Developmental Eye Movement test). Also conduct retinoscopy/refraction, binocular and accommodative measurements (vergences, phorias, fixation disparity, near accommodative flippers and amplitude of accommodation), a slit lamp evaluation, intraocular pressure testing and a dilated retinal evaluation.

During an exam, focus on these areas:

***History.*** Patients may report blur at distance or near, headaches, dizziness, visual discomfort, double vision, dry eye, light sensitivity, depth perception issues, peripheral vision complaints and reading-related issues. These areas are addressed in the Brain Injury Vision Symptom Survey, a standardized survey developed by the Pacific University College of Optometry.[4] You can mail this survey and the intake/history form to the patient at the time of scheduling the appointment or present them with it when they arrive at their appointment. Mailing the items in advance will give the patient and/or caregiver time to complete them at their leisure.

***Visual acuity issues.*** Patients may complain about intermittently blurred vision. In these cases, a minimal prescription may be effective following retinoscopy and a refraction. Another cause of intermittent blurred vision is tear film instability. At this point, consider a dry eye evaluation that includes a blink evaluation. TBI patients may have a delayed blink reflex, an incomplete blink reflex or no blink reflex at all. Consider that the blink rate may be low (compared with 17 blinks per minute) when measuring.[5] Note that TBI patients may have a blank stare as they are processing their visual information. This stare can induce or exasperate a dry

**BIVSS CHECKLIST** (Brain Injury Vision Symptom Survey)

Patient Name: _____ Today's date: _____

My brain injury was: ____ years ago My age is: ____ years today's date: _____

☐ I have had a medical diagnosis of brain injury (check box if true) Cause of injury: _____

☐ I sustained a brain injury without medical diagnosis (check box if true) _____

☐ I have NOT ever sustained a brain injury (check box if true)

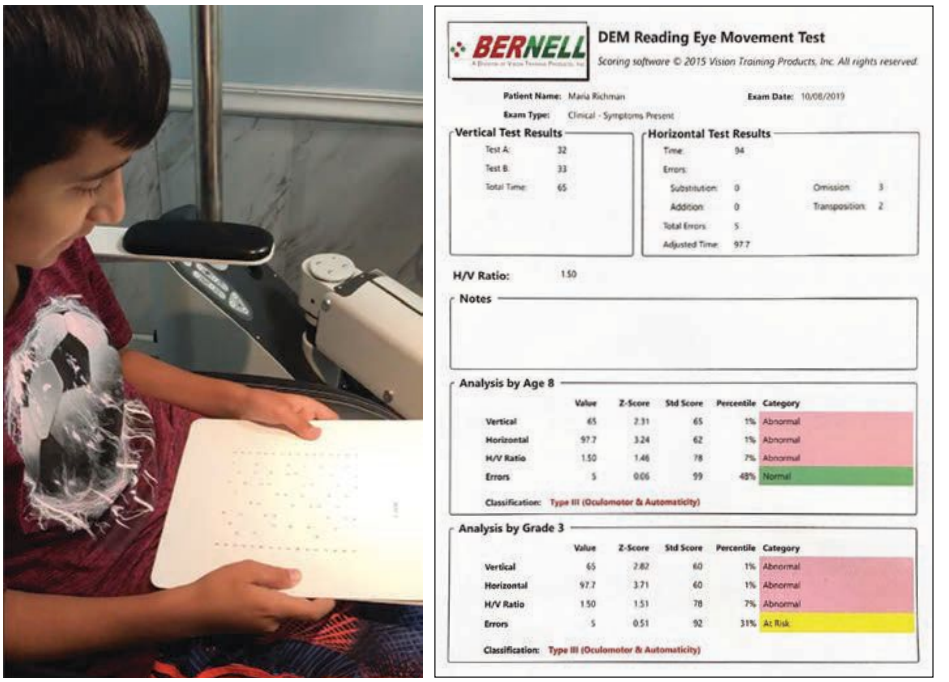
*Please check the most appropriate box, or circle the item number that best matches your observations. All information will be held in confidence. Thank you for your help!*

**SYMPTOM CHECKLIST** *Circle a number below:*

| Please rate each behavior. How often does each behavior occur? (circle a number) | Never | Seldom | Occasionally | Frequently | Always |
|---|---|---|---|---|---|
| ***EYESIGHT CLARITY*** | | | | | |
| Distance vision blurred and not clear -- even with lenses | 0 | 1 | 2 | 3 | 4 |
| Near vision blurred and not clear -- even with lenses | 0 | 1 | 2 | 3 | 4 |
| Clarity of vision changes or fluctuates during the day | 0 | 1 | 2 | 3 | 4 |
| Poor night vision / can't see well to drive at night | 0 | 1 | 2 | 3 | 4 |
| ***VISUAL COMFORT*** | | | | | |
| Eye discomfort / sore eyes / eyestrain | 0 | 1 | 2 | 3 | 4 |
| Headaches or dizziness after using eyes | 0 | 1 | 2 | 3 | 4 |
| Eye fatigue / very tired after using eyes all day | 0 | 1 | 2 | 3 | 4 |
| Feel "pulling" around the eyes | 0 | 1 | 2 | 3 | 4 |
| ***DOUBLING*** | | | | | |
| Double vision -- especially when tired | 0 | 1 | 2 | 3 | 4 |
| Have to close or cover one eye to see clearly | 0 | 1 | 2 | 3 | 4 |
| Print moves in and out of focus when reading | 0 | 1 | 2 | 3 | 4 |
| ***LIGHT SENSITIVITY*** | | | | | |
| Normal indoor lighting is uncomfortable – too much glare | 0 | 1 | 2 | 3 | 4 |
| Outdoor light too bright – have to use sunglasses | 0 | 1 | 2 | 3 | 4 |
| Indoors fluorescent lighting is bothersome or annoying | 0 | 1 | 2 | 3 | 4 |
| ***DRY EYES*** | | | | | |
| Eyes feel "dry" and sting | 0 | 1 | 2 | 3 | 4 |
| "Stare" into space without blinking | 0 | 1 | 2 | 3 | 4 |
| Have to rub the eyes a lot | 0 | 1 | 2 | 3 | 4 |
| ***DEPTH PERCEPTION*** | | | | | |
| Clumsiness / misjudge where objects really are | 0 | 1 | 2 | 3 | 4 |
| Lack of confidence walking / missing steps / stumbling | 0 | 1 | 2 | 3 | 4 |
| Poor handwriting (spacing, size, legibility) | 0 | 1 | 2 | 3 | 4 |
| ***PERIPHERAL VISION*** | | | | | |
| Side vision distorted / objects move or change position | 0 | 1 | 2 | 3 | 4 |
| What looks straight ahead--isn't always straight ahead | 0 | 1 | 2 | 3 | 4 |
| Avoid crowds / can't tolerate "visually-busy" places | 0 | 1 | 2 | 3 | 4 |
| ***READING*** | | | | | |
| Short attention span / easily distracted when reading | 0 | 1 | 2 | 3 | 4 |
| Difficulty / slowness with reading and writing | 0 | 1 | 2 | 3 | 4 |
| Poor reading comprehension / can't remember what was read | 0 | 1 | 2 | 3 | 4 |
| Confusion of words / skip words during reading | 0 | 1 | 2 | 3 | 4 |
| Lose place / have to use finger not to lose place when reading | 0 | 1 | 2 | 3 | 4 |

**total score for all 28-items:** _____

**Having the patient fill out the Brain Injury Vision Symptom Survey before their appointment will allow them to answer the questions at their own pace. You can download a full-size PDF of this survey in the online version of this article at www.reviewofoptometry.com/article/concussion-care.**




**A pediatric patient takes the DEM test (left). This sample of the reading eye test's results note oculomotor dysfunction and reduced attention (right).**

eye. Testing for dry eye can lead you to treating the poor quality of the refractive surface, which, in turn, will increase the patient's visual acuity stability.

***Visual field loss.*** While not as common in concussion cases, more advanced TBI patients may bump into things or miss items in their peripheral field of vision. Once confrontation fields document a defect, confirm it with standardized, computerized field testing. This will narrow down the level of impairment, as defined by the Social Security Administration, and also document any future improvement. If appropriate, consider prisms or rehabilitation therapy (whether vision, neuro-optometric, sports or physical medicine) either in your office or refer out to an optometrist who has special interests in that area. Unfortunately, computerized visual fields may be difficult in some cases since visual field testing is dependent on attention, and this population may have attention deficits, reduced speed of processing and/or a delay in reaction time.

If the patient is within their first year and a half of recovery and you can measure visual fields initially, repeat testing in six months to note any improvements. While traditional visual field loss is usually irreversible, this population demonstrates it may be possible to recover some field loss within that early time period.[6] This is due to neural plasticity, and the use of the prisms or therapy may contribute to improvements in visual attention, spatial awareness and ultimately visual fields. Keep in mind each case is very different, and sometimes the original visual field loss remains the same.

***Oculomotor dysfunction.*** TBI patients may exhibit reduced or altered saccades, pursuits and/or other near point convergence irregularities. Use a quick eye movement test, such as the Developmental Eye Movement (DEM) test, to quantify the level of impairment. This test measures number-naming speed and differentiates language processing speed from oculomotor dysfunctions, which may be quite helpful in the treatment plan. The DEM allows for better specificity of oculomotor dysfunctions than the King-Devick test, as it eliminates the language speed and potential oral injuries from the calculation. The test may also assist in documenting improvements made following optometric vision therapy treatment. As every patient is different and every concussion impacts the brain differently, some people need to start slow while others can be pushed to work on higher-level activities.

***Accommodative disorders.*** Problems focusing at near often benefit from eyeglasses and vision therapy. It has been found that even small amounts of plus lenses (as small as +0.25D) can have a profound impact on this population.[7] Consider additional investigation on binocular balance at near, as unequal adds are sometimes warranted. Addressing these accommodative issues may also improve convergence and visual attention abilities.

***Photophobia/glare issues.*** Primary care optometrists can respond immediately to these by recommending sunglasses, special tints, transitions, a brimmed hat or limited outdoor activities. While there are many lens options, specific wavelengths seem to work best for certain patients. Prescribing lenses usually includes a sequential assessment of various tints, which will ultimately result in the best color/transmission/wavelength/design for the individual patient.

***Reduced visual attention/perception skills.*** When patients demonstrate that they are distracted by


**TBI patients can use tinted lenses and a brimmed hat to reduce photophobia.**

## Helpful Resources

For more information, there are many organizations that provide education on brain injuries for optometrists. The American Optometric Association (AOA) Vision Rehabilitation Committee and the Brain Injury Task Force have developed guidelines, manuals, briefs and articles to assist their members. There are opportunities at the national level of the AOA and its state affiliates to become active in their respective Vision Rehabilitation Sections and Committees. In addition to the AOA's resources (aoa.org/VR), there are other organizations, such as the College of Optometrists in Vision Development (covd.org), the Neuro-Optometric Rehabilitation Association (noravisionrehab.org), the American Academy of Optometry (aaopt.org) and the Optometric Extension Program Foundation (oepf.org), that offer tremendous education to practitioners and patients alike.

less relevant information when trying to attend to something, they may be exhibiting reduced visual attention. If these issues last more than a few weeks, it's time to consider vision therapy, specifically visual processing therapy treatment options. If this service is not provided in your office, have your patient serviced at an optometric office that does.

When patients complain of trouble copying text, reversing letters or words, poor reading comprehension, confusing directions and difficulty telling right and left, consider standardized testing and vision therapy activities. These too should be done in your office or you should work with an optometric colleague who will share in the care of your patient for these specific activities.

## Comanage and Educate

Optometrists routinely perform much of the necessary baseline information in a comprehensive exam, such as visual acuity, pupils, visual fields, accommodative amplitude, saccades, binocular measurements and more. These findings are valuable to in evaluating, diagnosing and managing treatment of the visual sequelae of concussion. Optometrists in primary care practices who identify these visual disorders and dysfunctions have the option to provide additional testing and care during their patient's evaluations and eventual rehabilitation or refer these cases to an optometrist who can.

However, comanagement within the optometric community is not enough. It is equally important to coordinate care with other members of the TBI care team, such as the physiatrist, neurologist, neuropsychologist, medical physicians, occupational therapist, physical therapist, speech therapist and nurses. As a member of the traumatic brain injury rehabilitation team, the optometrist's role increases the overall effectiveness of and may even reduce the time needed in the rehabilitation program, which is highly dependent upon vision.

After diagnosis, the optometrist can direct the other members of the rehab team in regards to treating visual dysfunction and providing rehabilitation options. In addition to working with the TBI care team, optometrists should educate the members of their community. While primary care optometrists are very good at servicing their own patients, promote the importance of gathering baselines pre- and post-concussion information to school nurses and coaches, sports teams and others. Also, educate the public and other healthcare professions on the importance of eye and vision health in reducing the impact and risk of TBI, and encourage helmet use, seat belts, area carpets, proper gates by stairwells and more. This does not only promote our profession to our local community but doing so also can quite likely improve care and treatment by providing higher quality outcomes for all of our patients. ■

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# PREGNANCY AND THE EYE:
## WHAT TO DO WHEN CARING FOR TWO

Clinicians must understand how to manage ocular changes and treatment contraindications. **By Cecelia Koetting, OD**

When pregnant patients present for eye care, clinicians must be up to date on the ever-changing do's and don'ts of clinical care. Just as clinicians comanage patients with other specialties, they should also feel comfortable reaching out to patients' obstetricians.

When seeing any female of childbearing age, clinicians should ask if they are pregnant, nursing or thinking of becoming pregnant.

### Medications

Historically, drugs were labeled based on a category, with category A being the safest medications to take during pregnancy.[1,2] Category B included those showing no risk in animal studies, but a lack of controlled studies on pregnant women.[1,2] Category C indicated that animal studies showed risk to the fetus, but no human studies have been performed or are not available.[1,2] Category D indicated positive evidence of potential fetal risk but benefits for the pregnant woman may be acceptable despite the risk.[1,2] Lastly, category X was contraindicated in women who are pregnant or may become pregnant because of known fetal risk and abnormalities.[1,2]

In 2015, the FDA implemented new pregnancy and lactation guidelines to help healthcare providers better assess benefit vs. risk. The updated labeling system removes the letter categories and instead provides narrated sections on risk for women who are pregnant and breastfeeding, as well as men and women of reproductive age.[3] Many clinicians still think of drugs based on their historic category, and this article includes categories when available.

When prescribing, keep in mind which medications can and cannot be administered.

***Systemic medications.*** Among the

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**Educational Objectives:** After completing this activity, the participant should be better able to:
- Understand the ocular changes pregnancy can induce.
- Manage the ocular changes associated with pregnancy.
- Determine when to treat an ocular condition and when to wait.
- Successfully comanage with a patient's obstetrician.

**Target Audience:** This activity is intended for optometrists engaged in the care of patients who are pregnant or nursing.

**Accreditation Statement:** In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine and Review Education Group. Postgraduate Institute for Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education, the Accreditation Council for Pharmacy Education, and the American Nurses Credentialing Center, to provide continuing education for the healthcare team. Postgraduate Institute for Medicine is accredited by COPE to provide continuing education to optometrists.

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oral antibiotics, which may be needed for gland and soft tissue infections, it is safe to use Augmentin (amoxicillin and clavulanate, GlaxoSmith-Kline), erythromycin, azithromycin and amoxicillin, which are all historic category B.[1,4] Commonly used oral antibiotics such as doxycycline, tetracycline, sulfonamides, trimethoprim, neomycin and fluoroquinolones are historic category C or D and should be avoided.[1,4]

For patients with herpes simplex virus or shingles, oral antivirals acyclovir, valacyclovir and famciclovir are all historic category B.[1,4] However, acyclovir is the only one approved for use in lactating women.[1,4]

When oral steroids are needed, clinicians should consult with the patient's obstetrician because this class of medication is considered historic category C.[5] Fetal changes such as cleft palate, heart defects and neural tube defects have been noted with the use of systemic corticosteroids.[5]

When a patient is in need of pain medication, acetaminophen is historic category B in all three trimesters and is considered safe.[6] Other over-the-counter (OTC) medications, such as aspirin and ibuprofen, are historic category D in at least one of the trimesters and should be avoided.[6] In patients who are breastfeeding acetaminophen and ibuprofen are safe to use but aspirin and naproxen are typically avoided.[6] Hydrocodone (historic category C) and oxycodone (historic category B) are sometimes given to women to help with pain after birth.[7] Although they are the preferred pain medications when OTC medications aren't enough, both have been found in breast milk and can affect the baby.[6] If considering recommending these, consult with the patient's obstetrician.

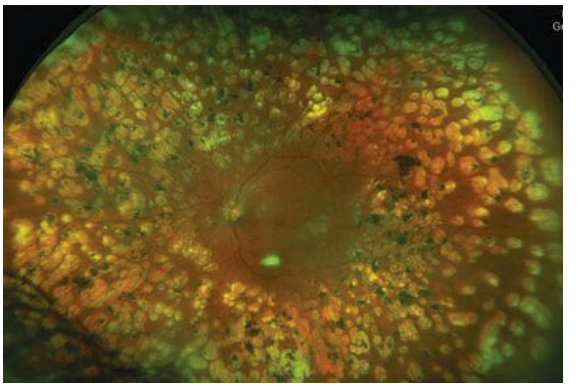

**Fig. 1. This pregnant patient has had significant panretinal photocoagulation treatment for proliferative diabetic retinopathy, leaving scaring 360° throughout the peripheral retina. Because of her history of poorly controlled Type 1 diabetes, she was monitored every three months with dilation for re-activation or progression.**

***Topical medications.*** Similar to systemic medication, fluoroquinolones are typically avoided unless the benefit outweighs the risk, such as in the case of resistant bacteria with fluoroquinolone sensitivity. If this prescription is necessary, clincians must consult the patient's obstetrician.

Tobramycin is historic category B, as is erythromycin, polymyxin B and topical azithromycin. In the case of severe ulcers or bacterial keratitis, fortified cephalosporins are also historic category B and are safe to use in this patient population.

Corticosteroids are often used to control a patient's inflammation, whether it be anterior surface or intraocular. All ocular formulations of corticosteroids are historic category C. Optometrists are familiar with the risks to their patients such as steroid-induced cataracts and intraocular pressure (IOP) increase.[5] No published studies have associated fetal changes, such as cleft palate, heart defect and neural tube defect, with topical ophthalmic corticosteroids.[5] Regardless, clinicians should discuss their use with the patient's obstetrician before initiating or continuing any steroid therapy.

For allergies, the only historic category B ocular allergy medication is Lastacaft (alcaftadine, Allergan). Anti-inflammatory medications for dry eye, such as cyclosporine A, are historic category C and come with concerns of teratogenic and fetal abnormalities; thus, the patient's obstetrician should be consulted first. Lifitegrast has no human data available; however, an animal study shows fetal changes with intravenous (IV) administration.[8]

Most glaucoma medications are historic category C. Prostaglandins are a cause for concern, as research shows they can induce labor and miscarriage.[5] Beta blockers are cautioned in the first trimester as well as shortly before birth to avoid neonatal beta blockade.[5] Carbonic anhydrase inhibitors have teratogenic and hepatorenal effects.[5]

The rho-kinase inhibitor Rhopressa (netarsudil, Aerie Pharmaceuticals) currently has no clinical data regarding use in pregnant women or its presence in breast milk, although animal data shows some teratogenic effects.[9] Oral Diamox (acetazolamide, Duramed Pharmaceuticals) is also historic category C and can cause fetal abnormalities.[5] Alphagan (brimonidine, Allergan), unlike the others, is historic category B and safe to use in all trimesters. However, it should be discontinued prior to breastfeeding due to concerns of sleep apnea and central nervous system (CNS) depression in infants.

Because IOP decreases during pregnancy, patients who are on one ocular medication may be stable without it, but should be monitored closely. In cases where an ocular medication is needed, brimonidine is a safe option, but the patient must stop while breastfeeding.

Other options such as minimally

invasive glaucoma surgery or selective laser trabeculoplasty may be considered in some patients.

Although not widely necessitated by women of child-bearing age, intravitreal anti-vascular endothelial growth factor (VEGF) treatment is needed for some retinal diseases such as proliferative diabetic retinopathy, neovascular glaucoma or chorioretinal neovascularization. During pregnancy, VEGF plays an important role for fetal and placental vasculature, and reduction has been linked with defective embryogenesis and fetal loss in humans.[10]

The use of anti-VEGF drugs during pregnancy may potentially cause systemic side effects in the mother and harm to the fetus, including spontaneous miscarriage and pre-eclampsia.[10] Therefore, anti-VEGF should only be used in cases where the potential benefit to the patient justifies the potential risk to the fetus. This requires consultation with the patient's obstetrician and careful patient education on the possible effects of the drug.

Breast milk contains VEGF to help with the infant's development and maturation of their digestive system.[11] Although the labeling of the anti-VEGF agents ranibizumab and aflibercept indicate that it is unknown if the drugs are excreted in breast milk, a recent study found that they are detected after intravitreal injection.[11] This raises safety concerns for the patient's infant. Women who are breastfeeding should be counseled prior to receiving treatment, including a discussion regarding risk vs. benefit and possible cessation of breastfeeding.

## Dilation: Yes or No?

In general, occasional dilation is acceptable, but repeated dilation is avoided in pregnant and breastfeeding patients because of risks to the fetus and newborn.[4] There are times when the benefits outweigh the risks and it is appropriate and necessary to dilate. Optometrists should not hesitate to have a discussion with a patient's obstetrician prior to administering medication.

When dilating, consider using shorter acting agents such as tropicamide 0.5% (historic category C) vs. 1%. Clinicians can have the patient punctal occlude after drops are administered or put in temporary punctal plugs to decrease systemic absorption. Avoidance of phenylephrine is suggested since systemic use of the drug may cause minor malformations during first trimester use as well as fetal hypoxia and bradycardia.[12]

If a patient is breastfeeding they should be advised that it is unknown if cycloplegics and mydriatics are excreted in human breastmilk.[12] However, low-weight infants are susceptible to systemic hypertension when 10% or 2.5% phenylephrine eye drops are used, so they should be avoided.[13] Atropine and homatropine may also cause minor fetal malformations when they are used systemically.[4,12]

Fluorescein and indocyanine green dyes both cross the placenta, although no reports of teratogenic effects on animals exist and no adverse effects are reported in humans.[12,14] Most vitreoretinal specialists avoid these tests on pregnant patients unless absolutely necessary.[14]

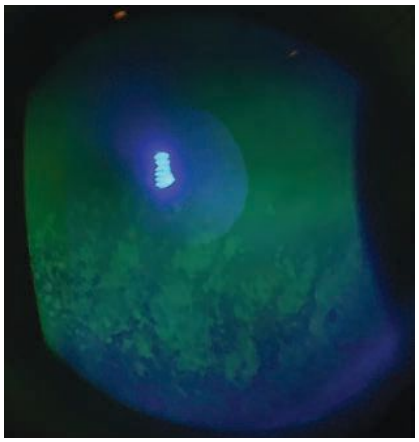

**Fig. 2. This patient experienced exposure keratopathy secondary to Bell's palsy shortly after giving birth. She has a defined area of punctate keratopathy staining on the lower third of her cornea.**

Specialists suggest that, despite the low toxicity, the mother avoid nursing for eight to 12 hours after topical fluorescein use since it has been detected in breast milk.[12,15]

## Ocular Changes and Complications

Pregnancy can induce a number of ocular changes that optometrists must understand to ensure they can manage patient's successfully.

***Refractive changes.*** During pregnancy, a patient's prescription and vision may change. More commonly it is a myopic shift, but hyperopic shifts may also occur. Studies show that approximately 40% to 75% of pregnant women experience a change in their distance vision.[16-19] Researchers found that during the second trimester 51% of patient's distance vision was affected and 11% of patient's near vision was affected.[16] By the third trimester the same study showed 74.7% of patient's distance vision was affected and 20.2% of patient's near vision.[16] Postnatal, only 8.2% of patients still had a change in distance vision and 4% in near vision.[16]

Most patients' refractive changes do resolve and are not long-term. Other studies had similar outcomes noting that most women's vision returned to pre-pregnancy refractive error shortly after birth and cessation of breastfeeding.[17]

These refractive changes are thought to be related to hormonal changes resulting in fluid retention in the cornea; however, causality requires further study.[16]

Less often, refractive shifts can occur because of cataract changes, diabetes, preeclampsia or an accommodative spasm. Both insufficiency

and paralysis of accommodation during lactation are possible.[18,19] These typically resolve shortly after breastfeeding is discontinued, but may require vision therapy.

***Dry eye disease.*** During pregnancy, this condition can worsen or develop.[4] One cause of this is likely physical dehydration due to nausea and vomiting, especially during the first trimester.[1] In addition, changes in the cornea and lacrimal system can lead to changes in tear film physiology.[20] There is a possible immune reaction to the lacrimal duct cells leading to destruction of acinar cells by prolactin.[20]

With the worsening of dry eye disease, secondary contact lens intolerance and discomfort are likely. This may be exacerbated by decreased corneal sensitivity common throughout pregnancy, peaking in the third trimester.[18,19] Sensitivity returns to normal eight weeks postpartum.[18,19]

Treatment can include adding punctal plugs and artificial tears, omega-3 and refitting soft contact lenses. Remember that topical ocular cyclosporine and steroids are historic category C, so these medications should be used only when absolutely necessary. However, it is important to consult with the patient's obstetrician prior to prescribing.

***Adnexal changes.*** Chloasma, also known as pregnancy mask, is increased pigmentation around the eyes and cheeks. This condition, caused by increased estrogen, progesterone and melanocyte stimulating hormones, will fade over time postpartum.[18,19] Another occasional adnexal change during or after pregnancy is unilateral ptosis. This is, in theory, caused by defects in the levator aponeurosis from fluid, hormones and other changes caused by the stress of labor and delivery.[18,19]

***Graves' disease.*** This condition is the most common cause of hyperthyroidism during pregnancy, leading to unilateral and bilateral proptosis.[18,19] Patients with preexisting Graves' disease may note an exacerbation during the first trimester that subsides during the rest of the pregnancy, only to flare up again postpartum.[18,19] Treatment is similar to that used for non-pregnant women, and ocular sequelae should be managed to decrease discomfort.[18,19]

***Preeclampsia and eclampsia.*** Preeclampsia is classified by a triad of symptoms in a normotensive pregnant woman: BP >140/90mm Hg, edema and proteinuria after 20 weeks of pregnancy. When the patient has the triad along with contractions, it is considered eclampsia.

Of the 5% of pregnant women who develop these conditions, one in three have ocular sequelae such as blurred vision, photopsia, scotoma and diplopia.[18] Up to 60% of those with preeclampsia or eclampsia will have hypertensive retinopathy with retinal arteriolar narrowing.[19]

If these changes are noted and the patient is undiagnosed, clinicians must convey these findings to the patient's obstetrician and monitor them during and after pregnancy. Severity of ocular symptoms is directly related to the severity of the preeclampsia.[19] Typically these changes dissipate postpartum.

In less than 1% of preeclamptic patients and 10% of eclamptic patients, exudative retinal detachment may occur.[19,21,22] The cause is thought to be choroidal ischemia, showing a delayed filing of choriocapillaris in the presence of normal retinal vasculature on intravenous fluorescein angiography.[19,22]

Approximately 10% of severe preeclampsia patients develop hemolysis, elevated liver enzymes and low platelets (HELLP).[19,22] These patients will develop bilateral serous retinal detachments with yellow/white subretinal opacities and possible vitreous hemorrhage.[19,22] Unfortunately, this syndrome is associated with poor prognosis for both mother and fetus. When a patient presents with these findings, clinicians must discuss them with the patient's obstetrician. They should also be referred to a retinal specialist for possible treatment of the ocular sequelae.

Preeclamptic patients with choroidal infarcts may also develop Elschnig spots that will resolve after delivery.[19,21,23] Infrequently, cortical blindness lasting four to eight hours associated with preeclampsia/eclampsia can occur as a result of petechial hemorrhages and focal edema in the occipital cortex.[24]

***Diabetes.*** Patients who develop diabetes during pregnancy—gestational diabetes—typically return to normal after delivery.[25] This usually occurs during the second to third trimester and glucose tolerance will return to normal approximately six weeks after giving birth (*Figure 1*).

These patients are at a higher risk of developing Type 2 diabetes during their lifetime and should be monitored with yearly dilated eye exams.[25] During pregnancy, given the relative shortness of the disease, these patients are at a small risk of developing diabetic retinopathy (DR).[18.19] According to the American Optometric Association (AOA) practice guidelines, retinal evaluation is not indicated for these patients.[26]

Patients who had Type 1 or Type 2 diabetes prior to pregnancy have a much higher risk of developing complications related to their diabetes during pregnancy. Patients who already have DR prior to pregnancy will note a quicker progression.[27]

According to one study, those with moderate to severe non-proliferative DR (NPDR) show a 54.8% progression during pregnancy.[27] The same study shows only a 21.1% progression in disease process for those with mild NPDR.[27] Approximately 22% of those with severe NPDR will

progress to proliferative DR (PDR).[18] Up to 45% of those who already have PDR will note worsening of the disease. The treatments are the same as those for non-pregnant patients.

To monitor for these changes, any diabetic patient who is pregnant or thinking of becoming pregnant should have regular eye exams and be counseled about their increased risk of DR progression both during and after pregnancy. Patients with Type 1 and Type 2 diabetes should have a comprehensive eye and vision exam prior to a planned pregnancy and once during every trimester with follow-up at six to 12 months postpartum, according to the AOA practice guidelines.[26]

***Bell's palsy.*** While pregnancy isn't a cause of Bell's palsy, it does lead to a higher risk of occurrence, especially during the third trimester and within the first weeks after giving birth.[28] This condition, caused by compression or inflammation and swelling of the facial nerve, has rapid onset of weakness or total paralysis on one side of the face. Typically, the face will droop and the patient will experience changes in the amount of tears and saliva produced. People generally recover with or without treatment, but both oral corticosteroids and antiviral drugs may be used. Resolution will occur over a few weeks to six months.[29]

With the paralysis leading to poor lid closure and incomplete blink, clinicians should be concerned about exposure keratopathy, erosions, punctate keratopathy, epithelial defects and corneal infiltrate (*Figure 2*).[29,30] In severe cases, this can lead to corneal thinning and subsequent perforation.[29,30]

***Toxoplasmosis.*** While this can be contracted by anyone, it is particularly risky for pregnant patients because it can be transferred to the fetus during pregnancy. The parasitic disease caused by *Toxoplasma gondii* can be contracted via infected cat feces and eating undercooked contaminated meat, as well as from mother to child during pregnancy.[19,31] Primary infection leads to congenital infection when it occurs during the pregnancy.

The timing of the infection during pregnancy will result in different levels of sequelae. First trimester fetal infection causes more severe complications, but most commonly the transmission occurs in the third trimester when the maternal and fetal circulation is greatest.[19,31] Latent infections may become active during pregnancy, resulting in retinochoroiditis findings, and should be monitored and treated appropriately.[19,31]

Before either systemic or ocular treatment is initiated, clinicians should consult with the patient's obstetrician. Systemic use of spiramycin is recommended over pyrimethamine as safer but equally effective.[4]

***Central serous retinopathy.*** Neurosensory retinal detachment with associated retinal pigment epithelium (RPE) detachment, RPE leakage and RPE and choroidal hyper permeability is known as central serous retinopathy (CSR).[19,31-33] Similar to non-pregnant patients, they will have complaints of decreased vision with unilateral or bilateral central metamorphopsia.

More often, pregnant women (90%) will have a subretinal exudate that is fibrous in nature compared with only 20% in their non-pregnant counterparts. This may be why, although the CSR resolves after pregnancy, it is more likely to reoccur in these patients.[19,31-33] Treatment is not necessary in these patients, but they should be monitored closely.

***Multiple sclerosis.*** Patients previously diagnosed with multiple sclerosis (MS) may note a decrease in attacks, including optic neuritis (ON), during pregnancy.[19,31] However, there is an increase in occurrence of ON within the first three months postpartum.[19,31] It is important that patients are aware of this so that they can report symptoms to their neurologist or optometrist quickly, ensuring a timely diagnosis and initiation of treatment, if indicated.

For these patients, pregnancy and delivery does not influence the patient's mid or long-term disability as related to MS.[31] It also doesn't seem to influence the pregnancy, delivery or child's health.[31]

Treatment is not indicated in every case of ON. For those whose visual

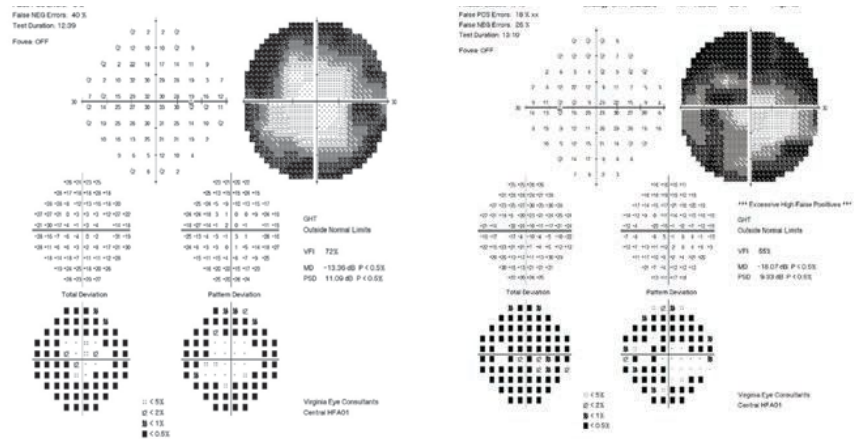

**Fig. 3. This previously diagnosed IIH patient was stable with no ONH swelling prior to pregnancy. During her pregnancy, her visual field, at left, shows constriction 360° with enlarged blind spot 360°, and her dilated exam revealed moderate ONH edema 360° OU. Because she was in her third trimester, consults with neurology and her obstetrician led to a plan to wait on any treatment and monitor closely for resolution after birth.**

acuity and field are not affected, the risk vs. benefit may not be worth initiating treatment. This requires consultation between the obstetrician, neurologist and optometrist. Treatment, for those who need it, both during pregnancy and while breastfeeding, is IV methylprednisolone for three days with an oral steroid taper of 1mg/kg/day for 11 days.[34,35]

Some physicians and optometrists do not follow the IV steroids with a oral steroid taper since there is no evidence suggesting efficacy of treatment is reliant on the oral taper.[35] Other physicians use it as a way to control withdrawal side effects.[35] Studies show that, although overall long-term visual outcome is the same as without treatment, it does delay the onset of clinically definite MS.[34]

Timing of treatment is also important; studies show that if steroids are started earlier in the course of ON it results in better outcomes and may help prevent vision loss compared with later treatment.[36]

***Idiopathic intracranial hypertension (IIH).*** This overproduction of cerebral spinal fluid (CSF) is typically triggered by hormonal changes or weight gain, both of which occur during pregnancy (*Figure 3*).[19,31,37] Ocular signs and symptoms include visual field defects, optic nerve head (ONH) elevation, diplopia, photopsia, headaches and tinnitus.[19,31,37]

For patients presenting with an edematous ONH without a diagnosis of IIH, testing is necessary to rule out alternative causes. An MRI and MRV with and without contrast of the head and orbits should be performed, followed by a lumbar puncture to confirm elevated CSF.

The standard treatment for IIH is oral medication Topamax (topiramate, Janssen Pharmaceuticals) or acetazolamide, which are historic category C. They may be considered if the obstetrician and neurologist determine that the benefits outweigh the risks.[37] In most cases, patients are monitored closely with repeat visual fields and optical coherence tomography of the ONH every three months along with neurology or neuro-ophthalmology appointments.

If the patient becomes symptomatic with severe visual field defects, they may be treated with serial lumbar punctures throughout pregnancy, although that carries a risk of spontaneous abortion.[19,37] In severe cases where vision is at risk, tube shunts or ONH fenestration may be needed.[37]

***Glaucoma.*** Most of these medications are historic category C. Studies note that IOP decreases approximately 19.6% in pregnant patients with normal IOP and 24.4% in those with ocular hypertension.[38-40] This occurs because of increased aqueous outflow, lower episcleral venous pressure due to decreased systemic vascular resistance and lower scleral rigidity resulting from increased tissue elasticity.[38-40] The pressure returns to normal approximately two months postpartum.[38-40]

To effectively treat pregnant patients, clinicians must have a comprehensive understanding of how pregnancy can affect the ocular structures as well as the therapeutic options and associated risks. It is the optometrist's job to help address patient concerns while providing safe, effective care. ■

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## OSC QUIZ

You can obtain continuing education credit through the Optometric Study Center. Complete the test form and return it with the $35 fee to: Jobson Healthcare Information, LLC, Attn.: CE Processing, 395 Hudson Street, 3rd Floor New York, New York 10014. To be eligible, please return the card within three years of publication. You can also access the test form and submit your answers and payment via credit card at *Review Education Group* online, revieweducationgroup.com.

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Please check with your state licensing board to see if this approval counts toward your CE requirement for relicensure.

1. Which of the following is a historic category B systemic antibiotic?
a. Trimethoprim.
b. Tetracycline.
c. Doxycycline.
d. Azithromycin.

2. Which of these statements is true regarding acyclovir, valacyclovir and famciclovir?
a. All are historic category D.
b. All are safe in pregnant women.
c. All oral antivirals are safe during lactation.
d. All are contraindicated in pregnant women.

3. Which of the following is suggested for pain relief and is historic category B in all three trimesters of pregnancy?
a. Aspirin.
b. Ibuprofen.
c. Acetaminophen.
d. Naproxen.

4. Which is the only ocular allergy medication that is historic category B?
a. Lastacaft.
b. Pataday.
c. Bepreve.
d. Alrex.

5. Which topical glaucoma medication is known to cause CNS depression in infants when breastfeeding?
a. Timolol.
b. Alphagan.
c. Rhopressa.
d. Travatan.

6. Which of the following statements about anti-VEGF treatments are *true*?
a. During pregnancy anti-VEGF drugs can have systemic side effects.
b. Anti-VEGF has been found in breastmilk after intravitreal injection.
c. Women who are pregnant or nursing should be counseled prior to use.
d. All of the above.

7. Which of the following may cause systemic hypertension in low weight infants?
a. Atropine.
b. Phenylephrine.
c. Tropicamide.
d. Vigamox.

8. All of these statements are true, *except*:
a. A patient's prescription and vision may change during pregnancy.
b. Most refractive changes during pregnancy will worsen after breastfeeding cessation.
c. Changes in refraction are thought to be related to hormones.
d. All of the above.

9. Dry eye disease may worsen during pregnancy because of all of these, *except*:
a. Physical dehydration.
b. Destruction of acinar cells.
c. Decreased corneal sensitivity.
d. Production of amniotic fluid.

10. Which of the following is an increase in pigmentation around the eyes and cheeks that can occur during pregnancy?
a. Chloasma.
b. Palmoplantar pigmentation.
c. Melanocytes.
d. Serpentine hyperpigmentation.

11. Pregnant patients with Graves' disease may experience which of the following?
a. Exacerbation during first trimester.
b. Improvement during first trimester.
c. Exacerbation during third trimester.
d. Improvement during postpartum.

12. Which of these is *not* a common ocular sequela of preeclampsia/eclampsia?
a. HELLP.
b. Elschnig spots.
c. Retinal tear.
d. Vessel tortuosity.

13. All of these statements about patients with gestational diabetes are true, *except*:
a. These patients typically return to normal after delivery.
b. They are at a lower risk of developing Type 2 diabetes in their lifetime.
c. These patients are at a small risk of developing diabetic retinopathy.
d. Retinal evaluation is not indicated.

14. The AOA guidelines suggest Type 1 and Type 2 diabetics who are pregnant should have a comprehensive eye and vision exam:
a. Prior to planned pregnancy.
b. Once a trimester.
c. After delivery.
d. All of the above.

15. All of these are possible issues related to exposure keratopathy from Bell's palsy, *except*:
a. Corneal erosions.
b. Punctate keratopathy.
c. Corneal infiltrate.
d. Proptosis.

16. During which trimester is the most common time for the fetus to contract toxoplasmosis from the mother?
a. First trimester.
b. Second trimester.
c. Third trimester.
d. They are all the same risk.

17. Which of the following statements about CSR is *false*?
a. Women who experience CSR while pregnant are less likely to have a reoccurrence.
b. Symptoms include decreased vision with central metamorphopsia.
c. Treatment is not necessary in pregnant patients, but close monitoring is warranted.
d. All of the above.

18. Which of the following statements regarding MS and pregnancy is *true*?
a. MS will worsen during pregnancy.
b. MS patients will have increased rate of optic neuritis postpartum.
c. MS will make the pregnancy and delivery more difficult.
d. MS patient's children will all have MS.

19. Which of the following is the preferred management of IIH in a pregnant patient?
a. Monitor closely.
b. Topamax.
c. Acetazolamide.
d. Gabapentin.

20. Glaucoma patients who are pregnant may experience which of the following?
a. An increase in IOP while pregnant.
b. A decrease in IOP while pregnant.
c. No change in IOP while pregnant.
d. Angle closure.

# Examination Answer Sheet

## Pregnancy and the Eye: What To Do When Caring For Two

*Valid for credit through June 15, 2023*

**Online:** This exam can be taken online at revieweducationgroup.com. Upon passing the exam, you can view your results immediately and download a real-time CE certificate. You can also view your test history at any time from the website.

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**Mail to:** Jobson Healthcare Information, LLC, Attn.: CE Processing, 395 Hudson Street, 3rd Floor New York, New York 10014

**Payment:** Remit $35 with this exam. Make check payable to Jobson Healthcare Information, LLC.

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**Answers to CE exam:**

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
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17. Ⓐ Ⓑ Ⓒ Ⓓ
18. Ⓐ Ⓑ Ⓒ Ⓓ
19. Ⓐ Ⓑ Ⓒ Ⓓ
20. Ⓐ Ⓑ Ⓒ Ⓓ

**Post-activity evaluation questions:**

*Rate how well the activity supported your achievement of these learning objectives:*
*1=Poor, 2=Fair, 3=Neutral, 4=Good, 5=Excellent*

21. Understand the ocular changes pregnancy can induce. ① ② ③ ④ ⑤
22. Manage the ocular changes associated with pregnancy. ① ② ③ ④ ⑤
23. Determine when to treat an ocular condition and when to wait. ① ② ③ ④ ⑤
24. Successfully comanage with a patient's obstetrician. ① ② ③ ④ ⑤

25. Based upon your participation in this activity, do you intend to change your practice behavior? (choose only one of the following options)
Ⓐ I do plan to implement changes in my practice based on the information presented.
Ⓑ My current practice has been reinforced by the information presented.
Ⓒ I need more information before I will change my practice.

26. Thinking about how your participation in this activity will influence your patient care, how many of your patients are likely to benefit? (please use a number): ☐

27. If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

ⓐ Apply latest guidelines ⓑ Change in pharmaceutical therapy ⓒ Choice of treatment/management approach ⓓ Change in current practice for referral ⓔ Change in non-pharmaceutical therapy ⓕ Change in differential diagnosis ⓖ Change in diagnostic testing ⓗ Other, please specify: _____

28. How confident are you that you will be able to make your intended changes?

ⓐ Very confident ⓑ Somewhat confident ⓒ Unsure ⓓ Not confident

29. Which of the following do you anticipate will be the primary barrier to implementing these changes?
ⓐ Formulary restrictions
ⓑ Time constraints
ⓒ System constraints
ⓓ Insurance/financial issues
ⓔ Lack of interprofessional team support
ⓕ Treatment related adverse events
ⓖ Patient adherence/compliance
ⓗ Other, please specify:

30. Additional comments on this course:

Please retain a copy for your records. Please print clearly.

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Last Name
E-Mail
The following is your: Home Address Business Address
Business Name
Address
City State
ZIP
Telephone # - -
Fax # - -
OE Tracker Number

*Rate the quality of the material provided:*
*1=Strongly disagree, 2=Somewhat disagree, 3=Neutral, 4=Somewhat agree, 5=Strongly agree*

31. The content was evidence-based. ① ② ③ ④ ⑤
32. The content was balanced and free of bias. ① ② ③ ④ ⑤
33. The presentation was clear and effective. ① ② ③ ④ ⑤

By submitting this answer sheet, I certify that I have read the lesson in its entirety and completed the self-assessment exam personally based on the material presented. I have not obtained the answers to this exam by any fraudulent or improper means.

Signature _____ Date _____

Lesson 119843 RO-OSC-0620

# Grab BKC by the Horns

The severity of this case requires equally aggressive action. **Edited by Joseph P. Shovlin, OD**

**Q A six-year-old Caucasian male presented with severe blepharokeratoconjunctivitis (BKC) associated with photophobia, watering, irritation and reduced acuity. He had significant corneal insult with vascularization and scarring. What are my options?**

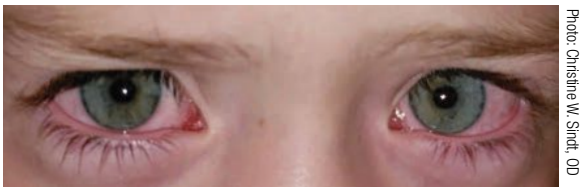

Photo: Christine W. Sindt, OD

**Aggressively treat BKC affecting a child's eyes.**

A BKC is a chronic inflammatory condition of the lid margin accompanied by conjunctivitis and keratopathy, says Paymaun Asnaashari, OD, who practices in California. The pathogenesis is associated with bacterial species that colonize the lids and ocular surface and release exotoxins.[1,2] This leads to a delayed hypersensitivity response, stimulating the production and release of proinflammatory molecules.[1,2] These cause the formation of prostaglandins, leukotrienes and other molecules that result in tear film destabilization and neutrophil chemotaxis inflammation.[3,4]

BKC signs and symptoms include tearing, photophobia, red eye, blepharitis, hordeolum, recurrent chalazium, phlyctenular conjunctivitis, keratitis and corneal complications.[1,2,3,5] While presentation is similar between children and adults, visual outcomes are generally worse in kids with corneal involvement.[1] The incidence of BKC in younger patients is 15%, with a mean age of disease onset of six years old.[1,5]

## Vision Preservation

Dr. Asnaashari recommends immediate treatment when a child's vision is affected. Paracentral and central opacity can lead to deprivation amblyopia and must be addressed early and aggressively to avoid permanent vision loss.

Treatment helps reduce the stimulus for the disease by lowering the population of *Staphylococci*, improving meibomian gland function and reducing the host's local immune response.[6] Options include lid hygiene, topical and systemic antibiotics and topical steroids.

Daily lid hygiene removes debris along the lid margin, and long-term oral antibiotics help control disease progression.[3] The severity of this case warrants the use of macrolides, with erythromycin being the preferred choice in children younger than eight for its safety profile.[6,7,8] Systemic macrolides work by penetrating the meibomian glands, affecting meibum composition and inhibiting bacterial protein synthesis and lipase production, notes Dr. Asnaashari.

He suggests short-term topical antibiotics when there is concomitant blepharitis or other infections within the lids and topical, broad-spectrum antibiotic ointments, drops or a combination to reduce bacterial colonization along the eyelid margin. Topical steroids are the most effective option to control ocular surface and corneal inflammation, according to Dr. Asnaashari. In this case, a short course of intensive treatment is needed to control the severe inflammation and minimize scar formation. If long-term treatment is warranted, he advises monitoring patients closely for ocular hypertension and cataract.

Oral omega-3 supplementation is an ancillary therapy in BKC.[1,3] Omega-3s inhibit synthesis of proinflammatory mediators by preventing the creation of prostaglandins and promoting a healthier lipid profile of meibomian gland secretions.[1,9] In more severe cases of BKC, however, omega-3s alone likely won't be sufficient to control the inflammation.

"BKC has the potential for severe corneal complications and vision loss," says Dr. Asnaashari. "Early treatment could prevent or minimize these complications. Many effective options are available, and understanding each is important in promoting successful outcomes." ■


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REVIEW® OF OPTOMETRY

Edited By Derek N. Cunningham, OD, and Walter O. Whitley, OD, MBA

# Break on Through to the Other Side

The Hydrus Microstent redirects aqueous flow directly into the canal, bypassing the trabecular meshwork. **By Brooke Mathie, OD**

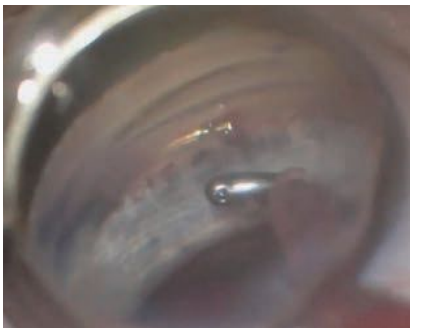
Gone are the days when there were no surgical options for patients with mild-to-moderate glaucoma. With the advent of minimally invasive glaucoma surgeries (MIGS), there now exists an ever-expanding list of options to treat these patients surgically and reduce dependence on drops.

FDA-approved in August 2018, the Hydrus Microstent (Ivantis) is a long, flexible structure roughly the size of an eyelash that research suggests can effectively lower intraocular pressure (IOP). It is only indicated for patients with mild-to-moderate open-angle glaucoma who are undergoing cataract surgery. It is not indicated for those with other forms of glaucoma or birth irregularities of the anterior chamber.

## Process and Progress

Taking an *ab interno* approach, the surgeon carefully places the 8mm device using incisions created during cataract surgery and a preloaded injector. It is inserted through the trabecular meshwork and into Schlemm's canal so that it spans 90° of the canal. There is no need for targeted insertion, as the length of the device accounts for one-fourth of Schlemm's canal, ensuring that multiple collector channels are targeted.

By bypassing the trabecular meshwork, the microstent redirects the flow of aqueous fluid and allows it to drain directly into Schlemm's canal for easier outflow. The flexible design of the device allows for gentle expansion of the canal, leaving the collector channels unaffected.



**After good stent placement is confirmed, the MIGS procedure is complete.**

This newer MIGS procedure has achieved successful clinical trial results. The Horizon study found 78% of Hydrus Microstent patients were able to remain medication-free after two years, a 30% improvement compared with cataract surgery alone.[1] This study further showed that 85.9% of Hydrus Microstent patients experienced an IOP reduction of 20% or more at one year and 77.2% retained this outcome after two years, indicating that the implant can both lower and maintain improved IOP levels.[1]

## Pros and Cons

One advantage of Hydrus is its safety profile, as procedures that bypass the trabecular meshwork and act on the canal are among the safest. However, all MIGS come with risks. The most common adverse events associated with this device include non-persistent anterior uveitis requiring a change in post-op steroid treatment, microstent malposition and microstent obstruction with or without peripheral anterior synechiae. All tend to occur at low incidences.[2]

Other complications include hyphema or microhyphema, transient anterior chamber shallowing, iris erosion, pupil peaking and early hypotony (IOP less than 6mm Hg within two weeks after surgery) accompanied by corneal folds.

Since the device is designed to enhance normal outflow mechanisms, post-op patients are protected against episodes of hypotony that sometimes occur after glaucoma surgery.

The device's effect on IOP is apparent early after surgery, allowing the surgeon to make a decision regarding the discontinuation of drops shortly after the procedure.

Research shows this low-risk MIGS can provide IOP-lowering effects as far out as two years after insertion. So far, it has proven to be yet another useful weapon in the battle against glaucoma. ■

*Dr. Mathie is an ocular disease resident at Virginia Eye Consultants in Norfolk, VA, and a graduate of The Ohio State College of Optometry.*

**For a video of this procedure, visit www.reviewofoptometry.com or scan the QR code.**

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"I was only seeing light flashes early on, but light FLASHES when you've not seen anything for so many years—it was wonderful"

—Keith H, retinal prosthesis recipient

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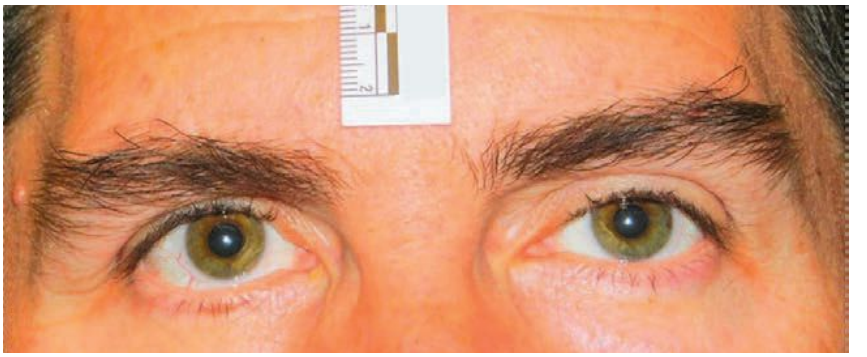
# Noninvasive Ptosis Management

Medical advances are offering more options for these patients. **By Paul M. Karpecki, OD**

Patients frequently present with bothersome blepharoptosis, but in the absence of pharmacologic options, optometrists could historically do little to improve their appearance or functioning. However, late last year, the FDA accepted a promising New Drug Application that, if approved, may soon alter the landscape of ptosis care as we know it.



**This clinical study subject is seen five minutes after instillation of RVL-1201 for the treatment of ptosis.**

## Etiology and Subtypes

Blepharoptosis is a common condition defined by either unilateral or bilateral eyelid drooping.[1] It can affect individuals of all ages and is caused by weakness of the levator palpebrae superioris and Müller's muscle, which are responsible for lifting the eyelid, or by a pathology of the nerves that cause innervation these muscles.[1,2]

Ptosis can be either acquired or congenital. The congenital form is the most common cause in children. It's defined as ptosis present at birth or that develops by age one.[1] Congenital blepharoptosis subtypes include blepharophimosis syndrome, congenital third cranial nerve (CN III) palsy, congenital Horner's syndrome, and Marcus Gunn jaw-winking syndrome.[3] Approximately 75% of congenital ptosis is unilateral, and leads to amblyopia in 20% of cases either due to occlusion of the pupil or by causing amblyogenic astigmatism in the affected eye.[1,4]

Acquired blepharoptosis can be divided into five subtypes:[5]

• ***Aponeurotic ptosis.*** This is the most common form of acquired ptosis.[1] It occurs secondary to stretching or dehiscence of the levator aponeurosis, typically acquired with repetitive traction or involution of the tissue. These patients present with a reduced margin to reflex distance 1 (MRD1), a high upper eyelid crease, a near normal levator function (LF), and decreased palpebral fissure in downgaze.[1]

• ***Neurogenic ptosis.*** This form of blepharoptosis may result from CN III palsy or Horner's syndrome.[3]

• ***Myogenic ptosis.*** Myogenic blepharoptosis can be found in myasthenia gravis (MG), chronic progressive external ophthalmoplegia, oculopharyngeal muscular dystrophy and myotonic dystrophy patients.[3]

• ***Mechanical ptosis.*** This can result from the presence of eyelid mass, such as neurofibroma or hemangioma or cicatrization secondary to inflammation or surgery.[1]

• ***Traumatic ptosis.*** Eyelid laceration with transection of the upper eyelid levators, or any disruption of the neural pathway can cause this type of acquired ptosis.[3]

## Diagnosis

Identifying ptosis is critical for neurologic and visual function. Ptosis is present when the upper eyelid is lower than its normal anatomical position, typically 1mm to 2mm below the superior corneoscleral limbus.[1,2] Evaluating the MRD1 can help determine the presence of ptosis, as well as its severity.[3] A normal value for MRD1 is 3.5mm to 5.0mm.[3] Levator function is also important and is a primary determinant of surgical technique. It is measured as the total excursion of the upper eyelid margin from maximum downgaze to maximum upgaze. A normal value is between 13mm Hg and 16mm Hg.[1]

Ptosis can foretell some potentially serious underlying conditions, such as Horner's syndrome and CN III palsy.[1] Research shows 20% of MG patients experience isolated ocular symptoms and 80% of patients who initially present with

ocular MG develop systemic symptoms.[1,2]

Horner's syndrome results from a disruption in the sympathetic nervous system pathway extending between the brain and the Müller's muscle, affecting the eye and ipsilateral side of the face.[3] While ptosis, miosis and anhydrosis are the classic Horner's syndrome triad, these clinical signs may be subtle and are rarely all present.[1]

Cosmetic botulinum toxin type A injection patients may also present with ptosis complaints. Here, upper lid ptosis occurs when the toxin diffuses through the orbital septum and affects the levator muscle as it traverses the pre-periosteal plane or when the toxin tracks along tributaries of the superior ophthalmic vein.[1] The side effects of this can persist for the whole duration of effect of treatment, but usually settle in three to four weeks.[4]

Finally, be sure to distinguish blepharoptosis from dermatochalasis.[5] Although true ptosis correction often requires surgery to elevate the position of the upper eyelid margin, isolated dermatochalasis can be corrected by removal of excessive skin with or without fat debulking or redistribution.[6] Importantly, correcting the ptosis alone may worsen the dermatochalasis as elevating the upper eyelid margin can increase the redundancy of the overlying skin. For this reason, some patients with both ptosis and dermatochalasis benefit from combined ptosis repair and upper lid blepharoplasty.[6]

## Surgical Options

The primary surgical approaches for ptosis include Müller's muscle-conjunctival resection, levator resection and the frontalis sling.[1] Levator function, the degree of ptosis and the patient's response to phenylephrine can help guide the surgeon select a surgical approach.[1]

Surgical ptosis correction can be performed at any age depending on the severity of the disease.[3] However, if the patient has strabismus and blepharoptosis, the strabismus must be corrected first.[3] A phenylephrine test can help determine if patients are good candidates for a conjunctivo-mullerectomy.[1] As an alpha-adrenergic agonist, phenylephrine stimulates the sympathetically innervated Müller's muscle when applied topically.[3]

## Pharmaceutical Treatments

ODs can consider one of three medical treatments for ptosis: apraclonidine ophthalmic drops, botulinum toxin injection and oxymetazoline.

Apraclonidine is not an appropriate long-term treatment for blepharoptosis, as it may cause sensitivity with longer-term use, but since upper eyelid ptosis after cosmetic botulinum toxin is generally short-lived and may be responsive to apraclonidine ophthalmic drops, this treatment is appropriate in cases of inadvertent migration of botulinum toxin injection into the levator palpebrae superioris muscle.[3,4]

In addition to creating a need for ptosis treatment, botulinum toxin injection is also a plausible treatment itself. As a neuromuscular-blocking agent, botulinum toxins weaken targeted muscles by inhibiting the release of acetylcholine from the presynaptic terminal of the neuromuscular junction.[4] As such, it can be a suitable option for the management of small eyelid margin asymmetries.[5] Indeed, with mild or micro-ptosis, surgery is rarely indicated for functional purposes and, in some cases, surgery can lead to secondary aesthetic complications, such as contour asymmetry or crease abnormalities.[6] In these cases, botulinum neurotoxin may be a desirable nonsurgical treatment option.[6,7] However, note that treatment is dose-dependent and large doses may induce complications, such as lagopthalmos, exposure keratitis and inadvertent induction or worsening of ptosis.[3]

More recently, researchers have been looking into RVL-1201 (oxymetazoline 0.1%, Vertical Pharmaceuticals) for use in patients with acquired ptosis.[3] Oxymetazoline is an α1 and partial α2 adrenergic agonist capable of contracting Müller's muscle through direct transconjunctival contact of this sympathomimetic agent.[3] In a Phase III study, the treatment was well tolerated and significantly improved the superior visual field, making this emerging therapy a potential nonsurgical treatment for upper eyelid ptosis.[1,3]

Optometrists are the first line of care for ptosis patients, yet we've had little opportunity to apply our deep understanding of the condition to approved treatments. Given the incidence of ptosis in the aging population, having an approved therapy—should it come to pass—will be a tremendous benefit in terms of providing comprehensive primary eye care. ■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# A Family Affair

Three boys have poor night vision—can imaging of one explain its cause?

By Rami Aboumourad, OD, and Mark Dunbar, OD

A 17-year-old Chinese male presented for evaluation of a presumed inherited retinal dystrophy. He had a longstanding history of poor night vision and carried a clinical diagnosis of retinitis pigmentosa (RP) since age six. The patient had two younger brothers, who shared the same biological parents and symptom of poor night vision. The parents denied consanguinity.

His best-corrected visual acuities were 20/40 OD and 20/50 OS. His intraocular pressures were 11mm Hg OD and 12mm Hg OS, extraocular motilities were full, confrontation visual fields were mildly constricted in both eyes, and pupils were equally round and reactive with no relative afferent pupillary defect. Anterior segment exam was unremarkable OU. Posterior segments contained bone spicule-like pigmentary changes in a midperipheral annular configuration and macular pigment changes. The optic nerves had an atypical presentation for which various studies are presented herein (*Figures 1-4*). The retina was otherwise flat and attached in both eyes with no other observed lesions OU.

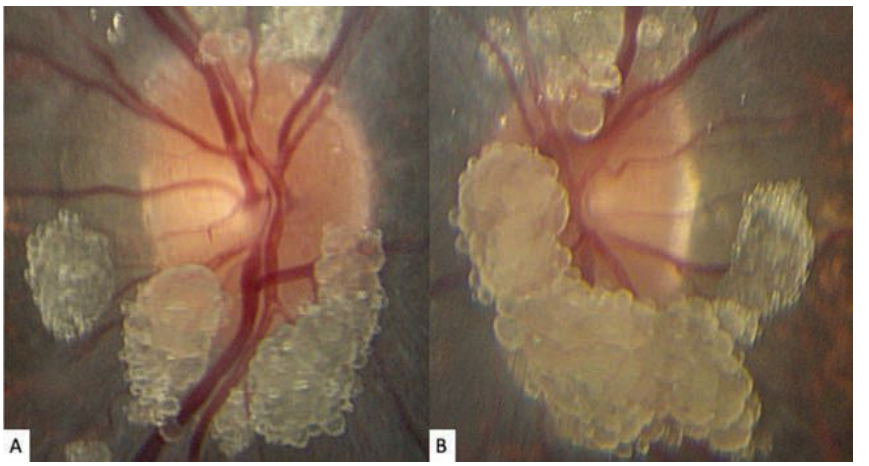



**Fig. 1. These photos of our young patient's right (A) and left (B) optic nerves show extensive elevated, globular lesions of both the optic nerve and peripapillary retina.**

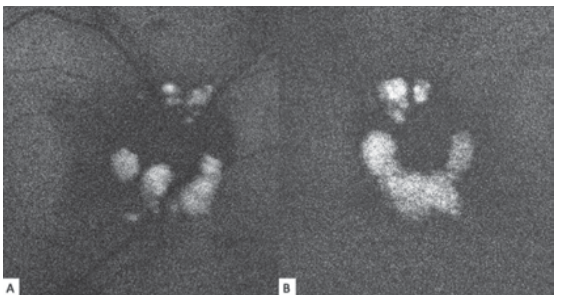



**Fig. 2. Fundus autofluorescence of the right (A) and left (B) optic nerves show discrete hyperautofluorescence corresponding with the lesions seen in Figure 1.**

## Take the retina quiz

1. Which of the following best describes the fundus autofluorescence findings depicted in *Figure 2*?
a. Hyperfluorescence of lesions at the optic nerve.
b. Hyperautofluorescence of the lesions at the optic nerve.
c. Hypofluorescence of the lesions at the optic nerve.
d. Hypoautofluorescence of the lesions at the optic nerve.

2. Optical coherence tomography (OCT) imaging suggests that this lesion arises from which ocular structure (*Figures 3 and 4*)?
a. The vitreous.
b. The inner retina.
c. The outer retina.
d. The retinal pigment epithelium.

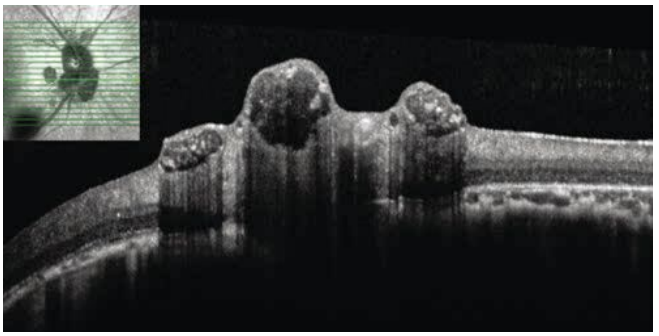
3. Which of the following is the most likely diagnosis of the optic nerve finding?
a. Retinoblastoma.
b. Optic nerve head drusen.
c. Retinal/optic nerve astrocytic hamartoma.
d. Retinal hemangioblastoma.

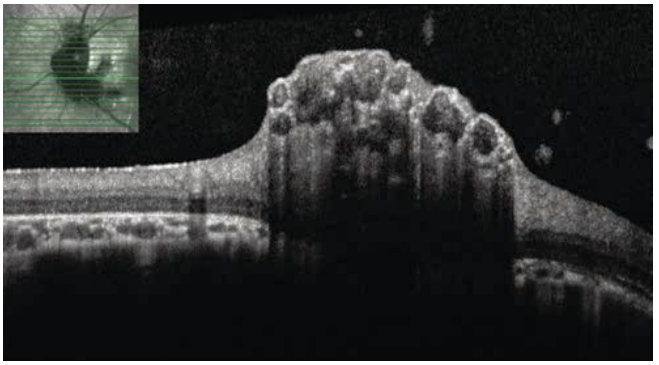
4. This lesion has been associated with which of the following conditions:
a. Tuberous sclerosis complex.
b. Neurofibromatosis.
c. Retinitis pigmentosa.

d. The lesions are associated with all of the above conditions.

5. Which of the following statements regarding the lesion is false?
a. They are composed of glial cells.
b. They are relatively benign, slow-growing tumors.
c. They are composed of hyaline bodies.
d. They can cause exudative retinal detachments.

*For answers, see page 94.*





**Figs. 3 and 4. SD-OCT through lesions of the right optic nerve. On SD-OCT, the lesions appear to have hyporeflective "moth eaten," optically empty spaces with foci of hyperreflectivity, likely reflecting areas of intralesional calcification.**

## Diagnosis

The striking appearance of both optic nerves show mulberry-like lesions of the optic nerve and peripapillary retina in both eyes (*Figures 1a and 1b*). Even though the lesions were elevated, the optic disc margins were sharp and the nerve itself was flat with no presence of fluid. Fundus autofluorescence (FAF) imaging showed hyperautofluorescence of the lesions in both eyes (*Figures 2a and 2b*). OCT imaging revealed hyporeflective optically empty spaces of the inner retina that appear confined to the retinal nerve fiber layer (RNFL) with focal intralesional hyper-reflective opacities (*Figures 3 and 4*). The lesions were clinically consistent with astrocytic hamartomas of the retina and optic nerve.

## Discussion

Retinal and optic nerve astrocytic hamartomas (RAH) are relatively rare, benign tumors of the retina and optic nerve that can be unilateral or bilateral.[1,2] They are most commonly seen in tuberous sclerosis complex (TSC), a systemic disorder defined by the triad of epilepsy, mental retardation and skin lesions that typically affect the head and face. In fact, RAHs are the most common ophthalmic manifestation of TSC and are present in up to 53% of cases.[1,3-6] In addition to TSC, RAHs have also been described in neurofibromatosis, RP or in isolation.[3,4]

Clinically, they appear as elevated, globular, yellow-white or translucent nodules; their appearance has been compared to that of fish eggs, tapioca and mulberries.[1,2,5,6,9,10] On OCT, they are RNFL tumors with hyporeflective, "moth-eaten" optically empty spaces with foci of hyperreflectivity, which researchers believe represent intralesional calcifications.[5,10-12] When calcified, the lesions hyperautofluoresce on FAF similar to optic nerve head drusen (ONHD).[5] While such findings are thought to be avascular, investigators have described cases where mild vascularity is evidenced on fluorescein angiography.[8] Vascularity can result in exudation and subsequent vision loss by way of retinal detachment.[8]

Typically, RAHs are endophytic tumors (arising from the RNFL and bulging toward the vitreous), but can rarely be exophytic (arising from the subretinal space).[1,5,6] Exophytic tumors tend to be more visually significant as a result of exudative retinal detachments and subsequent neovascular glaucoma.[1,6] Histologically, RAHS are RNFL tumors composed of fibrillary astrocytes (glial cells); they typically begin as flat lesions that slowly progress to elevated nodules in the first few decades of life with variable foci of calcification.[1,3,5,7-10]

Differential diagnoses include retinoblastoma, ONHD, acquired retinal astrocytoma, retinal hemangioblastoma, posterior amelanotic uveal melanoma, choroidal metastases and Coats' disease. Cavitary retinoblastoma, a unique variant of retinoblastoma of low-grade malignancy, is characterized by similar OCT features of focal hyperreflective opacities within hyporeflective

cavities, making distinction especially challenging.[10,13] In contrast to RAHs, ONHD are hyaline bodies within the substance of the optic nerve that undergo calcification with age.[7,8] By virtue of anatomy, ONHD result in a congested or elevated appearance to the optic nerve, while RAHs rest superficial to a flat optic nerve with distinct margins.[7,8]

Management of RAHs involves observation.[1,5,8] While ophthalmic complications are rare, they include retinal neovascularization, vitreous hemorrhage or seeding, macular edema, intraretinal or subretinal exudation and neovascular glaucoma.[1,5,8]

Treatment options include intravitreal anti-VEGF, intravitreal steroids, photodynamic therapy and pars plana vitrectomy either in combination or isolation.[1,5,8]

Our patient indeed had RP, in addition to the RAH. Given that both parents were asymptomatic and that all three male kin exhibited the disease, it was presumed to be of autosomal recessive or X-linked recessive inheritance. A blood sample was obtained and sent for genetic analysis. Genetic testing revealed a mutation in the RPGR gene, which is known to be pathogenic for X-linked RP. A genetically confirmed diagnosis of X-linked RP was obtained, and the patient and family were genetically counseled.

Although our patient did not have any apparent systemic manifestations of TSC, he was recommended to follow-up with internal medicine for further studies to rule it out. ■

*Dr. Aboumourad practices at the Bascom Palmer Eye Institute in Miami.*

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# Back on the Horse

A patient returns after years away from the OD, perhaps just in the nick of time.

By Andrew S. Gurwood, OD

## History

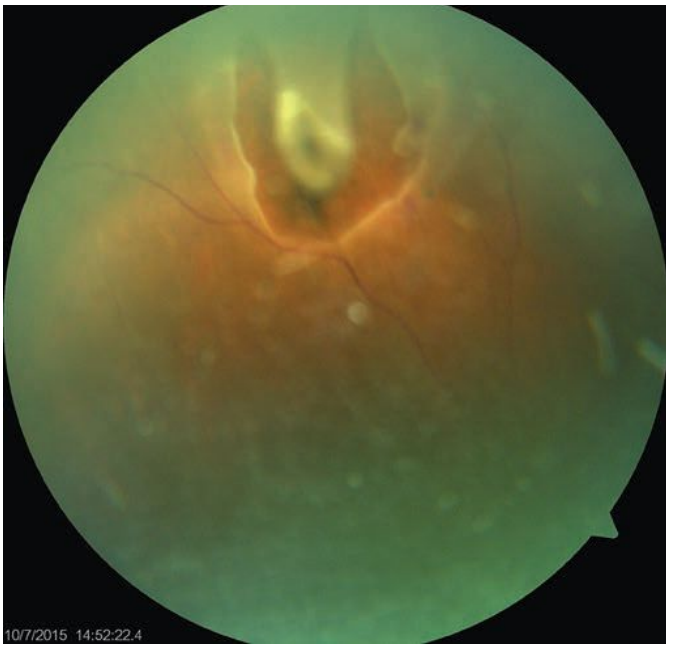
A 57-year-old black female presented for an eye examination with a chief complaint of near blur. She explained she had lost her job two years earlier and, with it, her vision and health insurance. She had no history of previous ocular or systemic disease, took no medication and reported no allergies.

## Diagnostic Data

Her best corrected entering acuities with her -6.25/+2.25 spectacles 20/30, OU at distance and near. Her external examination was normal and no evidence of afferent pupil defect was noted. Her refraction uncovered -7.00D of myopia, correctable to 20/20.

Her biomicroscopic examination found normal anterior segment structures, open angles, mild cataracts and Goldmann applanation pressures measuring 15mm Hg in both of her eyes.

The pertinent dilated fundus finding in the right eye is documented in the photograph.




**Although this patient only presented for near vision blurring, imaging found something more pressing. Do you recognize this presentation?**

## Your Diagnosis

Does the case presented require any additional tests, history or information? Based on the information provided, what would be your diagnosis? What is the patient's most likely prognosis? To find the answers, visit us at www.reviewofoptometry.com. ■

### Next Month in the Mag

Coming in July, *Review of Optometry* will present its Annual Glaucoma Report. Topics will include:

- Six Ways Glaucoma Care is Changing
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**Retina Quiz Answers** *(from page 90):* 1) b; 2) b; 3) c; 4) d; 5) c.

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# The Dangers of DNR

In glaucoma, optometrists can do more than detect and refer. **By James L. Fanelli, OD**

A 62-year-old Caucasian male presented to our office with concerns about his changing vision. Years before, he had a melanoma in his right eye, which was irradiated and treated with plaque therapy. He noted gradually changing vision in both eyes, and that prompted him to see another optometrist in the area earlier, but that doctor said that he "had too many things going on" and referred the case to a glaucoma surgeon. The patient found his way to me first, and it's a good thing he did because, despite the many factors complicating his glaucoma, he wasn't yet a surgical patient—so why send him to a surgeon?

He only reported using a statin for management of hypercholesterolemia. He reported no allergies to medications.

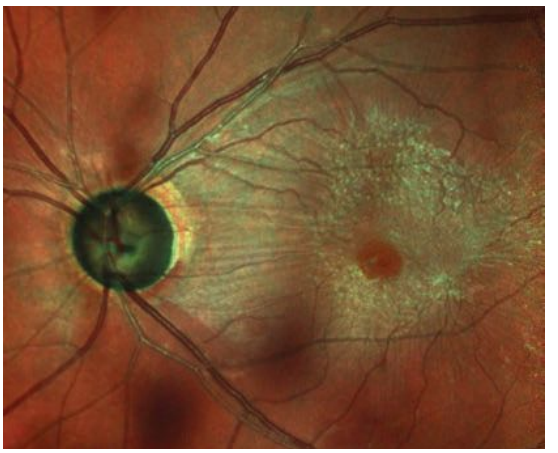

**Fig. 1. This multicolor image of the left optic nerve and macula shows the patient's thinned neuroretinal rim as well as the moderate ERM. Also, note the wedge defect inferotemporally. Other wedge defects, if present, were obscured by the ERM.**

## Examination

His best-corrected visual acuities were 20/400 OD and 20/40+ OS. His intraocular pressure (IOP) readings were 24mm Hg OD and 23mm Hg OS. Pachymetry measurements were 501µm OD and 507µm OS.

Through dilated pupils, his crystalline lenses were clear in both eyes. A large macular scar was visible in his right eye, most likely consistent with the post-radiation plaque years ago. The macula in the left was characterized by a moderate epiretinal membrane (ERM).

The optic nerve evaluations were consistent with moderately advanced glaucomatous damage in the right and left eyes, with very thin neuroretinal rims in both eyes. The retinal vasculature was characterized by moderate arteriolarsclerotic retinopathy OU. His peripheral retinal evaluations were unremarkable. Optic nerve multicolor images were obtained at the initial visit.

## Making a Diagnosis

Clearly, he had glaucoma bilaterally. He was subsequently scheduled for several follow-up visits to ascertain the level of damage and stabilize the situation. He was compliant with his visits. His average IOPs over three pretreatment visits were 22mm Hg OD and OS.

Visual fields showed moderate loss in his left eye related to the glaucoma, with field defects encroaching on fixation; the field in the right was uninterpretable, as he was unable to fixate due to the macular scarring.

OCT evaluation of both eyes demonstrated advanced damage as seen on the Bruch's membrane opening-minimum rim width (BMO-RMW) neuroretinal rim scans, as well as moderate damage in the circumpapillary retinal nerve fiber layer (RNFL).

A trial of Xelpros (latanoprost, Sun Pharmaceuticals) was initiated, and on four subsequent follow-up visits, post-treatment IOPs had averages of 13mm Hg OD and 12mm Hg OS. He continues using drops and his glaucoma is currently stabilized.

## Finding the Right Optometrist

The lesson here is one of case management. In the initial encounter, the patient mentioned that the previous doctor claimed he "had too many things going on" and that he needed to see a surgeon. I didn't probe as to what the "things" were, but I have a pretty good guess. The

patient was, essentially, visually monocular (insofar as acuity was concerned). He had advanced cupping OU. He had a moderate ERM in his better-seeing left eye. Because of these things, I assume, he was told he needed to see a surgeon.

The term "DNR" usually stands for the medical directive *do not resuscitate*. However, I used the term to describe a trend I'm seeing that worries me: *detect 'n' refer*. I am fully aware that many ODs do not manage glaucoma at all. That is perfectly OK, as I don't practice all aspects of optometry. I don't see pediatric cases, I don't fit specialty contact lenses, I don't do vision therapy. However, I know ODs who do take on these types of cases.

I often hear of situations like this one, where a patient is referred out to a "specialist." This patient needed glaucoma management. In 49 states, that's within optometry's domain. If you don't treat glaucoma yourself, why not send your patient to another optometrist?

## If You Treat, Keep Treating

Even those who do treat glaucoma can be guilty of detecting and referring. I've heard cases where the patient is referred to a surgeon because they didn't respond to the initial treatment, or the drop reddened their eyes or for fear of liability. Certain cases ultimately will need to go to a glaucoma specialist for surgical management, yes, but the large majority of glaucoma cases do not need surgical intervention. In other words, non-surgical glaucoma care is optometric glaucoma care. These patients, even advanced cases, are in our wheelhouse! We can't cherry-pick the cases we see. If we're going to treat glaucoma, then we need to treat the difficult cases as well as the easy ones.

**At top, this circumpapillary RNFL scan of the patient's left eye demonstrates significant loss in the superiotemporal and inferiotemporal sectors of the scan. Below, the same eye's BMO-MRW scans demonstrates advanced neuroretinal rim loss and thinning. Both scans are consistent with moderately advanced glaucoma.**

I'm sure a letter to the editor will follow from this analogy, but how many ODs have an upper limit of refractions that they will do? Do ODs cut off and refer out patients with refractive errors over a certain myopic level? My guess is not. Though the higher myope may carry more risk, it's certainly the practice of optometry to see them and not refer them for refractive care because they are "too myopic." The same holds true for glaucoma.

Sure, some glaucoma does get worse, despite the best therapeutic decisions. But that happens to ophthalmology as well. Fix it. Adjust the medications. Try different therapies. If things are still not stable, then an upstream referral is necessary. Why stop at one drop? Why refer out if the eye is red when that issue could be solved with a different drop? Why worry when a long-standing glaucoma patient worsens? That's what diseases do. Adjust. Recalculate. Rethink management. You can do this. We all can do this.

These are challenging times. Optometrists feel the pressure from all sides. Decreased reimbursements. Increased government intrusion. Patients who are less than pleasant. Coronavirus. It might seem harder to sustain a practice than ever these days. But, there will always be patients with sick eyes who need you. In fact, there may be more than ever. Those sick eyes can sustain a practice very nicely.

If you're going to DNR, at least refer to an optometrist who works in that field. If your practice doesn't allow you to manage diseases, an OD near you likely can do it. And if you are in a practice where you state that you 'treat ocular disease', but Detect 'N' Refer most of those patients out your door, you've figuratively put a sign with that other DNR on your practice's door: Do not resuscitate this practice, for it is on its way out. ■

**TOBRADEX® ST (tobramycin/dexamethasone ophthalmic suspension) 0.3%/0.05%**

**Brief Summary**

**This Brief Summary does not include all the information needed to use TOBRADEX ST safely and effectively. Please see Full Prescribing Information for TOBRADEX ST at MyTobraDexST.com.**

## INDICATIONS AND USAGE

TOBRADEX ST is a topical antibiotic and corticosteroid combination for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies.

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

## DOSAGE AND ADMINISTRATION

**Recommended Dosing:** Instill one drop into the conjunctival sac(s) every four to six hours. During the initial 24 to 48 hours, dosage may be increased to one drop every 2 hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

## CONTRAINDICATIONS

**Nonbacterial Etiology:** TOBRADEX ST is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

**Hypersensitivity:** Hypersensitivity to any component of the medication.

## 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. IOP should be monitored.

**Aminoglycoside sensitivity:** Sensitivity to topically applied aminoglycosides may occur.

**Cataracts:** May result in posterior subcapsular cataract formation.

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

**Bacterial infections:** 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:** Treatment in 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 with long-term use. Fungal invasion must be considered in any persistent corneal ulceration.

**Use with systemic aminoglycosides:** Use with systemic aminoglycoside antibiotics requires monitoring for total serum concentration of tobramycin.

## ADVERSE REACTIONS

The most frequent adverse reactions to topical ocular tobramycin (TOBREX®) are hypersensitivity and localized ocular toxicity, including eye pain, eyelids pruritis, eyelid edema, and conjunctival hyperemia. These reactions occur in less than 4% of patients. Similar reactions may occur with the topical use of other aminoglycoside antibiotics.

Non-ocular adverse events occurring at an incidence of 0.5% to 1% included headache and increased blood pressure.

The reactions due to the steroid component are: increased intraocular pressure (IOP) with possible development of glaucoma, and infrequent optic nerve disorder; subcapsular cataract; and impaired healing.

Secondary Infection.
The development of secondary infection has occurred. Fungal infections of the cornea are particularly prone to develop with long-term use. Fungal invasion must be considered in any persistent corneal ulceration. Secondary bacterial ocular infection following suppression of host responses also occurs.

## USE IN SPECIFIC POPULATIONS

**Pregnancy and Nursing Mothers**

There are no adequate and well controlled studies in pregnant women. TOBRADEX® ST ophthalmic suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Caution should be exercised when TOBRADEX® ST is administered to a nursing woman.

**Pediatric Use:** Safety and effectiveness in pediatric patients below the age of 2 years have not been established.

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

**Rx Only**

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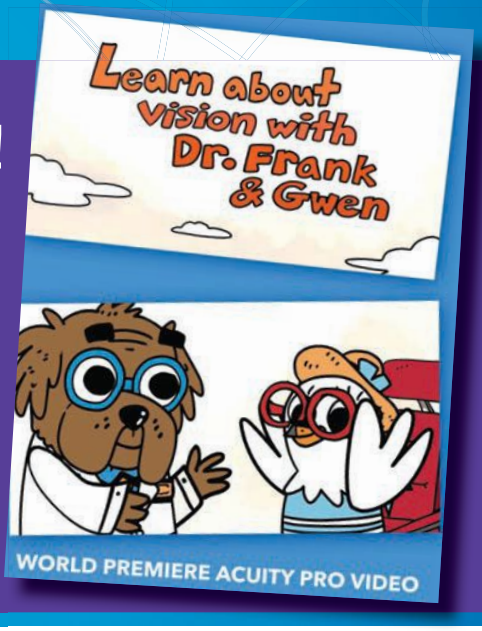
# Now Showing on Version Ten!

Acuity Pro™ is excited to announce the release of the new pediatric fixation target video, “Learn About Vision with Dr. Frank and Gwen”! We have had numerous requests for new pediatric video content for the video library. Therefore, working with Frankie Fontana, we created a video in honor of Dr. Frank Fontana, known affectionately as “Uncle Frank”. So join the fun as Dr. Frank, our canine eye doctor, provides Gwen, a nearsighted seagull, with a new pair of spectacles. And keep your pediatric patients “fixated” while you complete the exam!

* also available for download on Versions 7, 8, and 9

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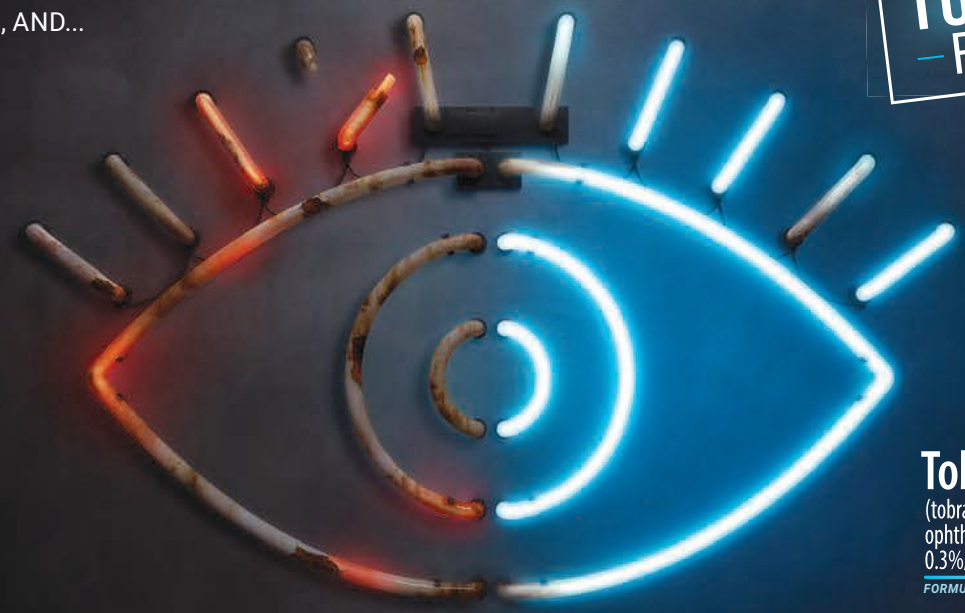


TobraDex® ST
(tobramycin/dexamethasone ophthalmic suspension) 0.3%/0.05%
FORMULATED WITH XanGen™

## PRESCRIBE TOBRADEX® ST to control ocular inflammation with risk of bacterial infection

- Rapid relief from blepharitis/blepharoconjunctivitis symptoms[1,a]
- XanGen™ suspension technology provides increased viscosity for improved ocular bioavailability of drug and consistent delivery[2]
- TOBRADEX ST contains half the dexamethasone as TobraDex®, yet similar ocular tissue exposure[2,b]

**Eligible patients could pay as little as $45 for TOBRADEX ST**
**LEARN MORE AT MYTOBRADEXST.COM**

## Indications and Usage

For steroid responsive inflammatory ocular conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe and chronic anterior uveitis, corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies for which a corticosteroid is indicated and where the risk of superficial bacterial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

## Important Safety Information

**CONTRAINDICATIONS:**
Most viral disease 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. Hypersensitivity to any components of the medication.

**WARNINGS & PRECAUTIONS:**

- **IOP increase** – Prolonged use may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. IOP should be monitored.
- **Aminoglycoside sensitivity** – Sensitivity to topically applied aminoglycosides may occur.
- **Cataracts** – Posterior subcapsular cataract formation may occur.
- **Delayed healing** – May delay healing and increase the incidence of bleb formation. Perforations of the cornea or sclera have occurred. Slit lamp biomicroscopy, and fluorescein staining should be conducted.
- **Bacterial infections** – May suppress host response and increase 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** – Use with history of herpes simplex requires great caution. The course and severity of many viral infections of the eye (including herpes simplex) may be exacerbated.
- **Fungal infections** – Fungal infections of the cornea may occur and should be considered in any persistent corneal ulceration.
- **Use with systemic aminoglycosides** – Total serum concentration of tobramycin should be monitored.

**ADVERSE REACTIONS:**
The most frequent adverse reactions (<4%) to topical ocular tobramycin are hypersensitivity and localized ocular toxicity, including eye pain, eyelid pruritus, eyelid edema, and conjunctival hyperemia.

The reactions due to the steroid component are increased intraocular pressure with possible development of glaucoma, and infrequent optic nerve disorder; subcapsular cataract; and impaired healing.

The development of secondary infection has occurred. Fungal infections of the cornea may occur. Secondary bacterial ocular infection following suppression of host responses also occurs.

Non-ocular adverse events (0.5% to 1%) included headache and increased blood pressure.

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

[a]Randomized, investigator-masked, active-controlled, parallel-group trial conducted at 7 private practice clinical sites in the United States with 122 adult patients who had moderate to severe blepharitis/blepharoconjunctivitis.[1]

[b]Multicenter, double-blind, parallel-group, single-dose study of 987 patients receiving a single dose of TOBRADEX ST or TobraDex ophthalmic suspension.[2]

**References: 1.** Torkildsen GL, Cockrum P, Meier E, et al. *Curr Med Res Opin.* 2011;27(1):171-178. **2.** Scoper SV, Kabat AG, Owen GR, et al. *Adv Ther.* 2008;25(2):77-88.

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