EARN 2 CE CREDITS: Visual Fields in the Era of OCT, p. 71

REVIEW® OF OPTOMETRY

May 15, 2019

www.reviewofoptometry.com

20TH ANNUAL DRY EYE REPORT

DID THE DREAM STUDY CHANGE YOUR THINKING?

The controversial findings led some ODs to question the role of omega-3s, while others dispute the study itself. Here, several experts share their views. p. 36

- Build a Better Dry Eye Protocol, p. 28
- Cyclosporine Shoot-out: How Do They Match Up?, p. 42

ALSO: A Guide to Conjunctival Tumors, p. 50 My Patient Has DR... Now What?, p. 60

SUBMICRON STRONG

Engineered with SM Technology™ for efficient penetration at a low BAK level (0.003%)[1,2]

~2× GREATER PENETRATION to the aqueous humor[2*]

*Compared to LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5%. Clinical significance of these preclinical data has not been established.

LOTEMAX® SM
(loteprednol etabonate ophthalmic gel) 0.38%

SMALL & MIGHTY
SUBMICRON PARTICLES

PROVEN STRENGTH

- 30% of LOTEMAX® SM patients had complete ACC resolution vs vehicle (15%) at Day 8 (N=371, $P<0.0001$)[1,3†]
- 74% of LOTEMAX® SM patients were completely pain-free vs vehicle (49%) at Day 8 (N=371, $P<0.0001$)[1,3‡]

†Pooled analysis of Phase 3 clinical studies. **Study 1:** 29% LOTEMAX® SM (N=171) vs 9% vehicle (N=172). **Study 2:** 31% LOTEMAX® SM (N=200) vs 20% vehicle (N=199); $P<0.05$ for all.

‡Pooled analysis of Phase 3 clinical studies. **Study 1:** 73% LOTEMAX® SM (N=171) vs 48% vehicle (N=172). **Study 2:** 76% LOTEMAX® SM (N=200) vs 50% vehicle (N=199); $P<0.05$ for all.

Indication

LOTEMAX® SM (loteprednol etabonate ophthalmic gel) 0.38% is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety Information

- LOTEMAX® SM, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If LOTEMAX® SM is used for 10 days or longer, IOP should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.

Important Safety Information (cont.)

- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those with diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections.
- Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.
- Contact lenses should not be worn when the eyes are inflamed.
- There were no treatment-emergent adverse drug reactions that occurred in more than 1% of subjects in the three times daily group compared to vehicle.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see brief summary of Prescribing Information on adjacent page.

References: 1. LOTEMAX SM [prescribing information]. Bridgewater, NJ: Bausch & Lomb, Incorporated. **2.** Cavet ME, Glogowski S, DiSalvo C, Richardson ME. Ocular pharmacokinetics of submicron loteprednol etabonate ophthalmic gel, 0.38% following topical administration in rabbits. Poster presented at 2015 ARVO Annual Meeting; May 4, 2015; Denver, Colorado. **3.** Data on file. Bausch & Lomb, Inc.

BAUSCH + LOMB

Visit www.LOTEMAXSM.com

LOTEMAX® SM
(loteprednol etabonate ophthalmic gel) 0.38%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

LOTEMAX® SM (loteprednol etabonate ophthalmic gel) 0.38%

For topical ophthalmic use
Initial U.S. Approval: 1998

INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops. Apply one drop of LOTEMAX® SM into the conjunctival sac of the affected eye three times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

Cataracts: Use of corticosteroids may result in posterior subcapsular cataract formation.

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

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

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

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

Contact Lens Wear: Contact lenses should not be worn when the eyes are inflamed.

ADVERSE REACTIONS

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. Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. There were no treatment-emergent adverse drug reactions that occurred in more than 1% of subjects in the three times daily group compared to vehicle.

USE IN SPECIAL POPULATIONS

Pregnancy: Risk Summary: There are no adequate and well controlled studies with loteprednol etabonate in pregnant women. Loteprednol etabonate produced teratogenicity at clinically relevant doses in the rabbit and rat when administered orally during pregnancy. Loteprednol etabonate produced malformations when administered orally to pregnant rabbits at doses 4.2 times the recommended human ophthalmic dose (RHOD) and to pregnant rats at doses 106 times the RHOD. In pregnant rats receiving oral doses of loteprednol etabonate during the period equivalent to the last trimester of pregnancy through lactation in humans, survival of offspring was reduced at doses 10.6 times the RHOD. Maternal toxicity was observed in rats at doses 1066 times the RHOD, and a maternal no observed adverse effect level (NOAEL) was established at 106 times the RHOD. 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 loteprednol etabonate by oral gavage on gestation days 6 to 18, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations at 0.1 mg/kg (4.2 times the recommended human ophthalmic dose (RHOD) based on body surface area, assuming 100% absorption). Spina bifida (including meningocele) was observed at 0.1 mg/kg, and exencephaly and craniofacial malformations were observed at 0.4 mg/kg (17 times the RHOD). At 3 mg/kg (128 times the RHOD), loteprednol etabonate was associated with increased incidences of abnormal left common carotid artery, limb flexures, umbilical hernia, scoliosis, and delayed ossification. Abortion and embryofetal lethality (resorption) occurred at 6 mg/kg (256 times the RHOD). A NOAEL for developmental toxicity was not established in this study. The NOAEL for maternal toxicity in rabbits was 3 mg/kg/day. Embryofetal studies were conducted in pregnant rats administered loteprednol etabonate by oral gavage on gestation days 6 to 15, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations, including absent innominate artery at 5 mg/kg (106 times the RHOD); and cleft palate, agnathia, cardiovascular defects, umbilical hernia, decreased fetal body weight and decreased skeletal ossification at 50 mg/kg (1066 times the RHOD). Embryofetal lethality (resorption) was observed at 100 mg/kg (2133 times the RHOD). The NOAEL for developmental toxicity in rats was 0.5 mg/kg (10.6 times the RHOD). Loteprednol etabonate was maternally toxic (reduced body weight gain) at 50 mg/kg/day. The NOAEL for maternal toxicity was 5 mg/kg. A peri-/postnatal study was conducted in rats administered loteprednol etabonate by oral gavage from gestation day 15 (start of fetal period) to postnatal day 21 (the end of lactation period). At 0.5 mg/kg (10.6 times the clinical dose), reduced survival was observed in live-born offspring. Doses ≥ 5 mg/kg (106 times the RHOD) caused umbilical hernia/incomplete gastrointestinal tract. Doses ≥ 50 mg/kg (1066 times the RHOD) produced maternal toxicity (reduced body weight gain, death), decreased number of live-born offspring, decreased birth weight, and delays in postnatal development. A developmental NOAEL was not established in this study. The NOAEL for maternal toxicity was 5 mg/kg.

Lactation: There are no data on the presence of loteprednol etabonate 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 LOTEMAX® SM and any potential adverse effects on the breastfed infant from LOTEMAX® SM.

Pediatric Use: Safety and effectiveness of LOTEMAX® SM in pediatric patients have not been established.

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in the chromosomal aberration test in human lymphocytes, or *in vivo* in the mouse micronucleus assay. Treatment of male and female rats with 25 mg/kg/day of loteprednol etabonate (533 times the RHOD based on body surface area, assuming 100% absorption) prior to and during mating caused preimplantation loss and decreased the number of live fetuses/live births. The NOAEL for fertility in rats was 5 mg/kg/day (106 times the RHOD).

Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

LSM.0091.USA.19
Based on 9669600-9669700 Revised: 02/2019

VOL. 156 NO. 5 ■ MAY 15, 2019

IN THE NEWS

The incidence and prevalence of **visual problems in acute stroke** is alarmingly high, affecting more than half of survivors. The prospective study found that **73% of 1,033 stroke survivor patients had visual problems**. The incidence of new-onset visual sequelae was 48% for all stroke admissions and 60% for all stroke survivors. The prevalence or incidence of visual problems was proportional to age at onset of stroke.

Rowe FJ, Hepworth LR, Howard C, et al. High incidence and prevalence of visual problems after acute stroke: an epidemiology study with implications for service delivery. PLoS One. March 6, 2019. [Epub ahead of print].

Researchers from the University of Florida found that **patients who had taken metformin had decreased odds of developing AMD**. The drug may have a therapeutic role in disease development or progression in those who are at risk. Metformin use was associated with an odds ratio of 0.58 and a 95% confidence interval. Further trials could prospectively investigate whether metformin has a protective effect in those at risk for developing AMD.

Brown EE, Ball JD, Chen Z, et al. The common antidiabetic drug metformin reduces odds of developing age-related macular degeneration. Invest Ophthalmol Vis Sci. 2019;60(5):1470-7.

The type of job you do may reflect your dry eye risk. Using data from a Netherlands population study, researchers found that **employees who work inside and log long hours in front of a computer** should be screened for symptomatic **dry eye**. People who worked in the agricultural industry and those employed in elementary occupations, such as cleaners, had the lowest risk of dry eye.

Bazeer S, Jansonius N, Snieder H, et al. The relationship between occupation and dry eye. Ocul Surf. April 2, 2019. [Epub ahead of print].

MG Expressibility, Lack of Obstruction Not the Same

Current therapies provide relief but do not address the loss of intraductal integrity.

By Mark De Leon, Associate Editor

Florida ophthalmologist Steven Maskin, MD, has developed a meibomian gland probing technique to assess obstructed glands that have been refractory to traditional treatments. A new study by Dr. Maskin—who has a commercial interest in devices used for this procedure—and his team looks at the probing technique's role in care and ways to improve the technology.

The study finds that targeting fixed, unyielding resistance and restoring intraductal integrity prevents progressive gland atrophy of nearby tissue. Also, expressible glands that are seemingly healthy were just as likely to have occult obstruction as non-expressible glands.

Researchers quantified probe findings of nearly 12,000 glands of 404 eyelids over a 34-month span. Of the glands, 84% showed mechanical resistance and 16% showed no resistance. Fixed, firm, focal unyielding resistance occurred in 79.5% of obstructed glands and nonfixed, nonfocal easily yielding soft resistance in 20.4%.

Researchers found no significant difference between mechanical resistance and fixed, unyielding resistance for lids between 0% and greater than 90% gland expressibility. Upper lids showed a greater incidence of both mechanical resistance and fixed, unyielding resistance. Soft resistance correlated with reduced expressibility, which researchers attributed to altered duct or duct contents.

These findings led researchers to believe that interventions to force meibum through fixed obstructions using pressure and heat could further elevate intraductal pressure and exacerbate inflammatory meibomian gland disease (MGD) and dry eye. The findings also suggest that early meibomian gland probing—before progression to whole-gland atrophy—could be beneficial because glands with expressible and non-expressible obstructive MGD have already developed fixed, unyielding resistance.

The study concludes that meibomian gland probing could enable more timely use of complementary procedures and therapies to provide optimal treatment of obstructive MGD.

Maskin SL, Alluri S. Expressible meibomian glands have occult fixed obstructions: findings from meibomian gland probing to restore intraductal integrity. Cornea. April 16, 2019. [Epub ahead of print].

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

essilor

GIVE YOUR PATIENTS THE BEST OF THEIR VISION

For many years, subjective refraction techniques have hardly changed.
The **Vision-R 800** phoropter ushers in a new era of refraction:

- More precise refraction, delivered by measurements up to 0.01 D
- Easier exam to perform, using unique algorithms to optimize the exam
- More comfortable experience for the patient due to smooth, continuous power changes

VISION-R™800
REINVENTING REFRACTION

ESSILOR INSTRUMENTS

855-393-4647 essilorinstrumentsusa.com info@essilorinstrumentsusa.com

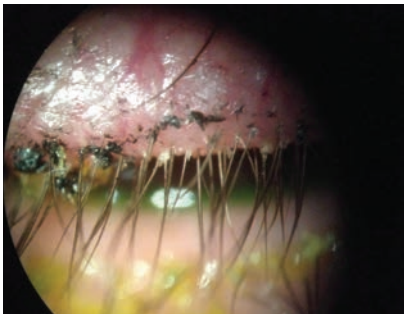
Lash Manipulation Better for *Demodex* Bleph

A better technique than eyelash removal, study says.

Lash manipulation may be a better technique than complete epilation for detecting *Demodex* blepharitis, a team of Irish researchers claims.

Investigators enrolled 107 subjects (428 eyelashes) and used a slit lamp biomicroscope to compare the quantity of *Demodex* folliculorum found first on a lash through manipulation and then on the same eyelash after epilation.

Researchers rotated individual eyelashes from each lid with sterile forceps *in situ* and counted the number of mites that emerged from each follicle. They then removed the same eyelash and noted the number found. While both techniques identified generally similar amounts of mites, the study found consistently higher quantities of *Demodex* folliculorum through the lash manipulation technique. The overall mean quantity of mites was also greater on eyelash manipulation (1.45 mites; range, 0 to 13) compared with the microscopic examination of the epilated eyelashes (0.81 mites; range, 0 to 16), the study noted.



Eyelash epilation alone often results in miscounting of *Demodex*.

The researchers also reported weak levels of agreement between the two methods for addressing the severity of infestation.

Eyelash epilation alone often results in miscounting because many *Demodex* mites will remain within the follicle even after the eyelash has been removed, the study reported.

Using eyelash manipulation without epilation was more comfortable for the patient. "This method was more accurate than epilation and microscopic examination for measuring quantity and assessing severity of infestation," the researchers wrote in their paper.

Murphy O, O'Dwyer V, Lloyd-McKernan A. The clinical use of eyelash manipulation in the diagnosis of demodex folliculorum blepharitis. Eye Contact Lens. April 2, 2019. [Epub ahead of print].

Peripheral Nonperfusion ID's Proliferative DR

A recent study found that peripheral ischemia is an important factor for proliferative changes in diabetic retinopathy (DR) and the presence of nonperfusion signifies the development of optic disc neovascularization.

The amount of retinal nonperfusion on fluorescein angiography also helps explain why some patients develop neovascularization only on the optic disc while others develop it elsewhere as the first manifestation of proliferative DR.

Researchers evaluated the association between retinal nonperfusion and DR severity on baseline ultra-widefield fluorescein angiograms in 92 patients: 59 in the proliferative group and 33 in the nonproliferative group. Regarding neovascularization location, 40 had it elsewhere and 19 had neovascularization of the optic disc with or without it elsewhere.

The study identified a retinal nonperfusion threshold of 118.3 disc areas (DA) with a specificity of 84.9% for proliferative DR. The median area of retinal nonperfusion was 67.8 DA in the nonproliferative DR eyes and 147.9 DA for eyes with proliferative changes. For peripheral nonperfusion, nonproliferative eyes measured 64.1 DA and proliferative eyes measured 130.6 DA. Eyes with neovascularization of the optic disc had the largest total area of retinal nonperfusion, with a difference of 65.1 DA compared with eyes with neovascularization only elsewhere.

Researchers suggest 118.3 DA as a possible threshold with a good specificity for the identification of proliferative changes. They also note that eyes with at least 107.3 DA of retinal nonperfusion are at risk for proliferative disease. The study concludes that identifying a threshold for the development of neovascularization is essential in eyes undergoing treatment. Cessation of treatment in eyes with more than 100 DA of retinal nonperfusion requires close observation.

Nicholson L, Ramu J, Chan EW, et al. Retinal nonperfusion characteristics on ultra-widefield angiography in eyes with severe nonproliferative diabetic retinopathy and proliferative diabetic retinopathy. JAMA Ophthalmol. April 11, 2019. [Epub ahead of print].

FRESHKOTE®

Preservative Free

LUBRICANT EYE DROPS

NEW and IMPROVED

FRESHKOTE® PF is now available— **preservative-free** in a multidose bottle

- For temporary relief of dry eye symptoms
- Unique phospholipid blend combats tear evaporation
- Gentle, preservative-free drops can be used with contact lenses
- Exclusive patented formulation
- State-of-the-art Novelia® multidose bottle dispenses drops with precision

For more information,
visit **FRESHKOTEPF.com**

NOW AVAILABLE
FROM
eyevance pharmaceuticals

FRE-004 12/2018

Anti-VEGF a Possible Solution for RVO

Effects temporary, as recurrent macular edema rids gains in visual acuity.

According to a new study from the Wilmer Eye Institute at Johns Hopkins University, patients with branch or central retinal vein occlusion (BRVO, CRVO) showed large improvements in best-corrected visual acuity (BCVA) after initiation of anti-VEGF injections; however, some visual gains were lost in many patients over time due to recurrent edema. Like AMD, both BRVO and CRVO are chronic diseases that require many years of injections in most patients.

The study prospectively recorded the number of anti-VEGF injections and improvements from baseline BCVA and central subfield thickness in 40 eyes of 39 CRVO patients and 50 eyes of 47 BRVO patients. Mean follow up was 58 and 78 months for BRVO and CRVO, respectively. Within six months of the last follow up, 58% of BRVO patients and 75% of CRVO patients required anti-VEGF injections to control edema.

For BRVO patients, their BCVA letter score increased by a mean of 24 from a baseline of 52 (20/100) to a peak of 76 (20/32) and subsequently decreased to 63 (20/50) at the final visit. CRVO patients gained a mean of 26 letters, from a baseline of 48 (20/100) to a peak of 74 (20/32) and subsequently decreased to 56 (20/80) at last follow up.

Recurrent macular edema and the related foveal damage caused any loss from peak BCVA. Researchers noted that loss of peak vision occurred in almost all patients. While it was greater in those with poor visual outcomes, it still occurred in patients with good ones too.

Researchers suggest suppression of VEGF as an alternative approach to frequent injections to try and avoid recurrent edema. The vast majority of patients with RVO would benefit from a durable, sustained delivery treatment. Only 14% of BRVO patients and 20% of CRVO patients had edema resolution without a large number of injections. Therefore, after proof-of-concept is obtained for new treatments that provide sustained suppression of VEGF in patients with neovascular AMD, the researchers find it reasonable to test them in patients with RVO as well.

Iftikhar M, Mir TA, Hafix G, et al. Loss of peak vision in retinal vein occlusion patients treated for macular edema. Am J Ophthalmol. April 4, 2019. [Epub ahead of print].

Video Imaging Captures Aqueous Flow

Aqueous outflow is a prime target of glaucoma therapy. However, visualizing this process can be challenging. Most *in vivo* techniques are static, invasive or involve some manipulation of physiological parameters. An international team of researchers from the United Kingdom and Australia has developed a non-invasive technology that might help: hemoglobin video imaging (HVI).

To test the technology, they added HVI to a typical clinical visit for patients at the Addenbrookes Hospital Glaucoma clinic. They viewed 30 eyes for a prospective, observational study to characterize aqueous veins and eight eyes slated for selective laser trabeculoplasty (SLT) for a pilot prospective interventional feasibility study. The team assessed the change in cross sectional area of the aqueous column within the episcleral veins and compared that with both intraocular pressure (IOP) reduction and change in visual field mean deviation before and after intervention.

HVI provided the researchers direct visualization of the aqueous flow. They noted the flow is "pulsatile" and fluctuates based on globe pressure and compression of the aqueous vein.

After SLT, HVI revealed an increase in the aqueous column, which correlates with a decrease in IOP and an improvement in the visual field mean deviation.

The researchers note the new technology could be added to a routine examination, allowing clinicians to assess and quantify aqueous outflow in real time. "It has the potential to be used to help target therapeutic interventions to improve aqueous outflow and further advance our understanding of aqueous outflow dysregulation in the pathogenesis of glaucoma," they concluded. ■

Khatib TZ, Meyer PAR, Lusthaus J, et al. Haemoglobin video imaging provides novel in vivo high-resolution imaging and quantification of human aqueous outflow in glaucoma patients. Ophthalmology Glaucoma. April 5, 2019. [Epub ahead of print].

DID YOU KNOW?

KEELER

has slit lamps!

For over 100 years, we have been creating innovative products. The Keeler slit lamp is one of them – designed with you and your patients in mind. The KSL delivers a visually pleasing, customizable device equipped with excellent, high-quality optics.

SLIT LAMP FEATURES

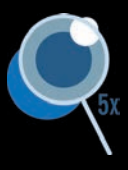
Sharp & clear Keeler Optics

KSL-H series: tower illumination

KSL-Z series: lower illumination

Digital-ready & full digital units

3x magnification drum (10x, 16x, 25x)



5x magnification drum (6x, 10x, 16x, 25x, 40x)

Unique 1mm square for Uveitis evaluation

Bright & white LED illumination

We also carry portable slit lamps!

VISIT OUR WEBSITE FOR MORE PRODUCT DETAILS

www.keelerusa.com / 800-523-5620

Keeler

COMING 2019

Open your eyes to what's on the horizon in dry eye.

Sign up for updates at **TearCare.com**

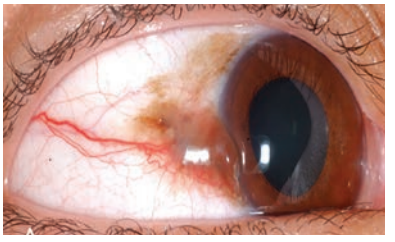
TearCare is indicated for the application of localized heat when the current medical community recommends the application of a warm compress to the eyelids. Such applications would include Meibomian Gland Dysfunction (MGD), Dry Eye, or Blepharitis.

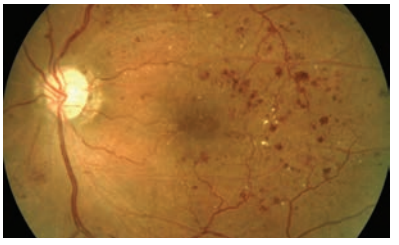
Contents

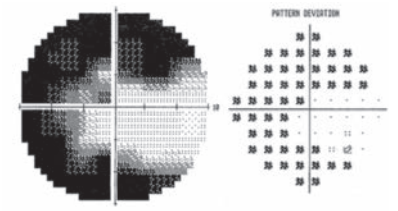
Review of Optometry May 15, 2019

20TH ANNUAL DRY EYE REPORT

ALSO INSIDE

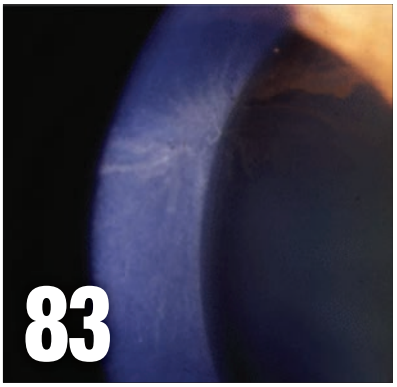


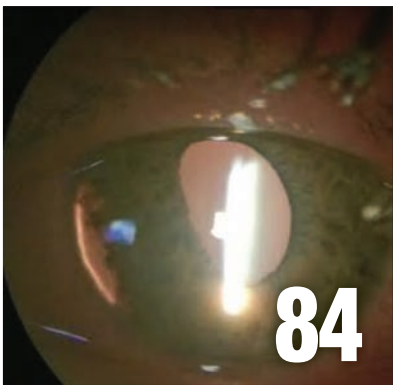


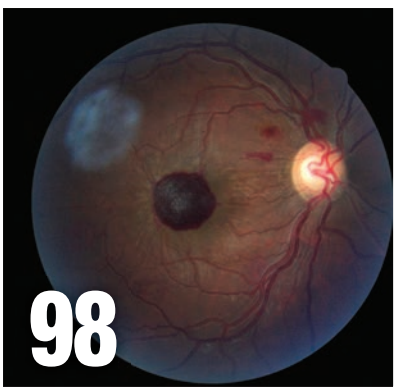


Departments

Review of Optometry May 15, 2019







REVIEW OF OPTOMETRY

BUSINESS OFFICES
11 Campus Blvd., Suite 100
Newtown Square, PA 19073

CEO, INFORMATION SERVICES GROUP
Marc Ferrara
(212) 274-7062 • mferrara@jobson.com

PUBLISHER
James Henne
(610) 492-1017 • jhenne@jobson.com

REGIONAL SALES MANAGER
Michele Barrett
(610) 492-1014 • mbarrett@jobson.com

REGIONAL SALES MANAGER
Michael Hoster
(610) 492-1028 • mhoster@jobson.com

VICE PRESIDENT, OPERATIONS
Casey Foster
(610) 492-1007 • cfoster@jobson.com

VICE PRESIDENT, CLINICAL CONTENT
Paul M. Karpecki, OD, FAAO
pkarpecki@jobson.com

PRODUCTION MANAGER
Scott Tobin
(610) 492-1011 • stobin@jobson.com

SENIOR CIRCULATION MANAGER
Hamilton Maher
(212) 219-7870 • hmaher@jhihealth.com

CLASSIFIED ADVERTISING
(888) 498-1460

SUBSCRIPTIONS
$56 a year, $88 (US) in Canada,
$209 (US) in all other countries.

SUBSCRIPTION INQUIRIES
(877) 529-1746 (US only)
Outside US Call: (845) 267-3065

CIRCULATION
PO Box 81
Congers, NY 10920
Tel: (Toll Free): (877) 529-1746
Outside US: (845) 267-3065

jmi

CEO, INFORMATION SERVICES GROUP
Marc Ferrara

SENIOR VICE PRESIDENT, OPERATIONS
Jeff Levitz

VICE PRESIDENT, HUMAN RESOURCES
Tammy Garcia

VICE PRESIDENT, CREATIVE SERVICES & PRODUCTION
Monica Tettamanzi

CORPORATE PRODUCTION DIRECTOR
John Anthony Caggiano

VICE PRESIDENT, CIRCULATION
Emelda Barea

DO YOUR DRY EYE PATIENTS WEAR CONTACTS?

Dry eyes are one of the most common reasons patients discontinue wearing contact lenses[1]

73%

OF CONTACT LENS WEARERS WERE DISSATISFIED OR DISCONTINUED USE **BECAUSE OF DRY EYE SYMPTOMS**[2]

Based on a survey of 730 contact lens wearers (n=730)

For patients who wear contact lenses, **screening for Dry Eye Disease is considered optimal**[1]

References:

1. TFOS DEWS II Research Subcommittee. Report of the Research Subcommittee of the Tear Film & Ocular Surface Society Dry Eye WorkShop II (2017). *Ocul Surf.* 2017;15(3):269-275.
2. Richdale K, Sinnott LT, Skadahl E, Nichols JJ. Frequency of and factors associated with contact lens dissatisfaction and discontinuation. *Cornea.* 2007;26(2):168-174.

Shire

REVIEW OF OPTOMETRY

PRINTED IN USA

FOUNDING EDITOR, FREDERICK BOGER
1891-1913

EDITORIAL OFFICES
11 CAMPUS BLVD., SUITE 100
NEWTOWN SQUARE, PA 19073

SUBSCRIPTION INQUIRIES
1-877-529-1746

CONTINUING EDUCATION INQUIRIES
1-800-825-4696

EDITOR-IN-CHIEF • JACK PERSICO
(610) 492-1006 • JPERSICO@JOBSON.COM

MANAGING EDITOR • REBECCA HEPP
(610) 492-1005 • RHEPP@JOBSON.COM

SENIOR EDITOR • BILL KEKEVIAN
(610) 492-1003 • BKEKEVIAN@JOBSON.COM

ASSOCIATE EDITOR • CATHERINE MANTHORP
(610) 492-1043 • CMANTHORP@JOBSON.COM

ASSOCIATE EDITOR • MARK DE LEON
(610) 492-1021 • MDELEON@JOBSON.COM

SPECIAL PROJECTS MANAGER • JILL HOFFMAN
(610) 492-1037 • JHOFFMAN@JOBSON.COM

ART DIRECTOR • JARED ARAUJO
(610) 492-1032 • JARAUJO@JOBSON.COM

DIRECTOR OF CE ADMINISTRATION • REGINA COMBS
(212) 274-7160 • RCOMBS@JOBSON.COM

EDITORIAL BOARD

CHIEF CLINICAL EDITOR • PAUL M. KARPECKI, OD

ASSOCIATE CLINICAL EDITORS • JOSEPH P. SHOVLIN, OD; ALAN G. KABAT, OD; CHRISTINE W. SINDT, OD

DIRECTOR OPTOMETRIC PROGRAMS • ARTHUR EPSTEIN, OD

CLINICAL & EDUCATION CONFERENCE ADVISOR
PAUL M. KARPECKI, OD

CASE REPORTS COORDINATOR • ANDREW S. GURWOOD, OD

CLINICAL CODING EDITOR • JOHN RUMPAKIS, OD, MBA

CONSULTING EDITOR • FRANK FONTANA, OD

COLUMNISTS

CHAIRSIDE • MONTGOMERY VICKERS, OD

CLINICAL QUANDARIES • PAUL C. AJAMIAN, OD

CODING CONNECTION • JOHN RUMPAKIS, OD

CORNEA & CONTACT LENS Q+A • JOSEPH P. SHOVLIN, OD

DIAGNOSTIC QUIZ • ANDREW S. GURWOOD, OD

THE ESSENTIALS • BISANT A. LABIB, OD

FOCUS ON REFRACTION • MARC TAUB, OD; PAUL HARRIS, OD

GLAUCOMA GRAND ROUNDS • JAMES L. FANELLI, OD

NEURO CLINIC • MICHAEL TROTTINI, OD; MICHAEL DELGIODICE, OD

OCULAR SURFACE REVIEW • PAUL M. KARPECKI, OD

RETINA DILEMMAS • DIANA L. SHECHTMAN, OD; JAY M. HAYNIE, OD

RETINA QUIZ • MARK T. DUNBAR, OD

REVIEW OF SYSTEMS • CARLO J. PELINO, OD; JOSEPH J. PIZZIMENTI, OD

SURGICAL MINUTE • DEREK N. CUNNINGHAM, OD; WALTER O. WHITLEY, OD, MBA

THERAPEUTIC REVIEW • JOSEPH W. SOWKA, OD; ALAN G. KABAT, OD

THROUGH MY EYES • PAUL M. KARPECKI, OD

URGENT CARE • RICHARD B. MANGAN, OD

JOBSON MEDICAL INFORMATION LLC

Outlook

By Jack Persico, Editor-in-Chief

The Unkindest Cut

A leading surgical society uses its antipathy toward optometry as a selling point, limiting its own prospects.

The year is 2025. Ten states permit optometrists to perform laser procedures like SLT and posterior capsulotomy, and 23 have given ODs the right to excise lid lesions. Use of injectable drugs is widely permitted and collagen crosslinking is the hot new growth opportunity. All across America, optometrists are using lasers, blades and syringes routinely and uneventfully. The scare-tactic stories the medical lobby once used to push back against optometric progress proved to be just that—stories.

Will the next six years play out like this? Hard to say. Prediction is difficult, especially about the future, Niels Bohr famously said. But reading that the American Society of Cataract and Refractive Surgery (ASCRS) has rebranded around advocacy for ophthalmologists got me thinking about the above scenario and the missed opportunity this shift represents.

Most optometrists are still prohibited from becoming members, or attending meetings, of the leading organization for anterior segment surgery; only ODs who work for an ophthalmologist are eligible to play even a limited role in ASCRS. The best source of education on ocular surgeries turns a blind eye to those who arguably need it most, doing a disservice to pretty much everyone, even its own core group of ophthalmic surgeons. Find me a cataract surgeon who doesn't want to offload pre- and post-op care so they could increase their procedure volume.

Optometry's legislative infrastructure will only continue to strengthen. Too many inescapable trends point toward it. They're so well known they hardly bear repeating, but the consequences of growth among both elderly patients and optometrists, while ophthalmology's numbers stagnate, aren't hard to suss out.

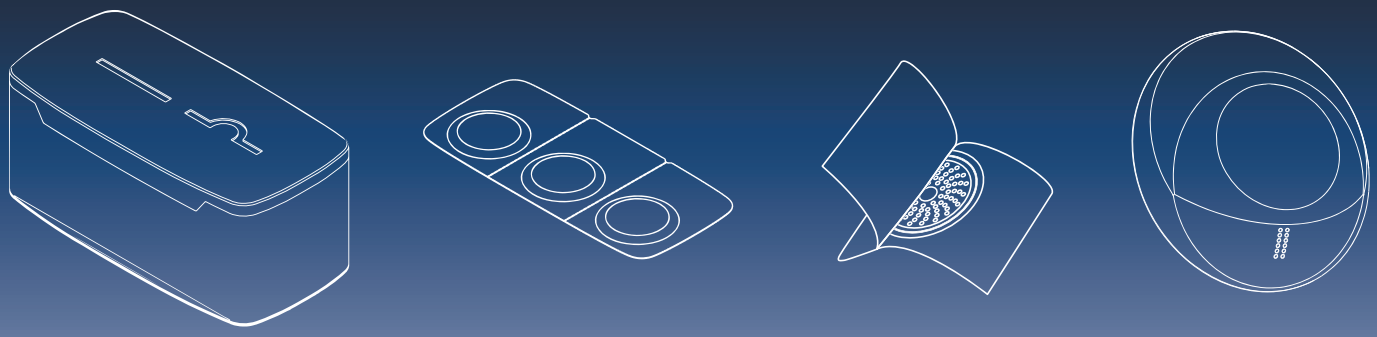
Granted, editors fixate on semantics more than most people but I've always thought the American Society of Cataract and Refractive *Surgery*, a name that makes no mention of ophthalmologists, had a unique opportunity to bridge the OD-MD divide. The powers that be could have interpreted that broadly enough to include optometrists, selling it to their established members as a way to help them gain referrals.

Instead, ASCRS saw the future—and flinched, reflexively retreating to its base. At its recent annual meeting, the group unveiled a new slogan: "For Surgeons. For You." The press release explains that "ASCRS is eager to advance its reputation as the home to all anterior segment surgeons at every career stage and across all associated subspecialties."

Psst, ASCRS: optometrists are anterior segment surgeons now, too. Not all by a long shot, and their work is limited to a handful of office-based procedures, but a good number of ODs already fit the bill and their ranks will only grow. Trouble is, yours won't.

And so once again a chance for mutual benefit between the professions goes wanting. Better luck next time. All eyes on you, American Glaucoma Society. Who do you think will benefit most from all those new AI-powered diagnostic technologies in the pipeline? ■

Now Available!



EASY, CLEAN, PORTABLE.

A Unique Approach to Daily Disposable Soft Toric Lenses

The 1day Miru Toric flat pack is designed using SmartTouch™ Technology which minimizes lens handling and contamination concerns so contact lenses can be worn more comfortably and hygienically.

1day Miru toric employs a unique Smart Fit™ design that naturally orients the lens correctly no matter which way it is inserted.

For a trial pair, please email information@menicon.com

Menicon

Miru 1day Menicon Flat Pack

Add Billions to Optometry

Managing dry eye can be a huge opportunity for your contact lens patients—and practice. **By Paul M. Karpecki, OD, Chief Clinical Editor**

More than 30 million people in the United States have dry eye disease (DED), which may be the single greatest opportunity in medical eye care.[1] But I'm not talking about treating dry eye patients specifically—even though this is critical, too—I'm referring to contact lens practices.

The Drop Out Rate

About 45 million Americans wear contact lenses, and up to 24% drop out each year.[2,3] Assuming conservative numbers, that's about 10 million people a year. A practice generates an annual income of about $330 per contact lens patient. So a loss of 10 million patients a year is a loss of $3.3 billion for the profession.

Imagine how much more we could thrive by trimming that dropout rate. The key isn't a focus on the money, it's a focus on what's really important: the patient. These patients want to stay in their lenses and don't want to develop chronic and progressive conditions such as DED.

A Better Exam

Uncovering early diagnostic clues is crucial for mitigating contact lens dropout. If a patient fully discontinues lens wear, it's difficult to get them back into their lenses; but, if you catch them at an early stage, you can address the problem and keep them happy in their contact lenses.

For starters, ask patients the right questions. Knowing they have end-of-day discomfort, fluctuating vision, burning, watering, dryness or irritation is the first clue to a problem. How long they spend on digital devices and whether they feel the urge to use, or are using, rewetting drops or artificial tears are also important.

Next, express the meibomian glands or obtain meibography. Most dry eye associated with lens wear is evaporative, and pushing on the lower eyelid can quickly determine its presence. The longer you allow meibomian glands to obstruct, the greater the likelihood of inflammation and atrophy—the more gland loss, the harder it will be to get patients back in contact lenses.

Don't Wait to Manage

If signs and early symptoms are present, address both the contact lens technologies and the DED/meibomian gland dysfunction (MGD).

Contact lenses. Today's advancements include daily disposable lenses and better modulus/Dk silicone hydrogels and water gradient designs. Find lenses that retain more than 90% of their moisture or water content after 12 to 16 hours. If patients don't want a daily disposable, consider recommending solutions with hyaluronic acid or preservative-free hydrogen peroxide.[4] Artificial tears that work well with contact lenses can help with comfort during the day.

Disease management. These simple steps may delay dropout, but they won't stop it. To give your patient the best chance at staying in contact lenses, address the underlying DED/MGD by treating three key components: biofilm, obstructed meibomian glands and inflammation.

For biofilm, the ideal treatment is belpharoexfoliation, lid scrubs or a combination of both. For MGD, consider thermal pulsation/expression and hydrating compresses. Research shows thermal pulsation can increase contact lens wear by as much as four hours.[5] Another study found a hydrating compress increased contact lens wear time by 3.5 hours.[6] For the inflammation, I have found topical treatment (lifitegrast or cyclosporine) works best, in addition to oral omega fatty acid supplementation and, potentially, doxycycline in advanced cases. In the end, your patient will have better contact lenses and use hydrating compresses, lid scrubs and omega fatty acids daily. That's not much to prevent a chronic, progressive, life-interrupting condition.

Not only is it worth it to patients, it's also worth it for our profession to the tune of about $3 billion a year. ■

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

1. Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthal. 2014;157(4):799-806.
2. Cope JR, Collier SA, Nethercut H, et al. Risk behaviors for contact lens–related eye infections among adults and adolescents—United States, 2016. MMWR Morb Mortal Wkly Rep. 2017;66(32):841-5.
3. Richdale K, Sinnott LT, Skadahl E, Nichols JJ. Frequency of and factors associated with contact lens dissatisfaction and discontinuation. Cornea. 2007;26(2):168-74.
4. Rah MJ, Merchea MM, Doktor MQ. Reducing dropout of contact lens wear with Biotrue multipurpose solution. Clin Ophthalmol. 2014 Jan 24;8:293-9.
5. Blackie C. A single vectored thermal pulsation treatment for meibomian gland dysfunction increases mean comfortable contact lens wearing time by approximately 4 hours per day. Clin Ophthalmol. 2018:12:169-83.
6. Ablamowicz AF, et al. The effect of the Bruder moist heat eye compress on contact lens discomfort in contact lens wearers. University of Alabama, Birmingham. 2018.

Dry Eye Disease

Many symptoms…
multiple solutions…
one company

Katena offers a broad range of solutions from the beginning to the end stage of dry eye treatment

- **Warm compress and lid hygiene - Fire and Ice Mask**
- **Punctal occlusion - EagleVision punctal plugs**
- **Meibomian gland expressors**
- **Amniotic membrane grafts - AmbioDisk™**

For more information on Katena's full line of dry eye solutions visit us at www.katena.com

800.225.1195•info@katena.com•www.katena.com

katena
DESIGNED FOR SIGHT®

KX-Adv-012419-Rev0

The Time March is On

It's not all bad. I've been doing this for 40 years now and I've survived—you can, too.

By Montgomery Vickers, OD

I'll never forget my first day practicing optometry without a preceptor or resident leaning over my ignorant shoulder. Mostly, I remember how clueless I was. The next thing I know, I'm zipping out to my 40th year in private practice. The question is this: What happened in between?

Let's break the history of our lives in optometry down to easily digestible bites. Your journey is different than mine, but some things are universal, so I think you'll see yourself in here somewhere.

The First 10 Years

A lot happens in these initial years of practice. They are marked by an unsteady progression that starts with eating macaroni and fish sticks while counting your last $10 that has to last you and the family for another two weeks until the next pay day. Later, you move up to pizza night when you come home to screaming, starving kids—or at least a screaming, starving you.

Then, one day when you least expect it, you realize you have enough money in the bank to splurge on a night out with friends or your spouse, except you need new tires on the minivan instead.

By now in your practice, you have a patient base of folks who, for the most part, love and support you (a few will never forgive you for that air puff test). Fortunately, you finally have a clue how to take care of them. And yes, it takes that long to figure it out.

The Next 10

Your next years of practice are an amazing blur. You know just what to do to help almost any patient, and you trade your education debt for a new house and car, both of which finally have working air conditioners. If you are blessed with children, they slide into the teen years. The bad news is, they think you are an idiot. The good news is, at the end of the day, you kinda are, especially when it comes to your kids' teen years.

Your practice has grown and has a life of its own, sort of like Godzilla; both Godzilla and your practice will happily devour you unless you carve out time to make the healthy choice of hiding under your bed from time to time.

30 Years and Counting

Before you know it, you have been in practice for more than 30 years. At CE meetings, young optometrists think you know way more than you do, so they show their respect by only talking smack about you when you are not around.

I am at the 40-year mark in optometry. My 40th class reunion is right around the corner, and while we used to reserve a basketball court and 50 pounds of chicken for everyone who attended, we can now feed everyone who has survived with seven loaves of bread and a few fish.

I have seen just about every advancement that's come and gone in our profession. I now carry a computer around in my pocket just like you. My office technology is so great that my brain has become a vestigial organ—not necessarily a bad thing, because I have rerouted my brain's blood flow to my taste buds. This reminds me… despite my cholesterol and triglycerides, I look back fondly on my macaroni-and-cheese and pizza decades.

Time is relentless, but there is only one alternative to birthdays. So learn, smile and enjoy your decades, colleagues. ■

The POWER of the PULSE

Advanced Doctor Treatment for Anterior Blepharitis*

Optometry's Meeting® Show Special - $1,495 for the AB Max™ Starter Kit

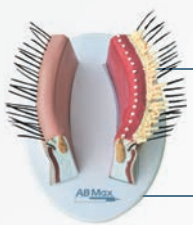
MAXimize Your Algerbrush** Investment

The advanced technology of the PATENT PENDING AB Max™ works seamlessly with your Algerbrush, transforming it into a multi-purpose device.

- Delivers PULSE action for more efficient and rapid debridement
- Treatment of the same conditions as a standard Algerbrush PLUS Anterior Blepharitis
- Removal of even the most tenacious scurf and debris
- Advanced Anterior Blepharoexfoliation
- BETTER treatment outcomes with HIGHER PROFITS
- Affordable Anterior Blepharoexfoliation
- 5X faster return on your investment
- Add $100,000 to your bottom line WITHOUT a major investment

AB Max™

www.AB-Max.com • 800-721-8006



Come see us during Optometry's Meeting® Booth #624 and ask how you can receive a FREE anatomical eyelid model

**Anterior blepharitis means blepharitis on the outer eyelid margin, including the eyelashes. **Algerbrush is a trademark of The Alger Companies. Myco Industries, Inc. is not affiliated with The Alger Companies. Patents pending Myco Industries, Inc. For use by medical professionals only.*

To Be Blunt

A calm, thorough evaluation of ocular trauma can determine the best course of action. **Edited by Paul C. Ajamian, OD**

Q A 70-year-old woman was walking her dog and tripped, landing on the left side of her face. What are some things I should think about before sending her to an orbital specialist?

A Orbital trauma can be overwhelming on initial presentation; however, breaking down your evaluation by ocular structure can help to focus your management," says Paige Thompson, OD, of SouthEast Eye Specialists in Chattanooga, TN. Initially, doctors should obtain a visual acuity measurement, assess pupillary function and evaluate the patient's extraocular motilities.

If visual acuity is reduced or an afferent pupillary defect is noted, investigate the underlying cause. Assess extraocular motilities to rule out any restriction or pain on eye movement, which may occur secondary to periorbital edema or orbital fracture.

Next, evaluate the orbits and adnexa for edema and ecchymosis. With palpation of the orbital rim, rule out focal tenderness and hypoesthesia, which may be associated with orbital fracture. Manage lid edema and bruising with cool compresses and head elevation. Rule out any conjunctival lacerations, corneal abrasions, or penetrating injuries.

"If a patient is found to have a ruptured globe, stop your exam, avoid applying any pressure to the eye and cover the patient's eye with a protective shield," Dr. Thompson says. Refer these patients immediately to a level one trauma center for appropriate management. Evaluate and treat the anterior chamber for traumatic hyphema, iritis or any combination.

Evaluate a patient who experienced ocular trauma by using a stepwise approach.

"Evaluate the lens to rule out phacodonesis or lens subluxation," says Dr. Thompson. "If the patient is found to have a subluxated lens, refer to a skilled cataract surgeon for evaluation and management."

Lastly, perform a dilated fundus examination to rule out commotio retinae, a common finding of whitening of the retinal tissue which typically resolves on its own within two weeks. Other potential posterior segment findings include retinal detachment, vitreous hemorrhage and traumatic optic neuropathy.

Orbital Fractures

Ultimately, an optometrist can appropriately manage many sequelae of ocular trauma. The main indication to refer to an orbital specialist would be with concern for orbital fracture, according to Dr. Thompson. An orbital fracture is most likely to occur in the orbital floor, followed by the medial orbital wall and commonly causes restricted upgaze, secondary to entrapment of the inferior rectus in the orbital floor.

If an orbital fracture is suspected, send the patient for neuroimaging to confirm the diagnosis with a CT scan, the preferred modality in traumatic cases. Specifically, axial views are preferred for evaluation of the orbital rim, and coronal views are ideal for detecting orbital floor fractures and muscle entrapment.

"Educate these patients to avoid nose blowing and valsalva maneuvers to prevent potential cellulitis," says Dr. Thompson. Most orbital fracture repairs are not emergency situations. The surgeon will typically wait for resolution of periorbital edema prior to surgical intervention. Treat orbital fractures emergently only in the case of muscle entrapment to prevent ischemia and persistent diplopia.

"We evaluated and diagnosed our patient with periorbital edema and ecchymosis," Dr. Thompson says. All other exam findings were unremarkable. She and her team conservatively managed the patient with cool compresses, and the patient's contusions and edema resolved over several weeks without any further sequelae. "Next time you evaluate a patient with blunt trauma, relax and examine the patient with a stepwise approach to determine if a referral is truly necessary," Dr. Thompson adds. ■

Analysis of Site Selection.

5 STEPS TO HELP GUIDE YOU ALONG TO A SUCCESSFUL AND STRESS FREE OPENING.

Did you know that building your new office will most likely be the single largest investment you will make for your practice? Taking the proper steps can make a big difference between success and possible failure.

Most of us have a limit on how much we can invest or borrow to fund this project, so it is very important that this process goes smoothly to minimize any costly delays or overages.

To do this, I suggest that you follow this simple "5 step" process that will help guide you along to a successful and stress free opening. Take the time prior to committing to the project to get organized and avoid as many obstacles as possible.

STEP 1: Determine the Needs of the Practice

Think about what your practice will need in order for it to flourish now, as well as in the future. Also look at both patient areas (testing rooms, exam rooms, optical, etc.) and non-patient areas (offices, conference and lounge areas, etc.) to make sure all of your needs are met.

Certain industry specialists are familiar with this process and can help guide you. In fact, Eye Designs, a leading design and display firm, offers a very detailed "Planning Survey" on their website to help you cover all of your bases.

STEP 2: How Much Space Will I Need

It is important to determine the correct amount of space for your new office. Not only should it meet your current needs, but it should include some room for future growth. It's also important that you factor in space for circulation aside from the actual room sizes when calculating office size. Finally, be sure you check the usable "net square footage" that you are committing to compared to what the landlord is actually giving you. In many cases you will actually be billed for common area spaces as well as your own space.

STEP 3: Who Do You Want To Be

Certain practices choose to have a more clinical image, while others want to maximize the retail experience for their patients, so knowing who you want to be is important in selecting a site. If you desire a strong retail presence that has strong "walk-by" or "drive-by" traffic then a strip mall may be best suited for you. If you want a more conventional clinical office, consider locating in a free standing building or a medical building, which may better suit your needs.

Example of displays & design by industry specialist the Eye Designs Group.

STEP 4: Site Selection

Before you sign on the dotted line be sure you've done your due diligence on the prospective location. Search local records for area demographic information to make sure you are targeting your desired patient profile and they have access to your practice. Other things to consider; who are the large employers in the area, as well as are there significant residential and commercial developments planned for the future. Finally, don't forget to scout out the local competition to ensure the area is not over saturated with ECPs.

STEP 5: Building Your Team

One of the most important elements of a successful new office is having a strong team to help you build your new office. A strong team will usually consist of an industry design specialist, who knows your business in both the retail and clinical areas. Also, a local architect who is familiar with the local codes can help expedite the process. A "recommended" and "proven" quality contractor is key to keep you on time and on budget. Your accountant, banker and real estate attorney are important to make sure you are receiving the most competitive and manageable deal. Finally, don't forget to discuss your new building with your vendors and peers. Your vendors can share detailed product information, which may effect the design and use of space. Meanwhile, always seek advice from your peers who have taken this journey, since they can share their own experiences to help you avoid any pitfalls that they had.

In closing, take the proper steps to plan your new office to help you avoid costly time delays and cost overruns. Specifically, follow this "5 step" program and your path to a new office will be manageable and organized, which will help you deliver a better patient and customer experience.

For more information contact the author:

Richard Winig
President / Senior Designer
Eye Designs LLC
www.eyedesigns.com
800.346.8890

Richard has over 25 years experience designing successful optical environments and has been a featured speaker at many industry events.

What Snellen Ain't Tellin'

Contrast sensitivity testing can help identify visual changes an acuity test might miss.

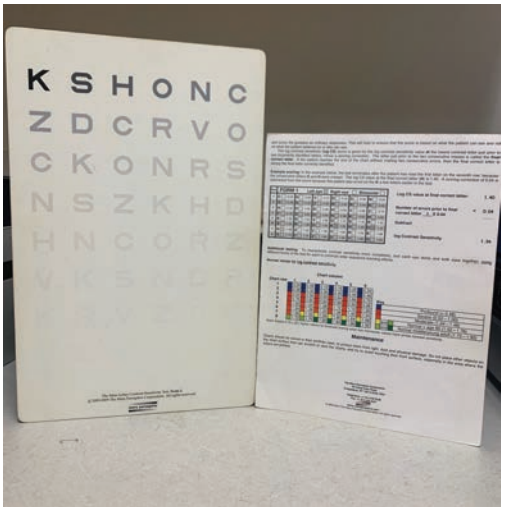
By Bisant A. Labib, OD

Oftentimes in practice, we encounter patients who subjectively report changes to their vision—but we then check their acuities and find no measurable difference in Snellen acuity. In these cases, we should consider an alternative measurement of vision quality: contrast sensitivity (CS). This brief, cost-effective screening tool can help us reveal factors relevant to their overall quality of vision.

Measuring visual acuity alone, using black letters on a white background, may not be completely representative of a patient's ability to perform their normal activities of daily living. There is also evidence that CS testing can provide early detection of ocular diseases, even before visual acuity or other entrance tests are affected.[1]

CS is defined as the capability of perceiving minimal luminance changes between objects and areas, or the ability to differentiate two objects from each other and the background.[1,2] CS testing measures the ability to discern patterns across a range of spatial scales and is implicated in several prevalent ocular diseases, such as amblyopia, glaucoma, diabetic retinopathy, cataracts and macular degeneration.[3]

Patients with affected CS will report trouble seeing street signs in the rain or fog, or greater difficulty reading the newspaper in the setting of normal or unchanged visual acuity.[2,4] There are several factors that affect CS, both in regards to the limits of normal human vision as well as the effect of ocular disease processes, discussed below.



The Mars letter contrast sensitivity test uses optotypes in decreasing contrast.

Light Scatter

The medium through which light normally travels contains numerous invisible particles suspended at various concentrations, causing light to scatter when encountering them. The greater the amount of light that is scattered, the less light is available to form a clear, distinct image with detailed contrast. This is the reason, for example, why it is more difficult to read street signs in rain or fog compared with a clear day.

The eye itself may also contribute to the increase in light scatter, such as in the presence of media opacities. A patient with a cataract will perceive a greater degradation in image quality and contrast due to the increase in light scatter by the hazy ocular media.[1,2] This is why patients with cataracts will report glare and yet normal visual acuity could be unaffected.[5] The same is true of patients who have undergone refractive surgery and report visual differences in the setting of good visual acuity.[1,2]

Retinal Photoreceptors

The angle that light hits the photoreceptors in the retina affects their response. For example, photoreceptors are most sensitive to light rays that strike them perpendicularly. This is known as the Stiles-Crawford effect and is the reason that light rays traveling through the pupil center form a clearer retinal image than those of the periphery. Also, if the orientation of the photoreceptors themselves is disrupted, such as in retinal diseases, the quality of the perceived retinal image is also diminished. An example of this would be age-related macular degeneration.[2]

Retinal and Neural Information Processing

The macula contains the highest number of cones which are responsible for fine, detailed acuity. Each cone contains blue, red or green pigment. When light strikes the cone photoreceptors, it is converted

into a neurochemical signal that is passed on to the inner retinal cells, first the bipolar and then ganglion cells. Each ganglion cell contains a receptive field made up of a varying number of bipolar cells, with the highest concentration at the fovea.

This process and anatomical variation is responsible for image information that is relayed to the visual cortex for processing through the optic nerve and perceived visual stimuli.[2]

As we are already aware, glaucoma is a disease that targets the retinal ganglion cells and optic nerve. As such, damage to these structures has a direct impact on vision. Since peripheral vision is first affected in early glaucoma, patients who report blur or affected central vision are more likely to be describing CS rather than reduced Snellen visual acuity.

Visual ability in low illumination and reduced contrast are important functions in daily life of patients with peripheral vision loss due to glaucoma.[6] Evidence suggests that recording CS in early glaucoma patients where central vision is not yet affected, or in very late stages where visual field defect progression is difficult to measure, can be beneficial in monitoring progression of the disease.[7]

Measuring and Managing

Though there is evidence regarding the effect of CS on image quality and visual function, there has yet to be a gold standard method of measuring CS in the clinical setting.[2] Options include printed charts as well as computerized methods. Generally, gratings or optotype targets at varying levels of spacing or contrast are used in these tests.

The Pelli-Robson letter sensitivity chart is a common chairside test at distance that uses letters of the same size in order of decreasing contrast.[2,4] The small-letter contrast test also uses rows of letters in decreasing contrast, but luminance is measured with a standard photometer. CS tests using the grating methods include the functional acuity contrast test and the VCTS 6500.[2]

In the event that a patient does suffer from reduced CS, many management options are available depending on their goals and affected activities of daily living. Something as simple as a referral for a lighting evaluation could offer great benefit for patients suffering from glare. The use of closed-circuit television aids or computer/smart phone apps or features to enhance contrast on their devices or displays are also a good option. These patients may also benefit from the use of filters and orientation and mobility services.[4]

With these options readily available, CS testing should be considered for patients with subjective visual complaints that do not match Snellen visual acuity to improve overall quality of vision and life. ■

1. Kara S, et al. Repeatability of contrast sensitivity testing in patients with age-related macular degeneration, glaucoma, and cataract. Arq Bras Oftalmol. 2016;79(5):323-7.
2. Amesbury EC, Schallhorn SC. Contrast Sensitivity and Limits of Vision. International Ophthalmology Clinics. 2003;43(2):31-42.
3. Thurman SM, Davey PG, McCray KL, et al. Predicting individual contrast sensitivity functions from acuity and letter contrast sensitivity measurements. J Vision. 2016;16(15):1-15.
4. Brilliant, Richard L. Essentials of Low Vision Practice. Butterworth-Heinemann, 1999.
5. Shandiz FH, Derakhshan A, Daneshyar A, et al. Effect of cataract type and severity on visual acuity and contrast sensitivity. J Ophthalmic Vis Res. 2011;6(1):26-31.
6. Bambo MP, Ferrandes B, Guerri N, et al. Evaluation of contrast sensitivity, chromatic vision, and reading ability in patients with primary open angle glaucoma. J Ophthalmol. 2016;2016:7074016.
7. Fatehi N, Nowroozizadeh S, Henry S, et al. Association of structural and functional measures with contrast sensitivity in glaucoma. Am J Ophthalmol. 2017 Jun;178:129-39.

Three Steps to Dry Eye Coding

Don't let the myriad testing and treatment options fool you into using all of them every time. **By John Rumpakis, OD, MBA, Clinical Coding Editor**

Managing clinically significant dry eye is all the rage in today's optometric practice—and with good reason. For one, surgeons need a pristine ocular surface prior to performing any refractive surgical procedure for the best outcomes. As providers on the frontline, ODs must capture this population presenting to their practices on a daily basis, whether it's obvious clinically significant dry eye, a contact lens dropout or that troublesome patient who complains that their eyes just don't feel as comfortable as they used to throughout the day. Once you capture the patient, here's how to capture the reimbursement for their care.

Dry eye management now boasts specialized equipment, tests and treatments, as well as various protocols. All of these come with differing economic returns for the practice. But many wonder if you really need all of this specialized equipment. Likewise, do you need to perform all of these tests for every patient to be considered a good practitioner? The answer is no, not really.

First Things First

More often than not, the clinical record does not support much of this testing and, in many cases, there is an absence of clinically specific tests that should be done if recommending certain therapies. Let's take a step-wise approach to this:

Step One: The Complaint. First, we must have a chief complaint related to the ocular surface. This can be a direct patient statement or a clinical finding discovered during a patient's regularly scheduled comprehensive examination.

Step Two: Testing. After properly documenting the complaint in the patient's medical record, you can start building the case of medical necessity for each clinical test you need to perform based on the specific patient. Clinical signs you might document include hyperemia, edema, meibomian gland dysfunction, inflammation, corneal staining and lid margin epitheliopathy, to name few. These signs warrant appropriate clinical testing.

For example, if you suspect an inflammatory component or need to rule it out, order a specific clinical test for inflammatory markers such as Quidel's InflammaDry (CPT 83516 – QW). The outcome of this test may also assist with getting a prior authorization for a specific medication, but the result must be in the medical record. Remember, to bill for any CLIA-waived clinical lab point-of-care tests, your office must be designated as a clinical lab and one physician must be designated as clinical lab director.

Other clinical tests such as meibography, previously coded as an anterior segment photograph (CPT – 92285), must meet the standard of medical necessity before you can order and perform them. If the clinical record shows the presence of obstructed orifices, you can perform meibography, but only if it is based on the clinical findings. As of January of this year, the code for meibography changed to a Category III code, 0507T, defined as: "Near-infrared dual imaging (i.e., simultaneous reflective and transilluminated light) of meibomian glands, unilateral or bilateral, with interpretation and report."

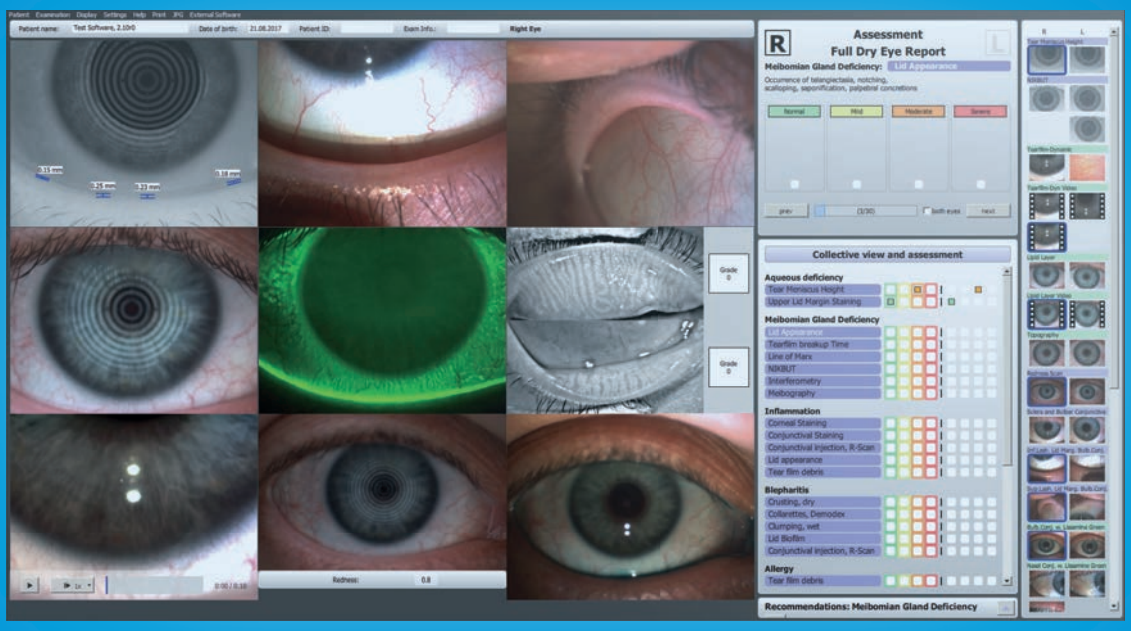
Most carriers now designate this as a patient pay code.

Step Three: Treatment. When treatment is indicated, be sure to follow the rules. For example, if you need to debride the lid margin or express the meibomian glands, neither have a specific CPT code to describe them. If you follow the CPT rules, the coding is easy. Because no CPT code currently exists for meibomian gland expression done in a non-surgical fashion, you have to use CPT code 92499 – Unlisted Ophthalmic Procedure to bill for it separately and distinctly. However, carriers generally do not reimburse for 92499, and coding with it simply allows the patient to pay you directly for it. If you choose to submit 92499 to the carrier, properly complete an ABN form, and collect from the patient in advance as directed in Option #1 of the ABN.

Clinical care protocols are wonderful if you use them properly. These tools can help you diagnose and manage the condition, but never feel compelled to do every test, every time, on every dry eye patient. That is not the purpose of a protocol, nor is it defendable in a carrier audit. Rather, use the tools with discretion to provide great care. ■

Send questions and comments to rocodingconnection@gmail.com.

Make Dry Eye Diagnosis Crystal Clear!



- Delegable measurements
- All results at a glance
- Comprehensive screening

OCULUS Keratograph® 5M with Crystal TEAR Report:

All relevant information at a glance!

Dry eye management has never been this easy. The Crystal TEAR Report helps you perform comprehensive screenings, using the measuring results as a basis for diagnosing dry eye syndrome. The workflow is optimized for time saving and patient friendliness. All results are documented and summarized for you and your patient in a neat and easily understandable printout.

Toll free 888-519-5375 Follow us!
ads@oculususa.com www.oculususa.com

OCULUS®

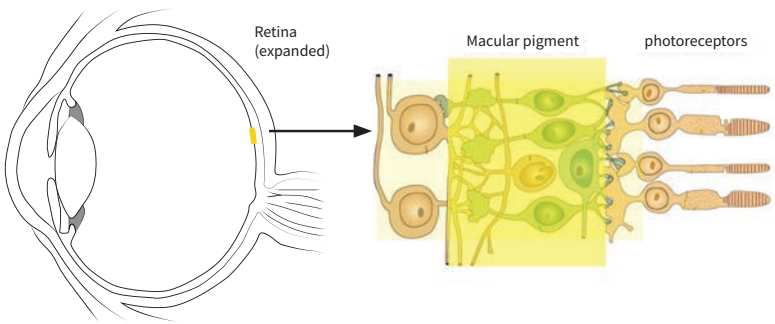
Macular Supplements for Optimal Vision Across the Life Cycle

James M. Stringham, PhD,
is a research scientist in the Visual Performance Laboratory at Duke Eye Center.

The idea that a select few dietary nutrients could 1) be crucial for normal retinal development, 2) enhance visual performance throughout life, and 3) help reduce the risk of developing age-related eye disease might at first seem preposterous. However, a wealth of recent evidence substantiates these roles for lutein (L), zeaxanthin (Z), and mesozeaxanthin (MZ).

L and Z are naturally-occurring carotenoid pigments found primarily in leafy-green vegetables, such as spinach and kale.[1] They are not synthesized by the body and so must be obtained from dietary sources or supplements. Those who have diets rich in leafy greens or supplement with sufficient L and Z tend to have higher blood and tissue concentrations of these carotenoids.[2,3] Although somewhat rare, MZ is present in the diet in various parts of the world—it is found in 21 species of fish, including trout flesh,[4] shrimp and sea turtles, as well as eggs (due to supplementation of chicken feed) in California and Mexico.[5,6] Importantly, MZ has been shown to be converted from L in the retina; it is found in high densities in the very center of the retina, where it affords protection and performance to the vulnerable neural tissue there. In terms of dietary response, MZ is readily deposited in the retina when taken in supplement form.[7,8]

L, Z, and MZ serve very important functions in the body. First, they are extremely potent antioxidants. L, Z, and MZ's antioxidant capability enables them to protect bodily tissues against damaging free-radical oxygen.[9] This is an extremely important function, because if free-radical reactions continue unabated they can lead ultimately to tissue degeneration, DNA damage, or in some cases, cancer. This is especially true for tissues with extremely high metabolism such as the macular retina, where the antioxidant potential of L, Z, and MZ is crucial for maintaining health and function. Secondly, L, Z, and MZ protect the vulnerable macula by absorbing high-energy, short-wavelength light. Their collective yellow-orange coloration and deposition in the macular region of the retina can be seen with ophthalmoscopic examination and has led to the term "macular pigment." This pigmentation effectively acts as a short-waveband filter, which further protects the macula from the cumulative damage that can manifest as age-related macular degeneration (AMD).[10]



Macular Pigment and Visual Performance The yellow macular pigment is most dense in the fovea, and is anterior to the photoreceptors; this enables pre-receptoral filtration of short-wavelength light, and mediates several positive effects on visual performance.
Image: James M. Stringham, PhD

We often fail to appreciate the high-energy, somewhat violent nature of the chemistry of our body; in some cases the body's endogenous antioxidant systems are no match for the assault. For this reason, the body supplements endogenous defense systems with nutrients via diet, and builds a defense against oxidation in key areas such as the retina and brain, where it is most needed. With regard to L, Z, and MZ, this preferential placement in vulnerable tissues starts very early.

The Macular Carotenoids in the Womb / Infancy / Childhood

Until fairly recently, the role of L, Z, and MZ in health was thought to be limited to helping protect against the development of AMD in one's senior years.[11] Ironically, however, over the last 10 to 15 years, solid evidence from prenatal and neonatal research indicates an important role for these carotenoids in the *start* of life. Recently it was determined that L & Z are the dominant carotenoids found in the placenta.[12] Surprisingly, these levels were not correlated with the mother's current diet. This is suggestive of long-term storage of these crucial carotenoids in the adipose tissue of women until pregnancy, whereby release of L & Z appears to occur. These findings are illustrative of an apparent prioritization of L & Z in terms of gestational development and health. This prioritization can be seen beyond the placenta, where it has been shown that L and Z play a major role in the early development of neural tissue in utero.

At about 6 weeks of gestation (before the retina starts to develop), L and Z are transferred via the umbilical cord[13] from the mother to the fetus and start to accumulate in an ocular reservoir called the vitreous humor. At week 20 of gestation, as the retina begins to be "built," L and Z are diverted from the vitreous humor into the now-forming retinal tissue, where they serve as antioxidants during the volatile, highly metabolic environment of neurogenesis and synaptogenesis.[14] Because oxygen is one of the major fuels for metabolism, the potential for free-radical oxidative stress and damage is high; based on the conspicuous timing of passage from the vitreous humor to the retina, coupled with the antioxidant capability of L and Z, it is not unreasonable to suggest that they play a crucial, early role in the protection and development of neural tissues. Additionally, because much development in the retina occurs after birth, L, Z, and MZ undoubtedly maintain this role well into childhood.

In fact, an argument could be made that children, despite their relatively small stature, actually need as much or more daily L, Z and MZ as adults. This is for two reasons: 1) Children are still developing and are thus using more oxygen to build tissues. More oxygen leads to increased potential for oxidative stress, and L, Z, and MZ can help to reduce it. 2) Tissue stores of L, Z, and MZ (such as the retina, brain, and adipose tissue) in children are relatively empty. By ensuring that a meaningful amount of these carotenoids is included in a child's diet, accumulation in these critical areas of the body is promoted. This would ultimately lead to enhanced protection into adulthood and beyond.

Lutein, Zeaxanthin, and Mesozeaxanthin in Adulthood / Old Age

In adults, L, Z, and MZ status in the retina (macular pigment) is associated with several notable visual performance advantages, including increased visual processing speed,[15,16] contrast sensitivity,[17-19] and better vision in dim lighting conditions.[20,21] Additionally, several studies have determined enhanced visual performance in glare, including reduced discomfort, faster photostress recovery time, and decreased disability glare.[22-25] Importantly, each of the performance parameters noted is *modifiable* via supplementation with L, Z, and MZ.[17]

Lastly, there is a well-established relationship between high concentrations of macular carotenoids and a reduced risk for developing AMD, a leading cause of vision loss in people over 50 in the United States. Importantly, there is evidence that even after the onset of AMD symptoms (e.g., mild distortions of central vision), macular carotenoid supplementation can slow down, or even stop progression of the disease.[19,27] It appears, therefore, that the macular carotenoids have not only long-term protective effects on tissues, but also acute benefits as well.

Given all of the existing research, L, Z, and MZ appear to provide meaningful, significant benefits across the lifespan. The more we learn about these carotenoids, the more apparent it becomes that they are crucial to normal development, health, and performance. From their early involvement in protecting developing neural tissues to reducing cumulative damage that results in age-related disease later in life, it is clear that L, Z, and MZ are meant to play a significant role in optimizing human development, performance, and aging. Importantly, supplementation with MacuHealth with LMZ3 will help augment the sometimes low dietary intake of these nutrients throughout life. Although L, Z, and MZ are not considered essential nutrients (i.e., vitamins), based on the available scientific evidence, they may certainly be considered essential for peak health and performance.

1. Sommerburg O, Keunen JE, Bird AC, van Kuijk FJ. Fruits and vegetables that are sources for lutein and zeaxanthin: the macular pigment in human eyes. Br J Ophthalmol. 1998;82(8):907-10. (NHANES 2003-2004).
2. Ciulla, TA, Curran-Celantano, J, Cooper DA, al. Macular pigment optical density in a midwestern sample. Ophthalmology. 2001;108(4):730-7.
3. Bone RA, Landrum JT, Guerra LH, et al. Lutein and zeaxanthin dietary supplements raise macular pigment density and serum concentrations of these carotenoids in humans. J Nutr. 2003. 133(4):992-8.
4. Prado-Cabrero A, Beatty S, Stack J, et al. Quantification of zeaxanthin stereoisomers and lutein in trout flesh using chiral high-performance liquid chromatography-diode array detection. J Food Compost Anal. 2016 Jul;50:19-22.
5. Maoka T, Arai A, Shimizu M, et al. The first isolation of enantiomeric and meso-zeaxanthin in nature. Comp Biochem Physiol B. 1986;83(1):121-4.
6. Nolan JM, Meagher K, Kashani S, et al. What is meso-zeaxanthin, and where does it come from? Eye (Lond). 2013 Aug;27(8):899-905.
7. Bone RA, Landrum JT, Cao Y, et al Macular pigment response to a supplement containing meso-zeaxanthin, lutein and zeaxanthin. Nutr Metab (Lond). 2007;11(4):12.
8. Loughman J, Nolan JM, Howard AN, et al. The impact of macular pigment augmentation on visual performance using different carotenoid formulations. Invest Ophthalmol Vis Sci. 2012;53(12):7871-80.
9. Krinsky NI, Landrum JT, Bone RA. Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye. Ann Rev Nutr. 2003;23:171-201.
10. Mares JA, Voland RP, Sondel SA, et al. Healthy lifestyles related to subsequent prevalence of age-related macular degeneration. Arch Ophthalmol Chic Ill 1960. 2011;129(4):470-80.
11. Seddon, JM, Ajani, UA, Sperduto RD, et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. JAMA. 1994;272:1413-20.
12. Thoene M, Anderson-Berry A, Van Ormer M, et al. Quantification of Lutein + Zeaxanthin Presence in Human Placenta and Correlations with Blood Levels and Maternal Dietary Intake. Nutrients. 2019;11(1).
13. Rubin LP, Chan GM, Barrett-Reis BM, et al. Effect of carotenoid supplementation on plasma carotenoids, inflammation and visual development in preterm infants. J Perinatol. 2012;32(6):418-24.
14. Panova I, Iakovleva MA, Feldman TB, et al. Detection of carotenoids in the vitreous body of the human eye during prenatal development. Bull Exper Biol Med. 2007;144(5):681-3.
15. Hammond, BR, Wooten BR. CFF thresholds: relation to macular pigment optical density. Ophthalmic & Physiological Optics. 2005;25:315-19.
16. Stringham NT, Stringham JM. temporal visual mechanisms may mediate compensation for macular pigment. Perception. 2015 Dec;44(12):1400-15.
17. Stringham JM, O'Brien KJ, Stringham NT. Contrast sensitivity and lateral inhibition are enhanced with macular carotenoid supplementation. Invest Ophthalmol Vis Sci. 2017 01;58(4):2291-5.
18. Nolan JM, Power R, Stringham J, et al. Enrichment of macular pigment enhances contrast sensitivity in subjects free of retinal disease: Central Retinal Enrichment Supplementation Trials - Report 1. Invest Ophthalmol Vis Sci. 2016 Jun 1;57(7):3429-39.
19. Akuffo KO, Beatty S, Peto T, et al. The impact of supplemental antioxidants on visual function in nonadvanced age-related macular degeneration: a head-to-head randomized clinical trial. Invest Ophthalmol Vis Sci. 2017 01;58(12):5347-60.
20. Hammond BR Jr, Wooten BR, Snodderly DM. Preservation of visual sensitivity of older subjects: association with macular pigment density. Invest Ophthalmol Vis Sci. 1998 Feb;39(2):397–406.
21. Stringham JM, Garcia PV, Smith PA, et al. Macular pigment and visual performance in low-light conditions. Invest Ophthalmol Vis Sci. 2015 Apr;56(4):2459-68.
22. Stringham JM, Garcia PV, Smith PA, et al. Macular pigment and visual performance in glare: benefits for photostress recovery, disability glare, and visual discomfort. Invest Ophthalmol Vis Sci. 2011; 52:7406-15.
23. Wenzel AJ, Fuld K, Stringham JM, et al. Macular pigment optical density and photophobia light threshold. Vision Res. 2006 Dec;46(28):4615-22.
24. Stringham JM, Hammond BR, Jr. The glare hypothesis of macular pigment function. Optom Vis Sci. 2007;84(9):859-64.
25. Stringham JM, Hammond BR. Macular pigment and visual performance under glare conditions. Optom Vis Sci. 2008;85(2):82-8.
26. National Eye Institute. Facts About Age-Related Macular Degeneration. Available at: https://nei.nih.gov/health/maculardegen/armd_facts (last accessed Feb. 19, 2019).
27. Richer S, Stiles W, Statkute L, et al. Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial). Optometry. 2004;75(4):216-30.

PEER • REVIEWED PRA ARTICLE

Build a Better Dry Eye Protocol

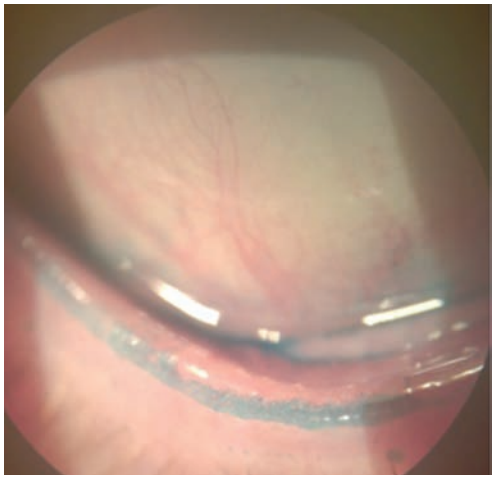
The DEWS II report provides a roadmap to help streamline your treatment regimens.

By Candice Tolud, OD

In 2017, the Tear Film & Ocular Surface Society updated the Dry Eye Workshop (DEWS II) to reflect a decade's worth of advances in our understanding, diagnosis, treatment and management of dry eye disease (DED). For the optometrist looking to better incorporate the findings of DEWS II into their practice, this article boils down the report's lengthy discussion into actionable recommendations.

Start With the Right Definition

One of the major developments of the DEWS II was the Definition and Classification subcommittee's revamping of the description of dry eye. Previously, DED was seen either as evaporative—as a result of deficient lipid layer from meibomian gland dysfunction (MGD)—or aqueous deficient (reduced tear volume).[1] However, many practitioners have noted that patients can exhibit features of both subtypes. As a result, the updated definition allows for a more comprehensive representation of DED, defining it as a "multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[2]



Lissamine green staining of the lid margin shows >2mm of stain, which would qualify as a positive sign of lid wiper epitheliopathy, a key diagnostic criteria for dry eye disease.

This expansive definition provides a more inclusive way to view a patient's presenting signs and symptoms. The expanded definition creates a spectrum of DED rather than a single process, sign or symptom that affects the entire ocular surface, including the tear film, cornea, conjunctiva, eyelids and lacrimal and meibomian glands.[3]

Categorize Carefully

The DEWS II Diagnostic Methodology subcommittee's algorithm begins with the assessment of symptoms. Patient questionnaires such as the Dry Eye Questionnaire-5 (DEQ-5) or the Ocular Surface Disease Index (OSDI) are important tools when DED is suspected, as they can often differentiate DED from other conditions that may mimic its symptoms.[1]

Adapted from: Jones L, Downie LE, Korb D, et al. Ocul Surf. 2017;15(3):575-628.

DEWS II staged DED recommendations.[4]

It's All About Balance

The new understanding of DED as a disruption of homeostasis on a spectrum of ocular surface dysfunction means identifying the factors contributing to a patient's profile is key. While there may be a predominant cause, concurrent contributing factors are also possible.

DEWS II recommends using three tests and techniques to identify and subtype DED. These are minimally invasive, clinically applicable and maintain high objectivity.[1] Clinicians should test for these key homeostasis markers in symptomatic patients using a positive screening questionnaire such as DEQ-5 (with a score >6) or OSDI (with a score >13). Testing should be performed in order from least to most invasive to minimize a test's effect on subsequent results:

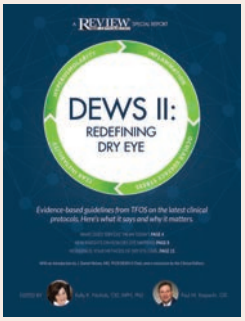
Noninvasive tear break-up time (TBUT). This is always recommended over traditional fluorescein TBUT, as fluorescein reduces tear film stability and impacts the accuracy of the measurement. Noninvasive TBUT can be measured with devices such as a corneal topographer.[1] However, if fluorescein is used, it is recommended that the test strip be dry and applied to the outer canthus to decrease any irritation of the ocular surface with measurements read one to three minutes after instillation.[1] A positive test result is tear break-up less than 10 seconds after blink.

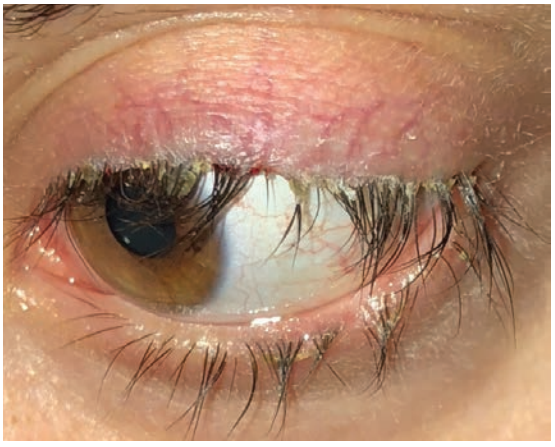
Tear hyperosmolarity. This has the highest correlation to DED severity of available clinical tests, and tear osmolarity is the single best metric to diagnose and classify DED, according to the DEWS II diagnostic and methodology report.[1] A positive result is any reading greater than 308mOsm/L or a difference of more than 8mOsm/L between eyes.

Ocular surface staining. Conjunctival and lid margin damage is best viewed with lissamine green staining, and corneal damage is best viewed with fluorescein dye.[1] Considered a late-stage sign of DED, staining in either eye is a positive test result. Ocular surface staining is defined as more than five corneal spots, greater than nine conjunctival spots or lid margin staining (lid wiper epitheliopathy) greater than 2mm in length.

DEWS II Revisited

Want to read more about the DEWS II reports and peruse the diagnostic and treatment algorithms? Check out our coverage of each subcommittee report at www.reviewofoptometry.com or follow the QR code:





This patient with anterior blepharitis required stage two treatment, which can include topical antibiotics or antibiotic-steroid combination medications, along with lid hygiene and warm compresses.

While only one abnormal test result is required to make a diagnosis, if a clinician only has access to a limited number of homeostasis markers, all of which come back negative, the clinician should refer the patient to rule out other markers of homeostasis before excluding the diagnosis of DED.[1]

Once DED is confirmed, further testing such as meibography, lipid interfermometry and tear volume measurement can further subtype and determine where on the DED continuum the patient falls, as well as determine the severity and help guide treatment.[3]

A Staged Treatment Approach

Because DED exists on a spectrum, the management and treatment requires a similar approach. DED can require several levels of care simultaneously. The DEWS II management and therapy algorithm is not a rigid sequential approach, but a guide to aid in the treatment.[4] In some cases, the initial therapy may be continued in addition to any new therapies in subsequent stages.[4]

Stage one. Patient education, as with any condition, is an important first step and helps to promote treatment compliance and guide patient expectations, especially in refractory cases. Additionally, patients with signs of dry eye without symptoms should be counseled on their condition along with potential worsening prior to any ocular surgery or when considering contact lens wear.

Patients can start by modifying their local environment by adding humidifiers in particularly dry conditions, as well as modifying other environmental issues such as prolonged digital device use and contact lens wear.[4] Dietary modifications may help as well, as evidence shows that diet and nutritional supplementation play a role in managing DED. Increasing water intake is a simple recommendation with significant benefits for patients with DED.[4] At the time of the DEWS II report, the use of omega-3 supplementation for dry eye was still unclear, with conflicting reports of efficacy.[4] Since DEWS II, the DREAM study found that fish oil did not perform significantly better than its olive oil placebo in treating dry eye.[5]

Clinicians should identify topical or systemic medications that may contribute to DED such as antihypertensives, antihistamines and antianxiety medication. Once identified, patients can consider dose adjustments, switching to another medication, discontinuing the medication or more aggressive management of the induced dry eye.[4] When the offending topical agent is preserved with benzalkonium chloride, clinicians should recommend switching to a different preservative such as Polyquad or a preservative-free solution to help minimize damage to the ocular surface, which may occur in those who require frequent dosing.[4]

Artificial tears are a mainstay of DED therapy and are used as palliative therapy; however, these over-the-counter products do not work to address the pathophysiology of DED.[4] Artificial tears vary in osmolarity, viscosity and pH—all of which impact their efficacy for individual patients. Higher viscosity agents such as carboxymethylcellulose, hyaluronic acid, HP-guar, polyvinyl alcohol and propylene glycol are typically recommended for overnight use.[4] In more advanced cases, higher viscosity agents are used more frequently to help prevent ocular surface desiccation. Lipid-containing drops are formulated with various oils such as mineral oil and phospholipids to help restore the tear film lipid layer, and are beneficial in cases of evaporative dry eye.[4]

Lid hygiene is important in managing any conditions that may further contribute to DED, such as blepharitis, MGD and ocular rosacea. Although lid scrubs using a mild dilution of baby shampoo have long been a common recommendation, studies show commercially available eyelid cleaners provide reduced ocular surface MMP-9 levels, improved lipid layer quality and are overall better tolerated compared with baby shampoo.[4] Research also suggests baby shampoo may have an adverse effect on goblet cell function, and the DEWS II recommends commercially available lid cleansing products over the use of baby shampoo.[4]

Warm compresses are a proven at-home treatment for MGD; however, compliance is typically poor due to the time required and the difficulty of maintaining the appropriate temperature of no more than 45°C

The One and Only Indicator of MMP-9 for Dry Eye Inflammation

QUIDEL | InflammaDry®

InflammaDry is the only test that detects elevated levels of MMP-9, a key inflammatory marker for dry eye. This rapid, point-of-care test produces results in 10 minutes allowing patients to be tested and treated in the same office visit. The test is easy to perform, is minimally invasive and requires no additional equipment. InflammaDry utilizes innovative patented technology, CE marked, and CLIA waived.

Quidel is a long-standing leader in the manufacture and sale of rapid, point-of-care diagnostics. Contact your Quidel Account Manager today at **800.874.1517** to learn more about how InflammaDry can help improve the health of your dry eye patients.

Visit us at Optometry's Meeting St. Louis
Booth 726, June 19–21

quideleyehealth.com

AD1022201EN00 (01/19)

for an extended period of time.[4] Patients can keep the cloth warm for longer by wrapping several cloths around each other in a bundle format. Patients should use a warm wet compress for at least five minutes.[4] Many commercially available devices can maintain the therapeutic temperature for longer periods of time; the Bruder mask (Bruder Healthcare), for example, maintains heat levels for 10 to 15 minutes.[6]

Stage two. Patients unresponsive to stage one therapies should initiate stage two treatment options. Switch to non-preserved artificial tears if corneal toxicity is a concern and recommend overnight treatments such as increased viscosity tears and ointments. Moisture chamber spectacles to slow tear evaporation and minimize airflow over the ocular surface may be beneficial.

If tear volume is a concern, punctual occlusion with collagen, silicone or surgical intervention in more advanced cases can help with tear conservation. Punctal occlusion is most successful in combination with other DED treatments.[4]

Stage two dry eye often responds to topical pharmaceutical agents such as cyclosporine A, which is an immunomodulatory drug with anti-inflammatory properties that inhibit the IL-2 activation of lymphocytes.[4] Topical cyclosporine, FDA-approved for moderate to severe DED, reduces markers of inflammation, decreases tear osmolarity, improves conjunctival goblet cell density and improves tear production measured via Schrimer's.[4] In 2018, Cequa (Sun Pharmaceuticals) gained FDA approval and provides a higher concentration of cyclosporine at 0.9% compared with the 0.05% of Restasis (Allergan).[7]

Xiidra (lifitegrast, Novartis) is a small molecule integrin antagonist that binds to the cell surface protein found on leukocytes and blocks the integrin lymphocyte function associated antigen-1 and cognate ligand intercellular adhesion molecule-1 interactions.[8-10] *In vitro* studies show Xiidra may inhibit the recruitment of previously activated T-cells, the activation of newly recruited T-cells and the release of pro-inflammatory cytokines—interrupting the perpetual cycle of inflammation that promotes DED.[8-10]

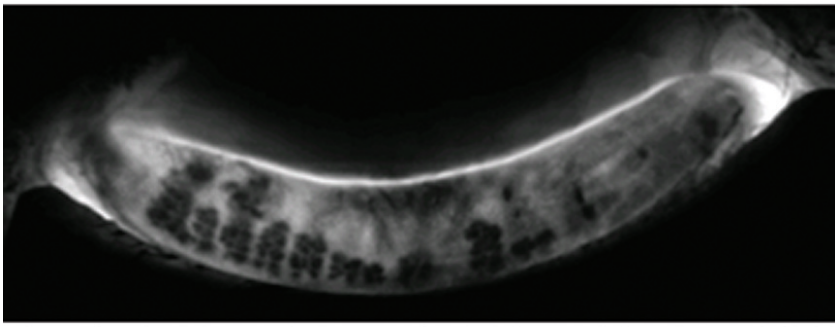
Clinicians can also consider using low-dose topical steroids such as Lotemax (loteprednol etabonate 0.5%, Bausch + Lomb) as a pretreatment or concomitantly with cyclosporine or lifitegrast in the early phases of treatment and tapered after a few weeks. A study found non-preserved steroids, such as 0.01% dexamethasone, can improve patient symptoms and findings of chronic ocular surface irritation that was previously unresponsive to various preserved topical steroids such as 0.2% loteprednol, 0.1% fluorometholone and 1% prednisolone.[4]

Stage two patients often present with lid involvement such as anterior blepharitis. A short course of topical antibiotics or an antibiotic/steroid combination ointment applied directly to the lid margin may help, in combination with lid hygiene and warm compresses.

Treatment of *Demodex*, if present (often with refractory blepharitis), will help alleviate patient symptoms and decrease any contributing impact on DED.[4] The use of tea tree oil, which exhibits antimicrobial, anti-inflammatory, antifungal and antiviral properties that are toxic to *Demodex* mites, has grown in popularity for its effectiveness in eradicating *Demodex* mites from the hair follicles at the lash margin.[4] One study shows weekly lid scrubs with 50% tea tree oil combined with daily lid hygiene with tea tree shampoo is an effective treatment for *Demodex*.[4,11]

Tea tree oil can be toxic to the ocular surface and can cause stinging and irritation if used in its pure form.[4] Pre-formulated wipes are now commercially available at 25% concentration and reduce the risk of toxicity to the ocular surface compared with stronger concentrations.[4]

Oral tetracyclines, such as doxycycline, can treat ocular rosacea, MGD and blepharitis that contribute to DED. These broad-spectrum antibiotics with anti-inflammatory properties can decrease several inflammatory mediators such as collagenase, phospholipase A2 and several MMPs.[4] No consensus exists on the optimal dosage of oral doxycycline for treating DED due to MGD, and regimens range from 20mg to 200mg daily in monthly intervals.[4] The lowest dose is always preferably to help minimize possible side effects



This Lipiscan image of a patient's meibomian glands shows extensive areas of gland loss and truncation consistent with the patient's complaints of dry eye.

new!

Gentle on Eyelids. Tough on Bacteria.

RECOMMEND

THE ONLY FDA-ACCEPTED ANTIMICROBIAL

EYELID CLEANSER

- ✓ Advanced Hypochlorous Acid (0.01%) formula for superior cleansing
- ✓ Cleanses away bacteria and irritants
- ✓ pH balanced formula is gentle on eyelids
- ✓ Effective daily eyelid and eyelash hygiene
- ✓ No rinse – soap free

Coming soon without a prescription at Walgreens, CVS Pharmacy®, Amazon, Rite Aid, and other retailers nationwide

Visit **theratears.com** to learn more

AKORN | CONSUMER HEALTH

Reference: 1. Results from an in vitro laboratory study. TheraTears® SteriLid® Antimicrobial Eyelid Cleanser and Facial Wash showed efficacy in reduction of colony forming units for eight common eyelid organisms. Data was captured at 30 and 60 seconds.

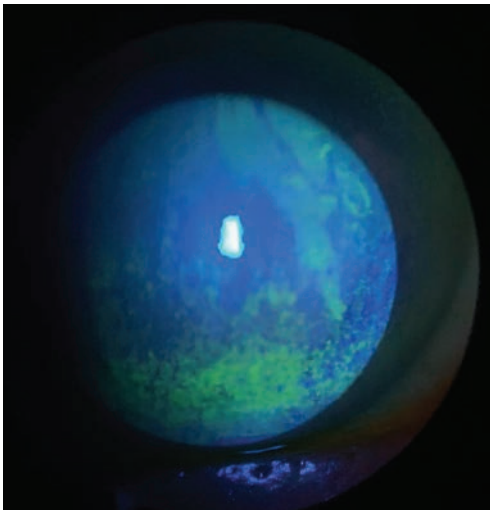
M18-069-00

of photosensitivity and gastrointestinal upset.

Oral macrolides, and azithromycin specifically, can be as effective as doxycycline in treating MGD.[4] Azithromycin works by inhibiting pro-inflammatory cytokines and is potent against gram-negative microorganisms associated with posterior blepharitis.[12] While the dosing of azithromycin for MGD remains controversial, clinicians should use a shorter course of treatment—500mg on first day and 250mg for four days after for a total of five days—to minimize gastrointestinal upset and boost cost efficiency.

MGD can be treated in office with instruments such as LipiFlow (Johnson & Johnson Vision) or intense pulsed light (IPL). LipiFlow is designed to simultaneously heat glands to therapeutic levels of 42.5°C and evacuate the gland contents, which can significantly improve patient symptoms, meibomian gland secretion and TBUT with one study showing efficacy of one treatment up to three years.[4] IPL therapy, which uses a handheld device to deliver pulses of non-coherent light between 500nm and 1200nm, can improve meibomian gland function and dry eye symptoms when used with manual meibomian gland expression. A retrospective multicenter review found that IPL therapy was a safe and effective treatment for evaporative dry eye.[4]

Stage three. These patients require more advanced dry eye therapies such as oral secretagogues. Pilocarpine and cevimeline, both cholinergic agonists, are commercially available for oral administration in the treatment of Sjögren's syndrome (SS)-associated DED.[4] One study found SS patients treated with oral pilocarpine had improvement of symptoms and ocular surface staining with rose bengal, goblet cell density and TBUT; however, it did not improve tear production via Schrimer's.[4] Cevimeline showed a better side effect profile compared with pilocarpine, and patients had significant improvements in subjective assessment of ocular dryness, dry mouth and increased salivary and lacrimal flow rates.[4]



This patient with dry eye has extensive punctate epithelial keratitis and decreased tear break-up time. Treatment requires consideration of patient symptoms, underlying contributory systemic conditions and medication use.

In more advanced cases of DED where topical pharmaceutical agents do not provide adequate relief (often in patients with underlying systemic conditions such as SS), autologous serum can be beneficial. Autologous serum is derived from the patient's own blood and contains many biochemical characteristics similar to that of human tears, such as pH, nutrients, vitamins, albumin, fibronectin and epithelial and nerve growth factors.[4] Research shows autologous serum and other blood-derived tear substitutes increase corneal epithelial wound healing, inhibit the release of inflammatory cytokine and increase the number of goblet cells and mucin expression.[4]

Autologous serum can be formulated at specialized compounding pharmacies at various concentrations, depending on severity of symptoms.[4] The formulations are non-preserved and can be kept frozen at -20°C for up to nine months, but are only good for about 24 hours after thaw.[4] One study found treatment with autologous serum improved patient symptoms as early as 10 days in 60% of patients and two months in 79%.[4] While patient symptoms, TBUT and corneal staining improved, Schirmer's scores remained the same and ocular surface disease recurred after discontinuation of treatment.[4]

Allogenic serum, which works similarly to autologous serum, is derived from the blood of a relative or individual of similar blood typing.

Bandage contact lenses can help maintain ocular comfort and corneal integrity and prolong ocular surface moisturization.[4] Soft contact lenses are typically used on an extended wear basis, although these patients should be advised of increased risk of infection and monitored regularly for complications. A recent study found silicone hydrogel lenses used as a bandage lens in SS patients provided significant improvement in visual acuity for up to six weeks after discontinuing wear, as well as improvement in OSDI scores, TBUT and corneal staining.[4]

Gas permeable scleral lenses are an option for moderate to severe DED and can provide a repository of tears between the lens and the ocular surface.[4] However, once a centralization of neuropathic pain occurs, the use of any bandage lens may be insufficient for reducing symptoms.[4]

Stage four. Treatment at this

stage is for refractory cases of DED. Chronic use of low-dose topical corticosteroids may be warranted to help control persistent ocular surface inflammation. Careful monitoring of secondary cataract formation or increased intraocular pressure is necessary for long courses of treatment.

Severe DED with persistent epithelial defects or corneal ulceration and scarring may be successfully treated by amniotic membrane grafts. These consist of cryopreserved human amniotic membrane, which contains a wide variety of neuropeptides and neurotransmitters.[4] These devices are inserted similarly to a scleral lens and typically dissolve in one week. One study showed symptom improvement for four months in dry eye patients treated with a Prokera Slim (Bio-Tissue) for five days.[4]

In the more severe cases of DED, surgical intervention may be necessary. Tarsorrhaphy is a temporary or permanent surgical procedure to partially or totally close the eyelids to decrease ocular surface exposure and tear evaporation in patients where all other treatments have failed. Removal of excessive conjunctivochalasis can help patients whose redundant conjunctival tissue exacerbates their dry eye symptoms as well as complaints of epiphora.[4]

The management options for dry eye have exploded over the past decade, and the DEWS II report provides the eye care community a much-needed road map to best identify patients who would benefit from treatment and tailor management to their individual needs. ■

Dr. Tolud practices at South Jersey Eye Physicians and specializes in ocular disease management.

1. Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II diagnostic methodology report. Ocul Surf. 2017;15(3):539-74.
2. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017;15(3):276-83.
3. Craig JP, Nelson JD, Azar DT, et al. TFOS DEWS II Report executive summary. Ocul Surf. 2017;15(3):802-12.
4. Jones L, Downie LE, Korb D, et al. TFOS DEWS II management and therapy report. Ocul Surf. 2017;15(3):575-628.
5. Dry Eye Assessment and Management Study Research Group, Asbell PA, Maguire MG, et al. n-3 fatty acid supplementation for the treatment of dry eye disease. N Engl J Med. 2018;378(18):1681-90.
6. Insight Optometry. Bruder Eye Hydrating Mask. https://insightoptometry.com/blog/bruder-moist-heat-eye-compress. Accessed March 19, 2019.
7. Sun Pharma Announces U.S. FDA Approval of CEQUA to Treat Dry Eye Disease. Sun Pharmaceutical Industries. https://cequapro.com/pdf/cequa-news-release.pdf. August 16, 2018. Accessed March 7, 2019.
8. Murphy CJ, Bentley E, Miller PE, et al. The pharmacologic assessment of a novel lymphocyte function-associated antigen-1 antagonist (SAR 1118) for the treatment of keratoconjunctivitis sicca in dogs. Invest Ophthalmol Vis Sci. 2011;52:3174-80.
9. Sun Y, Zhang R, Gadek TR, et al. Corneal inflammation is inhibited by the LFA-1 antagonist, lifitegrast (SAR 1118). J Ocular Pharmacol. 2013;29:395-402.
10. Zhong M, Gadek TR, Bui M, et al. Discovery and development of potent LFA-1/ICAM-1 antagonist SAR 1118 as an ophthalmic solution for treating dry eye. ACS Medicinal Chemistry Letters. 2012;3:203-6.
11. Gao Y, Di Pascuale MA, Li W, et al. In vitro and in vivo killing of ocular Demodex by tea tree oil. Br J Ophthalmol. 2005;89:1468-73.
12. Kashkouli MB, Fazel AJ, Kiavash V, et al. Oral azithromycin versus doxycycline in meibomian gland dysfunction: a randomised double-masked open-label clinical trial.Br J Ophthalmol. 2015;99(2):199-204.

DID THE DREAM STUDY CHANGE YOUR THINKING?

The controversial findings led some ODs to question the role of omega-3s, while others dispute the study itself. Here, several experts share their views. **By Jane Cole, Contributing Editor**

For more than a decade, omega-3 fatty acid supplements have been hailed for their role in helping to alleviate dry eye symptoms with no significant side effects. While they're not effective in every case and are typically used in conjunction with other methods, this avenue of care is pretty well-established. Then came the Dry Eye Assessment and Management (DREAM) study last May, which seemed to upend the validity of fish oil, as it found omega-3 fatty acids offered no benefit over the olive oil placebo.[1]

In light of these findings, should optometrists think about tossing omega-3 supplements from their dry eye treatment arsenals? Not so fast, caution some experts who suggest peeling back the layers of the study and taking a closer look before making up your mind.

"Be sure to read the scientific study, not just the headline and abstract, before making a decision on how to treat patients," says Jeffrey Anshel, OD, of Encinitas, CA. "The protocol of a study must cover many bases and not be influenced by flaws in the design of the study. Also, no one study should represent the gold standard for treatment in any disease."

Not everyone has taken the DREAM study with a grain of salt, however. According to Paul Karpecki, OD, of Lexington, KY, some doctors have stopped using fish oil altogether because of the results. He notes that those who had been on the fence about omega-3 supplements have now ruled them out as a dry eye treatment option and are wondering what neutraceuticals or other alternatives they should offer instead.

"Some people think the study results mean fish oil doesn't work for dry eye, and that's not the case," Dr. Karpecki adds. "The fish oil treatment arm had a phenomenal statistical improvement from baseline. So, fish oil does work, and it's very effective. But, why did the placebo arm work too?" It's that parallel effect seen among the placebo group that has some doctors now questioning the role of omega-3 supplementation.

Meanwhile, the DREAM researchers stand by the study's methodology and findings, and readily dispute the criticisms lobbed at the work.

In this article, experts in dry eye and ocular nutrition weigh in on the controversy.

Omega-3 Faces Scrutiny

The first mention of using omega-3 as a treatment for dry eye was in a 2005 study that showed women who ate regular amounts of tuna in their diets had lower rates of dry eye symptoms.[2] It wasn't until 2011, however, that a pilot study

INTRODUCING

Next Generation Hypochlorous Acid

Essential Daily Eyelid Health Management

- **HyClear™ is Pure.**
  With the antimicrobial activity* of pure hypochlorous acid .01%, HyClear™ is a non-cytotoxic, non-irritating solution.

- **HyClear™ is Affordable.**
  Now your patients on Medicare or without commercial insurance can enjoy affordable daily eyelid health management.

- **HyClear™ is Stable.**
  HyClear™ (Balanced Anolytic Hypochlorous Acid™) provides up to 18 months shelf life after opening.

- **HyClear™ is Exclusive.**
  HyClear™ is an exclusive brand for Optometry and Ophthalmology practices.

Contamac® is pleased to introduce HyClear™, the next generation Hypochlorous Acid for daily eyelid health management.

HyClear

Call 833-266-8262 or visit gethyclear.com for information on how HyClear™ can improve your dry eye practice.

Contamac

*in solution

was specifically designed to determine if omega-3 would alleviate dry eye symptoms.[3] The study concluded that dietary supplementation with omega-3 fatty acids for dry eye had no significant effect on meibum lipid composition or aqueous tear evaporation rate.[3] On the other hand, the average tear production and volume increased in the omega-3 group, as indicated by Schirmer testing and fluorophotometry.[3] Dr. Anshel notes that many studies since have found that omega-3 essential fatty acids have a positive effect on dry eye.

The DREAM Study—a one-year, double-masked, randomized multicenter study by the National Eye Institute—took a fresh look at the benefits, or lack thereof, of omega-3 supplements in a dry eye patient population.[1]

The study recruited patients from private and academic optometry and ophthalmology practices throughout the United States.[1] Eligible participants included those who had signs and symptoms of moderate-to-severe dry eye on two consecutive examinations performed two weeks apart, dry eye symptoms for at least six months, an Ocular Surface Disease Index (OSDI) score ranging from 25 to 80 at a screening visit and an OSDI score ranging from 21 to 80 at the baseline eligibility visit.[1] Patients also had to be willing to continue their current dry eye treatment regimens, use or want to use artificial tears at least twice daily in the previous two weeks and have at least two of the following four signs of dry eye in the same eye at the screening and baseline eligibility visits:[1]

- Conjunctival staining score ≥1
- Corneal fluorescein staining score ≥1
- Tear break-up time (TBUT) ≤7
- Schirmer's test with anesthesia ≥1mm and ≤7mm in five minutes

Since nutritional supplementation is often used as an adjunct to other dry eye treatments, the inclusion criteria were broad to mimic "real-world" clinical application, says Whitney Hauser, OD, of Southern College of Optometry in Memphis. A total of 329 patients were enrolled in the treatment group and 186 in the placebo group.

The clinical trial was considered "real-world" because it included patients with dry eye disease who sought relief of symptoms despite the use of other interventions. "Patients were allowed to continue their current treatments for dry eye disease, which is not the case in most industry-sponsored trials of treatments for this disease," the DREAM researchers wrote in their paper.

Additionally, patients with a history of thyroid disease, Sjögren's syndrome, rheumatoid arthritis or inflammatory diseases could be included in the trial if they were otherwise eligible.


Getty Images

The 3000mg daily dosage of n-3 fatty acids was the highest dose used to date in clinical trials of fish-derived n-3 fatty acids.[1] The daily placebo was approximately 1tsp of olive oil, which primarily delivered n-9 oleic acid, a substance considered to be neutral with respect to changes in signs and symptoms of dry eye.[1]

After 12 months, the study authors did not find significant differences in mean OSDI (primary outcome measure) or conjunctival staining, corneal staining, TBUT and Schirmer's test (secondary outcome measures) between both groups.[1]

Penny Asbell, MD, who helped conduct the DREAM study, says that because there was no difference between the groups, you can't conclusively say omega-3 actually works.[4] "In fact, some people have said what really worked is seeing [patients] four times a year," Dr. Asbell suggested in an online interview following release of the study. "Just seeing them seemed to make everybody feel better." She noted that while dry eye signs and symptoms both improved, the effect was more pronounced among symptoms, which may lend credence to her supposition than the effect was more a subjective experience influenced by the higher level of care provided.

"Within the profession, the study results stimulated a lot of talk and, in my opinion, a return to our scientific roots to read into the study to better understand the methodology and what was really being tested," says Cecelia Koetting, OD, of Norfolk, VA.

Dr. Anshel notes that the DREAM results also raised a lot

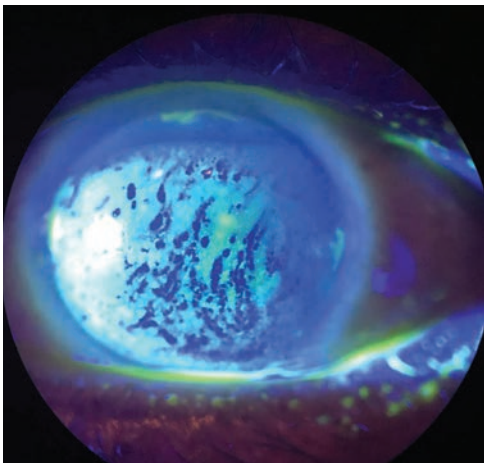


Photo: Cecelia Koetting, OD

This patient displays diffuse superficial punctate keratitis (SPK) with a decreased TBUT.

of eyebrows in the profession. "Most eye care professionals were surprised at the results of this study since many of them use just omega-3 fish oil to treat dry eye patients and have positive outcomes," he says.

He adds that he was also slightly surprised omega-3 fell short with how well he usually hears it works for dry eye treatment.

DREAM Interpretation

In the year since the DREAM study's release, elements of its methodology have come under fire. In particular, the choice of placebo and whether the olive oil played a confounding role have been under the most intense scrutiny.

"What's interesting in the study is that both the treatment and placebo groups saw improvements in signs and symptoms of dry eye," says Mile Brujic, OD, of Bowling

DREAM Extension Study Corroborates Original Findings

If fish oil therapy had effected a decrease in clinical signs and symptoms in the DREAM study, a worsening of outcomes might be expected following cessation. However, in a follow-up study recently presented at ARVO 2019, the DREAM researchers found no significant difference in outcomes between patients who stopped taking the omega-3 supplements and those who continued taking them over an additional 12-month period. This finding conforms with the original study results of no demonstrable benefit from omega-3 supplementation, the researchers say.

The team pulled a subset participants (n=43) from the original treatment arm, randomizing them into two groups: those who continued with therapy (21 patients) and those who switched to the olive oil placebo (22 patients). The primary outcome was a mean change from baseline (month 12 of the primary trial) in Ocular Surface Disease Index (OSDI) score. Secondary outcomes included changes in conjunctival and corneal staining scores, tear break-up time (TBUT), Schirmer's test results and adverse event incidences.

After 12 months, the study authors reported that the mean change in the total OSDI score (-0.6 points) was not significantly different between the omega-3 and the placebo groups. Additionally, they did not observe any significant differences between the groups in mean changes from baseline in conjunctival staining scores (-0.5 points), corneal staining scores (-0.6 points), TBUTs (-0.8 seconds) and Schirmer's test results (1.2mm). They add that the rates of adverse events were also similar between both groups.

These latest discoveries are consistent with the results of the primary clinical trial released last year, which also found that there was no beneficial effect of omega-3 relative to olive oil.

Hussain M, Shtein RM, Pistilli M, et al. DREAM extension study—comparison of placebo and omega-3 fatty acid supplement groups on OSDI, 4 key signs of DED and adverse events. ARVO 2019. Abstract 6729-B0253.

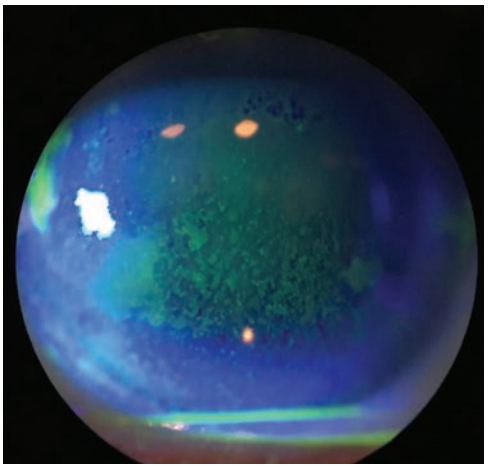


Photo: Cecelia Koetting, OD

Staining shows this dry eye patient's diffuse dense superficial punctate keratitis.

Green, OH. He notes that the oils are similar in a way, as they both have strong anti-inflammatory properties.

"It seems that the treatment and the placebo improved outcomes in the study," Dr. Brujic adds. "Not that the treatment arm didn't work, but the placebo arm (olive oil) had a strong level of efficacy that met the omega-3's."

These results prompt an obvious question: why did the olive oil group do so well?

The olive oil used in the study was refined, meaning it had no significant levels of antioxidant and anti-inflammatory polyphenol compounds, Dr. Karpecki notes. He says oleic acid—an olive oil component and seemingly unlikely placebo candidate—wasn't incorporated to any significant degree in either group and no other olive oil components offered a plausible explanation on why the placebo group did so well, especially at a dosage of just 1tsp per day.

Compared with the Mediterranean diet (which uses 60g of olive oil), DREAM investigators have suggested the olive oil placebo dose (5g, the equivalent of one tablespoon) was too low to have a therapeutic effect.[4,5]

"That's less than you usually put on your salad," Dr. Asbell noted in her recorded comments.[4] "It's really not comparable to a Mediterranean diet, where it's 12 times as much per day." She explained that the study measured blood levels of each group, and found a fourfold increase from baseline in omega-3 levels in the study group but no change in oleic-9 levels among the olive oil users.[4]

Some critics, however, have fixated on the study's purported demonstration of a treatment effect from olive oil as a rationale to continue use of omega-3 supplements. "If you want to continue believing that, stop buying omega-3 and tell them to use olive oil," Dr. Asbell observed in response to the criticism. "It's a lot less expensive."[4]

The researchers defended their choice of placebo by arguing that the anti-inflammatory effects associated with olive oil are attributed mainly to polyphenols not found in the refined olive oil used in the study.[6] However, research shows that oleic acid can alter the microbiome and reduce dysbiosis, conferring anti-inflammatory effects elsewhere in the body.[6] Oleic acid may also counter the negative impact of saturated fat on the microbiome.[7]

Dr. Koetting notes that the omega-3 used in the treatment arm was 3000mg of fish-derived n-3 eicosapentaenoic and docosahexaenoic acids but did not include gamma-linolenic acid (GLA), which has been validated in six dry eye clinical trials for treating dry eye and is an anti-inflammatory omega not found in fish, flax or the average diet.[8-13] Given the "real-world" study design, the results of the placebo would have made everything a challenge even if GLA was included and ended up being superior, Dr. Karpecki adds.

"It's a mystery, but with a p-value of 0.005, I find it hard to believe it could all be a placebo effect," Dr. Karpecki says. "My only hypothesis is that the 'real-world' study design led to murky data, so the dry eye improvements were more due to outside factors that were unaccounted for."

Further complicating things was the lack of strict inclusion and exclusion criteria, Dr. Karpecki notes. Including moderate-to-severe dry eye patients of different demographics and health profiles makes it increasingly difficult to come to a definitive conclusion and say that all oral omegas are ineffective, says Dr. Koetting.

"The study shows that not all omegas perform the same in treating dry eye symptoms," she notes, "and that olive oil and omegas can both improve dry eye symptoms."

Dr. Karpecki believes the study did measure a good indicator of dry eye by including osmolarity as an endpoint. He says, however, that unless osmolarity is a factor for enrollment, findings will be too variable and, consequently, inconclusive. And that's exactly what he thinks happened.

Additionally, while the study was promoted as "real-world," it assumed most dry eye patients are already using excessive amounts of fish oil, Dr. Anshel notes.

"I have to wonder if the investigators considered the safety of large amounts of omega-3 on a daily basis," he says, adding that studies have linked excessive omega-3 fatty acids with high blood sugar and other negative side effects.[14-16]

The Profession Reacts

The DREAM Study did not change Dr. Koetting's current practice of recommending omega-3 fatty acid supplements to her dry eye patients, and she believes the study's findings shouldn't sway others either. "I have found, in practice, that omega supplementation, especially one that is GLA-based, is an effective part of treatment for these patients," she notes.

The results of the study also haven't altered Dr. Anshel's nutraceutical recommendations for dry eye, as he doesn't use stand-alone omega-3 fish oil as a treatment.

For Dr. Karpecki, the study reinforced the rationale for recommending a GLA (or possibly flaxseed oil/alpha-linolenic acid) along with fish oil. "I think it's quite notable that the DREAM protocol discusses GLA metabolism and anti-inflammatory pathway at length," he says.

The DREAM study likely hasn't had a significant impact on prescribing practices for nutritional supplements in optometry, according to Dr. Hauser. While many would like to dismiss the study based on its design or choice of placebo, she says the results cannot be ignored and it's possible that nutraceuticals can play a valuable role in dry eye through evolving formulations or the addition of new components. "The study offers an opportunity to talk to patients about their whole food nutrition, which is a conversation many doctors do not have," Dr. Hauser says.

As a dry eye patient herself, Dr. Hauser continues to take omega-3 supplements and recommends the supplements to her patients. "Doctors committed to omega products use them because they have seen clinical improvement in their patients and believe in the supplements' anti-inflammatory effects," she adds. "However, the study does raise the question of whether some patients would have potentially experienced improvement regardless. The DREAM study opened a dialogue about nutrition and supplementation in dry eye. I don't think it's the end of the conversation but rather the beginning." ■

1. Asbell PA, Maguire MG, Pistilli M. n-3 fatty acid supplementation for the treatment of dry eye disease. N Engl J Med. 2018;378(18):1681-90.
2. Miljanovi B, Trivedi KA, Dana MR, et al. The relationship between dietary n-3 and n-6 fatty acids and clinically diagnosed dry eye syndrome in women. Am J Clin Nutr. 2005;82(4):887-93.
3. Wojtowicz JC, Butovich I, Uchiyama E, et al. Pilot, prospective, randomized, double-masked, placebo-controlled clinical trial of an omega-3 supplement for dry eye. Cornea. 2011;30(3):308-14.
4. Galor A, Asbell PA. DREAM Study: can omega-3 treat dry eye disease? American Academy of Ophthalmology. www.aao.org/interview/dream-study-can-omega-3-treat-dry-eye-disease. Published 2018. Accessed April 17, 2019.
5. Gorzynik-Debicka M, Przychodzen P, Cappello F, et al. Potential health benefits of olive oil and plant polyphenols. Int J Mol Sci. 2018;19(3).
6. Dennis Ruskin, Julie Poteet, Stuart Richer. Four Great Debates in Ocular Nutrition, Wellness Essentials for Clinical Practice. A Supplement to Review of Optometry. Pages 24-25, Sept. 15, 2018.
7. Alcock J, Lin HC. Fatty acids from diet and microbiota regulate energy metabolism. F1000Res. 2015;4(F1000 Faculty Rev):738.
8. Aragona P, Bucolo C, Spinella R, et al. Systemic omega-6 essential fatty acid treatment and pge1 tear content in Sjögren's syndrome patients. Invest Ophthalmol Vis Sci. 2005;46(12):4474-9.
9. Barabino S, Rolando M, Camicione P, et al. Systemic linoleic and gamma-linolenic acid therapy in dry eye syndrome with an inflammatory component. Cornea. 2003;22(2):97-101.
10. Rashid S, Jin Y, Ecoiffier T, et al. Topical omega-3 and omega-6 fatty acids for treatment of dry eye. Arch Ophthalmol. 2008;126(2):219-25.
11. Macrì A, Giuffrida S, Amico V, et al. Effect of linoleic acid and gamma-linolenic acid on tear production, tear clearance and on the ocular surface after photorefractive keratectomy. Graefes Arch Clin Exp Ophthalmol. 2003;241(7):561-6.
12. Brignole-Baudouin F, Baudouin C, Aragona P, et al. A multicentre, double-masked, randomized, controlled trial assessing the effect of oral supplementation of omega-3 and omega-6 fatty acids on a conjunctival inflammatory marker in dry eye patients. Acta Ophthalmol. 2011;89(7):e591-7.
13. Sheppard JD Jr., Sing R, McClellan AJ, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate-to-severe keratoconjunctivitis sicca: a randomized double-blind clinical trial. Cornea. 2013;32(10):1297-304.
14. Brasky TM, Darke AK, Song X, et al. Plasma phospholipid fatty acids and prostate cancer risk in the SELECT trial. J Natl Cancer Inst. 2013;105(15):1132-41.
15. Gow RV, Hibbeln JR. Omega-3 fatty acid and nutrient deficits in adverse neurodevelopment and childhood behaviors. Child Adolesc Psychiatr Clin N Am. 2014;23(3):555-90.
16. Link R. 8 little-known side effects of too much fish oil. www.healthline.com/nutrition/fish-oil-side-effects. Published July 17, 2018. Accessed April 30, 2019.

Cyclosporine Shoot-out:

How Do They Match Up?

After more than a decade with just a single agent to use, your options are expanding. This story explains their differences. By Michelle Hessen, OD

Nearly all eye care providers will treat dry eye and, while we have many arrows in our dry eye treatment quiver, one, cyclosporine, is of particular interest. This agent first gained prominence in the United States when Restasis (cyclosporine A ophthalmic emulsion 0.05%, Allergan) launched in 2003. Since then, a number of similar pharmaceutical options have entered the domestic and foreign markets, with even more new formulations in clinical trials. With this expansion, optometrists should understand how the array of options differ, how they're similar and other details of their mechanisms to pair them with the appropriate patients. This article reviews what the academic literature and published clinical trials show regarding the various cyclosporines around the globe.

Photo: Jakiah Varikooty

This positive lissamine green conjunctival staining indicates dry eye, whereas the lid margin staining is indicative of lid wiper epitheliopathy. Cyclosporine drugs offer these kinds of patients relief.

Inflammation's Role

Dry eye—a multifactorial disease of the tears and ocular surface that causes discomfort, visual disturbance and tear film instability—is estimated to affect more than 40 million Americans, and that number is anticipated to increase drastically.[1-4] Inflammation is a major factor of dry eye and it is primarily mediated by CD4+ T cells.[5]

The initial induction of inflammation varies and can include one of two systemic autoimmune diseases. One is Sjögren's syndrome (SS), which results in lymphocytic infiltration of the lacrimal gland, leading to aqueous-deficient dry eye. The other is meibomian gland dysfunction (MGD), which reduces the lipid component of the tear film leading to evaporative dry eye.[4,6] Irrespective of any identifiable underlying local or systemic inflammatory disorder, dry eye seems to be invariably associated with chronic inflammation of the ocular surface, although it is not known whether the local inflammation

Pathophysiology Review

Evidence from the past decade shows dry eye-related ocular surface inflammation is mediated by lymphocytes.[9] Based on earlier immunohistopathological evaluations, patients with both SS-related as well as non-SS dry eye have identical conjunctival inflammation manifested by T-cell infiltrates and upregulation of CD3, CD4 and CD8 as well as lymphocyte activation markers CD11a and HLA-DR.[10] These results suggest symptoms of dry eye may be dependent on T-cell activation and resultant autoimmune inflammation.

Multiple other studies followed and demonstrated the role of pro-inflammatory cytokines and matrix metalloproteinases (MMPs) in the pathogenesis of dry eye disease. Interleukin (IL)-1 is one of the most widely studied cytokines accompanying dry eye. An increase in the proinflammatory forms of IL-1 (IL-1α and mature IL-1β) and a decrease in the biologically inactive precursor IL-1β have been found in the tear film of dry eye patients.[11] The source of the increased levels of IL-1 was thought to be the conjunctival epithelium based on immunohistochemical studies.[11] More recently, reactive nitrogen species expressed by conjunctival epithelial cells have been recognized as playing a role in the pathogenesis or self-propagation of SS-related dry eye.[12]

In the same study, IL-1β, IL-6, IL-8, and tumor necrosis factor (TNF)-α also play a significant role in SS-related dry eye compared with normal eyes.

The response of cells to extracellular stimuli, such as ocular surface stress (including changes in the composition of the tear film or hyperosmolarity and ultraviolet light exposure) is mediated in part by a number of intracellular kinase and phosphatase enzymes.[13] Mitogen-activated protein (MAP) kinases are integral components of parallel MAP kinase cascades activated in response to a number of cellular stress, including inflammatory cytokines (e.g., IL-1 and TNF-α), heat shock, bacterial endotoxin and ischemia. Activation of these MAP kinase homologues mediates the transduction of extracellular signals to the nucleus and is pivotal in regulation of the transcription events that determine functional outcome in response to such stresses.

Researchers have identified these stress-activated protein kinases in the tear film of patients with dry eye. Activation of these stress pathways results in transcription of stress-related genes, including MMPs, mainly MMP-9.[14] In another study, MAP kinases were found to stimulate the production of inflammatory cytokines including IL-1, TNF-α and MMP-9 and thereby causing ocular surface damage.[15]

Hyperosmolarity induces inflammation in human limbal epithelial cells by increasing expression and production of pro-inflammatory cytokines and chemokines such as IL-1β, TNF-α and IL-8.[16] This process appears to be mediated through activation of the C-Jun N-terminal kinases and MAPK signalling pathways.

The science of dry eye pathogenesis may be complex, but it gives researchers numerous targets for potential therapies. All of these inflammatory mediators and pathways should be considered important, and should also be kept in mind when discussing treatment strategies.

is causative or simply occurs as a consequence of ocular dryness. Regardless, recognition of the role of inflammation in dry eye has been a crucial factor in facilitating dry eye treatment.

Since inflammation plays such a significant role in dry eye, promoting ocular surface disruption and symptoms of irritation, a number of anti-inflammatory treatments are currently available for its management. Many more anti-inflammatory medications are in the development or clinical trials phases. These agents inhibit the expression of inflammatory mediators on the ocular surface, thereby restoring the secretion of a healthy tear film and reducing the signs and symptoms of afflicted patients.

CsA Overview

Cyclosporine A (CsA) has principal pharmacologic action of suppressing the activation and function of T-lymphocytes, acting as an immunosuppressant and inhibitor of cell death. Patients with severe dry eye often have a poor response to the standard twice-daily dosing of Restasis, even after several months of treatment, and often benefit from an increased dosing application of three or four times per day.[8] Since frequent dosing can be a hassle for patients, researchers are seeking better drug delivery systems that can increase the concentration of CsA in the cornea and conjunctiva. While CsA drops may be compounded for patients at higher concentrations, the access for patients to obtain them from a compounding pharmacy may be limited and cost-prohibitive. But new options include the recently FDA-approval of Cequa (CsA 0.09%, Sun Pharmaceuticals), the compounded drop Klarity-C (Imprimis) and formulations not yet available in the US, including Ikervis (CsA 0.1%, Santen), Modusik-A Ofteno, TJ Cyporin and Papilock Mini.

CsA Mechanism of Action

Research shows commercially available topical cyclosporine 0.05%, such as Restasis, or 1% compounded preparations are effective in several inflammatory conditions including vernal conjunctivitis, Thygeson's superficial punctate keratitis, non-infectious keratitis

and MGD.[17] The American Academy of Ophthalmology now considers CsA a dry eye treatment option in its Preferred Practice Pattern.[18] The immunomodulating effects of cyclosporine A are achieved through binding with cyclophilins, which are a group of proteins. Cyclophilin A, which is found in the cytosol, and the cyclosporin-cyclophilin A complex inhibits a calcium/calmodulin-dependent phosphatase, calcineurin, which is thought to halt the production of the transcription of T-cell activation by inhibiting IL-2.[19] Cyclophilin D is located in the matrix of mitochondria. Cyclosporine A-cyclophilin D complex modulates the mitochondrial permeability transition pore thereby inducing a mitochondrial dysfunction and cell death.[20] The reduction in inflammation, via inhibition of T-cell activation and down-regulation of inflammatory cytokines in the conjunctiva and lacrimal gland is thus thought to allow enhanced tear production.[21-25] Topical cyclosporine also increases goblet cell density and decreases epithelial cell apoptosis.[26]

Treatment Protocol

When starting CsA treatment for a patient, we commonly educate them on the somewhat extended and variable duration of using the eye drop before it may result in improvement of their symptoms. Relief may take three weeks to three months after initiating CsA.[27]

In a survey of 144 patients in an extension study of the initial clinical trial of CsA (both the 0.05% and 0.1% formulation), 62.5% reported that their dry eye symptoms began to resolve after three months of treatment.[27] Patient reports of onset of symptom relief was faster in two larger survey studies involving more than 8,000 dry eye patients in which more than half of patients reported CsA was effective within three to five weeks.[28,29] It is unclear if the reduction in symptoms and staining (sodium fluorescein and rose bengal) was secondary to active CsA vs. lubrication from CsA vehicle.[28,29] In a prospective study of 158 patients treated with CsA, 22% reported no change in their symptoms as measured by the ocular surface disease index (OSDI) over an average of eight to 10 months of follow-up.[30] That large range in time to improvement may be because severe DED is so severe that patients notice slight improvements faster than someone who has more moderate symptoms.

Patient education regarding side effects of CsA is also an important conversation to improve compliance. The most commonly reported side effect of CsA 0.5% is ocular burning (reported in 17% of patients), which is also the most cited reason for discontinuation of CsA.[23,30-32] Topical steroid use prior to instillation of CsA may help reduce this burning sensation.[33] Pretreatment with topical Lotemax (loteprednol etabonate 0.5%, Bausch + Lomb) induction two weeks before the initiation of topical CsA 0.05% can provide more rapid relief of dry eye signs and symptoms and greater efficacy than CsA and artificial tears alone.[33] No studies currently demonstrate findings that would suggest systemic absorption of topical CsA for ophthalmic use.

New CsA Options

The option of cyclosporine therapy is evolving from a single agent to a burgeoning category of choices. As Restasis is quite familiar to practicing optometrists, we will concentrate on the newer agents.

Cequa (Sun Pharmaceutical)—preclinically referred to as OTX-101—is a nanomicellular topical 0.09% formulation recently FDA approved for DED treatment. This aqueous-based solution (as opposed to the oil-based emulsion of Restasis), aims to deliver therapeutic concentrations of CsA with minimal discomfort.

Investigators believe oil-based preparations are poorly tolerated by patients and lead to low bioavailability due to higher attraction of CsA to the lipophilic vehicle in contrast to the highly hydrophilic tissue.[34] Therapeutic levels of emulsion forms are reached in the tissues only after a large number of instillations, raising concerns for patient compliance. CsA ocular emulsions have increased CsA tissue levels; however, manufacturing problems are associated with high cost and potential toxicity over long-term use.[35]

The non-ionic surfactant polymers included in the Cequa formulation are FDA approved. Such safety from these polymers can be justified by the lack of toxicity from the preliminary results performed in human-derived corneal and retinal cells.[36] In addition, the negligible charge of the formulation helps prevent repulsion of the formulation with negatively charged cell surfaces, improving its interaction with the ocular cells.[37]

A comparative pharmacokinetics study between cyclosporine concentrations after single topical administration of Restasis 0.05% and of Cequa 0.05%—another CsA nanomicellar formulation—shows 3.84-fold higher CsA concentrations in the tears for Restasis than Cequa.[34] This is likely due to interaction of the oil-based vehicle with the outer oily layer of the tear. Similarly, the superior eyelid, which is primarily composed of a thin skin, absorbed significant CsA concentrations (1.98-fold) from oil-based Restasis in contrast to Cequa.[34] Systemic CsA exposure was also substantially lower for both of the formulations in comparison with ocular tissues, indicating lower chances

lombartinstrument.com/pre-owned

LOMBART

Table 1. Topical Cyclosporines[1-4]

Product	Form	Regimen	Indication
Restasis (0.5mg/mL, Allergan)	Anionic emulsion	BID	DED (KCS with presumed suppression of tear production)
Cequa (0.09%, Sun Pharma)	Solution	BID	KCS
Ikervis (1.0mg/mL, Santen)	Cationic emulsion	QD	DED (severe keratitis which has not improved with tear substitutes)
Cyclasol (0.5% and 0.1%, Novaliq)	Solution	QID, BID	KCS
Klarity-C (0.1% cyclosporine in chondroitin sulfate, ImprimisRx)	Emulsion	BID or QD	KCS
Papilock Mini (1.0mg/mL, Santen)	Solution)	TID	VKC
Modusik-A Ofteno (1.0mg/mL, Laboratorios Sophia)	Solution	BID	KCS with a functional decrease of lacrimal glands
Lacrinmune (0.5mg/mL, Bausch + Lomb)	Emulsion	BID	KCS with a functional decrease of lacrimal glands
TJ Cyporin (0.5mg/mL, Taejoon)	Solution	BID	Ocular inflammation associated with KCS
Cyporin (0.5mg/mL, Aristopharma)	Solution	BID	Ocular inflammation associated with KCS
Cyclorin (0.5mg/mL, Ibn Sina)	Solution	BID	Ocular inflammation associated with KCS

1. Lallemand F, Schmitt M, Bourges J, et al. Cyclosporine A delivery to the eye: a comprehensive review of academic and industrial efforts. European Journal of Pharmaceutics and Biopharmaceutics.2017;117(8):14-28.
2. Mandal A. Ocular pharmacokinetics of a topical ophthalmic nanomicellar solution of cyclosporine (Cequa) for dry eye disease. Pharm Res. 2019;36(2):36
3. Roesky C. Breaking the vicious circle of dry eye disease. On Drug Delivery. www.ondrugdelivery.com/breaking-the-vicious-circle-of-dry-eye-disease/. January 14, 2019. Accessed May 1, 2019.
4. Lindstrom R. New dry eye drop provides balance of compliance, cost. Ophthalmology Times. www.ophthalmologytimes.com/dry-eye/new-dry-eye-drop-provides-balance-compliance-cost. June 11, 2018. Accessed May 1, 2019.

of systemic side effects. The favorable pharmacokinetic *in vivo* results obtained for Cequa led to its advancement into clinical trials.

The majority of the ocular adverse events were mild and transient only at the instillation site with Cequa treatment groups, but no serious ocular adverse effects were reported in the Phase II/III study. Cequa 0.05% and 0.09% treatment groups demonstrated an equivalent safety and tolerability profiles.

Cequa is also the first DED product candidate that has demonstrated significant improvement for both conjunctival staining and anaesthetized Schirmer's test, apart from reduction in corneal staining.[38] The results of a Phase III study demonstrate that Cequa 0.09% significantly improved sign- and symptom- end points of DED.[39] The trial also proved the ocular safety of Cequa is consistent with the previous studies.[39]

Cyclasol (Novaliq) is another preservative-free clear solution the treatment of moderate-to-severe DED. Using the company's EyeSol technology based on semi-fluorinated alkanes, the new formulation does not use water, oils, surfactants or preservatives. An *ex vivo* model supports the higher bioavailability potential whereby, after initial application, Cyclasol 0.05% passes through the corneal barrier in as little as two and a half hours; after 8.5 hours, Restasis had not penetrated.[40]

Researchers believe Cyclasol has a significantly greater local bioavailability based on penetration into the cornea, compared with Restasis and Ikervis (eightfold and twofold respectively).

Efficacy, safety and tolerability of a 0.1% formulation of Cyclasol were evaluated in a Phase II, multicenter, randomized, vehicle-controlled clinical trial, double-masked between Cyclasol (0.5% and 0.1%) and vehicle with open-label comparator (Restasis) at twice daily for 16 weeks.[42] Cyclasol showed a consistent reduction in corneal and conjunctival staining compared with both vehicle and Restasis over the 16-week treatment period with an early onset of effect (at day 14).

A mixed-effect-model approach demonstrated that the Cyclasol drug effect was statistically significant over vehicle.[42] This analysis suggests a significant Cyclasol effect for OSDI as a symptom parameter. The number of ocular adverse events were low in all treatment groups. No clear differences between the two Cyclasol concentrations were observed in signs, symptoms or safety parameters analyzed for the clinical data, and this finding was supported by the modeling data.

Ikervis (Santen) is a preservative-free formulation being evaluated, yet unavailable, in the United States.

In a clinical trial, 246 DED patients with severe corneal fluorescein staining were randomised to one drop of Ikervis or vehicle daily at bedtime for six months.[43] The primary endpoint was the proportion of patients achieving by month six at least a two-grade improvement in corneal staining and a 30% improvement in symptoms, measured with the OSDI.[43] The proportion of responders in the Ikervis group was not statistically significant (28.6%, compared with 23.1% in the vehicle group).[43]

The severity of corneal staining improved significantly from baseline at six months with Ikervis compared with the vehicle. The proportion of Ikervis-treated patients

BAUSCH + LOMB
See better. Live better.

BALANCE

POWER AND SIMPLICITY

Zenlens™

*#1 DOCTOR-PRESCRIBED SCLERAL LENS**

SIMPLIFIED FITTING
with SmartCurve™ technology

FCLSA-CERTIFIED CONSULTANTS
offer individualized support

EXPANDED OFFERINGS
with Tangible® Hydra-PEG® and Zen™ Multifocal

*Based on US lens sales between December 2018 and February 2019.

with a three-grade improvement in corneal staining at six months (from four to one) was 28.8% compared with 9.6% of vehicle-treated subjects, but this was a *post hoc* analysis. The mean change from baseline in the 100-point OSDI score was -13.6 with Ikervis and 14.1 with vehicle at month six.[43] In addition, no improvement was observed for Ikervis compared with vehicle at month six for other secondary endpoints, including ocular discomfort score, Schirmer test, use of concomitant artificial tears, investigator's global evaluation of efficacy, tear break-up time, lissamine green staining, quality of life score and tear osmolarity.[43]

In a different six-month trial, 492 DED patients with moderate-to-severe corneal staining were also randomized to Ikervis or vehicle daily at bedtime for six months.[44] The two primary endpoints were the change in corneal staining score, and the change in global score of ocular discomfort unrelated to study medication instillation, both measured at six months.[44] Researchers noted a small but statistically significant difference in corneal staining between the treatment groups at six months in favor of Ikervis.[44]

Klarity-C (ImprimisRx) is yet another formulation to be used in the treatment of signs and symptoms of dry eye.[45] It contains 0.1% cyclosporine in a chondroitin sulfate ophthalmic emulsion, which is said to have short-term anti-inflammatory properties.[46] The product is supplied in a multi-dose bottle for convenience and potential cost savings. In a three-month study of 75 patients, OSDI scores improved in all patients, and 56% had at least a 20 point change in OSDI.[45] In addition, 81.2% of eyes had a reduction in corneal staining after three months of topical therapy.[45]

International medications. A few other cyclosporine formulations, unavailable in the US, have been mentioned in the literature; however, minimal research has been published to support efficacy and safety. Papilock Mini was approved in 2008 in Japan to treat vernal keratoconjunctivitis (VKC) at a dosage of three times daily. Lacrinmune (topical cyclosporine 0.05% emulsion, Bausch + Lomb) launched in Argentina and is dosed twice daily for the treatment of keratoconjunctivitis sicca (KCS). TJ Cyporin (cyclosporine 0.05% solution, Taejoon Pharmaceuticals) is available in some countries in Asia. Modusik-A Ofteno (cyclosporine 1%, Labratorios Sophia) was approved in 2003 to treat KCS and is available in Mexico, Chile, Columbia, Peru and Equador.

Future Directions

Additional research is being performed to evaluate the use of CsA-eluting contact lenses to treat dry eye.[47] These lenses showed an initial burst and sustained release of CsA until 48 hours. New Zealand rabbits exhibited improved clinical parameters and conjunctival goblet cell density as well as decreased inflammatory cytokines. Advancements in drug delivery continue to be explored for the treatment of this multifactorial ocular disease.

The inflammatory nature of dry eye disease has been widely accepted; thus, the direction for treatment research is geared toward the reduction of inflammatory cytokines. Cyclosporine A inhibits the immune reaction. There are documented drawbacks to this drug in regards to its somewhat poor tolerability, instability and low bioavailability. Several pharmaceutical companies are working on formulations to maximize the effects while minimize side-effects and keep dosing infrequent.

The above formulations of cyclosporine differ in their concentration and preparation and thus bioavailability to ocular tissue. That being said, future clinical research may assist us in choosing the right medication for treatment of ocular surface inflammatory conditions by understanding if one formulation will provide greater improvement in ocular surface staining, increased tear production, as well as tolerability. ■

Dr. Hessen is a clinical instructor at the Wilmer Eye Institute's Ocular Surface Diseases and Dry Eye Clinic at Johns Hopkins School of Medicine, where she specializes in ocular surface disease.

1. Yu J, Asche CV, Fairchild CJ. The economic burden of dry eye disease in the United States: a decision tree analysis. Cornea. 2011;30(4):379-87.
2. Hawkes N. US's $2bn annual spend on dry eye disease "brings tears to your eyes," says critics. BMJ 2018;360:k492.
3. Gayton JL. Etiology, prevalence, and treatment of dry eye disease. Clin Ophthalmol. 2009;3:405-12.
4. Lemp MA, Baudouin C, Baum J, et al. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international dry eye workshop (2007). Ocul Surf. 2007;5:75-92.
5. Niederkorn JY, Stern ME, Pflugfelder SC, et al. Desiccating stress induces T cell-mediated Sjogren's syndrome-like lacrimal keratoconjunctivitis. J Immunol. 2006;176:3950-3957.
6. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017;15:276-283.
7. Murphy CJ, Bentley E, Miller PE, et al. The pharmacologic assessment of a novel lymphocyte function-associated antigen-1 antagonist (SAR 1118) for the treatment of keratoconjunctivitis sicca in dogs. Invest Ophthalmol Vis Sci. 2011;52(6):3174-80.
8. Dastjerdi MH, Hamrah P, Dana R. High frequency topical cyclosporine 0.05% in the treatment of severe dry eye refractory to twice-daily regimen. Cornea. 2009;28:1091-1096.
9. Kunert KS, Tisdale AS, Stern ME, et al. Analysis of topical cyclosporine treatment of patients with dry eye syndrome: effect on conjunctival lymphocytes. Arch Ophthalmol. 2000;118:1489–96.
10. Stern ME, Gao J, Schwalb TA, et al. Conjunctival T-cell subpopulations in Sjögren's and non-Sjögren's patients with dry eye. Invest Ophthalmol Vis Sci. 2002;43:2609–14.
11. Solomon A, Dursun D, Liu Z, et al. Pro- and anti-inflammatory forms of interleukin-1 in the tear fluid and conjunctiva of patients with dry-eye disease. Invest Ophthalmol Vis Sci. 2001;42:2283–92.
12. Cejková J, Ardan T, Simonová Z, et al. Nitric oxide synthase induction and cytotoxic nitrogen-related oxidant formation in conjunctival epithelium of dry eye (Sjögren's syndrome) Nitric Oxide. 2007;17:10–7.
13. Paul A, Wilson S, Belham CM, et al. Stress-activated protein kinases: activation, regulation and function. Cell Signal. 1997;9:403–10.
14. Pflugfelder SC, de Paiva CS, Tong L, et al. Stress-activated protein kinase signaling pathways in dry eye and ocular surface disease. Ocul Surf. 2005;3(Suppl 4):154–7.
15. Luo L, Li DQ, Doshi A, et al. Experimental dry eye stimulates production of inflammatory cytokines and MMP-9 and activates MAPK signaling pathways on the ocular surface. Invest Ophthalmol Vis Sci. 2004;45:4293–301.

16. Li DQ, Luo L, Chen Z, et al. JNK and ERK MAP kinases mediate induction of IL-1beta, TNF-alpha and IL-8 following hyperosmolar stress in human limbal epithelial cells. Exp Eye Res. 2006;82:588–96.
17. Utine CA, Stern M, Akpek EK. Clinical review: topical ophthalmic use of cyclosporin A. Ocul Immunol Inflamm. 2010;18(5):352-61.
18. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Dry Eye Syndrome. San Francisco, CA: American Academy of Ophthalmology.
19. Matsuda S, Koyasu S. Mechanisms of action of cyclosporine. Immunopharmacology. 2000;47(2-3):199-125.
20. Stevenson W, Chauhan SK, Dana R. Dry Eye Disease: an immune-mediated ocular surface disorder. Arch Ophthalmology. 2012;130(1):90-100.
21. Pflugfelder SC, Wilhelmus KR, Osato MS, et al. The auto-immune nature of aqueous tear deficiency. Ophthalmology. 1986;93;1513-1517.
22. Stern ME, Gao J, Siemasko KF, et al. The role of the lacrimal gland functional unit in the pathophysiology of dry eye. Exp Eye Res. 2004;78;409-416.
23. Stevenson D, Tauber J, Reis BL. Efficacy and safety of cyclosporine A ophthalmic emulsion in the treatment of moderate to severe dry eye disease: a dose-ranging, randomized trial. The Cyclospoine A Phase 2 Study Group. Ophthalmology. 2000;107:967-974.
24. Sall K, Stevenson OD, Mundorf TK, et al. Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. CsA Phase 3 Study Group. Ophthalmology. 2000;107:631-639.
25. Laibovitz RA, Solch S, Andriano K, et al. Pilot trial of cyclosporine 1% ophthalmic ointment in the treatment of keratoconjunctivitis sicca. Cornea. 1993;12;315-323.
26. Kunert KS, Tisdale AS, Gipson IK. Goblet cell numbers and epithelial proliferation in the conjunctiva of patients with dry eye syndrome treated with cyclosporine. Arch Ophthalmol. 2002;120:330-337.
27. Benitez del Castillo JM, del Aguila A, Duran S. Influence of topically applied cyclosporine a in olive oil on corneal epithelium permeability. Cornea. 1994;13(2):136-40.
28. Sy A, O'Brein KS, Liu MP, et al. Expert opinion in the management of aqueous deficient dry eye disease (DED). BMC Ophthalmol. 2015;15:133.
29. Parrilha LR, Nai GA, Giuffrida R, et al. Comparison of 1% cyclosporine eye drops in olive oil and in linseed oil to treat experimentally-induced keratoconjunctivitis sicca in rabbits. Arq Bras Oftalmol. 2015;78(5):295-9.
30. Friedman NJ. Impact of dry eye disease and treatment on quality of life. Curr Opinion Ophthalmol. 2010;21(4):310-316.
31. Research in dry eye: report of the Research Subcommittee of the International Dry Eye Workshop (2007). The Ocular Surface. 2007;5(2):179-193.
32. Perry HD. Dry eye disease, pathophysiology, classification, and diagnosis. Am J Manag Care. 2008;14(3 Suppl):S79-87.
33. Sheppard JD, Donnenfeld ED, Holland EJ, et al. Effect of loteprednol etabonate 0.5% on initiation of dry eye treatment with topical cyclosporine 0.05%. Eye Contact Lens. 2014;40(5):289-96.
34. Mandal A, Gote V, Pal D, et al. Ocular pharmacokinetics of a topical ophthalmic nanomicellular solution of cyclosporine (Cequa) for dry eye disease. Pharm Res. 2019;36(2):36.
35. Luschmann C, Herrmann W, Strauss O, et al. Ocular delivery systems for poorly soluble drugs: an in-vivo evaluation. Int J Pharm. 2013;455(1–2):331–7.
36. Cholkar K, Gilger BC, Mitra AK. Topical, aqueous, clear cyclosporine formulation Design for Anterior and Posterior Ocular Delivery. Transl Vis Sci Technol. 2015;4(3):1.
37. Ashim K. Mitra PRV, Ulrich M. Grau Topical Drug Delivery Systems For Ophthalmic Use. In.: Aurinia Pharmaceuticals Inc Apr. 28, 2015.
38. Tauber J, Schechter BA, Bacharach J, Toyos MM, Smyth-Medina R, Weiss SL, 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;12:1921–9.
39. Jodi Luchs M. Phase 3 clinical results of cyclosporine 0.09% in a new nanomicellar ophthalmic solution to treatment keratoconjunctivitis sicca. International American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting Washington, DC; 2018.
40. Detuscu RM, Panfil A, Merkel UM, et al. Semifluorinated Alkanes as a liquid drug carrier system for topical ocular drug delivery. E J Pharm Biopharm 2014;88:123-8.
41. Agarwai O, Scherer D, Günther B, Rupenthal ID. Semifluorinated alkane based systems for enhanced corneal penetration of poorly soluble drugs. Int J Pharm 2018;538:119-29.
42. Wirta D, Torkildsen G, Moreira H, et al. A clinical phase 2 study to assess efficacy, safety and toleratbility of CyclASol for treatment of dry eye disease (DED). Ophthalmol. www.aaojournal.org/article/S0161-6420(18)32132-8/fulltext. November 11-14, 2017. Accessed May 1, 2019.
43. Leonardi A, Van Setten G, Amrane M, et al. Efficacy and Safety of 0.1% cyclosporine A cationic emulsion in the treatment of severe dry eye disease: a multicenter randomized trial. Eur J Ophthalmol 2016;26(4):287-296.
44. Baudoin C, Figueiredo FC, Messmer EM, et al. A randomized study of the efficacy and safety of 0.1% cyclosporine A cationic emulsion in the treatment of moderate to severe dry eye. Eur J Ophthalmol 2017;27(5);520-30.
45. Matossian C, Trattler WB, Loh JM. Tolerability and Efficacy of topical 0.1% cyclosporine in chondroitin sulfate ophthalmic emulsion: an open-label registry study. ASCRS annual meeting 2019.
46. Moon JW, Lee H-J, Shin KC, et al. Short term effectsof topical cyclosporine and viscoelastic on the ocular surfaces in patients with dry eye. Korean J Ophthalmol 2007;21(4):189-94.
47. Choi JH, Li Y, Shrestha T, et al. The efficiency of cyclosporine A-eluting contact lenses for the treatment of dry eye. Curr Eye Research. 2018;44(5):486-96.

A Guide to Conjunctival Tumors

These are benign half the time—but when they are malignant, you need to be ready to refer. By Carol L. Shields, MD, Sara E. Lally, MD and Jerry A. Shields, MD

Conjunctival tumors include a spectrum of benign and malignant neoplasms.[1-5] The types differ based on age and race, systemic immune status and long-term exposures. A large study of 5,002 cases from an ocular oncology center revealed that 52% were benign, 18% were premalignant and 30% were malignant (*Table 1*).[1,2] Even though this report was from an ocular oncology center and malignancies might be over-represented, it is important for clinicians to understand the variety of conjunctival tumors.

The five most common tumors were nevus (23%), ocular surface squamous neoplasia (OSSN, 14%), primary acquired melanosis (PAM, 12%), melanoma (12%) and lymphoid tumor (9%).[5] Malignant tumors were seen most often in adults and included melanoma (12%), squamous cell carcinoma (SCC, 9%), lymphoma (7%), Kaposi's sarcoma (<1%), metastasis (<1%) and others.[1] Conjunctival tumors in children demonstrate malignancy only 3% of the time.[5]

This review of the most common conjunctival tumors will prepare you to manage them appropriately, whether in your office or through referral.

Ocular Surface Squamous Neoplasia

The general clinical term of OSSN includes a spectrum of malignancies that ranges from mild epithelial dysplastic changes, such as conjunctival intraepithelial neoplasia (CIN), to more severe invasive carcinoma that invades through the basement membrane into the substantia propria, such as squamous cell carcinoma.

Clinical features. Conjunctival OSSN classically occurs in older Caucasian males, particularly those with chronic sun exposure. In the United States, conjunctival SCC is five times more common in males and Caucasians. However, in Africa, conjunctival SCC is nearly equally common in men and women, and it occurs at a younger age than in the United States.[6]

Ocular surface squamous neoplasia usually presents as a unilateral, vascularized gelatinous mass, located

Table 1. Type, Frequency of Conjunctival Tumors[2,5]

Category and Specific Diagnosis	All Patient Ages (n=5,002)	Children <21 (n=806)
Choristomatous tumors	101 (2%)	65 (8%)
Epithelial tumors (benign)	95 (2%)	9 (1%)
Epithelial tumors (premalignant, malignant)	729 (15%)	2 (<1%)
Melanocytic tumors (including nevus, PAM, melanoma)	2590 (52%)	553 (69%)
Vascular tumors	212 (4%)	54 (7%)
Fibrous tumors	15 (<1%)	4 (<1%)
Neural tumors	5 (<1%)	1 (<1%)
Xanthomatous tumors	8 (<1%)	6 (1%)
Myxomatous tumors	7 (<1%)	1 (<1%)
Lipomatous tumors	44 (1%)	3 (<1%)
Lacrimal gland tumors	15 (<1%)	1 (<1%)
Lymphoid/leukemic tumors	474 (10%)	47 (6%)
Metastatic tumors from remote cancers	6 (<1%)	0 (0%)
Secondary tumors from adjacent tumors	66 (1%)	2 (<1%)
Non-neoplastic masquerader	635 (13%)	58 (7%)

in the sun-exposed conjunctiva at the nasal or temporal limbus (*Figure 1*). Overlying leukoplakia, dilated feeder vessels and foamy infiltration of the adjacent corneal epithelium can occur and can rarely invade into the globe or orbit.

Predisposing factors. The most important environmental factors for OSSN include chronic sun exposure and cigarette smoke exposure. Two key host predisposing factors include fair complexion and underlying human immunodeficiency virus (HIV) and human papillomavirus.[6] Patients with immune deficiency, particularly those with HIV, are at risk for OSSN and can have advanced, bilateral and invasive tumors.[1] This is especially seen in Africa, where HIV is prevalent and OSSN occurs in both males and females and at a younger age.[6] Other immune dysregulation can predispose a patient to OSSN, including organ transplant immunosuppression, eczema/atopy, ocular cicatricial pemphigoid, xeroderma pigmentosum and autoimmune conditions.[7]

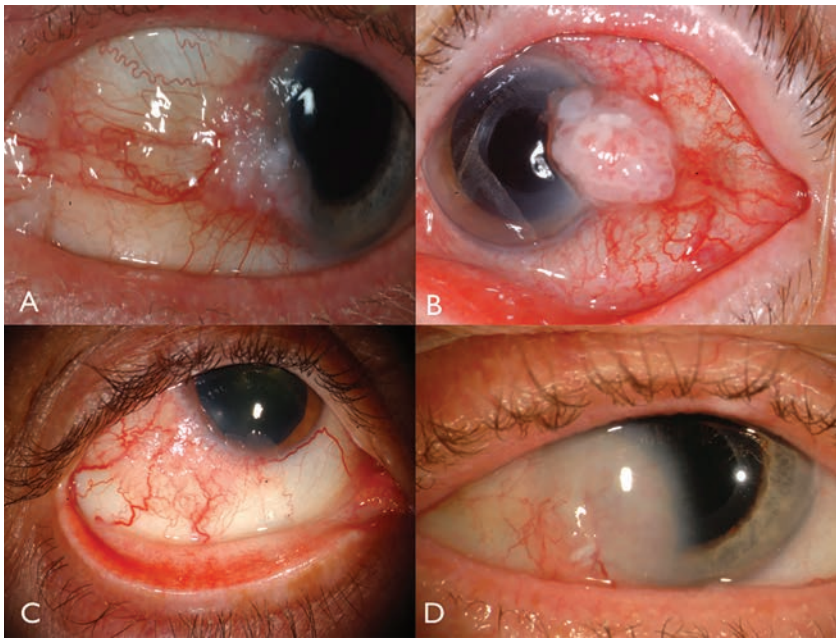


Fig. 1. Limbal OSSN: with leukoplakia and corneal involvement (A), with prominent intrinsic vascularity and feeder vessels (B), in a HIV patient (C), and with deep corneal invasion requiring resection and plaque radiotherapy (D).

Classification. The American Joint Committee on Cancer (AJCC)'s 8th edition manual provides the most recent classification for conjunctival carcinoma, including SCC and CIN (*Table 2*).[8]

Management. This involves surgical resection using the "no-touch" technique or nonsurgical therapies such as topical chemotherapy with mitomycin C (MMC) or 5-fluorouracil (5-FU), topical or injected immunotherapy with interferon alpha-2b (IFN), topical antiviral medication (cidofovir) or photodynamic therapy.[7,9-11]

The surgical no-touch technique involves detailed evaluation of the tumor using slit-lamp biomicroscopy to visualize all tumor margins, including bulbar, forniceal and tarsal components, to understand the entire extent of the tumor and enable the clinician to hand-draw a template recording.[9] This template is then taken into the surgery to ensure the entire tumor is removed.

At the time of surgery, only the surrounding normal tissue is held with forceps, and the tumor is never touched to avoid seeding of tumor. In addition, balanced salt solution is not employed during surgery to avoid liquid-dispersion of cancer cells. Following tumor removal, closure with clean instruments is crucial. Using this technique for OSSN, tumor persistence or recurrence is found in fewer than 5% of cases.

Topical chemotherapy with 5-FU or MMC is efficient in resolving the OSSN, often within two to four weeks of therapy, although a risk for stem cell

Table 2. Classification of Conjunctival Carcinoma[8]

Definition of Primary Tumor	
CATEGORY	**CRITERIA**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*
T1	Tumor (≤5mm in greatest dimension) invades through the conjunctival basement membrane without invasion of adjacent structures
T2	Tumor (>5mm in greatest dimension), invades through the conjunctival basement membrane without invasion of adjacent structures
T3	Tumor invades adjacent structures excluding the orbit
T4	Tumor invades the orbit with or without further extension
T4a	Tumor invades orbital soft tissues, without bone invasion
T4b	Tumor invades bone
T4c	Tumor invades adjacent paranasal sinuses
T4d	Tumor invades brain

deficiency exists. Our topical therapy preference is immunotherapy with IFN, as it is well tolerated with good tumor control, often over three months and with little complication and only minor follicular conjunctivitis.[10,11] These medications can be locally toxic to the corneal epithelium, but less so with interferon, and patients should be followed closely while on them. If cost is a factor to the patient, topical 5-FU is the least expensive, followed by MMC and then IFN.

Conjunctival Lymphoid Tumors

Lymphoid neoplasms range from low- to high-grade tumors and arise from monoclonal proliferation of lymphocytes. The lymphoid tumors that occur in the periocular region often involve several tissues such as the conjunctiva, orbit and eyelid and are termed "ocular adnexal" lymphoid tumors, including benign reactive lymphoid hyperplasia (BRLH) and lymphoma.

BRLH and lymphoma are on opposite ends of the spectrum, with BRLH appearing clinically as a localized "salmon patch" and histopathologically benign whereas lymphoma also appears as a "salmon patch" but with more aggressive histopathologic features, with mitotic activity and classified as malignant.

Ocular adnexal lymphoid tumors are typically of B-cell origin. A multicenter study of 268 patients with conjunctival lymphoma found the four most common types included extranodal marginal zone lymphoma (ENMZL, previously termed mucosal-associated lymphoid tissue) in 68%, follicular lymphoma (FL) in 16%, mantle cell lymphoma (MCL) in 7% and diffuse large B-cell lymphoma (DLBCL) in 5%.[12] Other types of conjunctival lymphoma include lymphoplasmacytic lymphoma and plasmacytoma.

Clinical features. Conjunctival lymphoma usually presents in older patients between the ages of 60 and 70. This tumor can manifest as primary lymphoma, limited to the periocular region, or as secondary lymphoma with disease elsewhere. Most primary lymphoma occurs with ENMZL and FL and secondary lymphoma with DLBCL and MCL. One analysis of 117 patients with conjunctival lymphoma found systemic involvement in 31%, most often in those with bilateral multifocal ocular adnexal lymphoma.[13]

Conjunctival lymphoma classically manifests as a pink salmon-colored, smooth-surfaced subconjunctival mass, sometimes with feeder vessels (*Figure 2*). This smooth, multilobulated mass can resemble follicular or papillary conjunctivitis. This tumor is most often located in the conjunctival fornix (44%) or midbulbar (42%) region and, rarely, in the caruncle (7%) or limbus (7%).[13] In addition to the conjunctiva, lymphoma can be found infiltrating the orbit, eyelid or uvea.[13] Most patients with conjunctival lymphoma do not exhibit an intraocular component, but if present, it generally resides in the uvea and not the retina or vitreous.

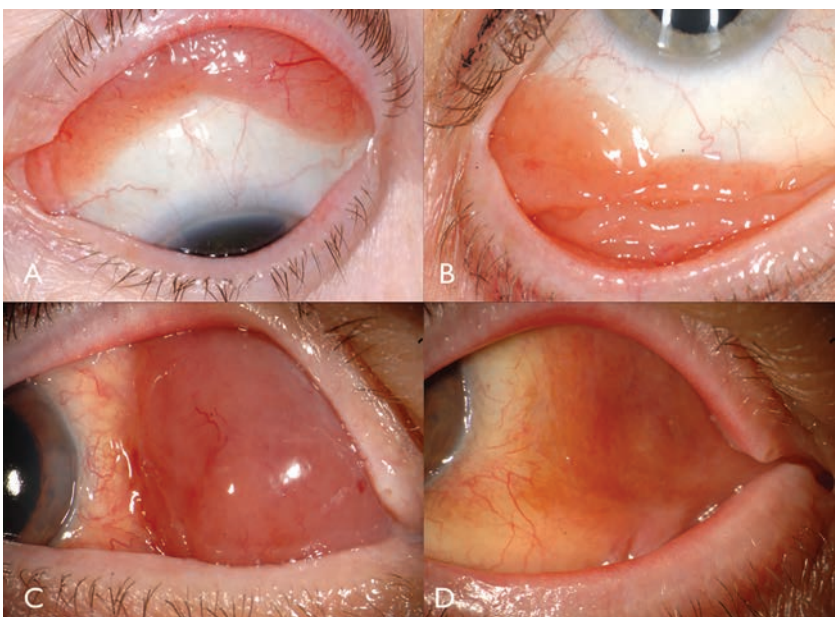


Fig. 2. Conjunctival lymphoma can be salmon-pink (A) or multilobulated forniceal (B). Medial forniceal conjunctival lymphoma before (C) and after (D) rituximab.

Predisposing factors. Immune dysfunction and autoimmune conditions, as well as infective etiologies such as *Helicobacter pylori* and *Chlamydia psittaci* are all predisposing factors for conjunctival lymphoma. BRLH may be a potential precursor to lymphoma and, while predominately found in adults, can occasionally occur in children.[5] In fact, the younger the patient at the time of diagnosis of a conjunctival lymphoid tumor, the more likely it is BRLH and not lymphoma.

Classification. Several classifications for conjunctival lymphoma exist, including the Ann Arbor, World Health Organization and AJCC 8th edition staging (*Table 3*).[8] The AJCC clinical staging is based on tumor location, regional lymph node and distant involvement.[8]

VITASIGHT™
Better Nutrition to Support Healthy Vision

O3+Maqui™

Omega-3 with Maqui Berry

COMBATS
DRY EYE SYMPTOMS
AND PROMOTES HEALTHY TEARS[Δ]

MaquiBright®
Clinical trials show Maqui Berry increases tear production and improves dry eye symptoms.

Omega-3 Fatty Acids
O3+Maqui contains 2420mg of highly refined omega-3 fish oil in a re-esterified triglyceride form.

Patented Unigel™ Technology
The only patended technology that combines a liquid & powder tablet in one convenient softgel.

LEARN MORE & ORDER

Visit **O3Maqui.com** or call **(866) 752-6006**

FocusLaboratories.com FOCUS Laboratories

Δ This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

FLM191-1218-01

Management. Caring for patients with conjunctival lymphoma primarily depends on the extent of periocular involvement, systemic involvement and their general health. In patients with only conjunctival lymphoma and no systemic involvement, treatment is focused on complete surgical resection. Treatment with external beam radiotherapy or rituximab are options if the tumor is nonresectable. For those with periocular and systemic lymphoma, treatment with systemic rituximab or the addition of chemotherapy are considerations.

Systemic prognosis with conjunctival lymphoma is directly related to each subtype, as one study found the five-year survival was 97% for ENMZL, 82% for FL, 55% for DLBCL and only 9% for MCL.[12]

Conjunctival Melanoma

Conjunctival melanocytic tumors are unquestionably common, representing more than 50% of cases in a large series of conjunctival tumors from an ocular oncology unit.[1,2] This class of melanocytic tumors includes many types such as nevus, complexion-related melanosis, PAM, secondary acquired melanosis, melanoma and metastases.[1-5] On some continents where patients have dark complexions, even OSSN can appear melanocytic. Of these lesions, conjunctival nevus represents 45% and primary conjunctival melanoma represents 23% of all melanocytic tumors in an ocular oncology practice.[2]

In the United States, the age-adjusted incidence of conjunctival melanoma doubled between 1973 and 1999 from 0.27 per million to 0.54 per million.[14,15] The incidence increased 295% in white men in the United States over the same 27-year period, especially among men aged 60 years or older.[14] Researchers speculate the increasing rate may be related to ultraviolet light exposure.

Clinical features. Conjunctival melanoma is a pigmented or non-pigmented malignancy that can arise from PAM, nevus or *de novo*.[16] Melanoma can be found on the limbal, bulbar, forniceal or palpebral conjunctiva and often demonstrates dilated, tortuous feeder and intrinsic vessels typically surrounded by flat PAM (*Figure 3*). In general, tumors measuring greater than 2mm in thickness are at significant risk for lymph node metastasis. Tumor invasion into the orbit is particularly serious with substantial metastatic risk.

Local tumor recurrence or new tumor is found in 50% of cases, often related to new PAM transformation. Distant metastasis—often to the preauricular, submandibular or cervical lymph node chain—is found in 25% of patients. Sentinel lymph node biopsy can help clinicians evaluate for subclinical lymph node infiltration. Multiple recurrences, especially those involving the orbit, necessitate orbital exenteration.

Table 3. Classification of Ocular Adnexal Lymphoma[8]

CATEGORY	CRITERIA
Definition of Primary Tumor	
TX	Tumor extent not specified
T0	Tumor absent
T1	Tumor in conjunctiva without eyelid or orbit involvement
T2	Tumor in orbit with or without conjunctival involvement
T3	Tumor in preseptal eyelid with or without orbital and/or conjunctival involvement
T4	Tumor in orbit plus additional bone, maxillofacial sinuses, and brain
Definition of Regional Lymph Nodes (N)	
NX	Regional lymph nodes not assessed
N0	Regional lymph node involvement absent
N1	Regional lymph node involvement present and superior to mediastinum (preauricular, parotid, submandibular, and cervical nodes)
N1a	1 lymph node region involvement superior to mediastinum
N1b	>2 lymph node regions involvement superior to mediastinum
N2	Regional lymph node involvement in mediastinum
N3	Regional lymph node involvement in peripheral and central lymph node regions (diffuse or disseminated)
Definition of Distant Metastasis (M)	
M0	Distant involvement at other extranodal site absent
M1a	Distant involvement in noncontiguous tissue (parotid gland, submandibular gland, lung, liver, spleen, kidney, breast)
M1b	Distant involvement in bone marrow
M1c	Both M1a and M1b present
Definition of Histologic Grade (G)	
GX	Grade cannot be assessed
G1	1 to 5 centroblasts/10 high power fields (HPF)
G2	5 to 15 centroblasts/10 HPF
G3	>15 centroblasts/10 HPF but with admixed centrocytes
G4	>15 centroblasts/10 HPF but without centrocytes

Predisposing factors. The most important predisposing factor for conjunctival melanoma is the presence of long-standing conjunctival nevus or PAM.[16-18] When studying conjunctival melanoma origin by histopathology, researchers found the origin was PAM in 74%, *de novo* in 19% and nevus in 7%.[16]

HOW TO SAVE
WITHOUT COUPONS

Help your patients get affordable eye drops without searching for coupons

TOTALTEARS®

The simple cash pay model of the Total Tears formulations* eliminates the need for patients to hunt down coupons and allows for them to purchase their eye drops at affordable prices

Preservative Free Formulations

Klarity Drops®	10mL	Chondroitin sulfate ophthalmic solution	$20/bottle
Klarity-A™ Drops	3.5mL	**Azithromycin 1%** / Chondroitin sulfate ophthalmic solution PF	As low as $40/bottle** When purchased as a pack of 3
Klarity-B™ Drops	5.5mL	**Betamethasone 0.1%** / Chondroitin sulfate ophthalmic solution PF	As low as $40/bottle** When purchased as a pack of 3
Klarity-C Drops®	5.5mL	**Cyclosporine 0.1%** / Chondroitin sulfate ophthalmic emulsion PF	$50/bottle
Klarity-L™ Drops	5mL	**Loteprednol 0.5%** / Chondroitin sulfate ophthalmic solution PF	As low as $40/bottle** When purchased as a pack of 3

No Prior Authorizations | No Coupons | No Pharmacy Hassles

Learn more at www.TotalTears.com

*For professional use only. ImprimisRx specializes in customizing medications to meet unique patient and practitioner needs. ImprimisRx dispenses only to individually identified patients with valid prescriptions. No compounded medication is reviewed by the FDA for safety or efficacy. ImprimisRx does not compound copies of commercially available products. References available upon request.

** Klarity-A, Klarity-B, Klarity-L offers tiered pricing at $59 for a single bottle, $99 for 2 bottles, and $119 for 3 bottles

imprimis Rx®
844.446.6979

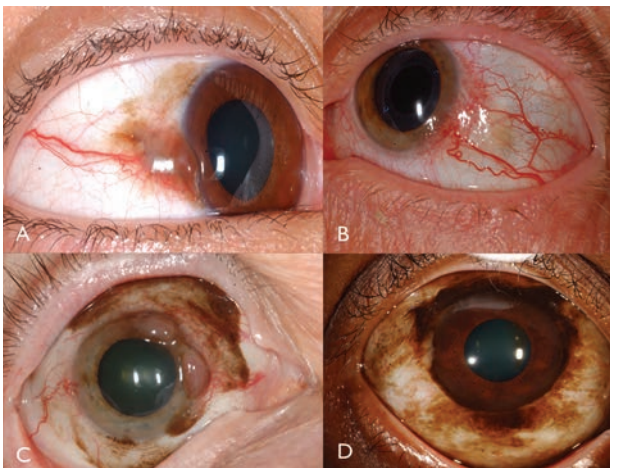


Fig. 3. Pigmented conjunctival melanoma can arise from PAM (A). Non-pigmented conjunctival melanoma may have intense vascularity (B). PAM could also cause mixed pigmented/non-pigmented conjunctival melanoma (C). PAM caused limbal melanoma in this African-American patient (D).

Clinical studies estimate that one in 300 nevi develop into melanoma.[17,18]

A large clinical study found that the 10-year risk for PAM transformation into melanoma was about 9%, and the greater extent of PAM promoted a greater risk for transformation into melanoma.[19] Hence, it is important to identify PAM and treat this condition with surgical excision, cryotherapy and even superficial keratectomy (if there is corneal involvement) with the intention of preventing melanoma.

The differentiation of conjunctival nevus from melanoma can be challenging. In a recent analysis of 510 cases of conjunctival nevus vs. melanoma in children, melanoma was more common in older children, with a relative risk (RR) of 4.80, greater tumor thickness (RR of 1.14), greater base (RR of 4.92), tumor hemorrhage (RR of 25.30) and lacking intrinsic cysts (RR of 5.06).[5] The researchers assigned these features, predictive of conjunctival melanoma in children, to a mnemonic: **CATCH Melanoma**, representing: **C**hildren **A**ge older, **T**hickness/base greater, **C**yst lacking, **H**emorrhage for **Melanoma**.[5]

Differentiation of PAM from melanoma can also be challenging; however, melanoma has thickness and PAM is completely flat. In an analysis of 1,224 cases of PAM vs. melanoma in all ages, melanoma with significantly greater based on median patient age (54 vs. 61 years); male sex (35% vs. 49%); location in fornix (2% vs. 6%) and tarsus (1% vs. 4%); larger median

basal diameter (6mm vs. 8mm), thickness (<1mm vs. 1mm), feeder vessels (10% vs. 48%) and intrinsic vessels (4% vs. 33%); and hemorrhage (<1% vs. 3%).[2]

Tissue biomarkers are important for the assessment of conjunctival melanoma and include BRAF mutation, TERT promoter mutation and PTEN mutation.[1] Identifying these biomarkers is critical when planning systemic therapy for treatment or prevention of metastasis, as targeted therapies against certain biomarkers are available, such as vemurafenib for BRAF-mutated malignancy.

Classification. The AJCC's clinical classification for conjunctival melanoma is based on tumor extent by quadrants, tumor location and invasive features (*Table 4*).[8] Our team studied outcomes of conjunctival melanoma based on the AJCC 7th edition and found this staging was highly predictive of prognosis.[20] Melanoma classified as T2 and T3 (compared with T1) showed significantly higher rates of local recurrence, regional lymph node metastasis, distant metastasis and death.

Management. Care for conjunctival melanoma basically involves complete surgical resection using the no-touch technique to avoid tumor seeding. The first surgery is the most important, as delicate removal of the entire tumor without tumor seeding is key to preventing future recurrences and metastases.[16]

Melanoma at the corneoscleral limbus is removed under the operating microscope also using the no-touch technique. The flat corneal component is removed with absolute alcohol, superficial epitheliectomy without disruption of Bowman's membrane. The conjunctival portion is removed with 2mm to 3mm margins and released at the limbus using flat episcleral dissection. If scleral invasion is present, plaque radiotherapy is applied. All conjunctival margins are treated with double freeze-thaw cryotherapy.

Reconstruction involves primary closure techniques, rotational flap or amniotic membrane transplantation, often with symblepharon ring with amniotic membrane draping. Melanoma that extends into the orbit requires orbital exenteration or, more recently, immunotherapy with checkpoint inhibition.[21]

Patients with conjunctival melanoma should be monitored by an ocular oncologist for local recurrence and by a systemic melanoma oncologist for metastatic disease, particularly with regional lymph node palpation and sentinel lymph node biopsy. Metastases initially appear in the preauricular or

submandibular lymph nodes, then later in the lung and brain. New evidence suggests that melanoma metastasis could be sensitive to BRAF inhibitors or immune checkpoint inhibitors.[21,22]

Conjunctival tumors encompass a broad spectrum of tumors. The most common malignancies include OSSN, lymphoma and melanoma. Recognizing the classic clinical features, understanding precursors and prompt and appropriate management of these malignancies are important for best patient outcomes. ■

Drs. Shields, Lally and Shields work in the Ocular Oncology Service at Wills Eye Hospital, Thomas Jefferson University, in Philadelphia. *Support provided by Eye Tumor Research Foundation, Philadelphia.*

1. Shields CL, Chien JL, Surakiatchanukul T, et al. Conjunctival tumors: review of clinical features, risks, biomarkers, and outcomes. The 2017 J. Donald M. Gass Lecture. Asia Pac J Ophthalmol. 2017;6:109-20.
2. Shields CL, Alset AE, Boal NS, et al. Conjunctival tumors in 5002 cases. Comparative analysis of benign versus malignant counterparts. The 2016 James D. Allen Lecture. Am J Ophthalmol. 2017;173:106-33.
3. Shields CL, Shields JA. Tumors of the conjunctiva and cornea. Surv Ophthalmol. 2004;49:3-24.
4. Grossniklaus HE, Green WR, Luckenbach M, et al. Conjunctival lesions in adults. A clinical and histopathologic review. Cornea. 1987;6:78-116.
5. Shields CL, Sioufi K, Alset AE, et al. Conjunctival tumors in children. Features differentiating benign from malignant tumors. JAMA Ophthalmol. 2017;135:215-24.
6. Gichuhi S, Sagoo MS, Weiss HA, et al. Epidemiology of ocular surface squamous neoplasia in Africa. Trop Med Int Health. 2013;18:1424-43.
7. Shields CL, Ramasubramanian A, Mellen P, Shields JA. Conjunctival squamous cell carcinoma arising in immunosuppressed patients (organ transplant, human immunodeficiency virus infection). Ophthalmology. 2011;118:2133-7.
8. Amin MB, Edge S, Greene F, et al., eds. AJCC Cancer Staging Manual. 8th ed. Chicago; Springer International Publishing: 2017.
9. Shields JA, Shields CL, De Potter PV. Surgical approach to conjunctival tumors. The 1994 Lynn B. McMahan Lecture. Arch Ophthalmol. 1997;115:808-15.
10. Shields CL, Kaliki S, Kim HJ, et al. Interferon for ocular surface squamous neoplasia in 81 cases: Outcomes based on the American Joint Committee on Cancer classification. Cornea. 2013;32(3):248-56.
11. Karp CL, Galor A, Chhabra S, et al. Subconjunctival/perilesional recombinant interferon α2b for ocular surface squamous neoplasia: a 10-year review. Ophthalmology. 2010;117(12):2241-6.
12. Kirkegaard MM, Rasmussen PK, Coupland SE, et al. Conjunctival lymphoma – An international multicenter retrospective study. JAMA Ophthalmol. 2016;134:406-14.
13. Shields CL, Shields JA, Carvalho C, et al. Conjunctival lymphoid tumors: clinical analysis of 117 cases and relationship to systemic lymphoma. Ophthalmology. 2001;108:979-84.
14. Yu GP, Hu DN, McCormick S, Finger PT. Conjunctival melanoma: Is it increasing in the United States? Am J Ophthalmol. 2003;135:800-6.
15. Tuomaala S, Kivela T. Correspondence regarding conjunctival melanoma: Is it increasing in the United States? Am J Ophthalmol. 2003;136:1189-90.
16. Shields CL, Markowitz JS, Belinsky I, et al. Conjunctival melanoma. Outcomes based on tumor origin in 382 consecutive cases. Ophthalmology. 2011;118:389-95.
17. Shields CL, Fasiuddin AF, Mashayekhi A, et al. Conjunctival nevi: clinical features and natural course in 410 consecutive patients. Arch Ophthalmol. 2004;122:167-75.
18. Gerner N, Norregaard JC, Jensen OA, Prause JU. Conjunctival naevi in Denmark 1960-1980. A 21-year follow-up study. Acta Ophthalmol Scand. 1996;74:334-7.
19. Shields JA, Shields CL, Mashayekhi A, et al. Primary acquired melanosis of the conjunctiva: risks for progression to melanoma in 311 eyes. The 2006 Lorenz E. Zimmerman lecture. Ophthalmology. 2008;115:511-9.
20. Shields CL, Kaliki S, Al-Dahmash S, et al. American Joint Committee on Cancer (AJCC) Clinical Classification predicts conjunctival melanoma outcomes. Ophthalm Plast Reconstr Surg. 2012;5:313-23.
21. Sagiv O, Thakar SD, Kandl TJ, et al. Immunotherapy with programmed cell death 1 inhibitors for 5 patients with conjunctival melanoma. JAMA Ophthalmol. 2018 Nov 1;136(11):1236-41.
22. Dalvin LA, Shields CL, Orloff M, et al. Checkpoint inhibitor immune therapy. Systemic indications and ophthalmic side effects. Retina. 2018;6:1063-78.

Table 4. Classification of Conjunctival Melanoma[8]

CATEGORY	CRITERIA
Definition of Primary Clinical Tumor	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor of the bulbar conjunctiva
T1a	<1 quadrant
T1b	>1 but <2 quadrants
T1c	>2 but <3 quadrants
T1d	>3 quadrants
T2	Tumor of nonbulbar conjunctiva (forniceal, palpebral, tarsal, caruncle)
T2a	Noncaruncular and <1 quadrant
T2b	Noncaruncular and >1 quadrant
T2c	Caruncular and <1 quadrant
T2d	Caruncular and >1 quadrant
T3	Tumor of any size with local invasion
T3a	Globe
T3b	Eyelid
T3c	Orbit
T3d	Nasolacrimal duct and/or lacrimal sac and/or paranasal sinuses
T4	Tumor (any size) with with invasion of central nervous system
Definition of Regional Lymph Nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	Regional lymph node metastasis absent
N1	Regional lymph node metastasis present
Definition of Distant Metastasis (M)	
M0	Distant metastasis absent
M1	Distant metastasis present
Definition of Primary Pathological Tumor	
TX	Primary tumor cannot be assessed
T0	No evidence or primary tumor
Tis	Tumor confined to conjunctival epithelium
T1	Tumor of bulbar conjunctiva
T1a	Tumor with <2mm thickness invasion of substantia propria
T1b	Tumor with >2mm thickness invasion of substantia propria
T2	Tumor of nonbulbar conjunctiva
T2a	Tumor with <2mm thickness invasion of substantia propria
T2b	Tumor with >2mm thickness invasion of substantia propria
T3	Tumor (any size) with local invasion
T3a	Globe
T3b	Eyelid
T3c	Orbit
T3d	Nasolacrimal duct and/or lacrimal sac and/or paranasal sinuses
T4	Tumor (any size) with invasion of central nervous system

“Because the **VeraPlug FlexFit** is so comfortable, **my patients are happier** — and with the easy insertion, the FlexFit has become my **plug of choice** for treating dry eye patients.”

Yun Jin Kim, M.D. | EyeCare Medical, Los Angeles, CA

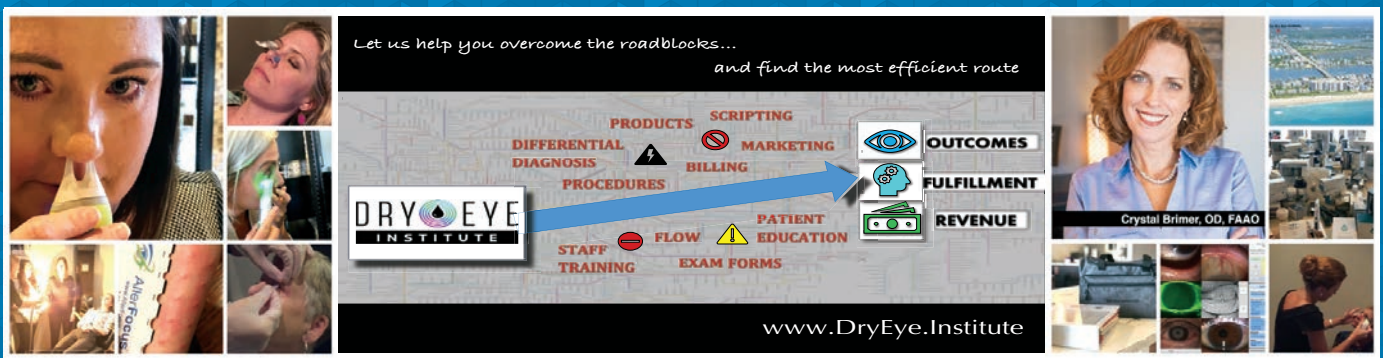
The word is out

Doctors are praising the **VeraPlug™ FlexFit™** for it’s simple sizing, ease of insertion and excellent patient comfort.

A FRESH PERSPECTIVE™

LACRIVERA

Lacrivera is a proud supporter of the Dry Eye Institute



lacrivera.com (855) 857-0518

2500 Sandersville Rd • Lexington KY 40511 USA

PEER • REVIEWED • RRA • ARTICLE

My Patient Has Diabetic Retinopathy... Now What?

The optometrist has a valuable role to play in monitoring the stages of this condition and guiding patients through treatment.

By Julie Torbit, OD, Anna Kathryn Bedwell, OD, Daniel Bollier, OD, and Brad Sutton, OD

You have dilated your diabetic patient and their fundus shows signs of retinopathy (*Figure 1*). Now it's time to determine your next step. Do you monitor the patient or refer to a retina specialist? The answer can be somewhat tricky because multiple practice guidelines for managing diabetic retinopathy (DR) exist, both from optometry and ophthalmology in the United States, as well as internationally.[1-3]

About this Series

To help optometrists strengthen their protocols for managing conditions that require ongoing—perhaps life-long—care, this series explains the steps to take after confirming a diagnosis, from day one through long-term management. Each installment in the five-part "Now What?" series will cover a different chronic condition:

March—glaucoma
April—RCE
May—diabetic retinopathy
June—scleritis
July—AMD

Be sure to check www.reviewofoptometry.com for any articles you may have missed.

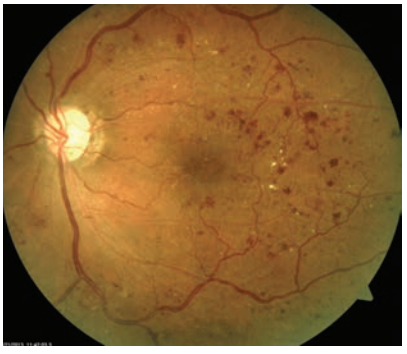


Fig. 1. This fundus shot shows a patient with signs of moderately severe NPDR.

Any therapeutic protocol will depend upon staging the severity of the DR. Note the location of any diabetic changes in the fundus. Next, classify the DR as either nonproliferative (NPDR) or proliferative (PDR). NPDR should be labeled as mild, moderate, severe or very severe. PDR can be further categorized into non-high risk and high risk (*Table 1*).

Finally, with all levels of retinopathy, you should definitively determine the presence or absence of macular edema. So, what are the signs for the various stages of DR that allow practitioners to effectively categorize the disease process?

Step One: Stage the Severity

In a sense, this is your most important task as it sets the tone for the management decisions to follow.

Mild NPDR. This stage is characterized by microaneurysms, dot/blot hemorrhages or hard exudates or a combination of all three. Further diagnostic testing is not indicated in mild NPDR, but fundus photography is often helpful to establish a baseline level of retinopathy to assess future progression, and is useful for patient education.

While traditional optical coherence tomography (OCT) is not indicated for mild NPDR unless retinal thickening is observed with stereoscopic clinical examination or visual acuity is reduced, OCT angiography (OCT-A) can be a useful tool to detect capillary dropout and small microvascular changes that are not otherwise noted on dilated fundus exam (*Figure 2*).

Moderate NPDR. This stage is considered more than just microaneurysms, but less than severe NPDR.[2] Moderate NPDR will show an increase in intraretinal hemor-

rhages and microaneurysms, as well as hard exudates and cotton-wool spots. Mild venous beading (VB) and intraretinal microvascular abnormalities (IRMA) are also seen in moderate NPDR. Fluorescein angiography (FA) may be indicated if VB or IRMA are present. OCT may be appropriate to confirm or rule out the presence of macular edema. Keep in mind that some patients have subclinical diabetic macular edema (DME), only observable with OCT. These patients are at significantly higher risk for worsening DME.[4]

Moderately severe NPDR. Historically, moderate NPDR was monitored and not treated. However, anti-vascular endothelial growth factor (anti-VEGF) injections are now considered primary therapy to improve DR severity.[5-8]

Data from anti-VEGF studies such as RISE, RIDE and PANOROMA show patients with moderately severe (or worse) retinopathy have the potential for at least a two-step improvement on the DR Severity Scale (DRSS) when given anti-VEGF drugs such as ranibizumab (Lucentis, Genentech) or aflibercept (Eylea, Regeneron).[5-8] Though these patients have not yet developed traditionally treatable disease with either macular edema or proliferative changes, there is value in decreasing the level of retinopathy, potentially delaying or preventing the development of sight-threatening complications.

This is an evolving paradigm, however, and many retina surgeons have not yet embraced this approach. Additionally, it can be difficult to convince patients without sight-threatening changes to undergo repeated intraocular injections.

So, what is the definition of moderately severe NPDR? The definition has not been clearly established in the literature, but many DR trials use the Early Treatment DR Study (ETDRS) severity scale score of 47 or higher.[8] This level of DR includes: hemorrhages or microaneurysms, or both, in two or more quadrants, mild IRMA (less than or equal to 0.4mm^2) or venous beading in one quadrant.[9-11] These findings would be considered severe enough to refer patients for potential anti-VEGF treatment.[8] FA may be performed at this stage to better understand the sources of leakage.

Severe NPDR. This stage consists of any one of the following with no signs of proliferative retinopathy: severe intraretinal hemorrhages and microaneurysms in each of four

Table 1. Level of Diabetic Retinopathy and Management[1-3]

Severity	Findings	Ancillary Testing	Follow-Up/ Referral
Minimal NPDR	MA only	Fundus photo +/- widefield imaging	12 months
Mild NPDR	Any or all of: Ma/H, HE, venous looping	Fundus photo +/- widefield imaging	12 months
Moderate NPDR	Ma/H Hard exudates CWS Mild IRMA	Fundus photo +/-widefield imaging	Six months
Moderately Severe NPDR	Retinopathy corresponding to DRSS levels 47 or 53: • Two or more quadrants of Ma/H Mild IRMA (< than SP8A) • VB in one quadrant	Fundus photo +/- FA +/- widefield imaging	Two to four months +/- retinal referral
Severe NPDR	4-2-1 Rule: MA/H in four quadrants or VB in >2 quadrants or Prominent IRMA in >1 quadrant (>SP8A)	Fundus photo +/- FA +/- widefield imaging	Two to four months +/- retinal referral
Very Severe NPDR	Two or more of the 4-2-1 rule (see above)	Fundus photo +/- FA +/- widefield imaging	Two to four months +/- retinal referral
Non-High Risk PDR	Any NVD, NVE, PRH, VH	Fundus photo +/- FA +/- widefield imaging	Retinal referral in one week
High Risk PDR	NVD >1/4 to 1/3DD or Any NVD with VH or PRH -or-NVE> ½ DD with VH or PRH	Fundus photo +/- FA +/- widefield imaging	Retinal referral within 48 hours
Non-CI DME	Retinal thickening outside 500µm microns (1/3DD) of fovea	Macular OCT Fundus photo +/- FA +/- widefield imaging	Two to four months
CI DME	Retinal thickening within 500µm (1/3DD) of the fovea	Macular OCT Fundus photo +/- FA +/- widefield imaging	Retinal referral in two weeks

CI=center involving
CWS=cotton-wool spot
DD=disc diameter
DME=diabetic macular edema
FA=fluorescein angiography
H=hemorrhage (blot/dot)
IRMA=intraretinal microvascular abnormalities
MA=microaneurysm
NVD=neovascularization of the disc
NVE=neovascularization elsewhere
PRH=preretinal hemorrhage
SP8A =EDTRS Standard photograph 8A
VB=venous beading
VH=vitreal hemorrhage

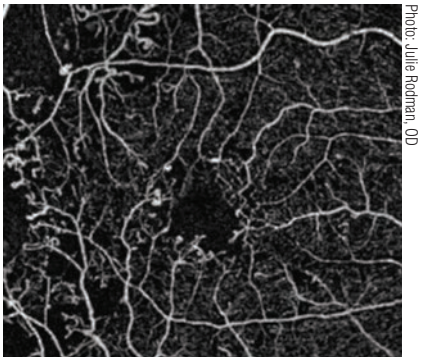


Photo: Julie Rodman, OD

Fig. 2. This OCT-A shows a patient with microaneurysms and capillary dropout.

quadrants (> 20 hemorrhages in each quadrant), two venous beading in two or more quadrants and moderate (or "prominent" by the international definition) IRMA in one or more quadrants, known as the 4-2-1 rule.

Very severe NPDR. To diagnose the most severe stage of NPDR, apply the 4-2-1 rule. The "4" in the rule stands for four quadrants of blot/dot hemorrhages, the "2" is two quadrants of venous beading, then finally the "1" is one or more quadrant of IRMA.

Close monitoring is absolutely necessary in these patients because the ETDRS found 52% risk of progression to PDR in one year and a 60% to 75% risk of progression to high-risk PDR in five years.[3,12]

Proliferative DR. The hallmark of this stage is neovascularization (*Figure 3*). Neovascularization is defined as either being NVD (on the disc or within one-disc diameter of the optic nerve head) or NVE, elsewhere in the retina. PDR can also include a pre-retinal or vitreous hemorrhage. High-risk PDR is defined as one or more of the following: NVD greater than one-fourth to one-third disc area in size, NVD with a fresh vitreous or pre-retinal hemorrhage or NVE greater than one-half a disc area in size associated with a pre-retinal or vitreous hemorrhage.

Step 2: Determine if Macular Edema is Present

DME can occur at any stage of retinopathy and can be difficult to observe clinically. In fact, even patients with 20/20 vision can have DME. It is best appreciated with careful slit lamp examination of the macula with a 78 or 90 diopter lens. Historically, clinically significant diabetic macular edema (CSME) was defined by the ETDRS as meeting one of the following criteria:

1. Thickening at or within 500µm of the center of the fovea.
2. Hard exudates at or within 500µm of the center of the fovea with associated thickening.
3. A one-disc diameter (DD) of thickening that is within one DD of the center of the fovea.

Traditional treatment for CSME was grid/focal laser surgery. Previous research showed that using focal laser for patients with CSME is effective at reducing moderate vision loss by 50%.[13] Rarely, however, was vision significantly improved by laser therapy. The hope was to stabilize vision and lessen further loss, not necessarily improve it. Over time, the concept of strictly defined CSME has evolved. With the widespread use of OCT, much of the literature now simply subdivides DME into center-involving (CI) when retinal thickening is located within the OCT central subfield zone (1mm in diameter) of the fovea, and non-CI DME when the thickening lays outside the central subfield zone.[2,14]

So, what central subfield thickness number on an OCT printout should prompt a referral for treatment? The exact number is hard to pinpoint because various studies of patients with diabetes use different center thickness values depending on the type of OCT instrument being used in the study. For example, the VIVID and VISTA studies used a central thickness of 300µm with a Cirrus OCT (Zeiss).[15] What happens in reality is that clinicians rely on the OCT's normative database to determine if the swelling warrants treatment. Clinically, if the center ring of the OCT printout is flagged as abnormally thick, the patient is referred for DME intervention. Some patients with diabetes have relatively thin retinas due to associated neurodegeneration of the retina, so looking for significant change from baseline may be more useful than reliance on 'color-flagged' OCT thickness abnormalities.

Routine screening of patients with OCT and FA is not necessary.[1,16] However, if you suspect that your patient has macular edema, or their vision is reduced, performing a macular OCT scan would be indicated. FA can be useful in identifying capillary nonperfusion at the macula or enlargement of the foveal avascular zone. It's important to identify CI-DME because the ETDRS found a 10-fold greater risk of moderate vision loss at one year in these eyes compared to eyes with non-CI DME.[3,17]

DME has historically been treated with laser. However, multiple clinical trials show that intravitreal anti-VEGF injections work better.[18,19] The advantage of injections is being able to improve vision instead of merely stabilizing it. The downside of anti-VEGF treatment is the necessity for repeated injections over a long period of time, which comes with a financial burden and the challenge of attending many office visits. In cases where anti-VEGF injections and additive laser therapy prove to be insufficient, intravitreal steroid injections or sustained-release implants can be considered. While frequently effective, they carry the risk of significant intraocular pressure elevation and unavoidable cataract formation.

Passionate About Patient Experience?

OF COURSE YOU ARE.

Exceed their expectations with our complete line of digital refraction devices.
Set your practice apart with the most advanced Phoroptor® ever, **Phoroptor® VRx**,
and our pixel-perfect **ClearChart® 4** family of digital acuity systems.

WATCH OUR NEW SERIES AT:
PASSIONATEABOUTEYECARE.COM

VISIT US AT **OPTOMETRY'S MEETING/AOA #816**

Reichert®
TECHNOLOGIES
PASSIONATE ABOUT EYE CARE

AMETEK®

What if your patient has non-CI DME? The ETDRS report #19 stated that patients with non-CI DME could be observed closely, which may be preferable to immediate treatment.[20] Currently, there is no established evidence for prompt anti-VEGF treatment versus observation versus laser regarding non-CI DME. If the clinician elects to observe, close monitoring of the patient every two to four months is warranted. Also, the discussion of treatment options such as laser or anti-VEGF injections for non-CI DME should be clearly documented in the chart.

The best approach for subclinical DME and center-involving DME without visual loss is not clearly defined in the literature. Subclinical DME describes a situation where macular thickening is present centrally on the OCT, yet thickening of the macula is not noted on clinical examination (*Figure 4*). The DR Clinical Research (DRCR) Network's Protocol G looked specifically at the issue of subclinical DME, and found that up to one-half of eyes in the study with subclinical DME progressed to clinically apparent DME within two years.[21]

In patients with CI DME and good vision (20/25 or better), DRCR Network's Protocol V research is still ongoing and is designed to answer the question if observation or prompt treatment is the best course of action.[22] Management of patients with these subcategories of macular edema will depend on your comfort level with observation vs. referral. If patients are not immediately referred to a retinal specialist for management, they should be seen every two to four months for close monitoring.

Consider Location

Certain retinal locations are more subject to high-risk characteristics of DR than others. Studies have found that the majority of NVE lesions are located inferonasal to the optic disc and along the superior arcades, while NVD has a predilection for the superior temporal rim.[23,24] While DR still exists outside these locations, it can be helpful to focus your fundus examination on these areas, especially in patients with small pupils or poor fixation. Remember, fundus photography can also be quite valuable in patients prove difficult to examine, since the photographic images can be magnified and closely scrutinized for subtle signs of retinopathy. This is also another area where OCT-A may prove useful for detecting NVD or NVE at the vitreo-retinal interface.

Ultra-widefield imaging allows for high resolution of the peripheral retina and can be performed using standard color photography, FA, autofluorescence and indocyanine green angiography. Widefield imaging typically allows up to 200 degrees of the retina to be photographed in a single image versus a 75-degree view of the fundus when using the conventional seven standard fields proposed in the ETDRS.[25]

Careful examination of the peripheral retina is important in diabetic patients because it can detect early signs of non-perfusion that can lead to disease progression. Research has shown a correlation between DME and peripheral retinal ischemia. Many experts feel that the severity of DR may be underestimated when the peripheral fundus is not closely observed and DRCR.net Protocol AA is underway to address the issue more conclusively.[25-28]

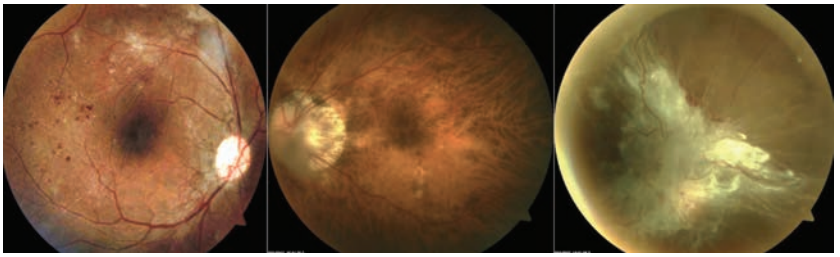


Fig. 3. These fundus images show, from left to right, a patient who has high risk PDR OD: >1/4D-1/3D of NVD inferiorly and NVE superiorly with fibrovascular tissue causing vertical retinal folds through macula; a patient with high myopia (-11.50DS), which can be protective against DR; large posterior vitreous detachment in front of the optic nerve head in the right eye of a patient who failed to seek treatment for PDR.

Systemic Risk Factors

In addition to the location and current stage of retinopathy, multiple systemic factors influence the follow-up schedule for a diabetic patient. A careful review of systems can reveal important information to better define the patient's risk of onset and progression of DR.

Non-modifiable risk factors for DR include duration of diabetes, age, ethnicity, genetics and pregnancy.[29] Because the duration of diabetes is one of the strongest predictors of the development and progression of DR, it is important to note how long your patient has had diabetes.[29-32] American epidemiological studies show African Americans, Latino Americans and Native Americans have the highest rates of visual impairment and blindness from DR.[33-35]

If your diabetes patient becomes pregnant, she should undergo a complete eye examination soon after conception or early during the pregnancy and every trimester, particularly if DR was more than mild

NuLids® – transformational dry eye therapy

Transforms your patients' lives

Finally… A doctor directed at-home treatment for dry eye disease that is safe, effective and easy to use.

A multi-center study[1] showed:

- 50% decrease in dry eye symptoms
- 65% improvement in TBUT
- 80% increase in meibomian glands yielding liquid secretions.

[1] Schanzlin, Olkowski, Coble, Gross. NuLids II Study, April 2018

Transforms your practice

The NuLids System helps reduce patient out-of-pocket expenses while creating an additional revenue stream for the practice – all without impacting overhead costs or disrupting other in-office treatments.

A multi-center study[1] showed 95% were satisfied or very satisfied with the treatment.

For more information visit www.NuSightMedical.com or call us at 833-468-5437

NuLids®

Doctor directed, at-home dry eye relief

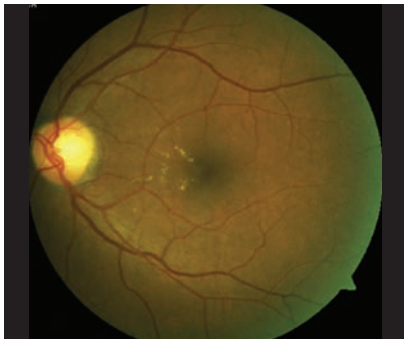
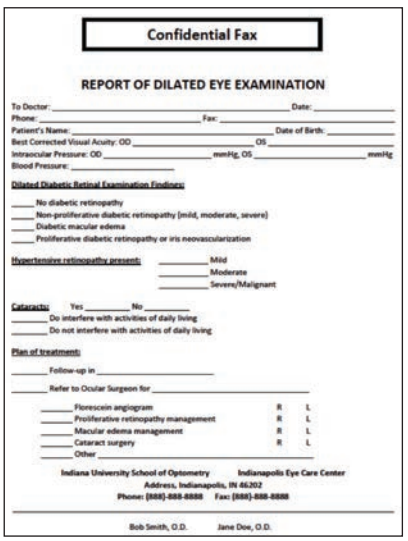


Fig. 4. This fundus image shows clinically significant macular edema with best-corrected visual acuity of 20/20.

at baseline. However, women who develop gestational diabetes do not require an eye examination during pregnancy.[1]

Step 3: Decide to Refer for Treatment or Monitor

Patients with minimal/mild DR can be monitored annually because only 5% to 10% of these patients will progress to more advanced stages of retinopathy over the course of one year.[1-3,30,36,37] Patients with moderate NPDR, in the absence of macular edema, should return every six to twelve months for a close examination of the fundus.[1-3] Moderately severe NPDR patients should be monitored every two to four months, as up to 27% of patients with moderately severe DR will develop PDR in one year.[11,38] If you decide to refer your patient for moderately severe NPDR, consult with your local retina specialist to ascertain their treatment preferences. In regards to DME, clinicians should make a referral to a retinal specialist within two weeks to treat CI macular edema.



Confidential Fax

REPORT OF DILATED EYE EXAMINATION

To Doctor: _____ Date: _____

Phone: _____ Fax: _____

Patient's Name: _____ Date of Birth: _____

Best Corrected Visual Acuity: OD _____ OS _____

Intraocular Pressure: OD _____ mmHg, OS _____ mmHg

Blood Pressure: _____

Dilated Diabetic Retinal Examination Findings:

_____ No diabetic retinopathy

_____ Non-proliferative diabetic retinopathy (mild, moderate, severe)

_____ Diabetic macular edema

_____ Proliferative diabetic retinopathy or iris neovascularization

Hypertensive retinopathy present: _____ Mild

_____ Moderate

_____ Severe/Malignant

Cataracts: Yes _____ No _____

_____ Do interfere with activities of daily living

_____ Do not interfere with activities of daily living

Plan of treatment:

_____ Follow-up in _____

_____ Refer to Ocular Surgeon for _____

_____ Florescein angiogram R L

_____ Proliferative retinopathy management R L

_____ Macular edema management R L

_____ Cataract surgery R L

_____ Other _____

Indiana University School of Optometry Indianapolis Eye Care Center

Address, Indianapolis, IN 46202

Phone: (888)-888-8888 Fax: (888)-888-8888

Bob Smith, O.D. Jane Doe, O.D.

For a full-size downloadable version of this referral form, read this article online at www.reviewofoptometry.com.

Severe cases involving vitreous hemorrhage and tractional retinal detachment often require surgical intervention. Consult with the specialist within 48 hours for high risk PDR and within one week for PDR. The DR Study found that with prompt treatment of high-risk PDR with PRP, the risk of severe vision loss (<5/200) was reduced by more than 50%.[39,40]

Step 4: Educate and Communicate

A key component to managing patients with diabetes is appropriate communication to those involved in the patient's care. This starts with a chairside discussion. Only half of all those with diabetes have a yearly eye exam.[41] To improve this statistic, our job as eye care providers is to educate our patients and the community at large. Our patients must understand DR, and its sight threatening complications. Educational resources include handouts, exam room posters, and incorporation of diabetes education within your website or social media accounts. Handouts can be self-designed or taken from pre-existing resources like the National Eye Institute or American Optometric Association.

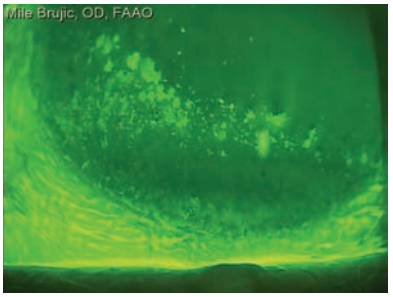
Regardless of your approach, it is important to emphasize modifiable risk factors:

- ***Glycemic control.*** Goal HbA1c in Type II diabetes varies depending on age and comorbidities. The American Diabetes Association recommends below 7.0% for most non-pregnant adults.[42]
- ***Smoking status.*** The exact relationship between smoking and DR progression is controversial. Regardless, from a public health standpoint, patients should be advised to lead a healthier lifestyle by not smoking. Encourage patients to kick the habit by providing them with local and state cessation programs. Ask them if they want to quit and focus efforts on those who answer affirmatively.
- ***Hypertension.*** Stress an ideal blood pressure below 130/80mm Hg. Understand that ACE inhibitors or angiotensin receptor blocking agents are standard of care for hypertension in diabetes, and have been shown to have a retino-protective effect in several studies.[43]
- ***Obesity.*** Emphasize weight loss through physical exercise and proper nutrition. Suggest a plant-based diet and elimination of processed foods and soft drinks.
- ***High cholesterol.*** Optimize cholesterol levels with a diet low in saturated and hydrogenated fats and relatively high in poly- and monounsaturated fats that can raise high-density lipoproteins (HDL). Current literature shows that statin treatment for dyslipidemia reduces the risk of DR in Type II diabetes, as does the triglyceride lowering agent fenofibrate.[44-46]

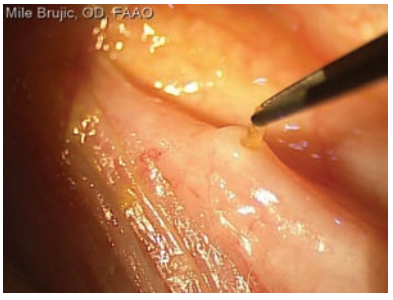
EyeRes™

Digital Imaging Systems

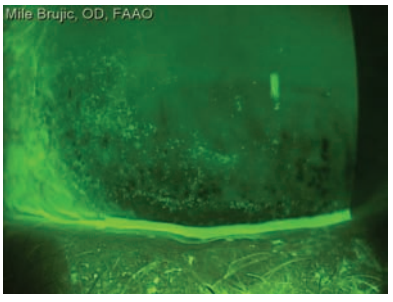
See *the condition.*



Treat *the condition.*



Monitor *the recovery.*

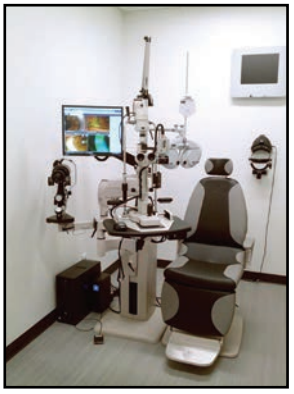


Photos courtesy of Mile Brujic, O.D.

Make A Difference by Using this Versatile System:

Anterior-segment imaging, Retinal imaging, and Infrared imaging all from an ***Eye*****Res**™ slit lamp and ***Eye*****Res**™ digital imaging system.

Save time, money, and space while enhancing the patient's appreciation for your expertise.



www.TelScreen.com

Call* 800.769.4933** ***today or email Wes Harris at Wes.Harris@TelScreen.com

TelScreen

Understanding Your Condition—A Guide for Patients

Diabetic retinopathy is the leading cause of blindness (20/200 or worse) in Americans of working age (20-74). Only 50% of patients with diabetes receive appropriate eye care. Diabetic retinopathy is a complication of diabetes that affects the eyes. It is caused by poorly controlled blood sugar, which damages the blood vessels in the retina. This is a painless eye disease that can slowly or quickly take away your vision. Vision that is lost often cannot be fully restored. About 95% of blindness can be prevented through early detection, timely treatment, and appropriate follow up.

Risk factors:

- How long you have had diabetes
- Blood sugar control
- Blood pressure control
- Lipid control
- Renal and heart disease
- Lifestyle: obesity, smoking, moderate to severe alcohol consumption, physical inactivity

What can and should you do?

- ***Get a dilated eye exam yearly*** or as recommended by your eye doctor
- Control your ABCs, (A1c, blood pressure, cholesterol)
- Adopt a healthy lifestyle, including diet and physical activity
- Limit processed foods and soft drinks
- Kick the smoking habit
- Get good sleep! Studies recommend six to nine uninterrupted hours a night
- Take your medications as prescribed by your primary doctor

Please do not hesitate to contact your health care providers, including your eye doctor, with any questions. Be active in your care as the health of your body is directly tied to the health of your eyes!

The text at left can be used to create a patient education handout. For a full-size downloadable version, read this article online at www.reviewofoptometry.com.

• ***Poor sleep habits.*** Getting six to nine hours of uninterrupted sleep each night reduces the risk of diabetes. Remember also that untreated obstructive sleep apnea (OSA) can worsen DR.[47] Encourage diabetic patients with OSA symptoms to have a sleep study.

• ***Vitamin D.*** Encourage patients to get outside. Vitamin D deficiency has been linked to diabetes and to increased risk of DR.[48]

• ***Nutrition.*** Consider a science-based nutritional supplement for those with DR.

• ***PCP/Endocrinologist.*** Communication must also occur with the patient's primary care doctor, endocrinologist, or both, after each diabetes-related office visit. Our preference is to send a one-page report focusing on important exam details, specifically visual acuity, blood pressure, presence of DR, level of hypertensive retinopathy (if applicable) and treatment plan. Most electronic health record systems can tailor a template for you.

If findings are atypical, or if you are suggesting the patient needs additional lab or diagnostic workup, a formal letter is indicated. A letter needs to appropriately address the target audience, include only pertinent information, follow an organized format and have a clear message. Often, letters contain extraneous information that dilutes the salient points. What needs to be included in a formal letter?

• ***Brief patient history.*** This includes the reason for communication and pertinent background information about the patient's complaint, condition(s) and medical history.

• ***Objective testing.*** Here is where providers have to focus on what is pertinent information. Best-corrected VA should always be included, as it is understood universally among all provider types. Refraction, though, is almost never necessary to include. Specifically, focus on the dilated fundus examination findings and the results of pertinent ancillary testing such as OCT. Non-ophthalmic providers have stressed that they prefer not to receive communications containing ophthalmic acronyms (e.g., NPDR, OD/OS/OU), so use formal diagnostic terminology.

• ***Assessment and recommendation.*** What is your diagnosis and treatment plan? Make it clear whether you are following up with the patient and when, or if you are referring the patient for specific management.

Formal letters, though more time-consuming, are an excellent means to provide thorough patient care and build better relationships with our medical colleagues. Whether you choose a short report, formal letter, or phone call will depend upon the clinical scenario and urgency of the message.

Retina Referral Tips

Most of us already have established relationships with our "go-to" ophthalmology providers for cataract, retina and glaucoma. Once you decide a patient needs retina specialist evaluation and possible treatment

for DR, have one of your staff members call to arrange an appointment and verify that the patient's insurance is accepted. After the patient is scheduled, it is a matter of faxing a short report or copy of the exam record to the retinal specialist. A formal letter is generally unnecessary if the referral is uncomplicated, as retinal specialists will understand all of the ocular findings included in the exam record or brief report.

When should optometrists hold 'em and monitor DR vs. fold 'em and refer for treatment? The paradigm is shifting as new research findings emerge. In the future, it may become standard of care to administer anti-VEGF treatments to reduce the severity of DR rather than to just treat already existing DME or PDR.

Proper management of DR starts with a good understanding of the different stages of retinopathy and the treatment options that are available. Modifiable risk factors for DR need to be discussed with the patient and effective communication with the patient, PCP, endocrinologist and retinal specialist is key. Optometrists should base the decision to monitor or refer on a combination of their knowledge that treatment would benefit the patient and their comfort level monitoring DR. ■

Dr. Torbit is an associate clinical professor at Indiana University School of Optometry.

Dr. Bedwell is an assistant clinical professor at Indiana University School of Optometry.

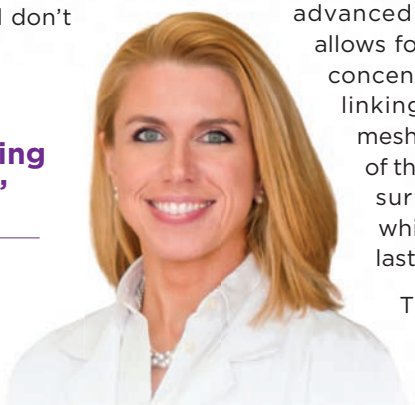
Dr. Bollier is a primary care resident at the Indianapolis Eye Care Center at Indiana University School of Optometry.

Dr. Sutton is a clinical professor at Indiana University School of Optometry and Service Chief of the Indianapolis Eye Care Center.

1. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Guidelines. DR. San Francisco, CA: American Academy of Ophthalmology; 2017. www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017. December 2017. Accessed Feburary 14, 2019.
2. International Council of Ophthalmology Guidelines for Diabetic Eye Care 2017. www.icoph.org/downloads/ICOGuidelinesforDiabeticEyeCare.pdf. January 2017. Accessed Feburary 14, 2019.
3. American Optometric Association. Eye Care of the Patient with Diabetes Mellitus. Evidence-Based Clinical Practice Guideline 2014. www.aoa.org/Documents/EBO/EyeCareOfThePatientWithDiabetesMellitus%20CPG3.pdf. February 7, 2014. Accessed February 14, 2019.
4. Bhavsar KV, Subramanian ML. Risk factors for progression of subclinical diabetic macular oedema. Br J Ophthalmol. 2011;95(5):671-4.
5. Ip M, Zhang J, Ehrlich J. The clinical importance of changes in DR severity score. American Academy of Ophthalmology. 2017;124(5):596-603.
6. Ip M, Domalpally A, Hopkins J, et al. Long-term effects of ranibizumab on DR severity and progression. Arch Ophthalmol. 2012;130(9):1145–52.
7. Ip M, Domalpally A, Sun JK, Ehrlich JS. Long-term effects of therapy with ranibizumab on DR severity and baseline risk factors for worsening retinopathy. Ophthalmol. 2015;122(2):367-74.
8. Wykoff C, Eichenbaum D, Roth D. Ranibizumab induces regression of DR in most patients at high risk of progression to proliferative DR. Ophthalmology Retina. 2018;2(10):997-1009.
9. Slakter J, Schneebaum J, Shah S. Digital Algorithmic DR Severity Scoring System (An American Ophthalmological Society Thesis). Trans Am Ophthalmol Soc. 2015;113:T9.
10. Staurenghi G, Feltgen N, Arnold J, et al. Impact of baseline DR Severity Scale scores on visual outcomes in the VIVID-DME and VISTA-DME studies. Br J Ophthalmol. 2017;102(7):954-958.
11. Baresegian A, Kotlyar B, Lee et al. DR: focus on minority populations. Int J Clin Endocrinol Metab. 2017;3(1):34-45.
12. Early Treatment DR Study Research Group. Early photocoagulation for DR. ETDRS report number 9. Ophthalmology. 1991;98(5 Suppl):766-85.
13. Early Treatment DR Study Research Group. Photocoagulation for diabetic macular edema. Early treatment DR study report number 1. Arch Ophthalmol 1985;103:1796-806.
14. Tomic M, Vrabec R, Poljicanin T, et al. Diabetic Macular Edema: Traditional and Novel Treatment. Acta Clin Croat. 2017;56(1):124-32.
15. Pieramici D, Singh R, Gibson A, et al. Outcomes of diabetic macular edema eyes with limited early response in the VISTA and VIVID studies. Ophthalmol. 2018;125(7):952-8.
16. Browning D, Fraser C, Clark S. The relationship of macular thickness to clinically graded DR severity in eyes without clinically detected diabetic macular edema. Ophthalmol. 2008;115(3):533-9.
17. Early Treatment DR Study Research Group. Photocoagulation for diabetic macular edema. ETDRS report No. 4. Int Ophthalmol Clin. 1987;27(4):265-72.
18. Heier J, Korobelnik J, Brown D, et al. Intravitreal aflibercept for diabetic macular edema: 148-Week Results from the VISTA and VIVID Studies. Ophthalmol. 2016;123(11):2376-85.
19. Gross J, Glassman A, Liu D, et al. Five-year outcomes of panretinal photocoagulation vs intravitreous ranibizumab for proliferative DR: A randomized clinical trial. JAMA Ophthalmol. 2018;136(10):1138–48.
20. Focal photocoagulation treatment of diabetic macular edema. Relationship of treatment effect to Fluorescein angiographic and other retinal characteristics at baseline: ETDRS Report No. 19. Arch Ophthalmol. 1995;113(9):1144-55.
21. Bressler N, Miller K, Beck R. Observational study of subclinical diabetic macular edema. DR Clinical Research Network. Eye. 2012;26:833-40.
22. Treatment for CI-DME in eyes with very good VA Study (Protocol V). DR Clinical Research Network. clinicaltrials.gov/ct2/show/NCT01909791. Accessed February 15,2019.
23. Ferman S, Leonard-Martin T, Semchyshyn T. The topographic distribution of the first sites of diabetic retinal neovascularization. Am J Ophthalmol. 1998;125(5):704-706.
24. Jansson RW, Frøystein T, Krohn J. Optic disc neovascularization in early stages of proliferative DR. Inves Ophthalmol Vis Sci. 2012;53(12):8246-52.
25. Bae K, Lee J, Kim T, et al. Anterior DR studied by ultra-widefield angiography. Korean J Ophthalmol. 2016;30(5):344-51.
26. Wessel M, Nair N, Aaker G, et al. Peripheral retinal ischaemia, as evaluated by ultra-widefield fluorescein angiography, is associated with diabetic macular oedema. Br J Ophthalmol. 2012;96(5):694-8.
27. Silva P, Dela Cruz A, Ledesma M, et al. DR severity and peripheral lesions are associated with nonperfusion on ultra-wide field angiography. Ophthalmol. 2015;122(12):2465–72.
28. Manjunath V, Papastavrou V, Steel D, et al. Wide-field imaging and OCT vs clinical evaluation of patients referred from DR screening. Eye. 2015;29(3):416-23.
29. Scanlon P, Aldington S, Stratton I. Epidemiological issues in DR. Middle East Afr J Ophthalmol. 2013;20(4):293-300.
30. Klein R, Klein B, Moss S, et al. The Wisconsin epidemiologic study of DR X. Four-year incidence and progression of DR when age at diagnosis is 30 years or more. Arch Ophthalmol. 1989;107(11):244-9.
31. Yau J, Rogers S, Kawasaki R, et al. Global prevalence and major risk factors of DR. Diabetes Care. 2012;35(3):556-64.
32. Ting D, Cheung G, Wong T. DR: global prevalence, major risk factors, screening practices and public health challenges: a review. Clin Exp Ophthalmol. 2016;44(4):260-77.
33. Barsegian A, Kotlyar B, Lee J, et al. DR: Focus on minority populations. Int J Clin Endocrinol Metab. 2017;3(1):34-45.
34. Varma R, Torres M, Pena F, et al. Prevalence of DR in adult Latinos: the Los Angeles Latino eye study. Ophthalmol. 2004;111(7):1298–306.
35. Munoz B, O'Leary M, Fonseca-Becker F, et al. Knowledge of diabetic eye disease and vision care guidelines among Hispanic individuals in Baltimore with and without diabetes. Arch Ophthalmol. 2008;126(7):968–74.
36. Modjtahedi BS, Theophanous C, Chiu S, et al. Two-year incidence of retinal intervention in patients with minimal or no DR on telemedicine screening. JAMA Ophthalmol. www.researchgate.net/publication/330943022_Two-Year_Incidence_of_Retinal_Intervention_in_Patients_With_Minimal_or_No_Diabetic_Retinopathy_on_Telemedicine_Screening. February 2019. Accessed April 22, 2019.
37. Vitale S, Maguire MG, Murphy RP, et al. Interval between onset of mild non-proliferative and proliferative retinopathy in type 1 diabetes arch Ophthalmol. 1997;115(2):194-198.
38. International Clinical DR Disease Severity Scale, Detailed Table. Authored by American Academy of Ophthalmology. The Eye MD Association. www.icoph.org/resources/45/International-Clinical-Diabetic-Retinopathy-Disease-Severity-Scale-Detailed-Table-.html. October 2002. Accessed February 15, 2019.
39. Photocoagulation treatment of proliferative DR clinical application of DR study (DRS) findings, DRS report number 8. The DR study research group. Ophthalmology. 1981;88(7):583-600.
40. Alvi R, Memon MS, Shera S, et al. Visual outcome of laser treatment in diabetic macular edema: Study from an urban diabetes care center. Pak J Med Sci. 2016;32(5):1229-33.
41. National Eye Institute. Diabetic Eye Disease. nei.nih.gov/nehep/programs/ diabeticeyedisease. Accessed February 12, 2019.
42. American Diabetes Association. 6. Glycemic targets: Standards of Medical Care in Diabetes—2019. Diabetes Care 2019;42(Suppl. 1):S61–S70
43. Wang B, Wang F, Zhang Y, et al. Effects of RAS inhibitors on DR: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2015 Apr;3(4):263-74.
44. Kang EY, Chen TH, Garg SJ, et al. Association of Statin Therapy With Prevention of Vision-Threatening DR. JAMA Ophthalmol. 2019 Jan 10.
45. Keech AC, Mitchell P, Summanen PA, et al. Effect of fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a randomised controlled trial. Lancet. 2007;370:1687–97.
46. Accord Eye Study Group, Chew EY, Ambrosius WT, Davis MD, et al. Effects of medical therapies on retinopathy progression in type 2 diabetes. N Engl J Med. 2010;363(3):233-44.
47. Atlaf Q. Obstructive sleep apnea and retinopathy in patients with Type 2 diabetes. A longitudinal study. Am J Respir Crit Care Med. 2017;196(7):892–900.
48. Luo B, Gao F, Qin L. The Association between vitamin D deficiency and DR in type 2 diabetes: A meta-analysis of observational studies. Nutrients. 2017;9(3):307.

Coaching for Dry Eye Success: SYSTANE® Complete

Dry eye is more important to your patients than you may realize. In my experience as a Dry Eye Coach, patients with dry eye are very concerned by the effect it has on their vision and ability to function, especially at work. My own history as a dry eye sufferer has helped me to understand its impact. I try to follow a healthy lifestyle that includes daily runs. On those days where I experience dry eye symptoms and don't have my lubricant eye drops handy, my daily workouts are abbreviated or even cancelled because it's too uncomfortable to pursue outdoor activities.



> **"SYSTANE® Complete is an excellent option for managing dry eye symptoms in many cases"**

Whitney Hauser, OD
DryEyeCoach®
Memphis, Tennessee

Although I'm familiar with the symptoms my dry eye patients may be experiencing, when patients come in for help, I still need to listen and uncover their needs—how long they have been suffering, the remedies they have tried and stopped using, what they would consider successful relief from dry eye all play a part in how I formulate a successful, individualized symptom management plan. I believe SYSTANE® Complete is an excellent option for managing dry eye symptoms in many cases.

SYSTANE® Complete is an important addition to the armamentarium for managing dry eye symptoms because it is formulated to provide relief for every major type of dry eye[1-5] and supports all layers of the tear film.[6-9] That is a significant attribute because the recent DEWS II Report described dry eye as a multifactorial condition that can be aqueous deficient or evaporative in nature, but more likely a combination of both.[10-12] SYSTANE® Complete's patented formulation[13] is designed to supplement and stabilize the tear film.[1] It accomplishes this through the use of advanced lipid nanotechnology that allows for the optimization of HP-guar concentration and improved cross-linking.[14] This enhanced HP-guar meshwork results in better retention of the active lubricant on the ocular surface vs SYSTANE® Balance which locks in moisture for long-lasting relief.[1,2,4,6,15,16]

There are many products on the shelves, so your recommendation is very important. I recommend SYSTANE® Complete to help simplify the management of my patients' dry eye symptoms.

Managing dry eye symptoms effectively is not just important to your patients, but also to your practice. Happy patients come back. Patients that don't find dry eye relief will continue to seek out other eye care providers until they do. With SYSTANE® Complete, you can meet the needs of your patients and provide relief for every major type of dry eye[1-5] and I can keep doing my morning runs.

Dr. Hauser was compensated by Alcon for her participation in this advertorial.

References **1.** Ketelson H, Rangarajan R. Pre-clinical evaluation of a novel phospholipid nanoemulsion based lubricant eye drops. *Invest Ophthalmol Vis Sci.* 2017;58:3929. **2.** Alcon data on file, 2017. **3.** Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. *Ocul Surf.* 2017;15:276-283. **4.** Benelli U. SYSTANE® lubricant eye drops in the management of ocular dryness. *Clin Ophthalmol.* 2011;5:783-790. **5.** Craig JP, Nelson JD, Azar DT, et al. TFOS DEWS II Report Executive Summary. *Ocul Surf.* 2017;15:802-812. **6.** Korb D, Blackie C, Meadows D, Christensen M, Tudor M. Evaluation of extended tear stability by two emulsion based artificial tears. Poster presented at: 6th International Conference of the Tear Film and Ocular Surface: Basic Science and Clinical Relevance; September 22-25, 2010; Florence, Italy. **7.** Davitt WF, Bloomenstein M, Christensen M, Martin AE. Efficacy in patients with dry eye after treatment with a new lubricant eye drop formulation. *J Ocul Pharmacol Ther.* 2010;26:347-353. **8.** Willcox MDP, Argueso P, Georgiev GA, et al. TFOS DEWS II tear film report. *Ocul Surf.* 2017;15:366-403. **9.** Moon SW, Hwang JH, Chung SH, Nam KH. The impact of artificial tears containing hydroxypropyl guar on mucous layer. *Cornea.* 2010;29:1430-1435. **10.** Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II Pathophysiology Report. *Ocul Surf.* 2017;15:438-510. **11.** Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II Diagnostic Methodology Report. *Ocul Surf.* 2017;15:539-574. **12.** Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. *Ocul Surf.* 2017;15:575-628. **13.** Alcon data on file, 2017. **14.** Alcon data on file, 2014. **15.** Lane S, Paugh JR, Webb JR, Christensen MT. An evaluation of the in vivo retention time of a novel artificial tear as compared to a placebo control. *Invest Ophthalmol Vis Sci.* 2009;50:4679. **16.** Torkildsen G. The effects of lubricant eye drops on visual function as measured by the Inter-blink interval Visual Acuity Decay test. *Clin Ophthalmol.* 2009;3:501-506.

SEE LOOK FEEL

Sponsored by Alcon A Novartis Division

2 CE Credits
(COPE approved)

PEER • REVIEWED • PRA • ARTICLE

VISUAL FIELDS IN THE ERA OF OCT

Is functional testing with visual fields still necessary in the age of advanced structural imaging with optical coherence tomography?

By Lauren Ristin, OD, and Andrew Rixon, OD

Early and optimal detection of glaucoma and its progression is critical in preventing a burden on optometry's patients and to society as a whole. The difficulty arises in how to optimally detect and gauge glaucomatous progression.

Traditionally, we were limited to functional testing of visual fields (VF) using standard automated perimetry (SAP). Although this is well understood and widely employed technology, the evolution of optical coherence tomography (OCT) gives us the ability to consistently gauge structural change.

The major, unresolved questions now are whether OCT technology should supplant VFs in detecting progression, whether visual

Release Date: May 15, 2019
Expiration Date: May 15, 2022
Estimated Time to Complete Activity: 2 hours

Jointly provided by Postgraduate Institute for Medicine (PIM) and Review Education Group

JOINTLY ACCREDITED PROVIDER™ INTERPROFESSIONAL CONTINUING EDUCATION

Educational Objectives: After completing this activity, the participant should be better able to:

- Explain why OCT is generally more sensitive than VF in detecting progression in early glaucoma, but not in moderate and advanced glaucoma.
- Interpret measurement of the peripapillary retinal nerve fiber layer, particularly in early glaucoma.
- Determine thickness of the macular ganglion cell complex to monitor progression from early to advanced glaucoma.
- Evaluate differences or inconsistencies between VF and OCT results.
- Incorporate VF and OCT as complementary tests for diagnosing, following and managing patients with glaucoma.

Target Audience: This activity is intended for optometrists engaged in the care of patients with glaucoma.

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.

Faculty/Editorial Board: Lauren Ristin, OD, Jesse Brown Veterans Affairs Medical Center (VAMC) in Chicago, IL, and Andrew Rixon, OD, Memphis VAMC.

Credit Statement: This course is COPE approved for 2 hours of CE credit. Course ID is **62379-GL**. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.

Disclosure Statements:

Drs. Ristin and Rixon have nothing to disclose.

Managers and Editorial Staff: The PIM planners and managers have nothing to disclose. The Review Education Group planners, managers and editorial staff have nothing to disclose.

field testing still takes precedence, whether the two are mutually exclusive, or whether integrating them is optimal for glaucoma care.

Structure-Function Relationship

Ultimately, both structural and functional tests, and the progressive changes gauged by those tests, are related to the pathological loss of retinal ganglion cells (RGCs) and their axons. The method in which current VF and OCT technologies measure the RGCs and their loss differs, leading to the often discordant structure-function (S-F) relationship, which is tied to various assumptions about which of the two technologies is superior for glaucoma management.

Speaking of technology, although research shows VF testing alternatives such as frequency doubling technology and flicker defined form perimetry have stronger correlation between S-F when compared with SAP, SAP is still the most frequently used form of perimetry and will be the form discussed in this structure-function conversation.[1-3]

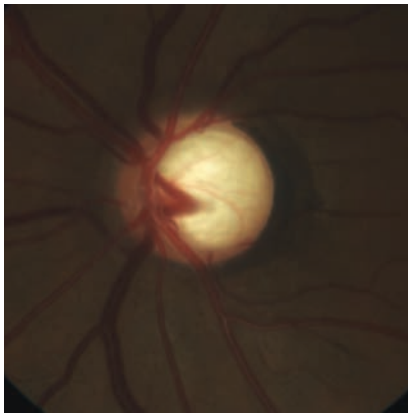
Significant structural change in early glaucoma—traditionally defined by SAP perimetry and, for the purposes of this article, specifically referring to Hodapp-Parrish-Anderson criteria (HPA)—is equivalent to much smaller relative functional change.[4] In advanced disease, the same amount of structural change results in substantial functional change.[5] As such, the S-F relationship is generally curvilinear, with retinal nerve fiber layer (RNFL) thickness becoming linearly related to SAP in moderate to advanced (per HPA) disease states.[6]

One estimate of this curvilinear relationship indicated that a loss of 100,000 RGCs in early glaucoma (baseline average mean deviation [MD] of -2 decibels [dB]) would result in a 1.79dB MD change on VFs. However, that same loss of 100,000 RGCs in a severe stage case (average MD of -15dB) would result in a 5.78dB MD change.[7]

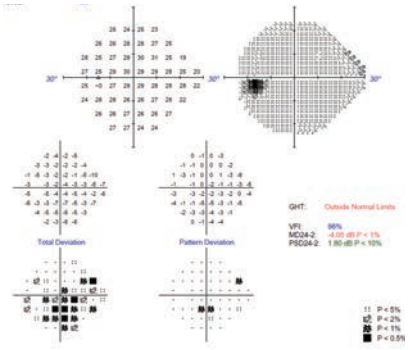
As a result, OCT is often favored over VFs in early disease, and multiple studies do support its superiority over SAP at that stage.[8] OCT has been shown to detect glaucomatous change on RNFL scans up to eight years prior to detection by VFs—in 19% of patients in one study.[9]

However, once the patient's disease reaches a moderate or severe level, functional testing may surpass OCT as the best method to detect progression because OCT may under-sample damage at that stage. Researchers explored OCT's ability to sample tissue thickness throughout the spectrum of disease, and estimated that a loss of 100,000 RGCs in early glaucoma (baseline average MD of -2dB) would result in a 5µm change on OCT. That same 100,000 RGC loss would result in just a 1.5µm change on OCT at a severe level.[7]

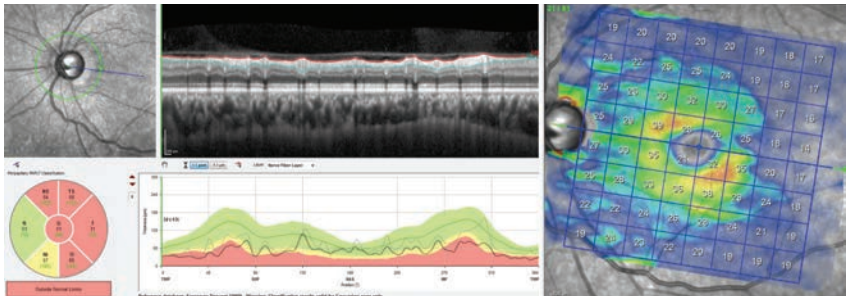
Ultimately, OCT testing is limited by the "floor effect"—when average RNFL measurements are approximately 50µm (a number that varies by platform).[10] At this level, RNFL tissue is no longer discernible. Although the machine will capture some quantity of tissue,



This 51-year-old patient's optic nerve shows extensive vertical neuroretinal rim loss and deep laminar cupping with laminar reconfiguration.



The patient's 24-2 VF is not as dense as expected based on the damage found on clinical and OCT evaluation. The pattern deviation's correction of diffuse changes masks the widespread field defect shown by the total deviation plot.



Cp-RNFL, at left, and isolated GCL, at right, shows RNFL tissue at "floor" (average RNFL of 51µm). The segmentation scan shows that the majority of the tissue thickness comes from the blood vessels, not neural tissue. Although a double arcuate loss of tissue exists on the GCL scan, there is sufficient tissue to track structural progression, whereas the RNFL scan is no longer useable.

it is thought to be non-neural in nature.[11] This has led to the notion that OCT is substandard in severe stages of glaucoma and visual fields alone are useful in monitoring progression in advanced states.

But this is not entirely accurate.

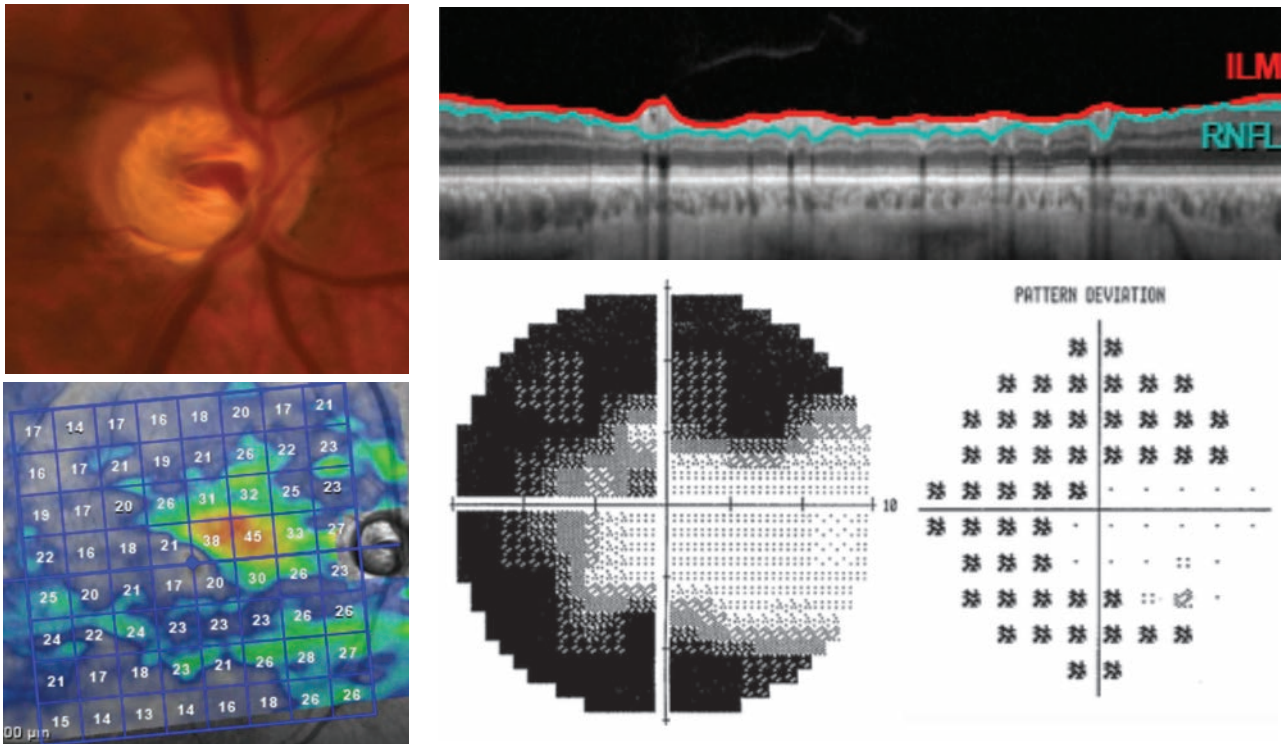
We know that the macula is involved at all stages of glaucoma while the papillomacular bundle is more resistant to damage in advanced disease when compared with RNFL.[12] Indeed, measuring the ganglion cell-inner plexiform layer (GC-IPL) shows the potential to identify structural progression not only in the early stage but also in late glaucoma, potentially extending the use of OCT into severe cases.

Why then does RNFL damage often "precede" functional damage seen on 24-2 VFs?

The answer is rooted in the difference between the two technologies. OCT (depending on the platform used) quantifies neuroretinal rim thickness (NRR), ganglion cell layer (GCL), RNFL, GC-IPL and total macular thickness (TMT) in linear units (mm^2 for NRR and µm for RNFL and respective macular thickness measurements). Subsequently, when RGCs die, GC-IPL, GCL, TMT, RNFL and NRR should also decrease linearly. A caveat to this is that RGC thicknesses vary depending on proximity to the foveal center and recent research shows isolation of both GCL and IPL can have diagnostic value.[13-16] The ability to capture the RGC bodies (GCL) and their dendrites (IPL) will vary across platforms.

Visual field sensitivity, however, is recorded in decibels, which are logarithmic units. Decibels do not express an absolute quantity, as linear µms do, but rather a ratio based on the maximum amount of background luminance provided by the specific perimetry unit employed. As an example of this logarithmic nature, a change of 3dB may actually represent a halving or doubling of light intensity.[17]

To complicate matters, values across different perimeters are not comparable due to differing maximal output stimuli and background luminance, meaning that a certain dB value on one perimeter is not equal to the same dB value on another.[18] Clearly, misalignment of the structural and functional measurement units results in discord. Interestingly, studies show that when perimetric sensitivity is expressed in linear units, there is good alignment with RGC density in the retinal region tested.[17] This underscores that the actual, real-world S-F relationship is complex and should not be oversimplified.



The right eye of this 65-year-old patient has severe stage glaucoma post-trabeculectomy. The segmentation scan, top right, shows no discernible RNFL thickness. The grayscale and pattern deviation plots, bottom right, show some remaining inferotemporal field on 10-2 testing. This corresponds well with the remaining superior nasal tissue found on isolated GCL analysis.

The detection ability of each of these technologies will vary according to the individual patient, and presumptions about structure preceding function do not apply to every patient.[19]

Specific VF-related factors that influence the discord and presumption that OCT is better in early disease, and VFs are better in more severe stages, include:

- The redundancy of the visual system, which results from the ability of RGCs neighboring dead or damaged RGCs to compensate for those cells. Any SAP stimulus projected onto a particular retinal region affects many different RGCs. Their redundancy is thought to prevent detection of functional change until most of the RGCs are no longer functional, rendering SAP insensitive in early disease.[6]
- Substantial intra- and inter-subject variability in SAP testing.
- Inadequate assessment of retinal loci damaged by glaucoma with standard 24-2 testing.
- The concept that RGC dysfunction precedes RGC death.[6,20]

Visual field variability is the result of the subjective, psychophysical nature of the test and is well known to have intra-subject test-retest variability, which only increases intra- and inter-subject variability, confounding diagnosis and assessment of disease progression with SAP.[17] Conversely, it is assumed that OCT, given its objective nature, exhibits low measurement variability and should therefore be more precise in determining change.

But it's not entirely clear whether this assumption holds true for all patients.[21] Recently, researchers confirmed the above assumption, determining that eyes with less severe disease (less than -10dB average MD) had a higher likelihood of having worsening disease detected by spectral-domain OCT than SAP, and those with more severe disease had a higher chance of being detected by SAP. However, they also found that progression could be detected by either method in all states of glaucoma, reinforcing that although OCT may be more precise, on average, than 24-2 SAP in early disease, this may not be the reality for the specific patient sitting across from you.[10]

10-2 + 24-2 = 24-2C?

Because the earliest damage from glaucoma involves local damage to the macula, some glaucoma specialists have advocated for performing a 10-2 visual field test in addition to a 24-2.[44] The clinical logistics of this suggestion are not ideal, so Zeiss recently developed the 24-2C test pattern for its HFA3 perimeter. It remains to be seen if this new strategy will improve structure-function agreement in early disease.

Another S-F presumption is that measuring tissue thickness is a surrogate way to measure RGC dysfunction.[17] RGCs exhibit a period of dysfunction prior to their death that structural measurements may not capture. For any given patient with the same RNFL thickness, a functional defect may arise prior to flagged structural loss, depending on RGC dysfunction.[6] This issue is highlighted by researchers who sought to determine the average RNFL thickness level where VF loss becomes manifest. Using Cirrus HD-OCT (Zeiss), the group found that the "tipping point" at which functional loss manifested was an average of 75.3µm.[22]

More detailed analysis of the data showed equal levels of VF loss at RNFL averages ranging from approximately 90µm to 50µm, signifying that RGC dysfunction might be captured by VF testing with presumably normal RNFL thicknesses. Of course, we have no way of knowing what our patient's RNFL thicknesses were prior to their initial visit. Baseline normals will vary, and an individual may start with a thicker or thinner RNFL, which will cause their individual "tipping point" to vary.[22]

A similar study using Spectralis OCT (Heidelberg) found the tipping point was an average of 89µm.[23] Analysis of the data showed a similarly wide range of RNFL levels where equal VF loss occurred. This reinforces that different patients and different instruments may show different levels of progression. RGC damage may be captured first by functional testing in spite of our preconceived notions of an abnormal RNFL thickness.

With the discordant S-F relationship sometimes favoring OCT and sometimes favoring VFs, the only consistent expectation we should have is that functional and structural progression will not be detected simultaneously, and if they do, will do so infrequently. So, if you see progression on structural testing during one visit, don't expect to confirm such progression on functional testing on that same visit, and vice-versa.[24,25]

OCT Pointers and Pitfalls

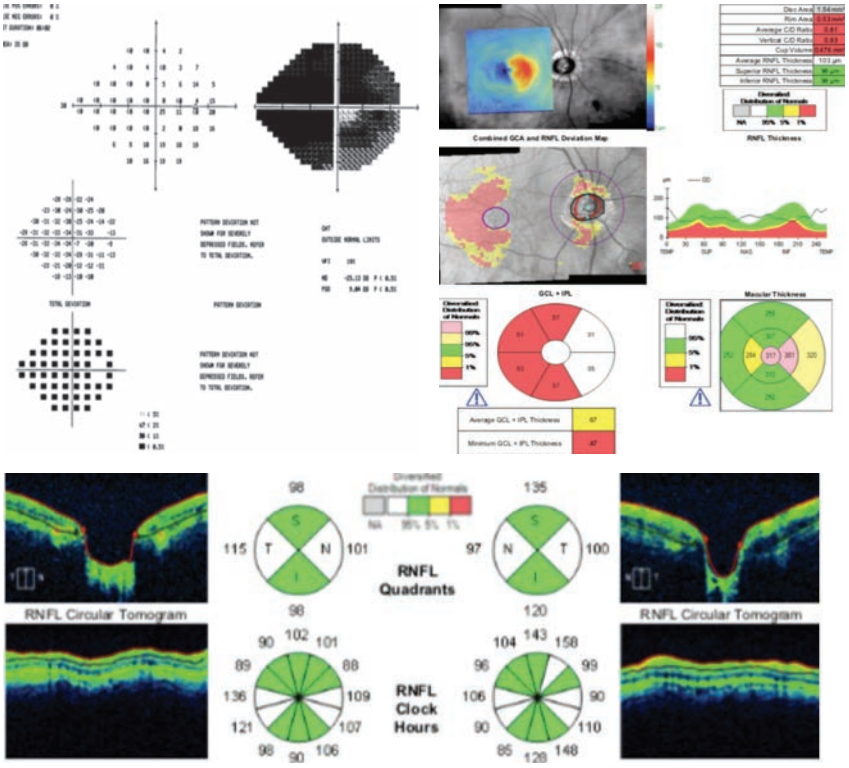
RNFL thickness and thickness deviation maps, as well as macular thickness parameters, have been shown to objectively discriminate between healthy and glaucomatous eyes, especially early in the disease.[26] However, these machines are not without limitations.

Awareness of the realities and pitfalls of OCT technology is important to avoid misinterpretation. While all major OCT platforms capture circumpapillary RNFL (cpRNFL) using a similar sized

measurement circle (3.46mm in diameter) and have been found to have similar abilities to help the clinician detect change, each is unique in its axial properties, axial resolution, segmentation algorithm and image processing capabilities. However, there is no standardization across platforms, which prevents direct comparison of measurements amongst them.[27,28]

When interpreting the peripapillary RNFL thickness parameters, there are a number of factors that a clinician needs to consider prior to determining whether their patient has glaucoma. First, attrition of RGCs is a normal part of the aging process and is expected. In OCT, the normal age-related attrition of RNFL varies according to the report, with recent studies showing an average global loss ranging from 0.33µm/year to 0.54µm/year.[27,29] Each instrument accounts for these natural changes by comparison with an age-matched normative database. While these databases are not exhaustive, a recent study has shown both the Spectralis and Cirrus databases successfully identified healthy patients.

But their specificity is much lower when trying to identify those who will develop glaucoma.[30]



This patient has advanced glaucoma in the right eye, which is masked on the RNFL and ganglion cell analysis by a large ERM between the ONH and the fovea (visible on the ganglion cell analysis printout), leading to anomalously normal "green" values. Artifacts should always be accounted for in analysis.

Normal population-based RNFL thickness variability is likely to blame for the reduced specificity. The database reports "normal" tissue using a green color code. This normal tissue is found within a dynamic range of tissue that represents 90% of patients in the reference database. Patients born with greater amounts of tissue compared with the reference database may have legitimate glaucoma but can be falsely flagged as being normal due to how the machine presents the data.[31] As such, substantial loss could occur within the normal range.[29]

The recognition of OCT scan artifacts and sources of error creating them is critical to accurately interpreting the data. Multiple sources of error exist and can generally be divided into patient-dependent, operator-dependent and device-dependent.

One of the most common causes of patient-dependent artifacts in

RNFL Thickness—Harbinger of Change

RNFL thickness has been the single most commonly studied OCT parameter in glaucoma. A repeatable 4µm or greater decrease in global RNFL thickness on two consecutive scans compared with baseline is considered a statistically significant change.[31]

Research shows global/average cpRNFL thickness is the most reproducible RNFL parameter and helpful in distinguishing normal patients from those with glaucoma.[36]

Average RNFL, likely due to its excellent reproducibility, is also the best parameter to detect change in glaucoma patients across multiple platforms and should be the first parameter looked at on RNFL trend analysis.[36] Although normal variability can confound things, patients with thinner RNFL averages are generally more likely to have glaucoma. Research has estimated the average rates of spectral domain OCT-based RNFL thinning in glaucoma patients ranges between -0.76µm and 1.5µm per year. At present, there is no universal standard as to what rate of RNFL progression is clinically important.[48]

More specific RNFL parameters, such as quadrants, sectors and clock hours are less reproducible than global averages, but still have excellent diagnostic value.

Across all platforms, the best diagnostic regions for clinical use are the inferior and superior quadrants, with the inferior regions having more value than the superior regions.[36]

VF Interpretation Dos and Don'ts

To assess findings on the VF, in the context of already having OCT information, it is important to review fundamental "dos and don'ts" of VF interpretation.

• **DON'T discard the initial field.** Just because it is the first field doesn't mean it isn't valid.

• **DO determine whether the field is reliable.** Traditionally, only the reliability indices (fixation loss, false negative and false positive [FP]) were used to substantiate reliability, with FPs the most important of the three. FP percentages in excess of 15% are often associated with poor test results, and some practitioners require even more stringent standards.[49]

The Finer Points of Reliability Indices

The traditional reliability indices do have limitations. The developers of the Humphrey Field Analyzer note that fixation loss is more indicative of technician inattention than patient gaze instability, and they prefer to turn off fixation loss catch trials in favor of gaze tracking.[49] They also eliminate false negative catch trials in their newest SITA-Faster. (Studies show that false negatives are more indicative of glaucomatous damage than poor reliability, making this parameter expendable.[57,58])

More recently, research shows gaze tracking parameters are closely related to reproducibility results and may be, in combination with false positives, the most useful way to assess reliability.[49,59,60] A recent study comparing gaze tracking with traditional reliability indices found gaze tracking was predictive of field variability, whereas traditional indices were not.[59]

• **DO compare the total deviation and pattern deviation.** Total deviation numerical maps compare the sensitivity of individual test points to age-matched normals, and total deviation probability maps identify which of these points are abnormal. Mean deviation approximately represents the average of these total deviation values. Pattern deviation maps show localized VF loss after filtering out general depression or elevation. Thus, if the total deviation is significantly more depressed than the pattern deviation, there is likely a cataract. If the opposite is true (pattern deviation more depressed than total deviation), the patient is most likely trigger happy with high false positives; alternatively, they may have performed at a level exceeding the expectations for their age.

• **DON'T ignore the total deviation.** Pattern deviation correction of diffuse changes in the visual field can paradoxically result in insufficiently assessing widespread damage from glaucoma.[50]

• **DO interpret the global indices.** This includes glaucoma hemifield test, visual field index, mean deviation and pattern standard deviation. It's important to stage glaucoma accurately with the HPA classification.[4] The HPA considers not only the extent of overall damage using mean deviation, but also the number of defective points in the pattern standard deviation probability map, as well as the proximity and density of loss near fixation.

• **DO repeat tests to account for variability in VF change.** The clinical significance of any visual field change usually depends on the number of exams given and the amount of intra-day and inter-visit variability of those exams. In general, peripheral test points not only vary more than central test points, but also exhibit progressively greater variability as the severity of the disease increases, with the variability peaking at -20dB on mean deviation and 8dB on pattern standard deviation.[51,52] Additionally, patients with more global diffuse loss tend to have more variability than patients with localized loss.[52]

• **DO acquire good baseline visual fields.** These are essential for accurately detecting progression. The World Glaucoma Association recommends at least two reliable baseline VFs in the first six months of management and at least two additional fields over the next 18 months.[53] More frequent visual fields may be necessary in advanced disease to detect fast progressors (-2dB/year or faster). The association recommends six VFs in the first two years in patients at risk for visual disability.

• **DON'T undertest.** Undertesting reduces the ability to compensate for variability. Research shows that three examinations per year are required to detect a -2dB change in mean deviation (considered rapid progression) over a two-year period.[54] It would take five years to confirm that same -2dB change if only two visual field exams are performed per year.

• **DON'T expect new defects to occur first as the disease progresses.** Progression typically occurs through deepening and expansion of preexisting defects, not by the development of new defects.[55] There can be substantial loss within the "black," and failure to look at the numerical deviation can result in missing a deepening defect.

• **DO look for glaucomatous patterns of loss.** The presence of classic patterns of visual field loss such as paracentral scotomas, nasal steps and arcuate defects shows that the patient has damage consistent with glaucoma.[49]

• **DON'T, however, disregard depressed test points.** This is true if a perfect traditional pattern of loss is not present. Glaucomatous VFs can exhibit a wide variety of patterns, so the lack of traditional defects should actually be expected in many of our patients.[45] It is important to assess visual fields in the context of where local and diffuse damage is found topographically on RNFL and macular OCT scans. If there is alignment between the area of damage on the OCT and the region of VF that samples the damage, a classic pattern is not required to substantiate the visual field defect's legitimacy.

• **DO consider switching from standard test strategies.** This can help to better detect damage. Multiple studies show 24-2 VFs can miss or markedly underestimate defects near fixation, whereas 10-2 strategies can better detect these defects.[43] Additionally, the use of 10-2 has been shown to correlate well with RGC thickness, improving the structure-function relationship.[56]

both the RNFL and ganglion cell complex (GCC) is the presence of an epiretinal membrane.[32,33] In one review, the upper boundary of the ERM was identified as the upper edge of the RNFL in 15.2% to 36.1% of scans, falsely inflating the RNFL or macular thickness.[32]

Errors of automated segmentation of the retinal layers represent device-dependent errors and can result in misinterpretation. These errors are more prevalent in highly myopic eyes whose axial length may be outside of the reference database and may confound the machine when the anatomy is altered in tilted disc, staphyloma and retinoschisis cases. Use of ganglion cell analysis may be more successful in these cases as they can be less influenced by the anatomy.[32]

This becomes particularly challenging in advanced disease, as there is greater segmentation variability. Clinicians should remember that it is critical in all stages of glaucoma to confirm the appropriateness of the segmentation.

Choosing OCT Parameters

Glaucoma preferentially affects the GCC, which is comprised of the GCL, the macular RNFL and the IPL. Experimental models of glaucoma show substantial loss of RGCs in the parafoveal region. Given that approximately 50% of the RGCs are concentrated within that parafoveal region and that negligible population variability exists there, it is an ideal location to assess throughout the entire spectrum of glaucomatous disease using OCT.[34]

Each platform measures the GCC differently, including the ILP and GC-IPL, the entire GCC by total macular thickness and by isolation of the GCL. The strongest structure-function relationship has been correlated with isolated GCL, GC-IPL and the GCC.[13] A weaker S-F relationship was observed with the full macular thickness parameters.

Let's take a look at some of these imaging parameters.

Average GC-IPL thickness. Studies show average GC-IPL has excellent intra- and inter-visit reproducibility, and a repeatable 2µm or greater decrease in average GC-IPL is considered a statistically significant change.[34] Additionally, because it removes macular RNFL from the segmentation, GC-IPL is less influenced by variability in that layer.[35]

Minimum GC-IPL thickness. This was designed to be sensitive to focal RGC loss and, not surprisingly, is consistently found across studies to be the most accurate GC-IPL parameter for the diagnosis of early, moderate and severe glaucoma.[35,36] It's followed in accuracy by inferotemporal and average GC-IPL thickness, respectively.

Tracking progression with minimum GC-IPL may be limited by its reproducibility. A change of 8µm to the average minimum GC-IPL over two exams is required to feel comfortable that the change is due to glaucomatous progression.[34]

In analyzing the rate of progression, no standard exists to designate a fast rate of average GC-IPL loss. For reference, researchers have reported the rate of average GC-IPL loss to be -0.014µm/year in healthy patients and -0.57µm/year in those with glaucoma.[37]

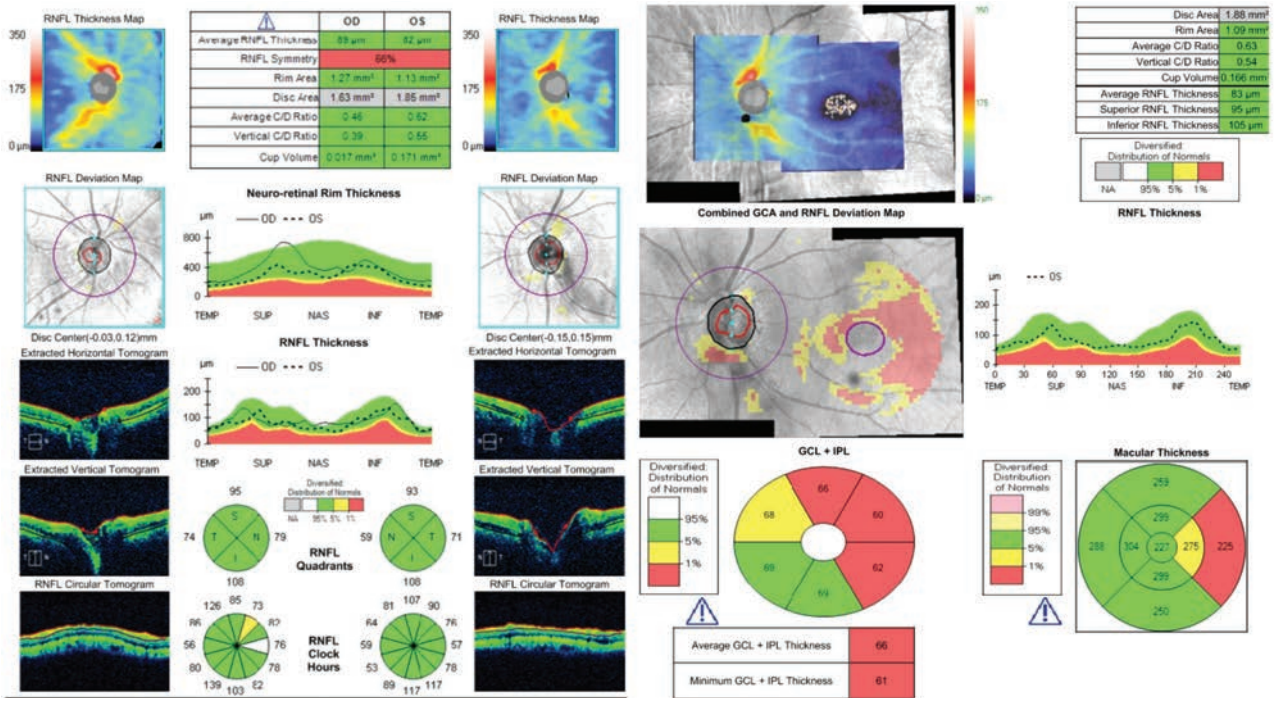
Inferior GC-IPL thickness. Research postulates the inferior macular ganglion cell layer is the earliest and most affected layer in glaucomatous changes.[38] However, isolation of GCL is limited by both machine segmentation and the small range of tissue thickness that can be captured, making it less useable for progression analysis than GC-IPL.[13] Segmentation becomes more challenging with advanced disease as thinner tissue layers become harder to find, increasing variability.[12]

Macular thickness asymmetry analysis. Comparison of tissue symmetry is another helpful diagnostic technique. Studies show inter-eye macular asymmetry analysis using TMT, termed posterior pole asymmetry analysis (PPAA), has equal, if not superior, diagnostic performance to circumpapillary RNFL (cpRNFL).[39-41] Research also shows intra-eye GC-IPL asymmetry can help diagnose glaucoma in highly myopic eyes, where RNFL scans may be limited due to optic nerve head anatomy.[42]

Ultimately, numerous studies have compared the sensitivity of macular, RNFL and optic parameters, finding similar diagnostic performance.[36] As a result, combining the data from all these parameters would likely provide better diagnostic value. One study did, in fact, find that combined analysis of GC-IPL and cpRNFL performed better diagnostically than the individual parameters by themselves.[14] The investigators recently validated the performance of this combined index, known as the University of North Carolina's UNC OCT Index, showing that it is likely a better tool for early detection than using individual parameters.[43]

Incorporating VF and OCT

Acknowledging that the structure-function relationship is complicated, how should we approach cases where VF and OCT results are inconsistent? First, by expecting the inconsistency, as we know structure and function rarely capture change at the same time. Given this expectation, a practical approach is to find the best strategy to detect change in the individual patient. Once glaucoma is diagnosed clinically, either VF or OCT may emerge as the most precise technology with which to gauge progression in that



This 62-year-old patient shows optic discs that appear glaucomatous OS>>OD funduscopically. Cursory analysis of the RNFL printout (at left) alone might give the false sense that there are no pathological changes compared with the reference database. The additional analysis of all tissues affected by glaucoma, at right, confirms the diagnosis of early glaucoma. This highlights the necessity of using all of the information these machines provide.

specific patient—and it generally depends on the stage of the disease.[8] For instance, an early glaucoma case that shows no 24-2 VF defect, yet shows glaucomatous loss of RNFL and GC-IPL, may benefit from greater reliance on tracking those OCT parameters. In that same scenario, changing the VF test strategy or stimulus size might increase the likelihood of S-F alignment and decrease perceived inconsistencies.[44]

If these testing modifications are undertaken and fail to elicit improved consistency, greater analytical emphasis would be placed on OCT for that patient. However, functional testing would not be abandoned here, as the point at which RGC dysfunction will be captured by VF testing in this scenario is unknown. Conversely, if a repeatable glaucomatous visual field defect precedes expected thinning on OCT, it would not result in abandoning the use of OCT testing.

The best strategy is to incorporate VF and OCT as complementary tests for the diagnosis and management of glaucoma. A recent editorial advocated discontinuing the debate about whether and when clinicians should use one form of testing over the other.[24] The authors pointed out that if either method was optimal, there would be no need for the other. Ideally, we would more effectively use the information gleaned from both technologies. Efficiently integrating VF, RNFL tissue segmentation and thickness maps, as well as RGC data in a meaningful way would allow us to maximize how we use that information.

Currently, the "Hood Report" (available on Topcon and Heidelberg platforms) is the only commercially available software to accomplish this. The Hood Report incorporates VF points overlaid by RNFL and either GCL+ (Topcon) or GCL (Heidelberg) thickness and significance maps produced from a single widefield cube scan. Research shows this single-page diagnostic report performs as well or better in classifying an eye as glaucomatous than that of glaucoma subspecialists who had fundus photos, 24-2 VFs and widely available commercial OCT RNFL.[45]

Looking to the future, integration of structural and functional data into one metric may streamline diagnosis, staging and determination of rate of change. One proposed metric is a combined S-F index (CSFI), based on experimental estimates of the percentage of RGCs lost compared with that expected for an age-matched healthy eye. Multiple studies show the CSFI successfully assesses rates

of change throughout the entire spectrum of disease, unlike with isolated structural or functional testing.[46] Newer technologies will likely individualize metrics in the future by estimating the quantity of RGCs in real time.[47]

Ultimately, in 2019 we must accept that both structural and functional testing have advantages and disadvantages, and neither are optimal. Their complementary use gives us the best opportunity to detect progression in our patients, which is key to preserving their quality of life. ■

Dr. Ristin is an attending optometrist at the Jesse Brown Veterans Affairs Medical Center (VAMC) in Chicago. She is the immediate past chair of the Glaucoma Section of the American Academy of Optometry (AAO).

Dr. Rixon is the residency coordinator at the Memphis VAMC, a member of the Optometric Glaucoma Society and is pursuing his glaucoma diplomate through the AAO Glaucoma Section.

1. Nouri-Mahdavi K. Selecting visual field tests and assessing visual field deterioration in glaucoma. Can J Ophthalmol. 2014;49:497-505.
2. Lamparter J, Russell RA, Schulze A, et al. Structure-function relationship between FDF, FDT, SAP, and scanning laser ophthalmoscopy in glaucoma patients. Invest Ophthalmol Vis Sci. 2012;53:7553-59.
3. Camp AS, Weinreb RN. Will perimetry be performed to monitor glaucoma in 2025? Ophthalmology. 2017;124(12S):S71-S75.
4. Hodapp E, Parrish RK II, Anderson DR. Clinical Decisions in Glaucoma. St Louis: CV Mosby Co; 1993: 52-61.
5. Malik R, Swanson WH, Nicolela MT. Structure-function relationships in glaucoma. In: Shaarawy T, Sherwood MB, Hitchings RA, Crowston JG. Glaucoma. London: Elsevier Saunders; 2015.
6. Lucy KA, Wollstein G. Structural and functional evaluations for the early detection of glaucoma. Expert Rev Ophthalmol. 2016;11(5):367-76.
7. Medeiros FA, Zangwill LM, Bowd C, et al. The structure and function relationship in glaucoma: implications for detection of progression and measurement of rates of change. Invest Ophthalmol Vis Sci. 2012;53(11):6939-46.
8. Zhang X, Dastiridou A, Francis BA, et al. Comparison of glaucoma progression detection by optical coherence tomography and visual field. Am J Ophthalmol. 2017;184:63-74.
9. Kuang TM, Zhang C, Zangwill LM, et al. Estimating lead time gained by optical coherence tomography in detecting glaucoma before development of visual field defects. Ophthalmology. 2015;122(10):2002-09.
10. Abe RY, Diniz-Filho A, Zangwill LM, et al. The relative odds of progressing by structural and functional tests in glaucoma. Invest Ophthalmol Vis Sci. 2016;57(9):421-428.
11. Bowd C, Zangwill LM, Weinreb RN, et al. Estimating optical coherence tomography structural measurement floors to improve detection of progression in advanced glaucoma. Am J Ophthalmol. 2017;175:37-44.
12. Belghith A, Medeiros FA, Bowd C, et al. Structural change can be detected in advanced-glaucoma eyes. Invest Ophthalmol Vis Sci. 2016;57(9):511-8.
13. Miraftabi A, Amini N, Morales E, et al. Macular SD-OCT outcome measures: Comparison of local structure-function relationships and dynamic range. Invest Ophthalmol Vis Sci. 2016;57(11):4815-23.
14. Mwanza J-C, Budenz DL, Godfrey DG, et al. Diagnostic performance of optical coherence tomography ganglion cell-inner plexiform layer thickness measurements in early glaucoma. Ophthalmology. 2014;121(4):849-54.
15. Kim Ek, Park HL, Park CK. Segmented inner plexiform layer thickness as a potential biomarker to evaluate open-angle glaucoma: dendritic degeneration of retinal ganglion cell. PLoS One. 2017;12(8):e0182404.
16. Lin JP, Lin PW, Lai IC, Tsai JC. Segmental inner macular layer analysis with spectral-domain optical coherence tomography for early detection of normal tension glaucoma. PLoS One. 2019;14(1):e0210215.
17. Malik R, Swanson WH, Garway-Heath DF. 'Structure-function relationship' in glaucoma: past thinking and current concepts. Clin Exp Ophthalmol. 2012;40(4):369-80.
18. Phu J, Khuu SK, Yapp M, et al. The value of visual field testing in the era of advanced imaging: clinical and psychophysical perspectives. Clin Exp Optom. 2017;100(4):313-32.
19. Tatham AJ, Weinreb RN, Medeiros FA. Strategies for improving early detection of glaucoma: the combined structure-function index. Clin Ophthalmol. 2014 Mar 26;8:611-21.
20. Susanna R, De Moraes CG, Cioffi GA, Ritch R. Why do people (still) go blind from glaucoma? Transl Vis Sci Technol. 2015;4(2):1.
21. Garway-Heath DF, Quartilho A, Prah P, et al. Evaluation of visual field and imaging outcomes for glaucoma clinical trials (An American Ophthalmological Society Thesis). Trans Am Ophthalmol Soc. 2017 Aug;115:T4.
22. Wollstein G, Kagemann L, Bilonick RA, et al. Retinal nerve fibre layer and visual function loss in glaucoma: the tipping point. Br J Ophthalmol. 2012;96(1):47-52.
23. Alasil T, Wang K, Yu F, et al. Correlation of retinal nerve fiber layer thickness and visual fields in glaucoma: a broken stick model. Am J Ophthalmol. 2014;157(5):953-59.
24. Medeiros FA, Tatham AJ. Structure versus function in glaucoma: The debate that doesn't need to be. Ophthalmology. 2016;123(6):1170-72.
25. Öhnell H, Heijl A, Brenner L, et al. Structural and functional progression in the Early Manifest Glaucoma Trial. Ophthalmology. 2016;123(6):1173-80.
26. Mwanza J-C, Budenz DL. Optical coherence tomography platforms and parameters for glaucoma diagnosis and progression. Curr Opin Ophthalmol. 2016;27(2):102-10.
27. Leung CK, Yu M, Weinreb RN, et al. Retinal nerve fiber layer imaging with spectral-domain optical coherence tomography: Patterns of retinal nerve fiber layer progression. Ophthalmology. 2012;119(9):1858-66.
28. Lee ES, Kang SY, Choi EH, et al. Comparisons of nerve fiber layer thickness measurements between Stratus, Cirrus, and RTVue OCTs in healthy and glaucomatous eyes. Optom Vis Sci. 2011;88(6):751-58.
29. Wu Z, Saunders LJ, Zangwill LM, et al. Impact of normal aging and progression definitions on the specificity of detecting retinal nerve fiber layer thinning. Am J Ophthalmol. 2017;181:106-13.
30. Silverman AL, Hammel N, Khachatryan N, et al. Diagnostic accuracy of the Spectralis and Cirrus reference database in differentiating between healthy and early glaucoma eyes. Ophthalmology. 2016;123(2):408-14.
31. Sayed MS, Margolis M, Lee RK. Green disease in optical coherence tomography diagnosis of glaucoma. Curr Opin Ophthalmol. 2017;28(2):139-53.
32. Asrani S, Essaid L, Alder BD, Santiago-Turla C. Artifacts in spectral-domain optical coherence tomography measurements in glaucoma. JAMA Ophthalmol. 2014;132(4):396-402.
33. Hardin JS, Taibbi G, Nelson SC, et al. Factors affecting Cirrus-HD OCT optic disc scan quality: a review with case examples. J Ophthalmol. 2015;2015:746150.
34. Mwanza J-C, Oakley JD, Budenz DL, et al. Macular ganglion cell-inner plexiform layer: automated detection and thickness reproducibility with spectral domain-optical coherence tomography in glaucoma. Invest Ophthalmol Vis Sci. 2011;52(11):8323-29.
35. Jeoung JW, Choi YJ, Park KH, Kim DM. Macular ganglion cell imaging study: glaucoma diagnostic accuracy of spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2013;54(7):4422-29.
36. Chen TC, Hoguet A, Junk AK, et al. Spectral-domain OCT: helping the clinician diagnose glaucoma: a report by the American Academy of Ophthalmology. Ophthalmology. 2018;125(11):1817-27.
37. Hammel N, Belghith A, Weinreb RN, et al. Comparing the rates of retinal nerve fiber layer and ganglion cell-inner plexiform layer loss in healthy eyes and in glaucoma eyes. Am J Ophthalmol. 2017;178:38-50.
38. Hood DC, Raza AS, de Moraes CG, et al. Glaucomatous damage of the macula. Prog Retin Eye Res. 2013 Jan;32:1-21.
39. Sullivan-Mee M, Ruegg CC, Pensyl D, et al. Diagnostic precision of retinal nerve fiber layer and macular thickness asymmetry parameters for identifying early primary open-angle glaucoma. Am J Ophthalmol. 2013;156(3):567-577.e1.
40. Dave P, Shah J. Diagnostic accuracy of posterior pole asymmetry analysis parameters of Spectralis optical coherence tomography in detecting early unilateral glaucoma. Indian J Ophthalmol. 2015;63(11):837-42.
41. Mori S, Hangai M, Sakamoto A, Yoshimura N. Spectral-domain optical coherence tomography measurement of macular volume for diagnosing glaucoma. J Glaucoma. 2010;19(8):528-34.
42. Kim YK, Yoo BW, Jeoung JW, et al. Glaucoma-diagnostic ability of ganglion cell-inner plexiform layer thickness difference across temporal raphe in highly myopic eyes. Invest Ophthalmol Vis Sci. 2016;57(14):5856-63.
43. Mwanza J-C, Lee G, Budenz DL, et al. Validation of the UNC OCT Index for the diagnosis of early glaucoma. Transl Vis Sci Technol. 2018;7(2):16.
44. Hood DC, De Moraes CG. Four questions for every clinician diagnosing and monitoring glaucoma. J Glaucoma. 2018;27(8):657-64.
45. Hood DC. Improving our understanding, and detection, of glaucomatous damage: An approach based upon optical coherence tomography (OCT). Prog Retin Eye Res. 2017;57:46-75.
46. Zhang C, Tatham AJ, Daga FB, et al. Event-based analysis of visual field change can miss fast glaucoma progression detected by a combined structure and function index. Graefes Arch Clin Exp Ophthalmol. 2018;256(7):1227-34.
47. Raza AS, Hood DC. Evaluation of the structure-function relationship in glaucoma using a novel method for estimating the number of retinal ganglion cells in the human retina. Invest Ophthalmol Vis Sci. 2015;56(9):5548-56.
48. Saunders LJ, Medeiros FA, Weinreb RN, Zangwill LM. What rates of glaucoma progression are clinically significant? Expert Rev Ophthalmol. 2016;11(3):227-34.
49. Heijl A, Patella VM, Bengtsson B. The Field Analyzer Primer: Effective Perimetry. 4th ed. Dublin, CA; Carl Zeiss Meditec: 2012.
50. Artes PH, Chauhan BC, Keltner JL, et al. Longitudinal and cross-sectional analyses of visual field progression in participants of the Ocular Hypertension Treatment Study. Arch Ophthalmol. 2010;128(12):1528-32.
51. De Moraes CG, Liebmann JM, Levin LA. Detection and measurement of clinically meaningful visual field progression in clinical trials for glaucoma. Prog Retin Eye Res. 2017 Jan;56:107-47.
52. Russell RA, Garway-Heath DF, Crabb DP. New insights into measurement variability in glaucomatous visual fields from computer modelling. PloS One. 2013;8(12):e83595.
53. Weinreb RN. Progression of Glaucoma: the 8th Consensus Report of the World Glaucoma Association. Amsterdam: Kugler Publication; 2011.
54. Chauhan BC, Garway-Heath DF, Goñi FJ, et al. Practical recommendations for measuring rates of visual field change in glaucoma. Br J Ophthalmol. 2008;92(4):569-73.
55. Nouri-Mahdavi K, Nassiri N, Giangiacomo A, Caprioli J. Detection of visual field progression in glaucoma with standard achromatic perimetry: a review and practical implications. Graefes Arch Clin Exp Ophthalmol. 2011;249(11):1593-616.
56. Lee J-W, Morales E, Sharifipour F, et al. The relationship between central visual field sensitivity and macular ganglion cell/inner plexiform layer thickness in glaucoma. Br J Ophthalmol. 2017;101(8):1052-58.
57. Katz J, Sommer A. Reliability indexes of automated perimetric tests. Arch Ophthalmol. 1988;106(9):1252-4.
58. Bengtsson B, Heijl A. False-negative responses in glaucoma perimetry: indicators of patient performance or test reliability? Invest Ophthalmol Vis Sci. 2000;41(8):2201-4.
59. Ishiyama Y, Murata H, Mayama C, Asaoka R. An objective evaluation of gaze tracking in Humphrey perimetry and the relation with the reproducibility of visual fields: a pilot study in glaucoma. Invest Ophthalmol Vis Sci. 2014;55(12):8149-52.
60. Ishiyama Y, Murata H, Asaoka R. The usefulness of gaze tracking as an index of visual field reliability in glaucoma patients. Invest Ophthalmol Vis Sci. 2015;56(11):6233-36.

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, www.reviewsce.com.

You must achieve a score of 70 or higher to receive credit. Allow four weeks for processing. For each Optometric Study Center course you pass, you earn 2 hours of credit from Pennsylvania College of Optometry.

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

1. The structure-function relationship is:
a. Linear.
b. Curvilinear.
c. Proportional.
d. Simple.

2. A person with early glaucoma who loses 100,000 RGCs will most likely:
a. Have a substantial change in their mean deviation.
b. Have a minimal change to their mean deviation.
c. Need to have a trabeculectomy.
d. Have a VFI of 50%.

3. A person with advanced glaucoma who loses 100,000 RGCs will most likely:
a. Have a substantial change in their mean deviation.
b. Have a minimal change in their mean deviation.
c. Be an excellent driver.
d. Have a VFI of 100%.

4. OCT has been shown to detect glaucoma up to how many years prior to SAP?
a. 12 years.
b. 10 years.
c. Eight years.
d. Six years.

5. Which is true in advanced glaucoma?
a. The average RNFL value is limited by the floor effect.
b. The GC-IPL cannot be used to monitor progression.
c. OCT findings are not valuable.
d. The central visual field remains unaffected.

6. The circumpapillary RNFL thickness map is based on a:
a. 2.46mm circle scan.
b. 3.46mm circle scan.
c. 4.46mm circle scan.
d. 5.46mm circle scan.

7. Different OCT platforms:
a. Are comparable.
b. Have similar abilities to detect change.
c. Are standardized.
d. Have the same image processing capabilities.

8. What is the average global loss of RNFL thickness?
a. 0.13µm to 0.23µm/year.
b. 0.23µm to 0.47µm/year.
c. 0.33µm to 0.54µm/year.
d. 0.54µm to 0.87µm/year.

9. The normative database is:
a. An exhaustive cross section of the population.
b. Standardized among OCT platforms.
c. Highly specific for identifying healthy eyes.
d. Equally representative of racial subgroups.

10. Patients with a thicker average RNFL value:
a. Do not have glaucoma.
b. Have a faster average rate of decline in the average RNFL value.
c. Are myopic.
d. Will be flagged "red" by the OCT.

11. What is considered a statistically significant change in global RNFL thickness?
a. Greater than 4µm on one exam.
b. Greater than 4µm on two consecutive exams.
c. Greater than 2µm on one exam.
d. Greater than 2µm on two consecutive exams.

12. What has been shown to be the best OCT RNFL parameter to detect glaucomatous change over time?
a. Superior temporal RNFL clock hour.
b. Average or global RNFL.
c. Inferior quadrant.
d. Vertical cup-to-disc ratio.

13. More specific RNFL parameters, such as quadrants, sectors and clock hours:
a. Have higher specificity for detecting change over time.
b. Are less reproducible.
c. Do not have diagnostic value.
d. Are the most accurate in the nasal quadrant.

14. Which parameter has the weakest structure-function relationship?
a. Isolated GCL.
b. GC-IPL.
c. GCC.
d. Full macular thickness.

15. Macular GC-IPL thickness measurement:
a. Has excellent inter-visit and intra-visit reproducibility.
b. Includes the macular RNFL.
c. Has an annulus that approximates the anatomical fovea.
d. Is not affected by imaging artifacts.

16. What is the most accurate GC-IPL parameter for diagnosis of early, moderate or advanced glaucoma?
a. Average GC-IPL thickness.
b. Minimum GC-IPL thickness.
c. Inferior-temporal GC-IPL thickness.
d. Superior GC-IPL thickness.

17. What amount of repeatable change is necessary to determine progression in the minimum GC-IPL parameter?
a. 4µm.
b. 6µm.
c. 8µm.
d. 10µm.

18. Combining structure and function into one index has been shown to?
a. Unsuccessfully assess the rates of change throughout the spectrum of disease.
b. Successfully assess the rates of change throughout the spectrum of disease.
c. Make diagnosis and staging more complicated.
d. Put the patient at higher risk of blindness.

19. The two most important visual field parameters to gauge reliability are:
a. Fixation losses and false negatives.
b. False negatives and false positives.
c. Gaze tracking and false positives.
d. VFI and gaze tracking.

20. Research shows 10-2 visual field testing can:
a. Sample less retinal loci than 24-2 testing.
b. Detect glaucoma loss earlier than with 24-2.
c. Reduce the structure function correlation.
d. Have limited use in glaucoma management.

Examination Answer Sheet

Visual Fields in the Era of OCT

Valid for credit through May 15, 2022

Online: This exam can be taken online at www.reviewsce.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.

Directions: Select one answer for each question in the exam and completely darken the appropriate circle. A minimum score of 70% is required to earn credit.

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.

Credit: This course is COPE approved for 2 hours of CE credit. Course ID is **62379-GL**.

Jointly provided by Postgraduate Institute for Medicine and Review Education Group.

Salus University has sponsored the review and approval of this activity.

Processing: There is a four-week processing time for this exam.

Answers to CE exam:

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
4. Ⓐ Ⓑ Ⓒ Ⓓ
5. Ⓐ Ⓑ Ⓒ Ⓓ
6. Ⓐ Ⓑ Ⓒ Ⓓ
7. Ⓐ Ⓑ Ⓒ Ⓓ
8. Ⓐ Ⓑ Ⓒ Ⓓ
9. Ⓐ Ⓑ Ⓒ Ⓓ
10. Ⓐ Ⓑ Ⓒ Ⓓ
11. Ⓐ Ⓑ Ⓒ Ⓓ
12. Ⓐ Ⓑ Ⓒ Ⓓ
13. Ⓐ Ⓑ Ⓒ Ⓓ
14. Ⓐ Ⓑ Ⓒ Ⓓ
15. Ⓐ Ⓑ Ⓒ Ⓓ
16. Ⓐ Ⓑ Ⓒ Ⓓ
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. Explain why OCT is generally more sensitive than VF in detecting progression in early glaucoma, but not in moderate and advanced glaucoma. ① ② ③ ④ ⑤

22. Interpret measurement of the peripapillary retinal nerve fiber layer, particularly in early glaucoma. ① ② ③ ④ ⑤

23. Determine thickness of the macular ganglion cell complex to monitor progression from early to advanced glaucoma. ① ② ③ ④ ⑤

24. Evaluate differences or inconsistencies between VF and OCT results. ① ② ③ ④ ⑤

25. Incorporate VF and OCT as complementary tests for diagnosing, following and managing patients with glaucoma. ① ② ③ ④ ⑤

26. 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.

27. 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): ☐

28. 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: _____

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

ⓐ Very confident ⓑ Somewhat confident ⓒ Unsure ⓓ Not confident

30. 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:

31. Additional comments on this course:

_____

_____

_____

_____

_____

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

First Name

Last Name

E-Mail

The following is your: ☐ Home Address ☐ Business Address

Business Name

Address

City State

ZIP

Telephone # - -

Fax # - -

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 118163 RO-OSC-0519

Rate the quality of the material provided:

1=Strongly disagree, 2=Somewhat disagree, 3=Neutral, 4=Somewhat agree, 5=Strongly agree

32. The content was evidence-based.
① ② ③ ④ ⑤

33. The content was balanced and free of bias.
① ② ③ ④ ⑤

34. The presentation was clear and effective.
① ② ③ ④ ⑤

2019 MEETINGS

Earn up to 12 CE Credits*

OPTOMETRIC SYMPOSIUM

MEETING CO-CHAIRS:

MURRAY FINGERET, OD

ROBERT N. WEINREB, MD

CE CONFERENCES

11th Annual

EAST COAST OPTOMETRIC GLAUCOMA SYMPOSIUM

October 4-5, 2019

Renaissance Baltimore Harborplace Hotel
202 East Pratt Street
BALTIMORE, MD

Register online: www.reviewsce.com/ECOGS2019

Please call the hotel directly at (410) 547-1200 and identify yourself as a participant of the East Coast Optometric Glaucoma Symposium.

11th Annual

WEST COAST OPTOMETRIC GLAUCOMA SYMPOSIUM

December 13-14, 2019

Hyatt Regency Huntington Beach
21500 Pacific Coast Highway
HUNTINGTON, CA

Register online: www.reviewsce.com/WCOGS2019

Please call the hotel directly at (714) 698-1234 and identify yourself as a participant of the West Coast Optometric Glaucoma Symposium.

Administered by REVIEW EDUCATION GROUP

cope *Approval pending

SALUS UNIVERSITY Pennsylvania College of Optometry

For up-to-date information, go to www.reviewsce.com/events
call 877-451-6514 or e-mail reviewmeetings@jhihealth.com

Review Education Group partners with Salus University for those ODs who are licensed in states that require university credit.

Pinpointing the Problem

Amiodarone doesn't usually have a significant effect on vision. But be more vigilant when it's used in a patient with other acuity-reducing issues.

Edited by Joseph P. Shovlin, OD

Q Several medications, such as amiodarone, quickly deposit in the cornea. Should I be concerned? Short of asking the prescriber to discontinue the drug, is there anything I can do to lessen the deposition and protect against acuity loss?

A "There's really nothing you can do clinically to halt the progression of the verticillata relative to amiodarone—or other new agents, such as Vyzulta (latanoprostene bunod, Bausch + Lomb)—other than discontinue the drug," says Jim Thimons, OD, medical director and founding partner of Ophthalmic Consultants of Connecticut. Fortunately, he says, acuity is most often unaffected.

These findings occur due to the deposition of cellular lipids in the basal epithelium secondary to the cationic amphiphilic properties of amiodarone and other drugs, Dr. Thimons explains. He notes, however, that in cases of severe symptomatology, an option is to debride the epithelium because the deposits are above Bowman's membrane. A new corneal surface will grow, improving vision and reducing the verticillata, if only transiently. If a patient continues taking the drug after their epithelium is debrided, Dr. Thimons says the verticillata will grow back, so intermittent debridement may be necessary.

Putting Things Into Perspective

"I have never had an experience where the reduced acuity was solely from or significant enough because of the verticillata that I've had to do much other than observe," Dr. Thimons says, adding that the idea that amiodarone severely impacts vision is misleading. While the drug rarely affects acuity related to verticillata, it is possible to demonstrate decreased acuity as a result of optic neuropathy—a rare but noted side effect.

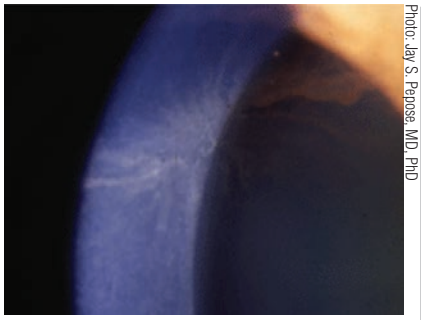


Photo: Jay S. Pepose, MD, PhD

Amiodarone causes corneal verticillata.

Throughout his extensive time in clinical practice, Dr. Thimons has seen a significant number of amiodarone patients. Of those, he only rarely had to intervene and debride the epithelium.

"The acuity issue has not been a big concern, at least in my experience," he says.

He adds that many of these patients have other issues that are both related (ocular surface disease) and unrelated to the drug and can cause acuity problems, such as cataract or macular disease.

The observed frequency of new amiodarone patients has declined in Dr. Thimons' area of the country. He notes that the drug isn't used as commonly because of competing agents that are being marketed as having fewer side effects (Multaq/dronedarone).

Working With Limited Options

Because amiodarone is intended for cardiac intervention and persistent ventricular fibrillation, Dr. Thimons recommends continuing drug therapy to avoid putting patients at cardiac risk.

"You tolerate the ocular symptomatology because the risk associated with cessation is actually quite real," he notes.

There are two steps Dr. Thimons would take, including maximizing the ocular surface.

"In patients with this treatment regimen, I would have no difficulty believing that the ocular surface is compromised as well, in that one of the more common side effects of the drug is dry eye," he says. "If you maximize the surface, you'll improve the overall visual function without having to be more aggressive with the management of the amiodarone complications."

The other is removing any cataracts that are present. Dr. Thimons notes that cataracts exacerbate effects on vision in patients with pre-existing corneal issues. Taking them out of the equation, he adds, will improve overall visual function without having to interfere with the amiodarone therapy, which could cause significant cardiac risk. ■

Getting Hosed

Blunt trauma can leave major damage. But optometrists can learn to treat and monitor to minimize long-term issues. **By Breanne B. McGhee, OD, and Richard Mangan, OD**

A 26-year-old Caucasian male presented with a red, painful, light-sensitive left eye after accidentally being injured when a compressed air hose nozzle hit his eye. He was wearing no safety eyewear protection. His entering unaided visual acuities were 20/20 OD and 20/400 OS with no improvement to pinhole. Pupillary testing revealed a distorted, irregular "D-shaped" left pupil with the absence of an afferent pupillary defect. Applanation tonometry measured 18mm Hg OD and 19mm Hg OS.

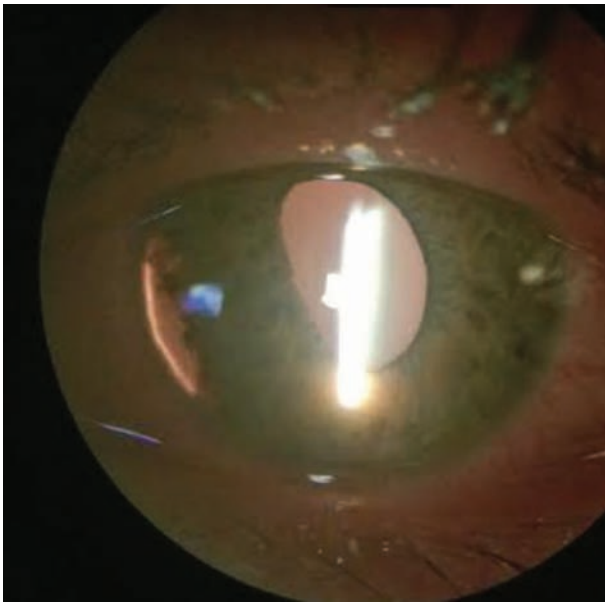


Fig. 1. This photo shows our patient's iridodialysis with accompanying inferior nasal transillumination defect.

Slit lamp examination demonstrated a mild nasal bulbar conjunctival abrasion with corresponding injection, grade 1+ traumatic iritis, moderately diffused central corneal edema, trace hyphema, and a sectoral disinsertion of the iris located inferior nasally from 8 o'clock to 10 o'clock with a corresponding transillumination defect (*Figure 1*).

Anterior segment findings in the right eye were unremarkable. Gonioscopy was deferred due to the presence of active inflammation and hyphema.

Diagnosis

A fundus examination revealed mild vitreous hemorrhage, diffuse radial striae within the macular zone (*Figure 2*). We also noted multiple pre- and subretinal hemorrhages peripherally in the left eye. Otherwise, the retinas were flat and intact with no holes, breaks or tears. A B-scan high resolution ultrasonography was performed and revealed the presence of fluid in the left eye's nasal suprachoroidal space (*Figure 3*). The test confirmed no signs of a retinal detachment.

Based on the clinical presentation and findings, the diagnosis of left large iridodialysis was made. The patient was prescribed topical cyclopentolate 1% BID, erythromycin topical ophthalmic 0.5 % ointment TID and Pred Forte (prednisolone acetate, Allergan) Q3H in the left eye until his follow-up in 24 hours. We advised he undergo a head elevation during sleep and begin topical lubricants for anterior surface irritation. The next day the patient exhibited significant improvement in ocular signs and symptoms. The conjunctival abrasion and iritis resolved, he showed improved corneal edema and a near-complete resolution of the hyphema.

Referrals were made to retina specialty for posterior segment evaluation and ophthalmology for possible surgery.

Discussion

Iridodialysis is the separation of the iris root from its ciliary body insertions, commonly sequela of blunt or penetrating ocular trauma.[1-6] However, intraocular surgical procedures or congenital causes are possible.[3] Occurrences are commonly unilaterally and sectoral, although complete dialysis of the iris have been reported.[1] The detachment of the peripheral iris root, the thinnest attachment, results in the classic "D-shaped" pupil sign where the pupillary margin, opposite of the dissection, flattens.[1]

Cases of iridodialysis may present with pain, traumatic uveal inflammation and possible associated findings, such as conjunctival injection, subconjunctival hemorrhage, hyphema, corneal abrasion, decreased or increased intraocular pressure (IOP), angle recession, vitreous hemorrhage or retinal detachments.[2,3] Photophobia and

unilateral diplopia are possible symptoms secondary to polycoria at the corneal limbus from the abnormal anatomical pupil shape created by the iridodialysis.[3,4]

Treatment

Management depends on the size and location of the iridodialysis. Cosmesis is also a concern. Superior dialyses are often covered by the upper lid and may present with fewer concerns, whereas temporal or inferior iridodialyses are more symptomatic.[1,2] Small, localized dialysis usually does not require treatment and may spontaneously resolve.[2] Larger dialysis (less than 2 clock hours) requires a non-emergent referral for surgical intervention, commonly done by suture and sutureless techniques via limbal peritomy and multiple sclerostomies.[1-6]

Sutureless techniques are often reserved for simple iridodialysis repair in conjunction with other intraocular procedures.[1,2] Associated collateral ocular trauma complications (e.g., corneal abrasion, elevated IOP, retinal detachment) must be addressed, treated and managed accordingly with topical ophthalmic preparations.[2-7]

Cycloplegics (anticholinergic drugs) are effective in alleviating pain by inhibiting ciliary body spasm, limiting the iris area to prevent the formation of a synechiae, and stabilizing the blood-aqueous barrier to reduce ocular inflammation.[8] Topical corticosteroids and non-steroidal anti-inflammatory agents can reduce acute immune responses.[6,7] Anti-glaucoma medications may be used to lower IOP in ocular hypertensive concurrent cases.[6,7]

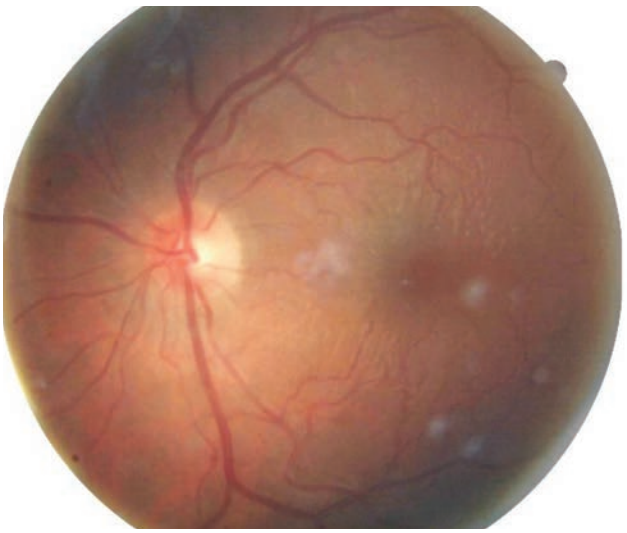


Fig. 2. This fundus image shows circular, radial striae concentrated within the macular aspect.

Following the resolution of any accompanying inflammatory reactions, gonioscopy can rule out any trabecular meshwork damage or angle recession.[6,7] Dialyzed angles with under 180° involvement have a lower risk for the development of secondary angle recession glaucoma.[6,7] The prognosis of iridodialysis is good post-surgical therapy.[2,6,7]

The patient returned asymptomatic and was happy with the cosmetic outcomes at his three-month follow up post-surgical iris repair. Visual unaided acuities were 20/20 OD, 20/20 OS. His anterior and posterior segment findings were unremarkable with normotensive IOP in both eyes. Sequential follow ups at six months revealed stable findings with the patient remaining stable at each visit. Being stable, annual clinic visits were recommended for observation. ■

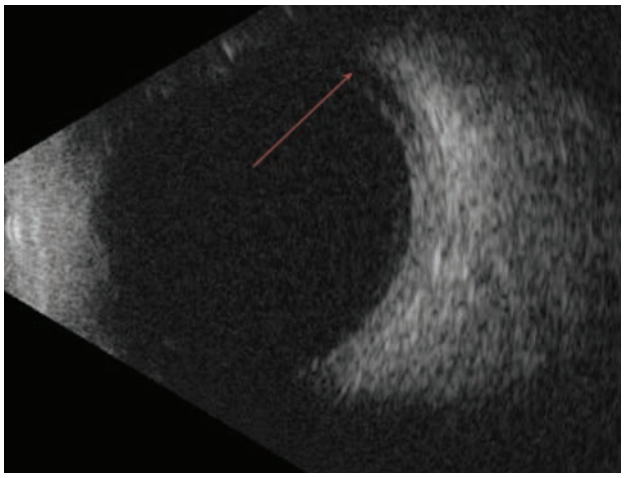


Fig. 3. Fluid in the superchoroidal space was observed using B-scan imaging.

1. Romanazzi F, Morano A, Caccavale A. Diagnostic and therapeutic approach in a case of severe post-traumatic hyphema with subtotal iridodialysis. Case Rep Ophthalmol. 2017;8(3):496-502.
2. Loiudice P, Casini G. Post-traumatic iridodialysis, crystalline dislocation and vitreous haemorrhage: how to manage. BMJ Case Reports. 2014;2014:bcr2014205595.
3. Pandey S, Sharma V. Commentary: Modified sewing machine technique: An innovative method for the management of iridodialysis, iris coloboma, and scleral fixation of intraocular lenses. Indian J Ophthalmol. 2018;66(8):1177-8.
4. Ravi Kumar K. Modified sewing machine technique for iridodialysis repair, intraocular lens relocation, iris coloboma repair, Cionni ring fixation, and scleral-fixated intraocular lens. Indian J Ophthalmol. 2018;66(8):1169-76.
5. Richards J, Kennedy C. Sutureless technique for repair of traumatic iridodialysis. Ophthalmic Surg Lasers Imaging. 2006;37:508-10.
6. Sihota R, Kumar S, Gupta V, et al. Early predictors of traumatic glaucoma after closed globe injury: trabecular pigmentation, widened angle recess, and higher baseline intraocular pressure. Arch Ophthalmol. 2008;126(7):921-6.
7. Abri Aghdam K, Aghaei H, Shokrollahi S, et al. Comparison of the effect of cycloplegic versus NSAID eye drops on pain after photorefractive keratectomy. J Current Ophthalmol. 2015;27(3-4):87-91.
8. Ellong A, Ebana Mvogo C, Nyouma Moune E, et al. Post-traumatic glaucoma with iridocorneal angle injuries in Cameroon. Bull Soc Belge Ophtalmol. 2005;(298):21-8.

OPTOMETRY GIVING SIGHT

TREK FOR SIGHT

Combine *travel* with purpose, **trek** and...

- **10-Day** Trek from 9-18 March 2020
- Take on the physical challenge while raising funds for eye care services
- **Volunteer** at Warakapola Vision Centre **for a day**

For more information contact Optometry Giving Sight on 303-526-0430
or email: jacqui@soulfulconcepts.com

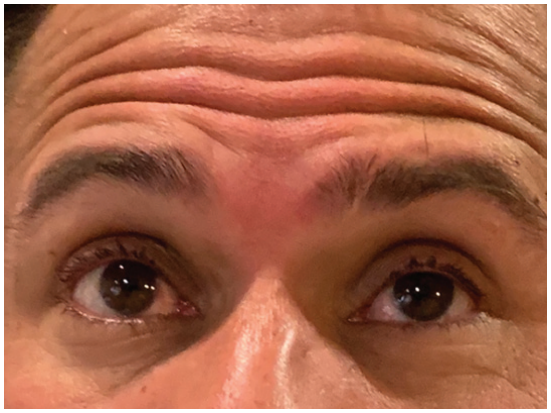
OPTOMETRYGIVINGSIGHT

When Things Aren't Looking Up

Lesions in the brain stem can be a sign of dorsal midbrain syndrome.

By Michael Trottini, OD, and Michael DelGiodice, OD

A 44-year-old male presented to the emergency room with a two-day onset of dizziness and diplopia. He felt the dizziness was worse when walking and seemed to be due to the imbalance from his vision. He denied any additional symptoms and otherwise has been in good health. The patient is originally from Honduras and moved to the United States eight years ago. His medical history is unremarkable, and he is not currently taking any medications.



This patient presented with dizziness and the inabilty to look upward.

His visual acuities were 20/70 OU. His extraocular muscle movements showed full right and left gaze; however, his downgaze was about 70% reduced, and his upgaze was 100% reduced. Both of his pupils were unreactive to light, and the left pupil was larger than the right by approximately 1mm to 2mm.

Although the pupils did not react to light stimulus, they did constrict when the patient fixated on a near target. Additionally, there was a subtle convergence-retraction nystagmus noted. His intraocular pressures were normal at 17mm Hg OU. His anterior and posterior segment exam was completely normal.

Ring Around

The pupil and motility findings were consistent with dorsal midbrain syndrome (DMS), also known as Parinaud's syndrome. Because of these findings, the team ordered a brain computerized tomography (CT) scan, which showed edema in the left basal ganglia with regional mass effect. A magnetic resonance image (MRI) was then ordered for further evaluation and showed three ring-enhancing lesions at the left midbrain, left basal ganglia and left temporal lobe with regional vasogenic edema.

These ring-enhancing lesions were most consistent with either metastatic disease or infection. Subsequently, the patient was admitted with neurosurgery and infectious disease consultations. His chest, abdominal and pelvic CT scans were all unremarkable, and his cerebrospinal fluid cytology was normal—the brain lesions were unlikely to be metastatic.

An infectious disease work-up revealed the patient to be human immunodeficiency virus (HIV) positive with a CD4 cell count of 96. Serum toxoplasmosis IgG was markedly elevated, and a lumbar puncture showed elevated cerebrospinal fluid toxoplasmosis IgG as well.

The patient was diagnosed with HIV, and his brain lesions were consistent with an opportunistic central nervous system (CNS) toxoplasmosis infection. The neurosurgeon did not recommend any acute surgical intervention, and the patient was treated with pyrimethamine, sulfadiazine and leucovorin.

Antiretroviral therapy (ART) was held initially until his opportunistic toxoplasmosis infection improved to avoid the risk of inducing immune reconstitution inflammatory syndrome (IRIS).

The patient remained hospitalized for approximately one month while he was receiving treatment for his CNS infection. Prior to his discharge, we ordered a repeat MRI that showed improvement of all three ring-enhancing lesions, with significant improvement of the associated edema. A repeat assessment of his ocular motilities showed improvement in his upward and downward gaze.

He still reported diplopia and some vision difficulties, but his upward gaze improved from a 100% limitation to about a 60% to 70% limitation. The downward gaze improved from a 70% limitation to about a 30% limitation. His pupils were now similar in size

with only 0.5mm of anisocoria and started to show some constriction to light stimulus.

The patient was discharged with instructions to take sulfamethoxazole-trimethoprim, leucovorin and pyrimethamine and later scheduled to start ART in a health clinic. He was also instructed to follow up in three months to reassess his ocular motilities.

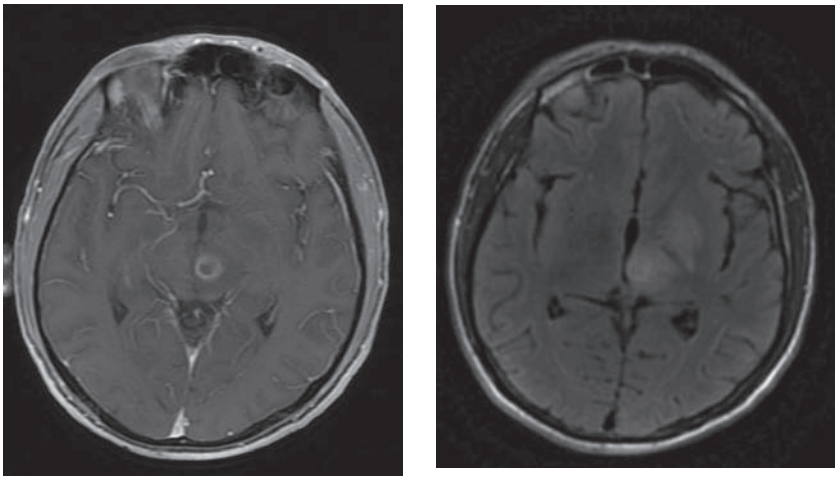
Discussion

The premotor pathways for vertical eye movements are located within the dorsal and tegmental midbrain and include the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) and the posterior commissure. Dorsal midbrain syndrome is a vertical gaze palsy that affects these structures and presents clinically with impaired vertical eye movements, light-near dissociation of the pupillary response and convergence nystagmus on attempted upward gaze.[1]

Pineal lesions exerting pressure on the midbrain are the classical cause of DMS, however primary lesions within the midbrain can be responsible as well.[1] Ischemia, hemorrhage, neoplasms and infectious or demyelinating processes also have all been reported.[1]

There is no specific treatment for DMS, and the prognosis is dependent on the underlying cause, extent of damage and treatment.[2] Any residual ischemia, atrophy or necrosis to the involved structures or damage from treatments, such as tumor resection or radiation, may prevent full recovery of vertical gaze.

In managing our patient, the first step was to identify the intracranial process that was causing DMS. The ring-enhancing lesions, specifically the one within his brainstem, were compressing around the posterior commissure with edema in the midbrain, correlating with his clinical presentation.



This axial MRI is able to show the ring-enhancing lesion (left). The edema surrounds the lesion, with compression around the posterior commissure (right).

The next step was to determine the etiology of these peripheral enhancing lesions. The underlying cause of ring-enhancing lesions is influenced in part by the immune status of the individual.[3]

Malignancy (primary or metastatic) tends to be the more common cause in immunocompetent individuals, while lymphoma and toxoplasmosis are often the cause in immunocompromised individuals.[3] Our patient presented with no prior medical issues, but a thorough work revealed he was HIV positive, was immunocompromised and had developed a CNS toxoplasmosis infection.

While neurology or infectious disease specialists typically perform these evaluations, an optometrist's role is important in a case such as this because the patient only presented with symptoms of diplopia. Localizing the source of the diplopia and the appropriate neuro-imaging helped to direct their work-up.

Lastly, in regards to management, the toxoplasmosis infection was treated and better controlled prior to starting the patient on ART. CD4 cells are suppressed due to HIV infection, and, if ART therapy is started simultaneously with treatment of the opportunistic infection, CD4 cells may rapidly increase, causing a significant inflammatory response.[4]

Although IRIS is generally self-limiting, it has a high mortality rate in the setting of opportunistic infections involving the CNS as seen in our patient.[4] Because of the potential for IRIS, ART was held initially to prevent this rapid increase of CD4 cells and the syndrome from developing.

While DMS is a rare clinical presentation, it's caused by brain stem dysfunction and often is a result of fatal diseases, if not treated appropriately. Early diagnosis and management are essential for patient survival and positive outcomes. ■

1. Shields M, Sinkar S, Chan W, Crompton J. Parinaud syndrome: a 25-year (1991-2016) review of 40 consecutive adult cases. Acta Ophthalmol. 2017;95:792-3.
2. Yiu G, Lessell S. Dorsal midbrain syndrome from a ring-enhancing lesion. Semin in Ophthalmol. 2012;27(3-4):65-8.
3. Chakraborty S. Multiple ring-enhancing lesions in a patient with unilateral limb jerking. Cent Eur J Med. 2014;9(3):391-3.
4. Sharma S, Soneja M. HIV and Immune Reconstitution Inflammatory Syndrome (IRIS). Indian J Med Res. 2011;134(6):866-77.

CLINICALLY PROVEN TO ENHANCE VISION

even in patients with perfect 20/20 vision.

Passing a standard vision test on a black and white eye chart may measure your visual acuity as "perfect," but anyone whose struggled with their vision driving at night knows that unlike an eye chart life doesnt occur at 100% contrast. For life's more colorful moments we have MacuHealth. MacuHealth is clinically proven* to improve contrast sensitivity, enhancing our visual performance no matter the conditions.

Because we've all been here!

SHARPER VISION

in situations of bright light, low light, glare, fog, etc...

Visit us at AOA Booth 605

MACUHEALTH WITH LMZ3

is the only dietary supplement to contain all three carotenoids found in the macula, Lutein, Meso-Zeaxanthin and Zeaxanthin, in a patented 10:10:2 ratio. MacuHealth is scientifically tested and clinically proven to enrich macular pigment, improve contrast sensitivity and enhance visual performance in both diseased and healthy eyes.*

*Data on file

MacuHealth®
With LMZ3 "TRUST THE SCIENCE"

TO PLACE AN ORDER OR LEARN MORE:

Call MacuHealth at 866 704 0845
Email us at info@macuhealth.com
Visit our website www.macuhealth.com

Edited By Carlo Pelino, OD, and Joseph J. Pizzimenti, OD

A Paralyzing Etiology

Patients with Guillain-Barré syndrome face significant systemic and ocular complications, including optic disc edema. By Sarah J. Bishop, OD, and Sandra M. Fox, OD

Symptoms of headache concurrent with clinical findings of bilateral optic disc edema are of serious concern. Papilledema is optic disc swelling due to high intracranial pressure (ICP). Its causative conditions can include hydrocephalus, spinal cord lesions, cerebral sinus drainage impairment, intracerebral mass, cerebral hemorrhage, meningitis and idiopathic intracranial hypertension (*Table 1*).

Visual function loss is the feared morbidity of papilledema. Treatment is directed at the underlying cause of the high ICP, and options include both medical and surgical modalities.

A thorough neuro-ophthalmic workup helps the clinician sort through the myriad differential diagnoses, which can include Guillain-Barré syndrome (GBS). This is an acute polyneuropathy in which the immune system attacks myelin within the peripheral nervous system. GBS manifests as an acute inflammatory neuropathy with weakness and diminished reflexes. Patients initially experience numbness and tingling in their extremities. The condition may progress, eventually resulting in paralysis.[1,2]

Case Example

While on active military duty, a 19-year-old Asian male experienced sudden numbness and loss of sensation in his lower extremities, causing him to fall down the stairs at his barracks. Prior to this episode, he was in excellent health without any medical conditions. He did, however, receive a flu vaccination a few weeks prior to his symptoms. He was immediately admitted to the hospital, where neuroimaging was performed and a lumbar puncture and serologic testing confirmed a diagnosis of GBS. Intravenous immunoglobulin treatment was initiated and a plasmapheresis (plasma exchange) was also completed.

The patient presented for an eye examination two months following his GBS diagnosis. He was now wheelchair bound. The patient had no visual or ocular complaints, though he reported occasional generalized headaches of low intensity. The patient was taking amitriptyline 100mg QHS, gabapentin 600mg TID, morphine ER 15mg QHS and metoprolol 25mg BID.

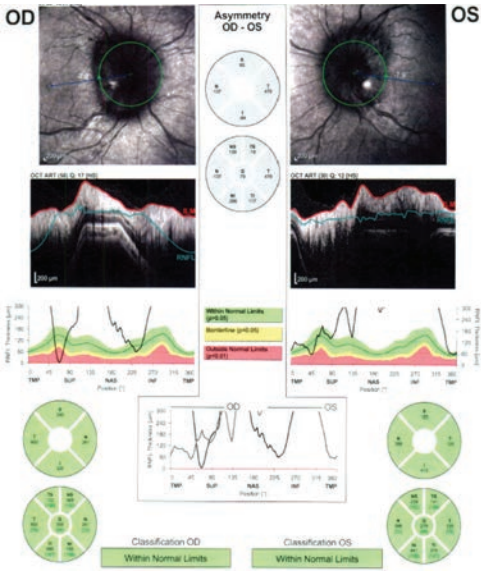


Fig. 1. SD-OCT revealed peripapillary retinal nerve fiber layer thickening in both eyes.

His best-corrected visual acuity was 20/20 OD and OS and all other preliminary findings were unremarkable. Posterior segment evaluation revealed bilateral small optic cups with 3+ optic disc edema OD and OS. A splinter hemorrhage was detected temporal to the disc OD. Spectral-domain optical coherence tomography (SD-OCT) revealed thickening of the peripapillary retinal nerve fiber layer (RNFL) OD and OS (*Figure 1*). A Humphrey 24-2 visual field revealed enlarged blind spots in both eyes.

The patient was diagnosed with bilateral disc edema. We ordered an MRI of the brain and orbits, with and without contrast, as well as targeted serologic workup.

The MRI revealed nonspecific T2/FLAIR hyperintense foci within the right frontal white matter. These lesions may result from migraine, demyelination or inflammation. No other intracranial or intraorbital abnormalities were detected. Serology was negative for HIV, syphilis, Lyme disease and neuronal antibodies. Copper levels and serum protein electrophoresis were within normal limits.

Lumbar puncture showed an elevated opening pressure of 40cm H_2O (the normal range for adults is 10cm to 20cm H_2O). The cerebrospinal fluid (CSF) showed elevated protein levels. The patient was diagnosed with papilledema associated

with GBS. He was prescribed 500mg acetazolamide BID PO. Following treatment, the patient's papilledema gradually began to resolve.

GBS: The Basics

GBS occurs more often in females (1.5:1) and its risk tends to increase with age. Ever since the eradication of polio, GBS has been the leading cause of acute paralytic disease within the western world.[1,2] Researchers speculate it is triggered by a viral infection, as approximately 60% to 70% of people with GBS had a preceding infection, most commonly gastroenteritis or an upper respiratory infection. Studies have also linked GBS and the flu vaccination, but have yet to establish causation. GBS frequency rose in 1976 and 1977 during the mass immunization campaign against the swine flu. However, no subsequent vaccines have been associated with an increased incidence of GBS.[1,2]

GBS develops over the course of a few days to a month. Early symptoms include numbness, tingling and weakness in the extremities. Later, paresthesia, quadriplegia and hyporeflexia can occur.[3] Approximately 15% of cases develop weakness in the muscles required for breathing. Diagnosis is made based on a combination of electrophysiological studies demonstrating slowed or blocked nerve conduction and CSF protein level testing. Glycolipid antibodies are observed in the sera of 60% to 70% of GBS patients during the acute phase, with gangliosides being the major target antigens.

Therapy aims to eliminate symptoms and speed recovery with immunoglobulin therapy, plasma exchange or a combination.[1-3]

GBS and The Eye

Ophthalmic manifestations of GBS include oculomotor palsy (which occurs in 10% of patients), accommodative dysfunction, optic neuritis and true papilledema, although the latter is exceedingly rare in GBS.[2,4] Approximately 80% to 90% of patients with papilledema first seek treatment for a headache.[5] In this case, our patient only mentioned occasional, mild headaches. However, the morphine may have been masking their intensity.

Other ocular symptoms and signs in papilledema secondary to GBS may include reduced visual acuity, enlarged blind spot, transient visual obscurations and diplopia secondary to a sixth cranial nerve palsy.[6] MRI with concomitant magnetic resonance venography (MRV) to rule out venous sinus thrombosis are the preferred neuroimaging studies for bilateral disc edema.

Although research does not widely report ICP with GBS, the increased ICP has been associated with an elevated CSF protein level—common in GBS.[7] Investigators hypothesize that the increased CSF protein decreases the rate of reabsorption of CSF through the brain's arachnoid granulations, leading to increased ICP.[8] CSF protein concentration is one of the main factors to consider in differentiating papilledema associated with GBS from idiopathic intracranial hypertension.

Treatment of papilledema involves addressing the underlying cause, as well as lowering the ICP. First-line treatment is usually a diuretic drug such as acetazolamide. If medical treatment is insufficient, serial lumbar punctures may be beneficial in providing temporarily relief from symptoms of intracranial hypertension. Other more invasive therapies such as a ventriculoperitoneal shunt or optic nerve sheath fenestration may be necessary in severe cases.[4]

Table 1. Differential Diagnosis of Bilateral Disc Edema

- Idiopathic intracranial hypertension
- Compressive optic neuropathy
- Hydocephalus/venous sinus thrombosis
- Optic neuritis
- Metabolic/toxic optic neuropathy
- Diabetic papillopathy
- Malignant hypertension
- Pseudopapilledema (optic nerve drusen)
- Anterior ischemic optic neuropathy

Patients with GBS may present to the optometrist with ocular manifestations, including true papilledema. In any case of bilateral disc edema, clinicians should comanage with neuro-ophthalmology to rule out serious threats to vision and life. MRI, MRV, serum analysis and, if indicated, lumbar puncture with CSF analysis, can help uncover the underlying cause. ■

Dr. Bishop, a graduate of the Pennsylvania College of Optometry with an advanced studies certificate in neuro-ophthalmic disease, is completing a residency in brain injury vision rehabilitation/ocular disease at the Audie L. Murphy Memorial VA Hospital in San Antonio.

Dr. Fox is the eye care provider at the Polytrauma Rehabilitation Center of Texas at the Audie L. Murphy Memorial VA Hospital in San Antonio. Her area of specialty is low vision rehabilitation with an emphasis on neuro rehabilitation.

1. van Doorn PA. Diagnosis, treatment, and prognosis of Guillain-Barré syndrome (GBS). Presse Med. 2013 Jun;42(6 Pt 2):e193-201.
2. Alrohimi A, Ba F. Headache and papilledema in Guillain-Barré syndrome. Canadian J Neurol Sci. 2018;42(3):351-53.
3. Gurwood AS, Drake J. Guillain-Barré syndrome. Optometry. 2006;77(11):540-46.
4. Rigi M, Almarzouqi SJ, Morgan ML, Lee AG. Papilledema: epidemiology, etiology, and clinical management." Eye Brain. 2015 Aug;7:47-57.
5. Sadun AA, Wang YM. Papilledema and raised intracranial pressure. In: Levin LA, Albert DM. Ocular Disease: Mechanisms and Management. Philadelphia: Saunders; 2010:883-86.
6. Farmakidis C, Inan S, Milstein M, Herskovitz S. Headache and pain in Guillain-Barré syndrome." Curr Pain Headache Rep. 2015;19(8):40.
7. Zhao PP, Ji QK, Sui RB, et al. Increased intracranial pressure in Guillain-Barré syndrome: A case report. Medicine (Baltimore). 2018;97(30):e11584.
8. Gardner WJ, Spitler DK, Whitten C. Increased intracranial pressure caused by increased protein content in the cerebrospinal fluid. N Engl J Med. 1954;250(22):932-6.

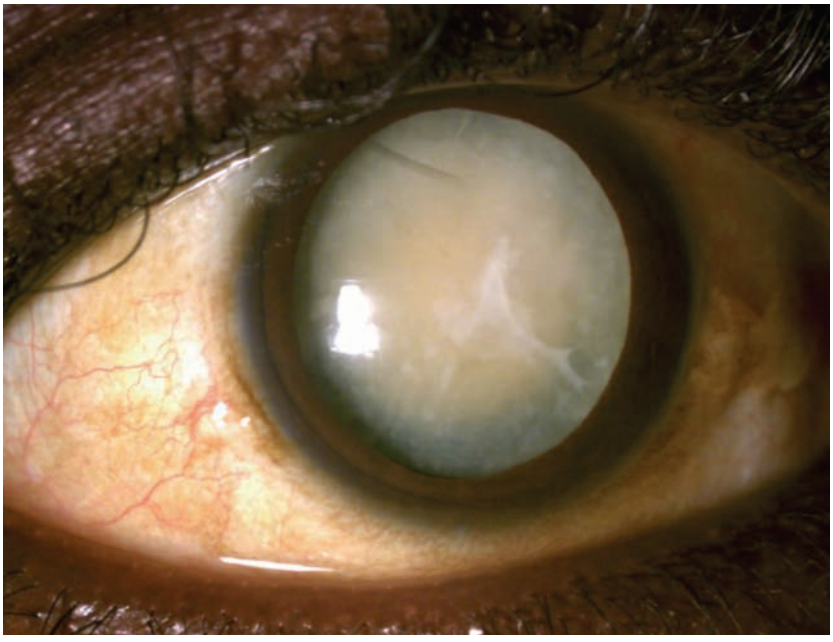
Hunting the Great White

Managing the complications from a hypermature cataract.

By Joseph W. Sowka, OD

A 53-year-old man previously treated for advanced glaucoma presented with slowly progressive painless vision loss in his right eye. He had missed his visits for the past year, though he had been obtaining medication refills through his pharmacy. His vision at this visit was light perception. A year earlier, it was 20/200 and three years earlier it was 20/70 with fixation loss and profound visual field loss from glaucoma.

His recent vision reduction was due to a hypermature cataract that fully developed in the year between visits. Intraocular pressures (IOPs) were 14mm Hg OD and 16mm Hg OS. He had neither pain nor inflammation and gonioscopically his anterior chamber angles were open and normal. However, with mature and hypermature cataracts, one must be concerned about phacomorphic and phacolytic glaucoma.



This 53-year-old patient's left eye's vision was reduced to light perception as a result of this hypermature cataract.

Discussion

Upon cataract hypermaturation, the lens cortex undergoes spontaneous lysis and absorption with secondary lens nucleus shrinkage and capsule wrinkling.[1-4] This allows internal lens proteins to leak out through an intact though permeable lens capsule.[1-4] While the internal lens proteins are the host's own body tissue, they have never been exposed to the anterior chamber due to their envelopment by the lens capsule. When the body detects these internal lens proteins, it interprets them as foreign and antigenic. Subsequently, a lens-induced inflammatory reaction ensues.[3] A pronounced macrophage response occurs in the anterior chamber.[6] Numerous macrophages containing phagocytized degenerated lens material (phacolytic cells) can be found in the anterior chamber. The lens-induced inflammation often causes a secondary rise in IOP with secondary glaucoma.

Phacolysis can be considered an innate evolutionary response to cataractogenesis. Prior to the advent of surgical lens removal, many individuals would become blind from cataracts. The subsequent lytic process and inflammatory degradation would effectively remove the visual obstruction. Unfortunately, the eye would be left aphakic and often irreparably damaged from inflammatory glaucoma. Spontaneous absorption of cataracts through the phacolytic process has been reported, which supports this evolutionary role of phacolysis.[5,6] While the cataract maturation process is generally slow, once a lens has become hypermature, the phacolytic process can develop rapidly.[7]

Phacomorphic glaucoma typically afflicts older females, often of small stature with moderate hyperopia and a nanophthalmic eye.[8] Frequently, an advanced, intumescent cataract will be present in the affected eye with commensurate reduced

vision. There will be a shallow anterior chamber and possibly iris bombé. In eyes with markedly asymmetric cataract formation, the depth of the anterior chambers may be accordingly disparate. Patients may present with an acute onset of ocular redness and pain with an edematous cornea and elevated IOP, as typically seen in an angle closure attack. During an acute attack, few to no anterior chamber angle structures will be visible on gonioscopy.[8-10] The resultant secondary angle closure may be either acute, subacute or chronic and can occur in eyes with previously open angles, as well as those with previously narrow, occludable angles.[11-13] In chronic angle closure cases that occur from phacomorphism, no symptoms will be seen.

Treatment

When managing the inflammatory component in phacolysis, topical corticosteroids are indicated, just as they would be for any anterior uveitis.[14] Cycloplegics are also indicated.[14] The choice should be dictated by the severity of the uveitic response and the patient's degree of discomfort. Typically, homatropine is an adequate choice.[14]

Patients with phacolysis may experience loss of zonular support to the lens, which manifests as phacodonesis.[14] In cases of poor zonular support, cycloplegia with attendant pupil dilation may result in anterior dislocation of the lens, possibly into the anterior chamber. If poor zonular support to the lens is suspected, cycloplegia should be avoided.

The secondary glaucoma accompanying phacolysis is often improved by the reduction in inflammation with topical steroid therapy. However, if additional pressure reduction is necessary, clinicians may turn to aqueous suppressants, barring any systemic contraindications. Avoid miotics and prostaglandin analogs due to their propensity to aggravate the disease.[14]

As with acute primary angle closure glaucoma, medical therapy is initially used to acutely lower the IOP in eyes with phacomorphic glaucoma. Beta-blockers, alpha-2 adrenergic agonists, topical corticosteroids, topical or oral carbonic anhydrase inhibitors and oral hyperosmotics may be all systematically employed. An exceptional effect of prostaglandin analogs in managing the IOP of patients with chronic angle closure glaucoma both before and following LPI has been reported.[15-17] In cases where pupil block precipitates the angle closure, LPI is indicated following medical treatment to attempt to relieve the resultant aqueous congestion and IOP rise. This is especially true where a relative pupil block, secondary to the unusual lens anatomy is the main pathogenesis.[18]

In most cases, it is necessary to remove the antigenic lens to fully manage phacolytic and phacomorphic glaucoma. Manual small-incision cataract surgery with trypan blue staining of the anterior lens capsule is a safe and effective method of cataract extraction for patients with phacolytic glaucoma, as is phacoemulsification.[19] Phaco combined with anterior vitrectomy is also an option in these cases.[20,21] Anecdotally, femtosecond laser-assisted cataract surgery may be a viable option.[22]

These hypermature lens conditions develop typically when a patient is deemed a poor candidate for surgery or otherwise cannot obtain or undergo cataract extraction. In the patient presented here, he already had longstanding severe vision loss from advanced glaucoma; thus his developing cataract was never addressed. With no future visual potential in this eye from pre-existing glaucoma, he will be monitored for the possible development of phacomorphism and phacolysis and then addressed accordingly should these complications develop. ■

1. Podhorecki J, Munir A. Result of operations for hyper-mature cataract complicated with phacolytic glaucoma. Klin Oczna. 2002;104(5-6):350-3.
2. Rijal AP, Karki DB. Visual outcome and IOP control after cataract surgery in lens induced glaucomas. Kathmandu Univ Med J (KUMJ). 2006;4(1):30-3.
3. Oprescu M. The etiopathology of phacoantigenic uveitis and phacolytic glaucoma. Oftalmologia 1992; 36(3):207-13.
4. Rosenbaum JT, Samples JR, Seymour B, et al. Chemotactic activity of lens proteins and the pathogenesis of phacolytic glaucoma. Arch Ophthalmol 1987;105(11):1582-4.
5. Blaise P, Duchesne B, Guillaume S, et al. Spontaneous recovery in phacolytic glaucoma. J Cataract Refract Surg. 2005;31(9):1829-30.
6. Mohan M, Bartholomew RS. Spontaneous absorption of a cataractous lens. Acta Ophthalmol Scand. 1999;77(4):476-7.
7. Sowka J, Vollmer L, Falco L. Rapid onset phacolysis. Optometry. 2004;75(9):571-6.
8. Abramson DH, Franzen LA, Coleman DJ. Pilocarpine in the presbyope: Demonstration of an effect on the anterior chamber and lens thickness. Arch Ophthalmol 1973; 89(2):100-2.
9. Gorin G. Angle closure glaucoma induced by miotics. Am J Ophthalmol 1966; 62(6):1063-6.
10. Gayton JL, Ledford JK. Angle closure glaucoma following a combined blepharoplasty and ectropion repair. Ophthal Plast Reconstr Surg. 1992;8(3):176-7.
11. Pradhan D, Hennig A, Kumar J, et al. A prospective study of 413 cases of lens-induced glaucoma in Nepal. Indian J Ophthalmol. 2001;49(2):103-7.
12. Prajna NV, Ramakrishnan R, Krishnadas R, et al. Lens induced glaucomas--visual results and risk factors for final visual acuity. Indian J Ophthalmol. 1996;44(3):149-55.
13. Angra SK, Pradhan R, Garg SP. Cataract induced glaucoma--an insight into management. Indian J Ophthalmol. 1991;39(3):97-101.
14. Sung VC, Barton K. Management of inflammatory glaucomas. Curr Opin Ophthalmol. 2004;15(2):136-40.
15. How AC, Kumar RS, Chen YM, et al. A randomised crossover study comparing bimatoprost and latanoprost in subjects with primary angle closure glaucoma. Br J Ophthalmol. 2009;93(6):782-6.
16. Chen MJ, Chen YC, Chou CK, et al. Comparison of the effects of latanoprost and bimatoprost on intraocular pressure in chronic angle-closure glaucoma. J Ocul Pharmacol Ther. 2007;23(6):559-66.
17. Chen MJ, Chen YC, Chou CK, et al. Comparison of the effects of latanoprost and travoprost on intraocular pressure in chronic angle-closure glaucoma. J Ocul Pharmacol Ther. 2006;22(6):449-54.
18. Tomey KF, al-Rajhi AA. Neodymium:YAG laser iridotomy in the initial management of phacomorphic glaucoma. Ophthalmology. 1992;99(5):660-5.
19. Venkatesh R, Tan CS, Kumar TT, et al. Safety and efficacy of manual small incision cataract surgery for phacolytic glaucoma. Br J Ophthalmol. 2007;91(3):279-81.
20. Dada T, Kumar S, Gadia R, et al. Sutureless single-port transconjunctival pars plana limited vitrectomy combined with phacoemulsification for management of phacomorphic glaucoma. J Cataract Refract Surg. 2007;33(6):951-4.
21. Miura S, Ieki Y, Ogino K, et al. Primary phacoemulsification and aspiration combined with 25-gauge single-port vitrectomy for management of acute angle closure. Eur J Ophthalmol. 2008;18(3):450-2.
22. Kránitz K, Takács AI, Gyenes A, et al. Femtosecond laser-assisted cataract surgery in management of phacomorphic glaucoma. J Refract Surg. 2013;29(9):645-8.

Merchandise Offered

Faculty

ASSISTANT PROFESSOR POSITIONS: PEDIATRICS, PRIMARY CARE/OCULAR DISEASE

Full-time non-tenure track faculty positions for the Chicago College of Optometry

Responsibilities: Candidates are expected to be highly knowledgeable in the field of pediatric or primary care and ocular disease and develop and teach courses and/or laboratories in the subject area. The primary care candidate must also be able to provide direct patient care and clinical instruction to professional students as well as residents, and be involved in interdisciplinary practice with other educational professionals.

Candidates must be willing to actively participate in curricular assessment, professional development, student counseling and service activities within the college, university and the scientific community. Successful candidates are also expected to be involved in research and scholarly activities, and have a sincere commitment to optometric education, community service and patient care. Primary duties include, but are not limited to:

a) **Teaching**
- Developing and delivering lectures and/or laboratories for related areas, as assigned;
- Embracing and enhancing the didactic
- philosophies in the O.D. program;
- Maintaining and expanding the high quality clinical practice environment for optometry students on rotation;
- Precepting students on clinical rotation at the Midwestern University Eye Institute;

b) **Service**
- Helping to maintain and grow the state of the art optometry program with a strong interdisciplinary focus that meets the needs of patients in the surrounding community; is efficient, patient friendly, and cost-effective;
- Working closely together with all optometry and ophthalmology faculty to provide a complete range of eye and vision care services;
- Participating in leadership roles in state, regional, and national optometry organizations;
- Participating on College and University committees, as assigned;
- Participating in College and University service activities.

c) **Scholarly activity**

Engaging in research and scholarly activity, including presentations at scientific meetings, research, and publication in peer reviewed journals sufficient to qualify for academic advancement in a non-tenure track position.

Qualifications: Candidates must possess a Doctor of Optometry degree from an ACOE-accredited institution, must have completed an ACOE-accredited residency, and must be eligible for an illinois optometric state license. Primary eye care clinical expertise is also required.

Salary will be commensurate with qualifications and experience
Review of applications will begin immediately and continue until the position is filled

Contact information: Interested applicants should apply online at www.midwestern.edu and include curriculum vitae and letter of interest specifying the position and college that he/she wishes to be considered for. Application packet should include curriculum vitae and letter of interest. Inquiries may be directed to Dr. Melissa Suckow, Dean; Midwestern University: msucko@midwestern.edu.

Midwestern University is an Equal Opportunity/Affirmative Action employer that does not discriminate against an employee or applicant based upon race, color, religion, gender, national origin, disability, or veterans status, in accord with 41 C.F.R. 60-1.4(a), 250.5(a), 300.5(a) and 741.5(a).

Continuing Education

Dr. Travel Seminars, LLC

In Partnership With The NJ Society of Optometric Physicians

Buenos Aires, Argentina to Santiago, Chile Cruise

NCL's Star

February 29 - March 14, 2020 (14 Night Cruise)

Sailing to Multiple Stops in Argentina & Chile

Optional Private Group Tours in all Ports-of-Call

Optional Pre & Post Cruise Stays & Tours in Argentina, Chile & Peru (Machu Picchu)

NJSOP Society of Optometric Physicians

All Programs Are in Partnership With the New Jersey Society of Optometric Physicians

cope

Dr. TRAVEL SEMINARS, LLC is a COPE approved provider Course approved for 12 CE

Special Amenities: $100 + Choose Free Drinks, Specialty Dining or Internet

"An Educational Feast for the Comprehensive Optometric Physician"
Presented by Ron Melton, OD, FAAO, & Randall Thomas OD, FAAO

Additional Seminar Cruises (12-16 C E):

Baltic Sea Cruise: July 22 - 31, 2020 - *NCL's 'Getaway'*
Round Trip Copenhagen - Leo Semes OD, FAAO, Professor Emeritus, UAB

Christmas Week: December 22-29, 2019 - Royal Caribbean's 'Allure of the Seas'
Eastern Caribbean Sailing - Edward Paul, Jr., OD, PhD, FIALVS

Presidents Week: February 15 - 22, 2019 - Whitney Hauser, OD, FAAO
Western Caribbean - Royal Caribbean's Symphony of the Sea's - Save $800 per person

www.DrTravel.com 800-436-1028

MEDICAL OPTOMETRISTS

The American Board of Certification in Medical Optometry (ABCMO) is recognized at Joint Commission (JC) accredited medical facilities as issuing board certification in the specialty of medical optometry and those ABCMO certifies are eligible for credentialing at these facilities as specialists rather than general optometry practitioners.^

The Joint Commission, the accepted national Gold Standard, reviews and accredits over 21,000 federal, state and local-chartered medical facilities.

To Be Eligible for ABCMO board certification:

1. Complete an accredited residency in medical optometry
2. Pass the national Advanced Competence in Medical Optometry Examination
3. Practice in a medical setting for a minimum of two years.#

www.abcmo.org

Visit **www.abcmo.org** to understand how JC accredited medical facilities credential specialists and why specialty certification can enhance the careers of optometrists who complete residencies in medical optometry.

For Application procedures see
www.abcmo.org
or contact myers.kenj@gmail.com

^ At this time, 127 JC accredited hospitals, clinics and teaching institutions recognize ABCMO specialist certification.
' www.jointcommission.org
Waived for two years after residency

Practice For Sale

For Sale
NEW YORK – ULSTER COUNTY

Exceptional opportunity to live and practice in a beautiful, vibrant community only 1½ hour drive from Manhattan. Grossing $700,000 in 2018 with $210,000 in owner net. Advanced diagnostic equipment includes Optovue OCT, corneal topographer, retinal camera, LipiView and LipiFlow.

100% Financing Available
Call for a Free Practice Evaluation
800-416-2055
www.TransitionConsultants.com

Practice Consultants

Practice Sales • Appraisals • Consulting
www.PracticeConsultants.com

PRACTICES FOR SALE NATIONWIDE

Visit us on the Web or call us to learn more about our company and the practices we have available.

info@PracticeConsultants.com

925-820-6758

www.PracticeConsultants.com

Equipment and Supplies

WHY PAY RETAIL???

Pretesting Tables of all shapes and sizes at Wholesale Prices.

Search the word PRETESTING at EBAY

Save hundreds even thousands on all your pretesting needs.
Or call: 316-734-4265

Do you have Equipment and Supplies for Sale?

REVIEW® OF OPTOMETRY

Contact us today for classified advertising:
Toll free: **888-498-1460** • E-mail: **sales@kerhgroup.com**

Career Opportunities

Staff Optometrist Wanted

Bard Optical is a family owned full-service retail optometric practice with 22 offices (and growing) throughout Central Illinois. Bard Optical prides itself on having a progressive optometric staff whose foundation is based on one-on-one patient service. We are currently accepting CV/resumes for Optometrists to join our medical model optometric practice that includes extended testing. The practice includes but is not limited to general optometry, contact lenses and geriatric care. Salaried, full-time positions are available with excellent base compensation and incentive programs and benefits. Some part-time opportunities may also be available.

Current positions are available in Bloomington/Normal, Decatur/Forsyth, Peoria, Sterling and Canton as we continue to grow with new and established offices.

Please email your information to **mhall@bardoptical.com** or call Mick at **309-693-9540 ext 225**.
Mailing address if more convenient is:
Bard Optical
Attn: Mick Hall, Vice President
8309 N Knoxville Avenue
Peoria, IL 61615

Bard Optical is a proud Associate Member of the Illinois Optometric Association.

BARD OPTICAL

www.bardoptical.com

Professional Opportunities

MACULAR DEGENERATION
Patients pay out of pocket for low vision glasses to keep reading and driving.

I'll teach you how to have them call you.
I'll teach you how to help them achieve their goals.
I'll teach you how to substantially increase your income.

I get paid only if you get paid!

THE INTERNATIONAL ACADEMY OF LOW VISION SPECIALISTS HAS THE FOLLOWING TERRITORIES AVAILABLE:
N. CALIFORIA S. CAROLINA MAINE S. MISSOURI MASSACHUSETTS IOWA S. GEORGIA W. VIRGINIA SAN DIEGO OHIO S. IDAHO

OUR CONNECTICUT DOCTOR IS RETIRING SOON. TAKE OVER A THRIVING LOW VISION PRACTICE!

RICHARD J. SHULDINER, OD, FAAO
LOW VISION DIPLOMATE / PRES. IALVS
DOCTOR@LOWVISIONCARE.COM / 951 286 2020 CELL

Targeting Optometrists?

CLASSIFIED ADVERTISING WORKS

• JOB OPENINGS • CME PROGRAMS
• PRODUCTS & SERVICES • AND MORE...

Contact us today for classified advertising:
Toll free: **888-498-1460**
E-mail: **sales@kerhgroup.com**

Meetings + Conferences

June 2019

■ **1-3.** *Annual Ocular Disease Update.* Big Cedar Lodge, Ridgedale, MO. Hosted by: Oklahoma College of Optometry. Key faculty: Kelly Malloy, Walter Whitley, Joseph Shetler. CE hours: 16. For more information, email Callie McAtee at mcateec@nsuok.edu or go to optometry.nsuok.edu.

■ **5-9.** *VT1/Visual Dysfunctions.* Nova Southeastern University, Fort Lauderdale, FL. Hosted by: Optometric Extension Program Foundation. Key faculty: Paul Harris. CE hours: 35. For more information, email Karen Ruder at karen.ruder@oep.org, call 410-561-3791 or go to www.oepf.org.

■ **6-9.** *UOA Annual Congress.* Zermatt Utah Resort, Midway, UT. Hosted by: Utah Optometric Association. CE hours: 21. For more information, email Alyssa White at alyssa@utaheyedoc.org, call 801-364-9103 or go to www.utaheyedoc.org.

■ **7-9.** *Everything Therapeutic: Houston.* University of Houston, Houston Health 1 Building. Hosted by: University of Houston College of Optometry. Key faculty: Bruce Onofrey, Seema Nanda, Joe Wheat, Susan Cotter, Justin Schweitzer. CE hours: 24. For more information, email optce@central.uh.edu, call 713-743-1900 or go to ce.opt.uh.edu.

■ **13-16.** *VOA Annual Conference.* Omni Richmond Hotel, Richmond, VA. Hosted by: Virginia Optometric Society. Key faculty: Peter Cass, Michael Chaglasian, Clark Chang, Jason Duncan, Scott Ensor, Tami Hagemeyer, Whitney Hauser. CE hours: 20 total, 17 per OD. For more information, email Bo Keeney at office@thevoa.org go to www.thevoa.org/annual.

■ **19-23.** *Optometry's Meeting.* America's Center Convention Complex, St. Louis, MO. Hosted by: American Optometric Association and American Optometric Student Society. CE hours: 247, 44 per OD. For more information, email Fran Ghannam at fghannam@aoa.org or go to www.optometrysmeeting.org.

■ **28-July 8.** *A Contemporary Look at Patient Eye Care—Dalmation Coast.* On Board Celebrity Cruise Line's Celebrity Constellation from Venice to Rome, Italy. Hosted by: Dr. Travel Seminars and NJ Society of Optometric Physicians. Key faculty: Randall Thomas. CE hours: 12. For more information, email info@drtravel.com or go to www.drtravel.com.

■ **30-July 6.** *Tropical CE–Costa Rica.* Los Suenos Marriott Ocean and Golf Resort, Herradura, Costa Rica. Hosted by: Tropical CE. Key faculty: Steven Ferrucci, William Miller. CE hours: 20. For more information, email Stuart Autry at sautry@tropicalce.com or go to www.tropicalce.com.

To list your meeting, please send the details to:

Mark De Leon, Associate Editor
Email: mdeleon@jobson.com
Phone: (610) 492-1021

Advertisers Index

This advertiser index is published as a convenience and not as part of the advertising contract. Every care will be taken to index correctly. No allowance will be made for errors due to spelling, incorrect page number or failure to insert.

Diagnostic **Quiz**

A Hairy Eyeball

By Andrew S. Gurwood, OD

History

A 39-year-old black male presented to the emergency department complaining of worsening blurred vision in both eyes over seven days. He also noted weight loss, palpitations and night sweats. A cursory work-up uncovered pancytopenia (deficiency of red blood cells, white blood cells and platelets) and splenomegaly. The patient was referred to ophthalmology to investigate the ocular issues.

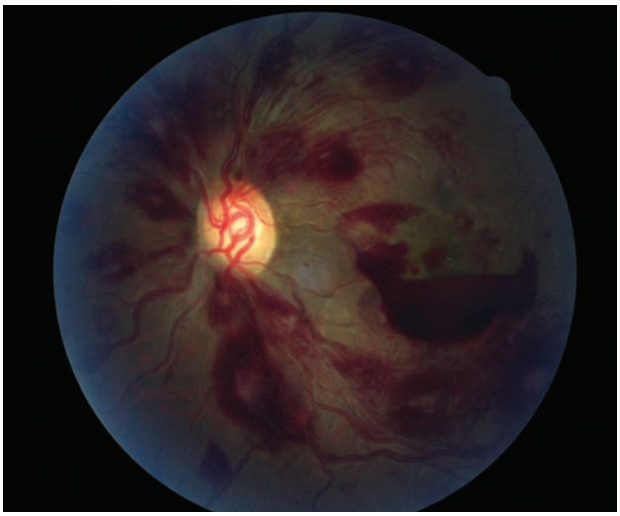
Upon initial presentation, his entering visual acuity without correction was 20/200 OD with no improvement upon pinhole testing and counting fingers at 10 feet with pinhole improvement to 20/200 OS. A 15% red cap color desaturation was present in the right eye. His pupils were round, equal, reactive and no relative afferent pupillary defect was observed. His confrontation fields were blurry but full-to-finger-counting, and extraocular muscle movements were full and smooth over both eyes.

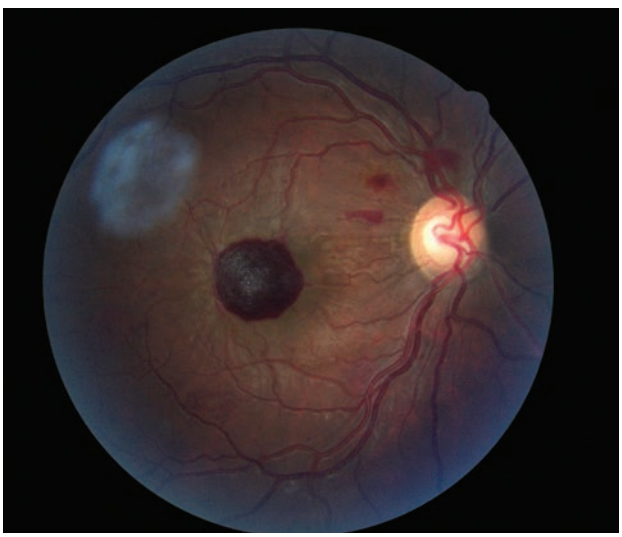
Diagnostic Data

A biomicroscopic anterior segment examination found normal structures with deep anterior chambers, no evidence of inflammation, open angles and intraocular pressures measuring 8mm Hg OD and 10mm Hg OS using Goldmann applanation tonometry. The pertinent findings are demonstrated in the photographs.

Your Diagnosis

Does the case presented require any additional tests, history or information? What steps would you take to manage this patient? Based on the information provided, what do you believe would be the patient's diagnosis? What is the patient's most likely prognosis? To find out, please visit us online at www.reviewofoptometry.com. ■





This 39-year-old patient went to the emergency room after experiencing blurred vision over the course of a week. Can these fundus images help identify his underlying condition?

REVIEW OF OPTOMETRY (ISSN 0147-7633) IS PUBLISHED MONTHLY, 12 TIMES A YEAR BY JOBSON MEDICAL INFORMATION LLC, 395 HUDSON STREET, 3RD FLOOR, NEW YORK, NY 10014. PERIODICALS POSTAGE PAID AT NEW YORK, NY AND ADDITIONAL MAILING OFFICES. POSTMASTER: SEND ADDRESS CHANGES TO REVIEW OF OPTOMETRY, PO BOX 81, CONGERS, NY 10920-0081. SUBSCRIPTION PRICES: US: ONE YEAR $56; TWO YEARS $97, CANADA: ONE YEAR $88, TWO YEARS $160, INT'L: ONE YEAR $209, TWO YEARS $299. FOR SUBSCRIPTION INFORMATION CALL TOLL-FREE (877) 529-1746 (USA); OUTSIDE USA, CALL (845) 267-3065. OR EMAIL US AT REVOPTOMETRY@CAMBEYWEST.COM. PUBLICATIONS MAIL AGREEMENT NO: 40612608. CANADA RETURNS TO BE SENT TO BLEUCHIP INTERNATIONAL, P.O. BOX 25542, LONDON, ON N6C 6B2.

TAKE A CLOSER LOOK

at the lens with a smart combination of performance and value

	Biotrue® ONEday	1-DAY ACUVUE MOIST	DAILIES AquaComfort Plus
Moisture content	78%	58%	69%
Oxygen level*	42 Dk/t	25 Dk/t	26 Dk/t
Spherical aberration control†	✓		
UVA/UVB protection‡	✓	✓	

Give your patients a **$200 REBATE**§ on the lens with the most moisture.[1]

‡WARNING: UV-absorbing contact lenses are NOT substitutes for protective UV-absorbing eyewear, such as UV-absorbing goggles or sunglasses, because they do not completely cover the eye and surrounding area. The effectiveness of wearing UV-absorbing contact lenses in preventing or reducing the incidence of ocular disorders associated with exposure to UV light has not been established at this time. You should continue to use UV-absorbing eyewear as directed. NOTE: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-blocking contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-blocking contact lenses reduces the risk of developing cataracts or other eye disorders.

*Oxygen levels for single vision spherical (SVS) lenses only.
†In SVS and toric lenses only.
§Terms and conditions apply. See www.bauschrewards.com for full terms and conditions.

REFERENCE: 1. Data on file. Bausch & Lomb Incorporated. Rochester, NY.

BAUSCH+LOMB
See better. Live better.

No other daily disposable toric contact lens gives you more parameters.

DAILIES® AquaComfort Plus® Toric contact lenses now offer 75% more parameters.*

Meet more of your astigmatic patients' needs with an expanded range of parameters, including new **-2.25D Cylinder, Around the Clock Axes in Core Parameters** and **Expanded High-Minus Sphere Powers.** All the more reason to recommend contact lenses that deliver **Dual Stability:**

- **Blink-Activated Moisture technology** for exceptional tear film stability[3,4]
- **Precision Curve® Lens Design** for on-eye stability and excellent visual acuity[5]

Fit your astigmatic patients in DAILIES® AquaComfort Plus® Toric contact lenses today.

*Compared to original DAILIES® AquaComfort Plus® Toric parameter offering of 1,350.

References: 1. Tyler's Quarterly soft contact lens parameter guide. 2018;36(1):1-64. **2.** Alcon data on file, 2019. **3.** Wolffsohn JS, Hunt OA, Chowdhury A. Objective clinical performance of 'comfort-enhanced' daily disposable soft contact lenses. *Contact Lens & Anterior Eye.* 2010;33(2):88-92. **4.** Laboratory study release profile; Alcon data on file, 2007. **5.** Alcon data on file, 2012.

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

Alcon A Novartis Division