REVIEW® OF OPTOMETRY

November 15, 2017

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THE RED EYE

Ocular surface anomalies and how to treat them.

Because I know their eyes are prone to discomfort, I prescribe the 1-DAY ACUVUE® MOIST Family.

§ 88% of all BLINK STABILIZED® Design contact lenses were fitted in the first attempt, and 99.5% within 2 trial fittings.

** Based on *in vitro* data. Clinical studies have not been done directly linking differences in lysozyme profile with specific clinical benefits.

* UV-blocking percentages are based on an average across the wavelength spectrum.

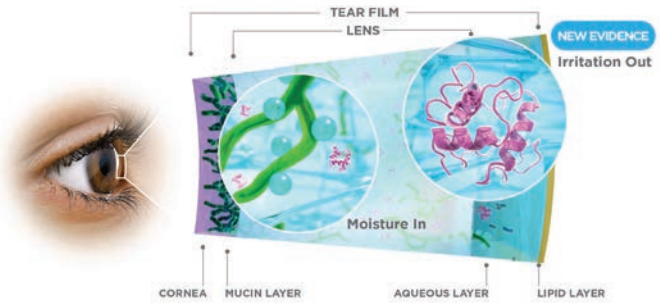
† Helps protect against transmission of harmful UV radiation to the cornea and into the eye.

‡ **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. 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. Consult your eye care practitioner for more information.

EYE-INSPIRED™ Design

Dual Action Technology helps keep moisture in and irritation out

1-DAY ACUVUE® MOIST Brand Contact Lens Family



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- **New evidence**—Etafilcon A uniquely attracts and retains more lysozyme in its natural state[1], which, along with an INFINITY EDGE™ Design and a low modulus, helps to keep irritation out. **

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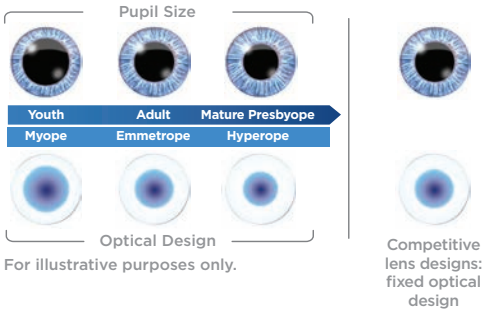

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ACUVUE® Brand Contact Lenses are indicated for vision correction. As with any contact lens, eye problems, including corneal ulcers, can develop. Some wearers may experience mild irritation, itching or discomfort. Lenses should not be prescribed if patients have any eye infection, or experience eye discomfort, excessive tearing, vision changes, redness or other eye problems. Consult the package insert for complete information. Complete information is also available by visiting acuvueprofessional.com, or by calling Johnson & Johnson Vision Care, Inc. at 1-800-843-2020.

Reference: 1. Suwala M, Glasier MA, Subbaraman LN, et al. Quantity and conformation of lysozyme deposited on conventional and silicone hydrogel contact lens materials using an in vitro model. *Eye Contact Lens.* 2007;33(3):138-143.

VOL. 154 NO. 11 ■ NOVEMBER 15, 2017

IN THE NEWS

After analyzing medical records of 365 patients with **posterior vitreous detachment (PVD) symptoms**, Swedish researchers found **those who sought care on the first day of their symptoms had a statistically significant higher risk of retinal tears**. Those with only floaters and long duration of symptoms were lower-risk patients, the investigators said, emphasizing the importance of prompt referral for those with sudden onset of symptoms.

Bond-Taylor M, Jakobsson G, Zetterberg M. Posterior vitreous detachment - prevalence of and risk factors for retinal tears. Clin Ophthalmol. 2017;2017(11):1689-95.

Studying a child's **central inner retinal function may be a future predictive measure for myopia**, according to a new study. Investigators measured cycloplegic refraction and axial length and took a global flash multifocal electroretinogram at baseline for 56 emmetropic children ages six to nine. The 43 children with myopic changes on follow up also had reduced response in the central inner retina. Because this reduced response preceded the myopia, the researchers speculate this might be an inducement to myopia, not a secondary effect.

Li SZ, Yu WY, Choi KY, et al. Subclinical decrease in central inner retinal activity is associated with myopia development in children. Invest Ophthalmol Vis Sci. 2017;58(10):4399-4406.

New research found **epithelium-off 15mW accelerated crosslinking pulsed-light therapy stabilized progression and improved vision in patients with stage two keratoconus**. The researchers suggest this treatment modality reduces treatment time, increases patient comfort and reduces post-op glare, subepithelial nerve plexus damage and postoperative haze.

Mazzotta C, Baiocchi S, Bagaglia SA, et al. Accelerated 15 mW pulsed-light crosslinking to treat progressive keratoconus: Two-year clinical results. J Cataract Refract Surg. 2017;43(8):1081-8.

California Relaxes OD Regulations

New legislation significantly widens scope of practice.

By Bill Kekevian, Senior Editor

Years of efforts by optometric advocates have paid off in California as Governor Jerry Brown recently signed a bill expanding optometry's scope of practice. The bill permits California ODs with proper certification to use therapeutic pharmaceutical agents (TPA) in a number of new ways, including expansions on treating pain, hypotrichosis, glaucoma and blepharitis. The bill also permits optometrists to use noninvasive medical devices and technologies FDA indicated for conditions optometrists already treat; they can even employ some invasive procedures that require needles.

Bill Highlights

Specifically, the legislation focuses on TPA use in cases of blepharitis and hypotrichosis and prescribing Tramadol for up to three days. It also clarifies that certified ODs are permitted to prescribe currently allowable drugs "off-label."

It opens up new diagnostic avenues for certified ODs, such as the ability to use intravenous injection for angiography, collect blood by skin puncture to test for diabetes, perform skin tests to diagnose ocular allergies and administer flu, shingles and pneumonia vaccines. Finally, ODs can now use a needle to remove foreign bodies and treat steroid-induced glaucoma.

Past Efforts

"California optometrists worked diligently over five years to advocate for scope of practice changes that strengthen our profession and our ability to care for Californians' eyes," said Sage Hider, OD, president of the California Optometric Association.[1]

Similar legislation proposed in the past faced adversity. A 2013 bill would have expanded the role of optometrists to diagnose and treat common systemic diseases, including diabetes, hypertension and hypercholesterolemia. It would have also authorized TPA use and removed limitations on the types of diagnostic tests ODs could order. By 2014 the bill merely authorized ODs to give limited immunizations before ultimately being pulled altogether.

Better Future

With this bill's passage, California ODs can finally expand their scope of practice and better serve their patients.

"This important legislation is a step forward for the optometric profession, empowering doctors of optometry to more fully utilize our extensive training, education and experience to help expand eye and health care access," Dr. Hider said.[1]

1. California Optometric Association. COA champions bill to expand optometric practice in California. October 9, 2017.

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Eye Dominance May Impact Dyslexia

Dyslexia, a significant problem for 5% to 17% of school-aged children, may have an ocular biomarker, according to new research.[1] A recent study suggests the blue cone-free area at the center of the fovea is different in eyes of patients with dyslexia compared with eyes of those without the condition.[2]

Investigators in France studied 30 control patients without dyslexia and 30 subjects with dyslexia. While the controls all had asymmetrical blue cone-free areas—leading to the normal dominant/non-dominant relationship between the eyes—the same was not true for the 30 patients with dyslexia. Each of the 30 patients with dyslexia had symmetrical blue cone-free areas, causing an undetermined eye dominance.[2]

Without a dominant eye, the researchers speculate the patient's brain is confused by the two different images, causing the characteristic blurring and distortion described by many dyslexic patients.[2]

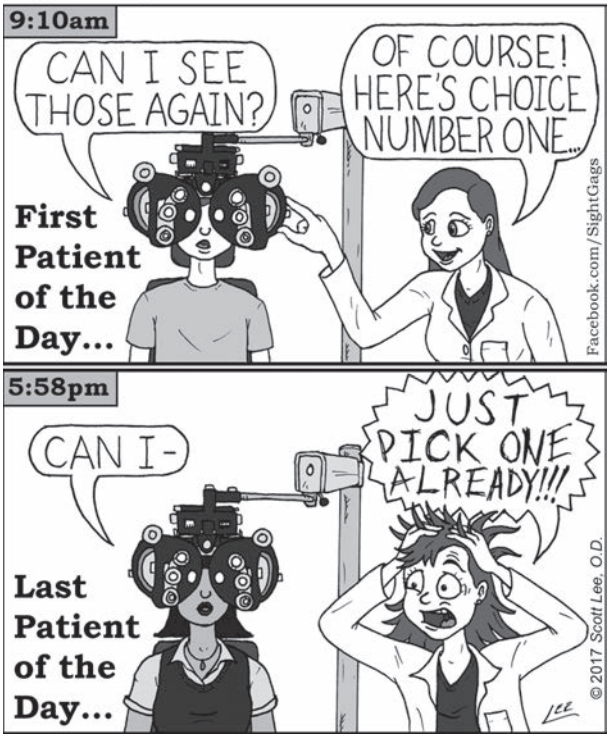
While the study authors believe these findings suggest eye dominance as a possible cause for dyslexia, research has a long way to go before its true relationship to the diagnosis is understood.

"I'd say the findings may represent a comorbidity, as opposed to cause and effect," says Bill Potter, OD, chief of Optometry and Contact Lens Services at Millennium Eye Care in West Freehold, NJ. Generally, "the brain is really good at suppressing the eye that is generating an aberrant image." Thus, according to Dr. Potter, the research raises more questions than it answers, such as, "Does dyslexia in a one-eyed patient, or a 20/200 amblyope, differ from that of the binocular patient? Cause vs. comorbidity remains the question."

More research is necessary to test this new theory—and work through all of the questions it raises, including possible treatment options.

1. Habib M, Giraud K. Dyslexia. Handb Clin Neurol. 2013;111:229-35.
2. Le Floch A, Ropars G. Left–right asymmetry of the Maxwell spot centroids in adults without and with dyslexia. Proceedings of the Royal Society B. October 18, 2017. rspb.royalsocietypublishing.org/content/284/1865/20171380. Accessed October 20, 2017.

Sight Gags By Scott Lee, OD



Drug Patents Under Fire

Allergan continues the battle to protect its control of the patents for its dry eye drug Restasis, this time in the Eastern District of Texas, where a federal judge recently invalidated four key patents.[1]

In September, the company transferred the patents to the Saint Regis Mohawk Tribe in upstate New York in response to a patent challenge filed in an administrative proceeding with the United States Patent and Trademark Office. By paying the tribe to take possession of the patents and then leasing them back, the company hopes to capitalize on the tribe's sovereign immunity to shield the patents from the challenge—a move met by criticism from Congress and consumer groups.[1]

Although the court case and the administrative patent challenge are separate proceedings, the Texas judge had harsh words for the company's move to avoid repercussions of the patent challenge: "Sovereign immunity should not be treated as a monetizable commodity that can be purchased by private entities as part of a scheme to evade their legal responsibilities," he wrote.[1]

The patent transfers have no bearing on the legal battle in Texas, where manufacturers continue to fight over the validity of the patents.[1] If the ruling stands, the

patents will be invalidated, regardless of the deal with the Mohawk Tribe.[2]

This recent push for a generic dry eye treatment option may not necessarily be in the patients' best interest, however. Cost has always been a barrier to proper prescribing, according to Marc Bloomenstein, OD, director of optometric services at Schwartz Laser Eye Center in Scottsdale, Ariz., and "the notion that a generic is more cost-effective will definitely make clinicians more inclined to reach for a pen and Rx pad. However, the perceived cost benefit will come at the price of choice." That choice, Dr. Bloomenstein says, is between a branded drug with "the best combination of molecule, strength and vehicle to maximize efficacy while minimizing side effects" and a generic drug with the same molecule but a different concentration and vehicle that lacks human testing to prove its efficacy.

"Optometry's interest is centered around providing our patients with safe and efficacious medications to treat their conditions," he says. "With this challenging disease, I worry that a generic market, without proper testing in humans, will dilute results and cause huge frustrations for doctors and patients."

Those wary of a generic option can rest assured it's far in the future still. Not only does Allergan plan to appeal the decision, but the Food and Drug Administration has yet to approve generic equivalents of Restasis, according to a press release.[1]

1. Thomas K. Patents for Restasis are invalidated, opening door to generics. New York Times. October 16, 2017. www.nytimes.com/2017/10/16/health/allergan-restasis-patent-.html. Accessed October 17, 2017.
2. Thomas K. How to protect a drug patent? Give it to a Native American tribe. New York Times. September 8, 2017. www.nytimes.com/2017/09/08/health/allergan-patent-tribe.html. Accessed October 17, 2017.

Potential DR Therapy

Scientists have identified a possible target for reducing dysfunctional blood vessel growth in diabetic retinopathy (DR). The researchers suspect a receptor stimulates glycolysis, which promotes pathological angiogenesis in retinopathies.[1,2]

"If we block the adenosine receptor A2a, the blood vessels will not leak, and not as many new blood vessels will grow," said Yuqing Huo, MD, PhD, chief of the Vascular Inflammation Program at the Vascular Biology Center at the Medical College of Georgia at Augusta University.[1]

Adenosine receptor A2a is found on the endothelial cells that line blood vessels. When oxygen levels are good, adenosine A2a receptor expression is low. But in diabetes, where oxygen levels go down, their expression increases.[1] The increased expression "means repairing existing blood vessels and growing new ones in a process called angiogenesis," said Dr. Huo. But when "cells don't use energy efficiently or build blood vessels well, it's actually called 'pathological angiogenesis.'"[1] With DR, the blood vessels "grow too much, too fast," says Dr. Huo, leading to bleeding or contraction, and then to hemorrhage, retinal detachment and blindness.[1]

The researchers hypothesize that adenosine, via the A2a receptor, helps endothelial cells in the diabetic eye use glycolysis.[2] The research shows that blocking glycolysis dramatically inhibits blood vessel proliferation and sprouting of endothelial cells that overexpress the receptor.[1,2] When oxygen levels were more normal, deleting adenosine receptor A2a didn't have that much impact on glycolysis, possibly because the receptor's expression is not that high when oxygen levels are normal, the scientists suspect.[1,2]

Luckily, an adenosine receptor A2a inhibitor is already in clinical trials for Parkinson's disease, paving the way for more studies.[1]

This is another fascinating scientific endeavor, says Mohammad Rafieetary, OD, of Charles Retina Institute in Germantown, Tenn. "Ultimately, diabetic retinopathy's complications, which include vision loss, are primarily the result of hypoxia or ischemia." Anything that can lessen this hypoxia-induced demise can help limit the degree and extent of the disease, which ends with loss of vision. "I am hopeful to see advancements in the basic science such as these translate into clinical applications." ■

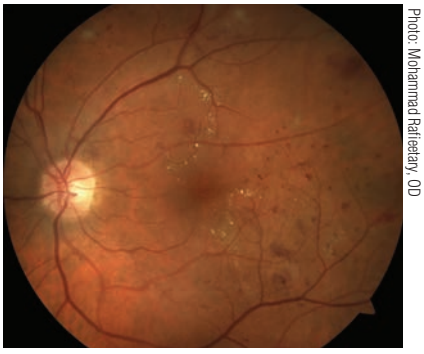


Photo: Mohammad Rafieetary, OD

Patients with diabetic retinopathy may one day have a new therapy option.

1. Baker T. Likely new treatment target identified for diabetic retinopathy. Jagwire News. October 2017. jagwire.augusta.edu/archives/48024. Accessed October 25, 2017.
2. Liu Z, Yan S, Wang J, et al. Endothelial adenosine A2a receptor-mediated glycolysis is essential for pathological retinal angiogenesis. Nature Comm. 2017;8(1):584.

Correction

On page 70 of the October 15, 2017 print edition, the ocular motility grading standards mentioned in "My Five Favorite Binocular Evaulation Tests" were incorrectly identified. They are from Northeastern State University College of Optometry.

REVIEW® OF OPTOMETRY

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HELP PUT RELIEF IN YOUR CORNER

INDICATIONS AND USAGE

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

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

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

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

IMPORTANT SAFETY INFORMATION

- ZYLET® is contraindicated in most viral diseases of the cornea and conjunctiva, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infections of the eye and fungal diseases of ocular structures.

IMPORTANT SAFETY INFORMATION (continued)

- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, and defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as a slit lamp biomicroscopy and, where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
- Employment of corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and exacerbate the severity of many viral infections of the eye (including herpes simplex).
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term, local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.
- Most common adverse reactions reported in patients were injection and superficial punctate keratitis, increased intraocular pressure, and burning and stinging upon instillation.

Please see Brief Summary of full Prescribing Information for ZYLET® on adjacent page.

BAUSCH+LOMB

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

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

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

Initial U.S. Approval: 2004

DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

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

2.2 Prescription Guideline

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

CONTRAINDICATIONS

4.1 Nonbacterial Etiology

Zylet, as with other steroid anti-infective ophthalmic combination drugs, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

WARNINGS AND PRECAUTIONS

5.1 Intraocular Pressure (IOP) Increase

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

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

5.2 Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

5.3 Delayed Healing

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

5.4 Bacterial Infections

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

5.5 Viral Infections

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

5.6 Fungal Infections

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

5.7 Aminoglycoside Hypersensitivity

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

ADVERSE REACTIONS

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

Zylet:

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

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

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

Loteprednol etabonate ophthalmic suspension 0.2% - 0.5%:

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

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

Tobramycin ophthalmic solution 0.3%:

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

Secondary Infection:

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

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

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

USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

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

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

8.3 Nursing Mothers

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

8.4 Pediatric Use

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

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

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

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

8.5 Geriatric Use

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

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

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

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

PATIENT COUNSELING INFORMATION

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

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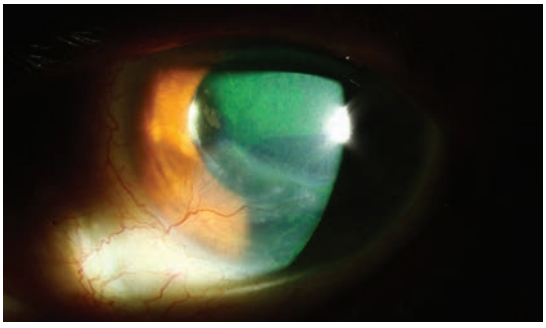
Based on 9007706-9004406 Revised 08/2016 ZYL.0053.USA.16

Contents

Review of Optometry November 15, 2017



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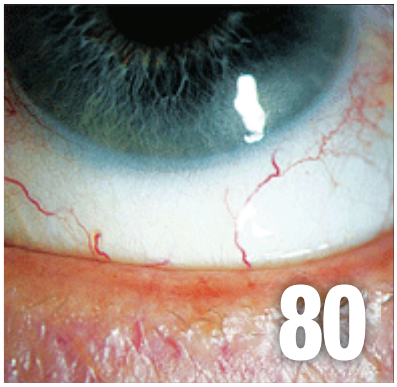
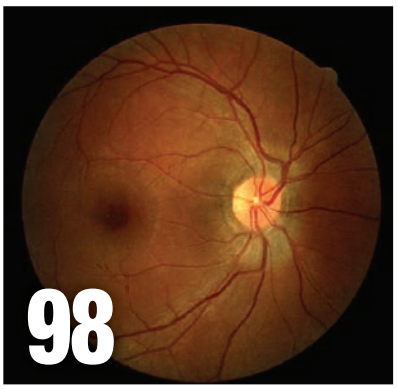
Review of Optometry November 15, 2017





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REVIEW OF OPTOMETRY

PRINTED IN USA

FOUNDING EDITOR, FREDERICK BOGER
1891-1913

EDITORIAL OFFICES
11 CAMPUS BLVD., SUITE 100
NEWTOWN SQUARE, PA 19073
WEBSITE • WWW.REVIEWOFOPTOMETRY.COM

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Outlook

By Jack Persico, Editor-in-Chief

Sugar Rush

November is Diabetic Eye Disease Awareness Month. So put away that leftover Halloween candy already!

Optometrists are often prodded—by people like me, on pages like this—to do more. See more patients, add new services, learn new things, sell more products, hire more people, buy more stuff. It must be wearying. So I thought I'd start by complimenting you, for something you've *already* done. According to the AOA, in 2016 optometrists diagnosed 320,000 new cases of diabetic eye disease in patients who otherwise didn't know they had diabetes. That's impressive unto itself (an average of eight new diagnoses per OD per year), but consider that, just two years prior, the number was 240,000. In a two-year span, the optometric community increased its diagnoses of diabetes by 33%. That achievement may have flown under the radar, especially on editorial pages that always nag, nag, nag. So, congratulations!

"Expanded scope of practice for doctors of optometry has produced historic gains in quality care, delivered superior outcomes, improved the lives of patients and established a primary care success story," says AOA president Christopher Quinn, OD. "It's not at all surprising that many people learn of their diabetes risk through a dilated, comprehensive eye examination from their doctor of optometry." And it "reinforces the importance of regular, in-person eye care," he adds.

But, if I may, there's still room for improvement. Because the state of diabetes awareness and attention is still dire. The AOA's 2016 Eye-Q survey of public knowledge of eye diseases found that only 41% of Americans know diabetes can be detected in an eye exam, even though 72% know that there's a connection between diabetes and blindness.

Consider that discrepancy a mandate for eye doctors to speak out about diabetes often and unabashedly. I know some doctors feel ill at ease talking with patients about weight, diet and other lifestyle choices that might seem to be beyond the purview of optometric practice. But they aren't. Too many people are at risk to be modest about it.

Whether you're just starting out or already established, diabetes is going to be a dominant part of your practice for, well, ever. Prevent Blindness America (PBA) says eight million people have diabetic eye disease right now, and that number will grow to 11 million over the next 15 years. PBA projects the Hispanic population will see the most growth, with cases nearly doubling by 2050. If these patients present a language or cultural barrier to non-Hispanic ODs, try to find other ways to reach them, such as Spanish-language educational videos and handouts, or a public health resource in your community that serves this audience.

It's for these reasons that PBA has declared November to be Diabetic Eye Disease Awareness Month. The AOA is doing its part to help by offering educational materials for ODs and their patients. A good place to start is www.aoa.org/news/clinical-eye-care/diabetes-month-17.

Optometrists have already done a great job of getting vulnerable diabetes patients diagnosed and treated. Keep up the good work! ■

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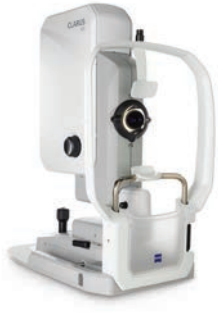

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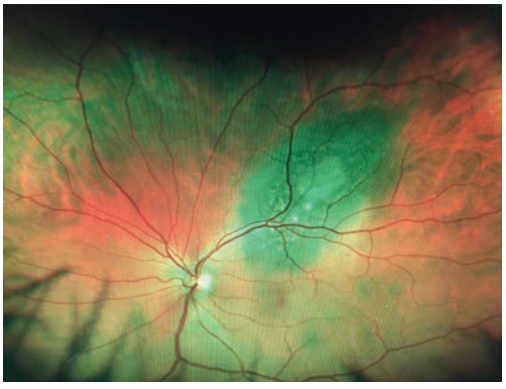
By Paul M. Karpecki, OD, Chief Clinical Editor

Red Eyes Mean Optometry

Patients still head to their primary care provider for this when they should be giving their OD a call. What we find could be far more troubling.

A patient who schedules an appointment for a red eye could walk through the door with any number of ocular issues. This month's feature articles hit the highlights: allergy, infection, dry eye, scleritis and episcleritis, to name only a few. But some patients still call their primary care provider for a red eye, especially if the patient is a child. Many parents aren't aware of where to take their children when they have 'pink eye.'



Although this patient had no complaints, his optometrists found a large retinal lesion during the dilated exam, later diagnosed as malignant choroidal melanoma.

We must continue to educate patients—starting with each parent or patient who enters our offices—on our services beyond the basic refraction that once defined us. We have to directly or indirectly convey to our patients that we manage anything related to the eyes, including "red eyes" and children. In addition to managing garden-variety conjunctivitis most effectively, we can also ensure that it is not an iritis, preceptal cellulitis, episcleritis, keratitis or some other potential differential diagnosis that could be more painful and problematic.

Optometrists also know to look for systemic findings in patients who present with conjunctivitis. The most common causes of bacterial conjunctivitis in children, for example, include *Haemophilus influenza* and *Streptococcus pneumonia*. Unlike adult conjunctivitis, which is most commonly caused by *Staphylococcus*, the pathogens in childhood conjunctivitis cause a significant number of systemic issues, including otitis, preceptal cellulitis and, in rare cases, encephalitis.

The first step when examining a child with conjunctivitis is checking their temperature and questioning the parents regarding systemic findings. A fever, ear infection, malaise or upper respiratory infection warrants systemic treatment, and only then would a referral to the pediatrician be best. The presence of a reddish sheen around the eyes indicates preceptal cellulitis and requires oral antibiotics in addition to topical treatment—something optometrists can handle.

Beyond the Ocular Surface

Now is a critical time for optometry to educate the masses. It is always in our interest to educate about the technology we use and the conditions we can treat, including everything from a common conjunctivitis to the most critical and rare findings. It may be 'pink eye' or another basic issue that brings them in; once they're in the chair, however, we can truly play a life-changing role.

Take a recent 50-year-old patient. He presented to a local optometrist simply because of symptoms related to presbyopia. He measured 20/20+ OD and OS. Because it was his first exam with an optometrist, he was dilated and received a comprehensive exam. The OD captured the image provided here, and immediately referred him to our retina specialty practice for further evaluation. Fundus exam revealed a large lesion, OCT imaging confirmed the presence of serous fluid, autofluorescence confirmed lipofuscin over the lesion and ultrasound confirmed a diameter of more than 3mm. All of this led to a confirmed diagnosis of a malignant choroidal melanoma.

Though he was referred to our specialty practice, every one of these tests could have been conducted by the primary eye care provider. OCTs are commonplace in optometry, as are ultra-widefield imagers and dilated fundus exams. Even B-scan ultrasounds are now inexpensive and have great image resolution.

This is just one more example of why it is so important to educate our patients about our knowledge, training and capabilities. Without optometric intervention, this melanoma would surely have resulted in devastating consequences. ■

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It's All About the Benjamins

Let's discuss the most important word in all of medicine—and it's not "patient," unfortunately. **By Montgomery Vickers, OD**

Right or wrong, for better or for worse, the most important word in medicine is "money." That's right! I said it!

As the great economist Cyndi Lauper so beautifully explained it, "Money Changes Everything." The Notorious B.I.G. expanded upon the thesis by wisely reminding us, "Mo Money, Mo Problems." I could go on, because "Money Makes the World Go Round" (Thanks, Liza Minnelli and Joel Grey).

After all, we have to make money or we go out of business; if we go out of business, we cannot help our patients. Why do they not understand that?

What should you do to make sure your doors stay open? Many sage business consultants can offer to you, for a hefty fee (so they can stay in business) some very effective advice. Or you could listen to Cyndi and Biggie. I would urge you to get good advice before you are in trouble, for sure. Here's what I do when worried about money:

1. Buy something. There's nothing like the rush when the checkout clerk says you just saved $30.

2. Check the change in your car's console. The other day, I found enough for a hot dog.

3. Go out to dinner with your grown children. When the waiter brings the check, head to the bathroom until the bill is settled. They owe you.

4. Count the golf shirts in your closet. So that's where all that money went!

5. Make a donation. You will always be rewarded for giving, especially if it's your state's optometry PAC or DVVF—Dr. Vickers's Vacation Fund is also not tax deductible, so what's the difference?

6. Reach out to an old friend and remind him about that lunch money you gave him in third grade. Explain compounding interest.

7. Ask your closest colleague/competitor to check your eyes. You can steal their best ideas and get smug satisfaction they didn't make any money while with you.

8. Carry a roll of quarters at all times so you can physically tell that you have money.

9. Buy a new piece of equipment that will benefit your patients and add potential income to your office. A gumball machine, perhaps?

10. Practice mindfulness, so when you are stressed and broke, you can be completely stressed and broke right where you are.

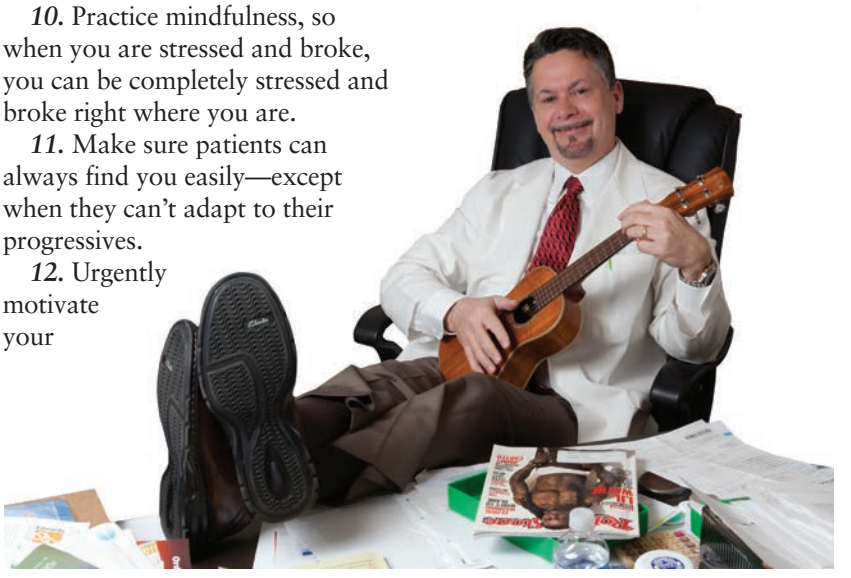
11. Make sure patients can always find you easily—except when they can't adapt to their progressives.

12. Urgently motivate your patients to refer friends, coworkers and family members. I find that promising not to key their car if they refer seems to work.

13. Accept any and all insurances and vision plans as long as they require policyholders to pay for everything out of pocket. This gives you more time to binge read my column.

14. Square your shoulders and stand up straight. Look that waiter right in the eye and ask if they have a senior citizen discount. If not, order a kid's meal.

I truly hope this helps. Lucky for me, when I was a kid, my mom told me: "Don't marry for money. Just hang around rich people until you fall in love with one of them." I was married three years before I realized Renee's dad was a coal miner, not a gold miner. Darn. ■



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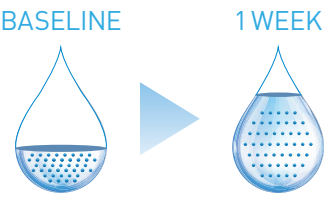

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AKORN | CONSUMER HEALTH

Red Alert

A routine conjunctivitis case could portend serious systemic illness.

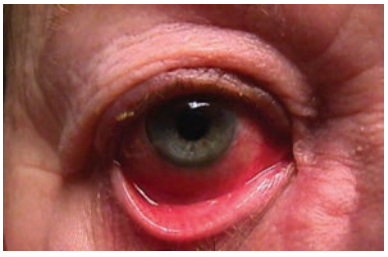
Edited by Paul C. Ajamian, OD

Q A 45-year-old female in good health presents with subepithelial infiltrates and a red eye. It looks like simple epidemic keratoconjunctivitis. However, the patient is lethargic with labored breathing. Do I just assume that her eye infection is causing her to feel bad?

A "When this patient presented to me, I suspected something else was going on," says Carlton Edwards, OD, in private practice in Douglasville, GA. Both eyes had been red for only three days, yet there were corneal infiltrates noted in both eyes, says Dr. Edwards. "It didn't add up, so I made an immediate referral to her internist, which led to hospital admission."

An obvious ocular condition in conjunction with non-specific systemic complaints should catch your attention, as a potentially life-threatening condition could be at work, says Joseph Shovlin, OD, a practitioner at Northeastern Eye Institute in Scranton, PA, and president of the American Academy of Optometry. "Always gauge the general health of your patient and respond to any symptoms that appear sinister or unexpected," says Dr. Shovlin. Although patients are often very uncomfortable with adenovirus infection, severe malaise or a feeling that they are very ill are out of the norm, Dr. Shovlin explains. "If these symptoms occur, it's imperative that clinicians evaluate the patient for additional systemic ailments."

Corneal signs, including infiltrates, can certainly be a manifestation of an underlying systemic disease, such as the nummular infiltrates found in Lyme disease and numerous corneal findings of the herpes family of infections, says Dr. Shovlin. He says to monitor patients for any unusual symptoms and follow closely when indicated. "As my mentor once said, 'When all else fails, re-examine,'" says Dr. Shovlin.



An ill eye, along with non-specific systemic complaints, could signal a serious systemic condition is afoot.

Back to Square One

To unravel the mystery of your patient's illness, Dr. Shovlin says to start by asking them for all the facts. "A detailed history is always a great place to start," says Dr. Shovlin. Ask about timing, onset and the exact symptoms, he says, as well as severity and frequency.

Investigate the Infiltrate

Next, see what the corneal disruption might suggest. Infiltrates—aggregates of white blood cells—have multiple causes, says Dr. Shovlin. He explains that the number, location and level of corneal involvement may provide some clues as to the etiology. "The central cornea and the periphery have key anatomical and physiological differences, and mitotic rates and corneal nerve density differ greatly," he explains. A careful history, along with patient symptoms and a detailed examination of the cornea and adnexa, are essential in differentiating a sterile from an infectious process.

"Remember that, histologically, all infections have infiltration with, or occasionally without, overlying defects or frank ulceration," he says. "In this case, the patient presents with diffuse subepithelial infiltrates that may signal a viral cause. Generally, infiltrates in adenovirus disease present the second week and, if vision is affected significantly, topical steroid drops such as loteprednol etabonate are indicated."

It just so happens that in this case, the viral cause wasn't located in the eye. Rather, it was located in the heart. Dr. Edwards spoke to the patient's internist a week later, and "the workup confirmed a systemic viral infection, which led to premature ventricular contractions. The cardiomyopathy that ensued could have taken the patient's life if it had been ignored," says Dr. Edwards.

As medical professionals, optometrists are responsible for the health of their patients in every area, across organ systems. The ocular system is often a window into the rest of the body. When practitioners remain vigilant and suspicious, they have the best opportunity to save the life of their patients. ■

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Steer Clear of the Coding Rut

Every patient's office visit is different and, often, so is the coding.

By John Rumpakis, OD, MBA, Clinical Coding Editor

As we fine-tune our practices, we often focus so intently on coding new technologies that we forget our practice's foundation: the office visit. Many ODs get into the habit of coding the same type of visits, which can leave money on the table by undercoding or create undue exposure by overcoding.

Eye exams can be coded at least 16 ways in an optometric practice. The 16 codes are comprised of four ophthalmic visit codes (920XX), 10 E/M codes (992XX) and two HCPCS "S" codes (S062X). Because S codes are not used for the medical management of a patient, we will eliminate them from consideration.

920XX

Ophthalmic office visits are either comprehensive or intermediate for both new and established patients. Remember, a new patient is one who has not received professional services from a physician of the exact same specialty and subspecialty in the same group practice in three years.

92002. Ophthalmological services: Medical examination and evaluation with initiation of diagnostic treatment program; intermediate, new patient.

92004. Ophthalmological services: Medical examination and evaluation with initiation of diagnostic treatment program; comprehensive, new patient, one or more visits.

92012. Ophthalmological services: Medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; intermediate, established patient.

92014. Ophthalmological services: Medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; comprehensive, established patient, one or more visits.

Comprehensive eye examination codes (92004, 92014). These describe a general evaluation of the complete visual system. According to the CPT definition, it "includes history, general medical observation, external and ophthalmoscopic examinations, gross visual fields and basic sensorimotor examination. It often includes, as indicated: biomicroscopy, examination with cycloplegia or mydriasis and tonometry. It always includes initiation of diagnostic and treatment programs."

Gross visual fields and a basic sensorimotor exam are also required for a comprehensive eye exam, while dilation is not; however, as part of the definition of each code, dilation is not a separately billable procedure should you choose to perform it.

Intermediate codes (92002, 92012). These are defined as: "an evaluation of a new or existing condition complicated with a new diagnostic or management problem not necessarily relating to the primary diagnosis, including history, general medical observation, external ocular and adnexal examination and other diagnostic procedures as indicated; may include the use of mydriasis for ophthalmoscopy." Some inappropriately use these codes to reduce the exam cost to a non-insured patient.

992XX

The E/M codes are typically used for patients with a medical complaint or a continuation of medical case management. The five levels of E/M codes are universally applicable for all medical eye care encounters; however, out of the 10 codes within this subset, only six are used routinely: 99201, 99202, 99203, 99212, 99213 and 99214.

These codes have more specific requirements regarding case history, elements of exam and medical decision-making. The higher level codes for a new patient, 99204 and 99205, require a comprehensive history, for which it is difficult, but not impossible, for ODs to qualify.

One of the most common misunderstandings is scoring the history. Properly scoring the review of systems, for example, includes only the systems pertinent to the patient encounter on that specific day. Too often, clinicians count all 14 systems toward their history score, when only a few are pertinent. When scored correctly, the highest E/M code achievable would generally be 99203 for a new patient and 99214 for an established patient.

Understanding office visit codes is critical to coding the proper type and level of examination. Don't get into a rut by performing a particular type and level of exam out of habit. Instead, be cognizant of the type and level of care your patients need and strengthen your practice's foundation for the future. ■

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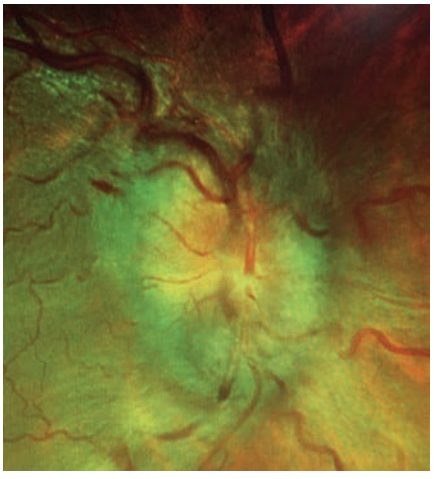
A Second Helping

Idiopathic intracranial hypertension sometimes returns. When it does, here's what to do.

By Michael DelGiodice, OD, and Michael Trottini, OD

A 24-year-old Hispanic female presented in consultation from her neurologist for intractable headache lasting three weeks, with a normal neurologic exam and blood pressure. Her history was positive for neck pain and transient "blackouts" in both eyes lasting less than 30 seconds. She was taking Avonex (interferon beta-1a, Biogen) for her MS. Her past ocular, family and social histories were unremarkable.

Her best-corrected acuities were 20/25 OU. Ocular motilities were full with no limitation. Pupil evaluation showed no afferent pupillary defect, and she was orthophoric in primary and lateral gaze in both eyes. She noted 10/10 color plates in each eye. Intraocular pressure (IOP) measured 18mm Hg OD and 16mm Hg OS. The anterior segment exam was unremarkable. Fundus exam showed bilateral blurring of the optic disc margins, peripapillary hemorrhages, absent venous pulsations and venous engorgement and tortuosity.



Two years after an IIH bout, this patient returned with grade four papilledema.

First Encounter

Because of her symptoms of transient visual obscurations, intractable headaches and neck pain, and in accordance with the findings of bilateral disc edema, we were concerned she was suffering from an intracranial process. We ordered fundus photography, spectral-domain optical coherence tomography (SD-OCT) and visual fields (VF). SD-OCT showed significant bilateral elevation of the retinal nerve fiber layer, and VF testing showed an enlargement of the physiologic blindspot and central-inferior hemifield defects OU.

Given her history and demographics, we formed a differential diagnosis of conditions that may result in elevated intracranial pressure (ICP): malignant hypertension, space-occupying mass, hemorrhage, infection, inflammation and, lastly, idiopathic intracranial hypertension (IIH)—also called pseudotumor cerebri—a diagnosis of exclusion.

Consequently, she was sent to the emergency department for emergent head computed tomography (CT) to discount intracranial pathologies such as hemorrhage, infection and mass lesion; her CT scan was unremarkable. She then underwent lumbar puncture (LP), which revealed an opening pressure of 550mm H_2O and normal cerebrospinal fluid (CSF). Because a reading above 250mm H_2O with normal CSF is consistent with intracranial hypertension secondary to IIH, she was diagnosed with IIH.[1]

After the patient was discharged from the hospital, we reviewed the laboratory tests to confirm there was no contraindication to starting her on acetazolamide; her potassium was within normal range between 3.5mEq/L to 5.0 mEq/L.[2] We started her on acetazolamide 250mg twice daily and slowly titrated up to 500mg twice daily and discussed a low-sodium weight loss plan of one pound per week for 12 weeks.

The patient was monitored monthly, and over the next six months she lost 10 pounds. The headaches, disc edema and visual field testing improved dramatically. However, she was lost to follow up for the next two years.

Back for More

She recently returned with complaints of severe headache, pulsatile synchronous tinnitus and bilateral transient vision loss despite taking 250mg of acetazolamide daily and a net loss of 20 pounds since her last visit.

Ophthalmologic examination revealed recurrent, grade four papilledema. We ordered a metabolic panel to evaluate her potassium before increasing the dose of acetazolamide. The potassium level was 3.3mEq/L, which was slightly lower than the 3.5mEq/L cutoff

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value. She was instructed to follow up with her primary care physician for clearance. Once cleared, we increased her dosage to 500mg of acetazolamide twice daily.

She returned four weeks later with no improvement in symptoms. We then ordered magnetic resonance venography (MRV) due to the recurrent nature and severity of the papilledema. The MRV revealed narrow dural venous sinuses without frank stenosis or thrombosis. Given the recurrent, aggressive nature of the condition and her lack of proper follow up, we alerted her neurologist and admitted her to the hospital for electrolytes, therapeutic LP and intravenous mannitol. Neurosurgery then evaluated her for an intracranial shunt.

Pseudo Tumor, Genuine Concerns

Even optometrists who see it infrequently know that papilledema is defined as bilateral disc edema secondary to increased ICP, and identification is often straightforward. To a clinician, the bigger challenge is determining what it signifies. Its pathophysiology involves axoplasmic stasis with swelling of axons and leakage.[3] The increased pressure is transmitted along the subarachnoid space, leading to increased pressure within the optic nerve tissues and clinical disc edema. Histopathology of papilledema shows displacement of the retina away from the optic disc with serous sensory detachment within the peripapillary area.[3]

The most common general symptoms of pseudotumor cerebri include headaches in the morning that intensify with movement, projectile vomiting, neck pain, tinnitus (whooshing or ringing in the ears) and loss of consciousness. Ocular symptoms include blurred vision, transient visual obscuration, vision loss, retro-orbital pain and horizontal diplopia.[4] Optic nerve findings include elevation of the disc with hyperemia, blurring of the disc margins, superficial retinal hemorrhages, edema of the peripapillary region, loss of venous pulsations, concentric retinal or chorioretinal folds around the optic nerve and macular exudates.[4] Other findings include retinal vascular tortuosity and hemorrhages within the posterior pole and retinal periphery.[4]

Diagnostic criteria. IIH is diagnosed based on the modified Dandy criteria, which include: signs and symptoms of increased ICP, no localized neurologic findings, normal neuroimaging with the exception of an empty sella (dark appearance of the sella tursica on T1-weighted MRI from increased CSF), opening LP pressure of greater than 250mm H_2O with normal CSF and no other causes of increased ICP.[5]

Grading. During clinical examination, it is important to initially grade the severity of papilledema to monitor the effects of therapy:[6]

Grade I: C-shaped halo of nerve fiber layer edema and blurred disc margins with a temporal gap.

Grade II: progressive circumferential edema and margin obscuration with blurring of the capillaries.

Grade III: Expanded nerve fiber layer edema and obscured major blood vessels as they leave the disc.

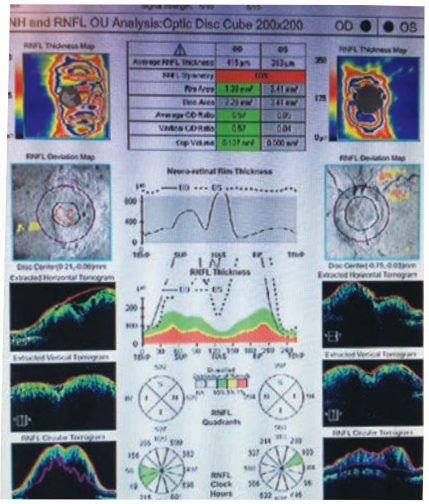
Grade IV: loss of major vessels on the disc.

Grade V: characteristics of grade IV plus partial or total obscuration of all vessels of the disc.[6]

Testing. Taking visual fields is necessary to monitor functional vision. According to research, over 90% of patients with papilledema had visual loss documented by perimetry.[7] The most common visual field deficits include enlargement of the blind spot, inferior nasal depressions and peripheral constriction.[8]

After diagnosing bilateral disc edema, it is important to check the blood pressure to discount primary malignant hypertension or secondary hypertension

from increased ICP. The next step is to send the patient to the local emergency department with the diagnosis and your recommendation for stat head CT, as well as LP—in the absence of intracranial pathology on neuroimaging—to record the opening pressure and check the CSF for pathology. CT is preferred over MRI in the emergency setting because it is readily available and quickly assesses for intracranial pathologies such as hemorrhages, space-occupying lesions, obstructive hydrocephalus and cerebral edema, all of which are neurologic emergencies.



Significant bilateral elevation of the nerve fiber layer can be seen on the patient's OCT.

In our case, we ordered MRV because the patient continued to show signs of intractable papilledema, headaches and tinnitus despite significant weight loss and long-term acetazolamide use. The MRV allowed us to discount abnormalities within the venous drainage system, identify potential additional causes for the recalcitrant nature of the condition, better establish a prognosis and determine whether surgical intervention was necessary. According to a recent study, MRV reveals bilateral narrowing of lateral sinuses in IIH, which is rarely seen in controls.[9]

OCT and fluorescein angiography (FA), in addition to recording the stage of papilledema, can be used to monitor the status of the disc during treatment. FA findings of the early phase of papilledema includes disc capillary dilation and leakage within the disc. Late findings show leakage beyond and pooling around the disc.[10] On OCT, papilledema causes a hyporeflective space above the retinal pigment epithelium within the papillary space, representing serous sensory retinal detachment.[11]

Treatment. The key goal is to decrease ICP to help preserve vision and eliminate intractable headaches. Medical therapies include acetazolamide, oral glycerol, IV mannitol and weight reduction.

Acetazolamide is the treatment of choice to manage IIH.[2] It reduces CSF production and flow from the choroid plexus. Prior to beginning therapy, a complete metabolic panel should be ordered to establish a baseline level of electrolytes and, if the results are concerning, consult with the patient's primary care physician before administering the drug.

In one study, treatment with 250mg of acetazolamide, divided into four doses, was administered and then increased by 250mg per week to a maximum dosage of 4g/d until the papilledema grade was less than one in both eyes and the mean deviation on VF testing improved to equal to or better than -1dB in each eye.[12] A low-sodium weight management plan should be implemented. Studies show as little as 6% weight loss is effective in improving signs and symptoms of ICP.[13]

During medical therapy, clinicians should measure the visual acuities, test the VFs and perform fundus photography, OCT and FA. Patients who do not show improvement in papilledema or systemic symptoms despite medical therapy and weight loss should be referred for neurosurgical consultation. Surgical treatment includes therapeutic LP, optic nerve decompression and intracranial shunting.

In IIH, medical management is necessary to preserve visual function and decrease systemic symptoms. Monthly follow up is recommended to test visual acuities, perform formal perimetry and record the grading of disc edema. In recurrent and refractory cases, consider MRV to discount venous sinus pathologies and better gauge prognosis. Patients who show narrowing of the venous system may follow a prolonged treatment course and require closer observation for surgery. ■

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NEW STUDY

EFFECTIVENESS OF ROHTO® DRY-AID™ VS. WIDELY USED ARTIFICIAL TEAR

ROHTO® DRY-AID™ Provides All-Day Dry Eye Symptom Relief

Dry Eye Disease (DED) is the most prevalent form of ocular discomfort and irritation, with estimates of affected individuals ranging from 1 in 20 to as high as 1 in every 5 adults in the United States experiencing some degree of mild to moderate dry eye[1], and is one of the leading causes of patient visits to eye care practitioners in the United States[2].

Over-the-counter artificial tears are often the first line of therapy to minimize dryness and related discomfort of patients who present with dry eye. There are few published studies that directly compare the effectiveness of different drop preparations, especially those formulated for dry eye.

*Source Euromonitor International Limited: Consumer Health Eye Care definition, retail value share, 2016 data.

ROHTO® DRY-AID™ - BREAKTHROUGH DRY EYE SYMPTOM RELIEF

According to a study recently published in the peer-reviewed journal ***Clinical Ophthalmology***[3] ROHTO® DRY-AID™, a new, breakthrough, non-blurring lubricant eye drop, was found to show superior relief of discomfort associated with visual tasking activities, and daily diaries indicate that it may provide a longer duration of symptomatic relief over the course of a day versus one of the most widely-used ocular lubricants in the United States.

ROHTO® DRY-AID™ features a unique formula that provides all-day relief from key symptoms of Dry Eye Disease. Unlike most eye drops that only work on the aqueous layer of the tear film, ROHTO® DRY-AID™ is formulated to help restore moisture to the entire tear film by working on all three layers to mimic a natural, healthy tear. It delivers immediate and long-lasting dry eye symptom relief by enhancing tear adhesion to the surface of the eye, providing uniform moisture to the aqueous layer, and slowing evaporation by replicating an even lipid layer without blur. *(see image 1)*

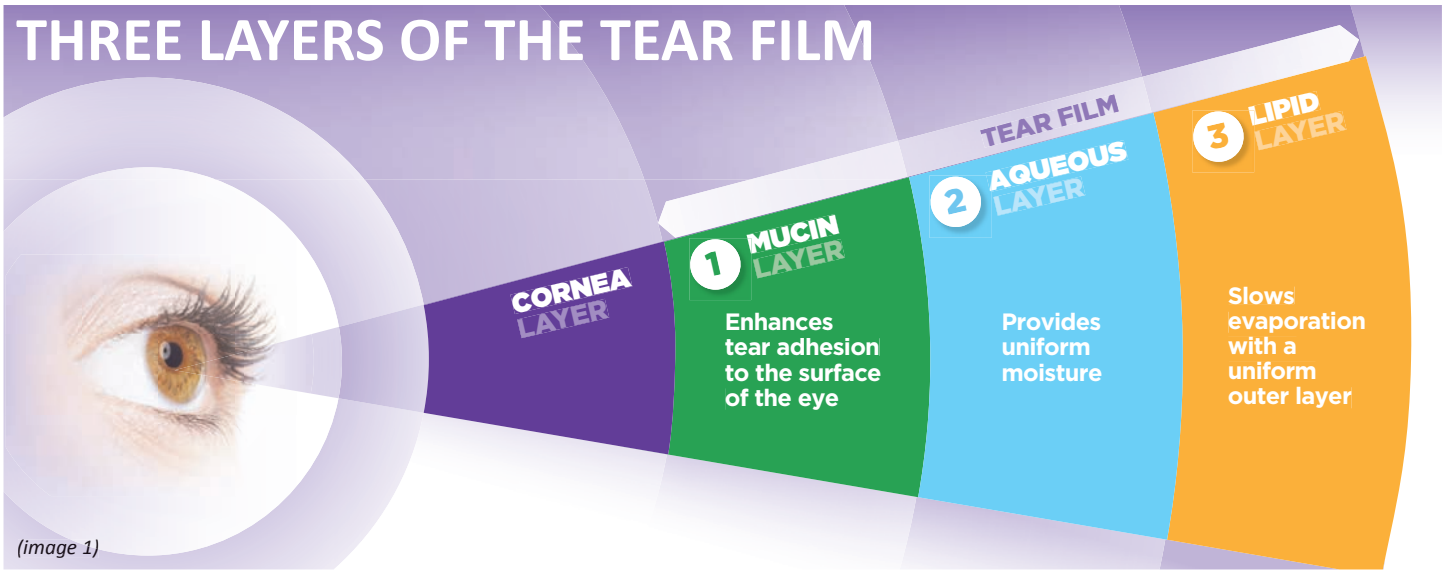
ABOUT THE STUDY

In a single center, parallel group study, the effects of ROHTO® DRY-AID™ were compared versus a leading artificial tear brand in patients 18 years of age or older (n=80) diagnosed with mild to moderate DED over approximately 30 days in a real-life, real-time setting. Subjects were assigned to one of the two products, and were monitored at two and four weeks during the course of the study. All subjects completed the entire 30-day duration.

"A key to the study design was that it represented an assessment conducted in a real-life, real-time setting rather than a strictly clinic-based trial," says study co-author Parag A. Majmudar, MD, President and Chief Medical Officer, Chicago Cornea Consultants. "For this reason, it may provide a more realistic picture as to its relative effectiveness compared to traditional dry eye therapies."

ALL-DAY RELIEF

Ocular comfort scores confirmed that both products provide an immediate, significant improvement in ocular comfort that was sustained for at least one hour after instillation. However, patients using ROHTO® DRY-AID™ (n=40) reported longer lasting relief of the ocular signs, symptoms, and visual function issues associated with DED versus the comparator product.



(image 1)

"One of the most intriguing distinctions between the two products was observed in diary data that showed ROHTO® DRY-AID™ mean scores for ocular discomfort and dryness remained approximately the same from morning to evening while the comparator product mean scores in these two areas trended upward from morning to evening," notes study co-author Michael S. Cooper, OD, Windham Eye Group, P.C., Willimantic, Conn.

"The effects of artificial tears are often short-lived, providing temporary relief and require repeated instillations," he adds. "Artificial tears should help maintain protection of the ocular surface. Patient-reported symptoms from this study suggest that ROHTO® DRY-AID™ balances the ocular surface throughout the day, which may help reduce patients' need for continuous dosing and allow for improved quality of life and visual measures."

IMPROVEMENT IN COMFORT SCORES

At each study visit, subjects were also queried using the Ora Calibra™ Quality of Life Questionnaire, which includes questions addressing visual function as well as other symptom assessments. Only the ROHTO® DRY-AID™ group reported significant improvements in comfort scores during visual tasking activities such as television or movie viewing and driving at night. *(see image 2)*

"Studies consistently show that DED has a measureable impact on several aspects of patients' Quality of Life, including their ability to perform certain activities requiring sustained visual attention (e.g. reading, driving)," says Dr. Majmudar. "Data from this study suggests that ROHTO® DRY-AID™ provides superior relief of discomfort associated with visual tasking activities."

LEARN MORE

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For further information, visit:
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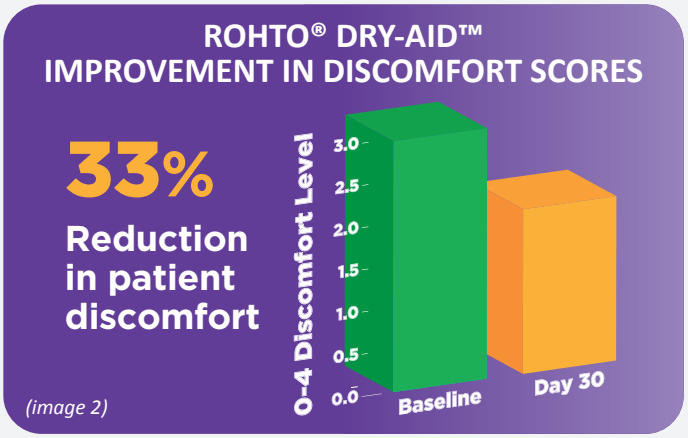
The study was sponsored by The Mentholatum Company, marketer of ROHTO® DRY-AID™.



(image 2)

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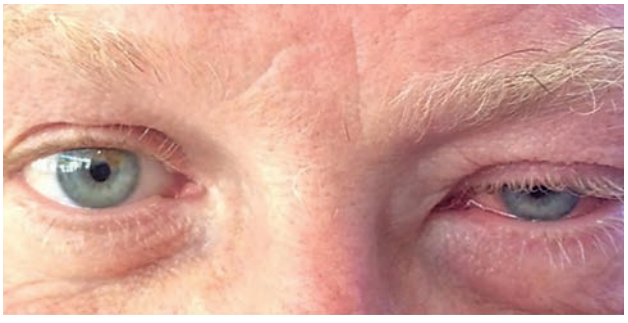
The Conjunctiva in Crisis: Ocular Irritation Unmasked

When conjunctival calamities strike, here's how to identify the cause and come up with a plan. **By Emily Bruce, OD, and Rodney Bendure, OD**

Perhaps no other ocular structure does so much yet receives such cursory clinical descriptions as the conjunctiva. 'Clear and quiet,' 'pinguecula nasal' and 'diffuse injection' dominate the lexicon as practitioners evaluate the state of this ocular structure. While it doesn't catch our attention with flashy biochemical processes or precisely change shape to focus light, the conjunctiva performs a number of essential functions. For instance, it acts as a defense of the globe and eyelids, produces the mucus portion of the tear film and facilitates the globe's freedom of movement. So, when the conjunctiva is insulted, it can be a calamity. Here's a closer look at the structure and the conditions that can compromise its integrity.



This patient presented with a unilateral ptosis, edema and injection, characteristic of viral conjunctivitis.

Anatomy

The conjunctiva is a mucous membrane that extends from the corneolimbus across the globe, down into the fornix and then returns back up the inner surface of the eyelid, terminating at the keratinized margin. It is composed of cuboidal epithelial cells interspersed with Langerhans cells, melanocytes and lymphocytes. Underneath the epithelium is a richly vascularized substantia propria containing lymphatics and additional immune cells.[1]

The conjunctiva is typically divided into three sections: the palpebral conjunctiva, the bulbar conjunctiva and the fornix. The average conjunctiva covers 16cm^2—13 times greater than the surface of the cornea, and 1.3 times greater than the area of the retina.[2] The conjunctiva allows for unencumbered movement of the globe, provides a protective barrier for the eyeball and orbit, contributes to production of the tear film and hosts ocular immune tissues.[1]

The ophthalmic division of the trigeminal nerve provides sensation, while autonomic efferents supply the vessels, accessory lacrimal glands and epithelium. Vascular supplies to the bulbar conjunctiva and fornices are provided by the long ciliary arteries and peripheral tarsal arcades. The palpebral conjunctiva is primarily supplied by the terminal branches of the ophthalmic artery and secondarily by the branches of the facial artery. Blood drains from the bulbar conjunctiva and fornices via the anterior ciliary and conjunctival veins, while the palpebral conjunctiva drains into the post-tarsal veins of the eyelids and the deep facial branches of the anterior facial vein and the pterygoid plexus.

The conjunctiva houses the only ocular lymph tissue. Nasal lymphatics drain into the submandibular nodes, while temporal vessels empty into the pre-auricular nodes.[1]

Diagnostic Considerations

When the eye is insulted, whether

from an allergen, microbe, chemical assault, physical trauma or autoimmune cause, the local tissue reaction is an inflammatory response—conjunctivitis. When a patient presents with a red, irritated eye, it can be challenging to determine the cause of their conjunctivitis. Each type has key characteristics, and checking the boxes off on your clinical checklist can help narrow down the etiological culprit *(Table 1)*.

Thorough history. It is crucial to ascertain as many details from the patient as possible, including onset, duration and laterality. Take note of symptoms, such as pain or itching, to further help distinguish etiology. For instance, a chief complaint of itching is highly suggestive of an allergic reaction, while severe pain is quite uncommon in isolated conjunctivitis and would warrant a check of the cornea for epithelial defects and foreign bodies.

Patient education. Because a high risk of transmission exists with bacterial and viral conjunctivitis, remember to thoroughly educate patients about rigorous hygiene.

Lab work. In many cases, cultures or other laboratory investigations are helpful to find the cause of the patient's conjunctivitis.

Here we focus on the three most common types of each conjunctivitis etiology—viral, allergic and bacterial—and the pearls regarding their diagnosis.

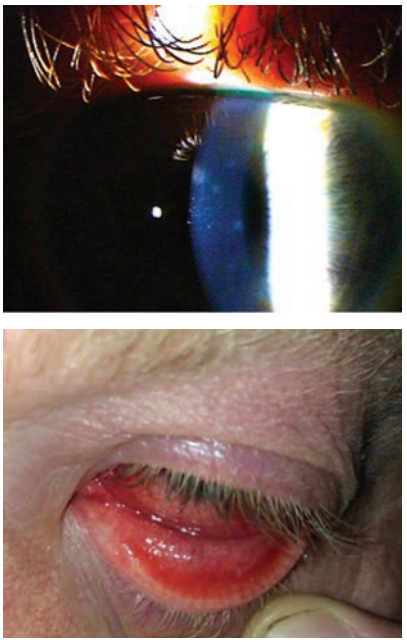
Viral Conjunctivitis

Practitioners often encounter patients with a chief complaint of the dreaded pink eye, and up to 80% of infectious cases of acute red eye are viral in origin.[3] When patients present with a red, irritated eye and you suspect a viral etiology, two virus types may be at play: adenovirus and coxsackie virus.[3,4]

Adenovirus. Of the 53 subtypes of adenovirus in existence, 19 are responsible for 90% of all viral conjunctivitis.[4] Infections can be present in relative isolation, but often occur as epidemics in places such as schools, hospitals and swimming pools. The virus is capable of surviving for weeks, even on dry surfaces. Patients begin to shed virus particles days prior to the onset of symptoms; therefore, many individuals may be affected before preventative measures can be employed.[5]

The adenoviridae infections manifest in four clinical presentations: non-specific follicular, pharyngoconjunctival fever (PCF), epidemic keratoconjunctivitis (EKC) and chronic adenoviral conjunctivitis. The exact incidence of each of the adenoviral presentations is unknown. Symptoms may be mild to severe, with unilateral redness and serous discharge spreading to the second eye one to two days later.

Follicular conjunctivitis is the most common variant and produces a mild bilateral conjunctivitis with watery discharge and no corneal involvement.[4] It is associated with serotypes 1 through 11 and 19.[6] PCF, which is caused by adenoviral serotypes 3, 4 and 7, can affect the cornea in about 30% of cases.[4] It is associated with pharyngitis, high fever and pre-auricular lymphadenopathy.[3] Both follicular conjunctivitis and PCF may be associated with a sore throat and are seen often in children. EKC, adenovirus serotypes 8 and 19, is the most severe form and involves the cornea about 80% of the time.[4-6] The initial ocular presentation of EKC and PCF is similar, making differentiation difficult on ocular presentation alone. Therefore, it is helpful to remember to check for the systemic manifestations of PCF, while corneal subepithelial infiltrates are much more commonly seen with EKC.[7]



In the same viral conjunctivitis patient, follicles and injection were present on the palpebral conjunctiva, and subepithelial infiltrates were present in the cornea.

Chronic follicular conjunctivitis, the rarest adenoviral conjunctivitis variant, is characterized by intermittent, relapsing episodes of follicular conjunctivitis, though papillae may predominate.[4] The clinical presentation is less severe than in other forms. The condition, though sometimes lasting for years, tends to resolve spontaneously. Adenoviral serotypes 2, 3, 4 and 5 have been isolated from affected individuals.[7]

Coxsackie virus. Acute hemorrhagic conjunctivitis creates a startling clinical presentation. It is more common in tropical areas and is usually caused by the enterovirus or coxsackie virus. Infectious outbreaks typically occur in underdeveloped countries with a prevalence of up to 50%.[8] Patients are often worried by the particularly red, bloody appearance of the petechial subconjunctival hemorrhages present with this type of infection.[4,5]

Table 1. Differential Diagnosis of Viral, Allergic and Bacterial Conjunctivitis

	Viral	Allergic	Bacterial
Laterality	Unilateral, then bilateral	Bilateral	Unilateral, then bilateral
Tissue response	Follicles Chemosis Petechial hemorrhages Subepithelial Infiltrates	Papillae Chemosis Corneal scarring, if severe	Papillae Subepithelial Infiltrates *Note: mixed papillary and follicular response with *Chamydia*
Discharge	Serous, mucoserous	Serous, mucoserous	Mucopurulent, purulent
Membrane/pseudomembrane	Yes	No	Yes
Lympadenopathy	Yes	No	Only with *Neisseria* and *Chlamydia*

Diagnosis. In viral conjunctivitis, clinical signs often govern the diagnosis. These include eyelid edema, as well as a swollen preauricular node and conjunctival redness, follicles, membranes and pseudomembranes. Corneal involvement includes superficial punctate keratitis in mild cases, or discrete whitish anterior stromal infiltrates, which may persist for months.[4,5]

Though diagnosis is typically made based on clinical presentation, Giemsa stain can reveal multinucleated giant cells in herpetic infection and mononuclear cells in adenovirus infection. Viral cultures, nucleic acid amplification and, more recently, in-office immunochromatography tests such as the AdenoPlus (Quidel), are available for point-of-care diagnosis. The AdenoPlus test kit identifies the presence of adenovirus with a sensitivity of 93% and specificity of 98%, according to research. The in-office test results are available within approximately 10 minutes.[9,10]

Allergic Conjunctivitis

Ocular allergy is comprised of several distinct clinical entities representing a veritable alphabet soup of acronyms. These include seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), contact allergic conjunctivitis (CAC), giant papillary conjunctivitis (GPC) and atopic keratoconjunctivitis (AKC). Some of these conditions are acute and visually benign, while others are chronic and pose the threat of permanent vision loss.[1,4,6,11]

Acute allergic conjunctivitis. SAC and PAC represent the milder and more common types of ocular allergy, and both are classified as acute. SAC is the most common form of allergic conjunctivitis, is often accompanied by allergic rhinitis, and its incidence and duration is tied closely to the arrival of plant-derived allergens.[12]

In PAC, allergens such as dust mites and pet dander are often triggers, and though patients often notice exacerbations and remissions, this condition occurs throughout the year. Itching is a hallmark sign of these conditions, and papillary response, watery or stringy discharge, conjunctival hyperemia and mild to moderate conjunctival chemosis are generally present to variable degrees.[1,13]

Despite the significant discomfort for patients, these two entities do not pose a significant risk to vision.

Chronic allergic conjunctivitis. VKC and AKC, chronic forms of allergic conjunctivitis, have prolonged, complex inflammatory reactions involving a number of immune responses, which includes T-cells, eosinophils, basophils, neutrophils and associated cytokines. While all types of allergic conjunctivitis have a type I hypersensitivity response, the cell-mediated type IV response typified in these conditions is responsible for their sight-threatening effects.[14,15] Risk of permanent vision loss rises sharply with these conditions due to the potential for secondary conjunctival and corneal scarring and, although rare, corneal perforation. VKC generally presents in males younger than age 30, while AKC exhibits a weaker gender predilection. AKC usually presents after the age of 30, with visual complications in the fourth and fifth decades. Ninety-five percent of cases are associated with a history of atopic dermatitis.[4,6,11]

GPC, the third form of chronic allergic conjunctivitis, is caused by chronic irritation, usually from contact lenses, ocular prostheses, exposed surgical sutures, scleral buckles, corneal surface irregularity and filtering blebs. GPC is a mechanically induced allergic reaction and generally resolves when the source of the mechanical irritation is removed. Later in the condition, giant papillae can be greater than 1mm in diameter.[4,15,16]

CAC occurs when the conjunctiva exhibits a type IV delayed hypersensitivity reaction to ocular medications or their preservatives. This usually presents after patients have been exposed to a medication, solution, contact lens material or preservative for several days.[4,6,11]

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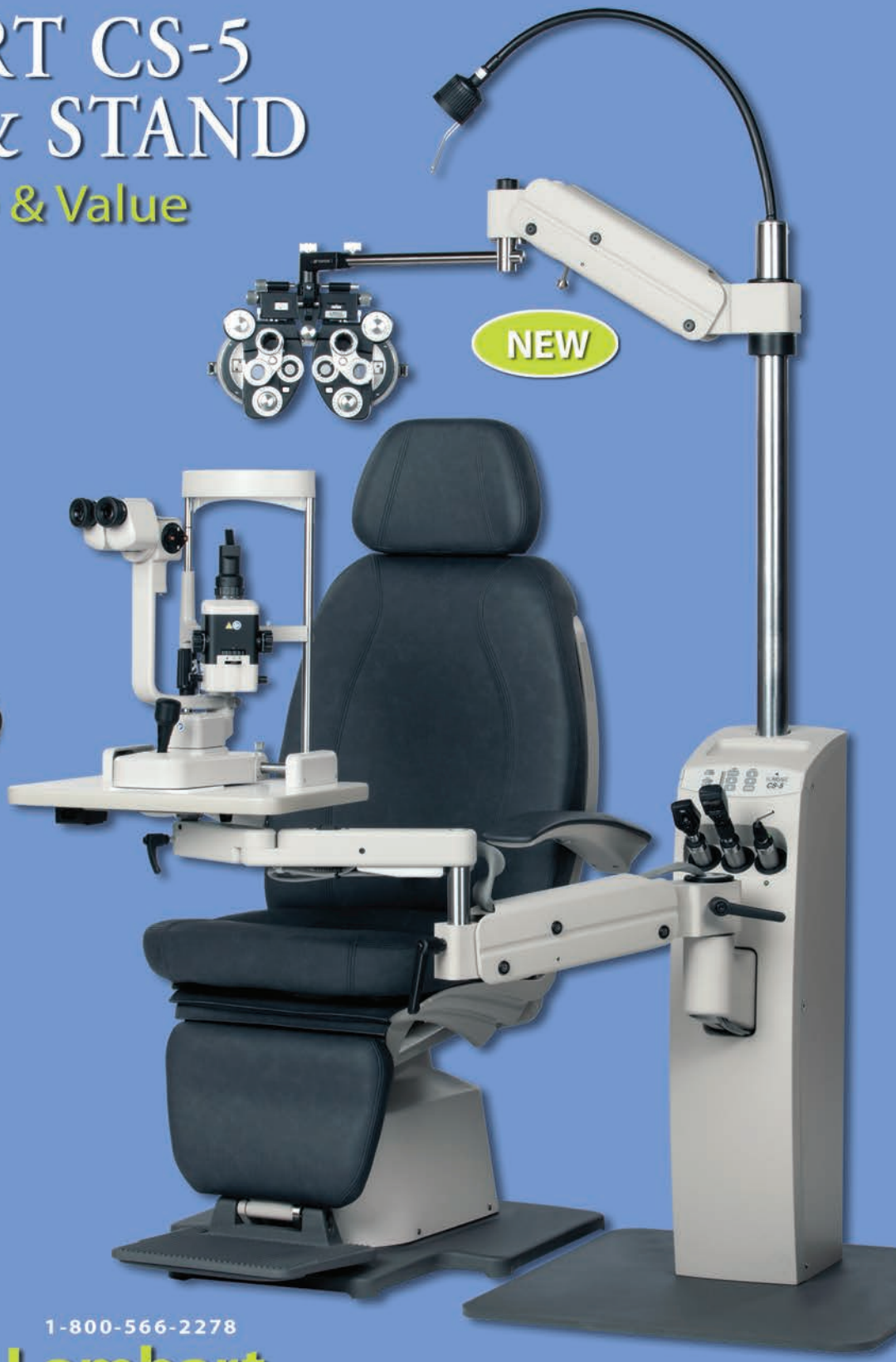

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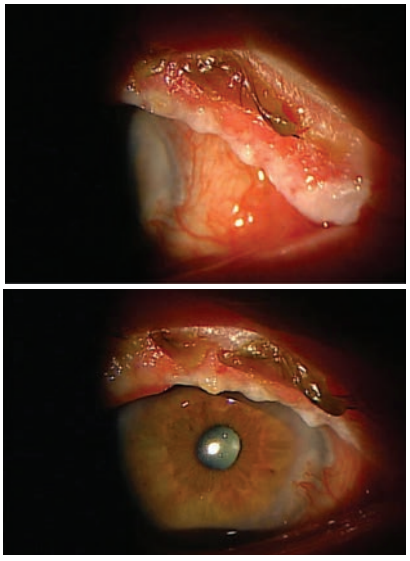
Diagnosis. All types of allergic conjunctivitis are diagnosed based on signs and symptoms. A family history of atopic disease or asthma may support suspicion of ocular allergies. Itching is the hallmark sign of ocular allergy, and its absence makes this diagnosis unlikely. In contrast, conjunctival scrapings may reveal eosinophils, but their absence does not rule out ocular allergies.

Conjunctival provocation testing with suspected allergens may help determine the effectiveness of therapeutics if a patient has a history of severe allergies. A blood test, the radioallergosorbent test or ELISA testing of tears may be performed to identify specific allergens.

Bacterial Conjunctivitis

Last but not least, bacterial conjunctivitis is caused by direct inoculation with infectious secretions. Three presentations of bacterial conjunctivitis exist: acute, hyperacute and chronic.



In the case of this acute bacterial blepharoconjunctivitis patient, a culture was obtained, which revealed *S. aureus* overgrowth. A pseudomembrane is seen emerging from the upper lid in the second picture (bottom).

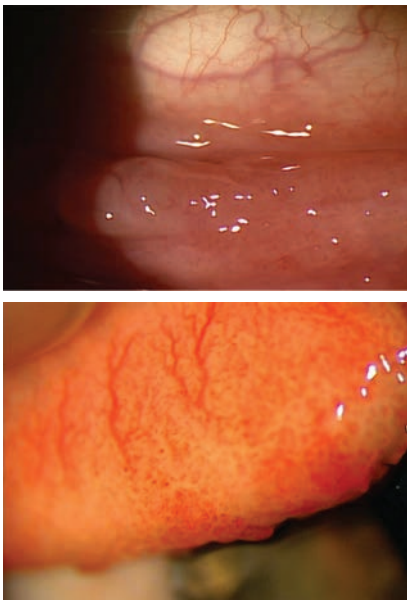
Acute bacterial conjunctivitis. The most common causes of acute bacterial conjunctivitis are *Streptococcal* pneumonia, *Staphylococcus aureus*, *Haemophilis influenzae* and *Moraxella catarrhalis*. Severe presentations should prompt suspicion of *Neisseria* species.[4]

Because *S. aureus* is ubiquitous in skin flora, it can present at any time and has no demographic predilection. *S. pneumoniae* infections are more common among children in cooler climates, while *H. influenza* is more commonly seen in children in warmer climates and tends to have a more severe presentation.[17]

Symptoms include sudden onset of redness, burning and discharge occurring in both eyes, though one may precede the other by one to two days. Clinical findings can include conjunctival and eyelid edema, erythema, papillae, mucopurulent discharge and punctate corneal staining. In contrast to viral or allergic conjunctivitis, bacterial discharge often has a yellow-green appearance along with matting of the eyelids. Lymphadenopathy typically seen in viral conjunctivitis is absent, except in cases of *Neisseria* infections. In rare cases, the cornea can become compromised.[4,18,19]

Hyperacute conjunctivitis. Although they are responsible for only a small number of cases of conjunctivitis, *Neisseria gonorrhoaea* and meningitides should be suspected in cases of severe conjunctivitis. Signs include hyperpurulent discharge, severe lid edema, corneal ulceration, lymphadenopathy and pseudomembranes. If a corneal ulcer is present, aggressive treatment is necessary due to the risk of perforation within 24 hours.[18,19]

In these cases of hyperacute conjunctivitis, culture is mandatory. Culture media include Giemsa stain, Chocolate agar and Thayer-Martin.



These images highlight the difference in appearance between follicles (above) and papillae (below).

Patients who test positive for *Neisseria* should also be tested for concurrent sexually transmitted diseases including syphillus, chlamydia and HIV.[4,6]

Chronic bacterial conjunctivitis. When the signs and symptoms of bacterial conjunctivitis have been present for more than four weeks, there are two likely infectious causes to consider: a chronic overgrowth of normal flora, typically seen as blepharitis, and chlamydia.[11,20]

The most common cause of blepharitis is *Staphylococcus*. If ulceration is seen near the lacrimal structures and puncta, *Moraxella lacunata* should also be considered as a causative agent. As practitioners, we see this every day, and we all know the typical signs and symptoms: tearing, foreign body sensation, conjunctival hyperemia, thickening of lid margins, telangectatic vessels, rosettes, collarettes, inferior superficial punctate keratitis and even sterile infiltrates. Blepharitis is easy to diagnose based on the

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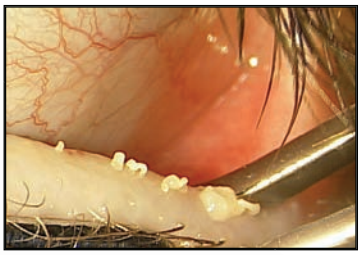

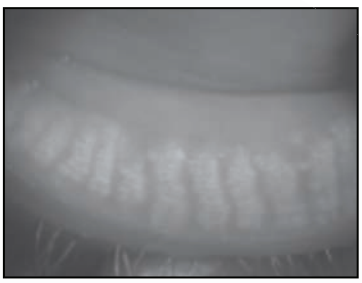

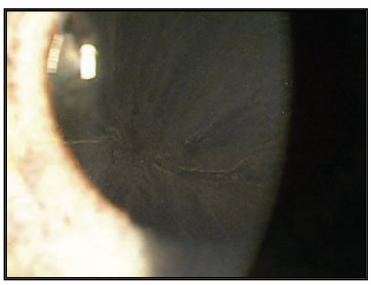

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clinical picture, but it is extremely difficult to eradicate due to the always-present skin flora.

Chlamydia, caused by *Chlamydia trachomatis*, is typically diagnosed in young, sexually active patients who present with a red eye that does not respond to other treatments and is present for three to four weeks. *Chlamydia trachomatis* is an intracellular obligate bacterial species and is capable of causing a mild unilateral or bilateral chronic conjunctivitis associated with redness, watering and discharge. Preauricular lymphadenopathy and large follicles primarily of the lower fornix are common findings. Mild conjunctival scarring and corneal infiltrates may also be seen. Tarsal conjunctival scrapings may be obtained for laboratory confirmation. Referral to a primary care or genitourinary physician is appropriate. Patients and their partner(s) should be tested for other sexually transmitted diseases.[4,5,11]

Diagnosis. This is based on clinical findings, but more specific information can be obtained with a culture, Giemsa and gram stains.

We strive to provide comprehensive, complete eye care for our patients. By successfully diagnosing conjunctivitis, you can help to alleviate or even eliminate a condition that diminishes quality of life—garnering increased patient respect and, hopefully, a lifelong patient. ■

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Table 2. Conjunctivitis Treatment Options

Type	Severity	Treatment
Allergic conjunctivitis	Mild	Allergen avoidance. Cool compresses. Artificial tears.
	Moderate	Add dual-acting histamine receptor antagonist and mast cell stabilizer.
	Severe	Add topical corticosteroid.
Bacterial conjunctivitis	Acute	Consider laboratory evaluation; treat empirically with broad-spectrum ophthalmic antibiotic for seven to 10 days.
	Hyperacute (purulent)	Laboratory evaluation is imperative. Ceftriaxone, saline lavage of fornices Q1hr, followed by ophthalmic antibiotic. Corneal involvement requires hospitalization with IV antibiotics. Consider evaluating and treating for concurrent STDs.
	Chronic	Warm compresses and eyelid massage in addition to eyelid hygiene Topical antibiotic; consider an oral tetracycline.
Viral conjunctivitis	Mild (PCF and nonspecific follicular conjunctivitis)	Cold compresses and artificial tears. Stress hygiene.
	Severe (EKC)	Add ophthalmic vasoconstrictor, removal of membranes/pseudomembranes. Consider ophthalmic steroid, particularly if corneal involvement is noted. Ophthalmic Betadine early can decrease infectivity of free virus.

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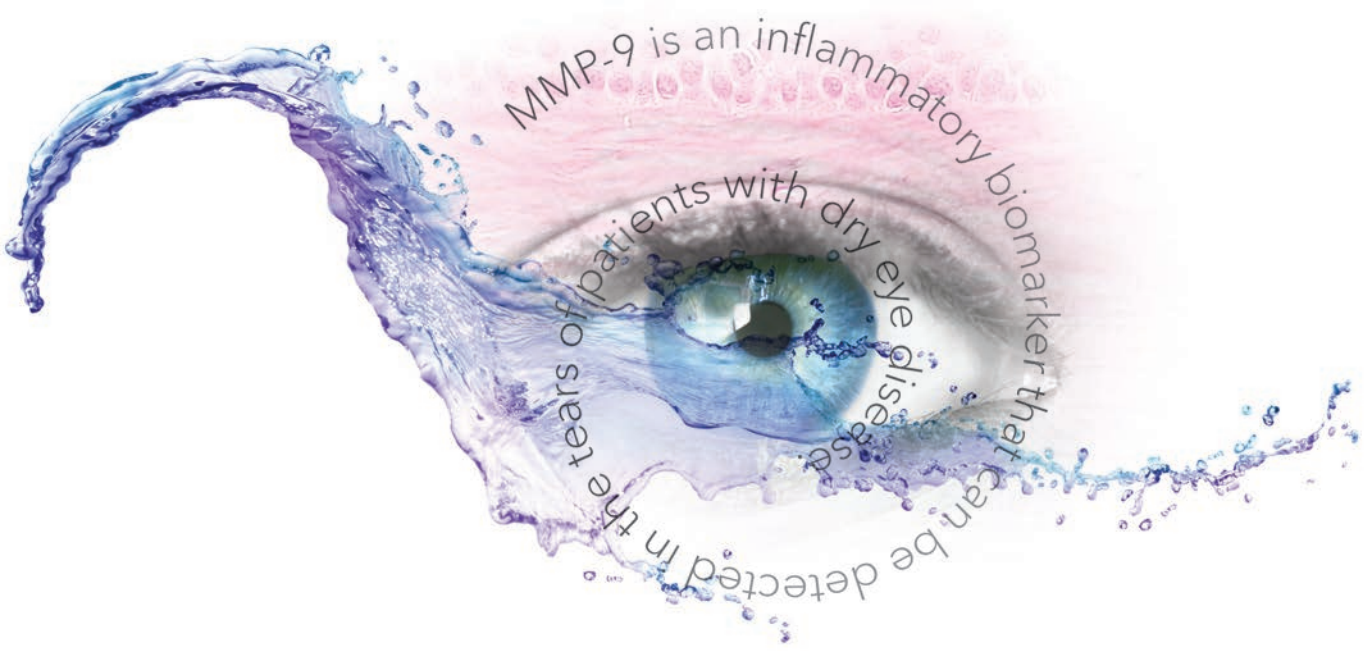

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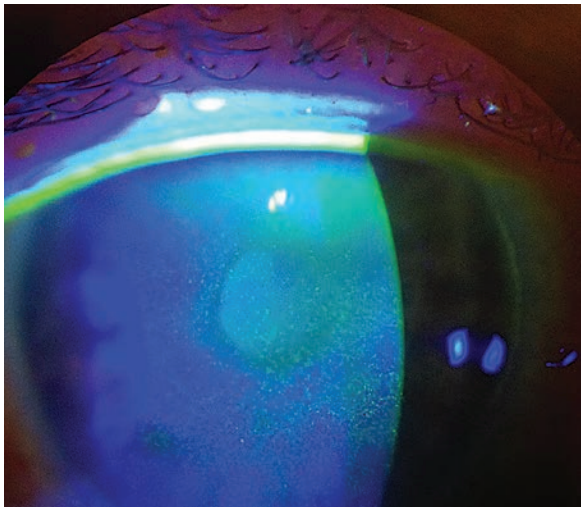
When Dry Eye COMPROMISES Corneal Integrity

Your patients' blurry vision, keratitis and infections could be caused by ocular surface disease. By Scott G. Hauswirth, OD

Dry eye disease (DED) affects all parts of the lacrimal functional unit—including the cornea, conjunctiva, meibomian glands, lacrimal glands and the interconnecting innervation. As clinicians, we tend to detect dry eye by listening to patient complaints for DED-related symptoms and closely examining the cornea. This isn't a misguided approach, considering the cornea is crucial to vision and is often the first structure compromised by DED.



This patient demonstrates diffuse punctate epitheliopathy, and shows decreased barrier function related to dry eye.

This article delves into DED's impact on the cornea, including what we know about the pathophysiology of the condition, the initiating insult and methods of progression.

Corneal Basics

The human cornea is an avascular structure comprised of several distinct layers.[1] The outermost layer, the corneal epithelium, is composed of three stratified layers of cells: basal epithelium, wing cells and apical cells.[1]

Basal epithelium. This is in contact with the underlying basement membrane and adheres the epithelial complex to the structural portion of the cornea.[1]

Wing cells. These are in the middle section of the epithelium, and represent upwards migration of a portion of the basal epithelium in an intermediary state towards the apical cells.[1]

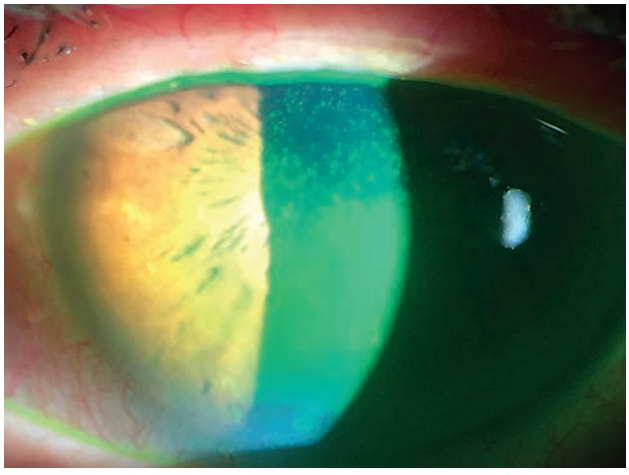
Apical cells. These are the outermost cells and are in direct contact with the tear film.[1] The apical cells contain microvillae and microplicae, which extend upwards into the tear film as much as 0.5µm and are coated with a dense glycocalyx. Composed of several transmembrane mucins that form a mucoadhesive complex, the glycocalyx anchors the tear film to the apical epithelium and defends against bacteria.[1]

The cornea derives nutrients and oxygen from two different regions. The peripheral cornea derives its supply from the limbal region, which contains the vascular loops of the conjunctiva. The central anterior cornea—specifically the corneal epithelium—obtains most of its oxygen and nutrients from the tear film.

The epithelial surface is generated by the stem cell niches at the limbus, which produce transient amplifying cells.[1] These migrate across Bowman's membrane

towards the central cornea, further from the limbus and blood supply. During normal cellular turnover, transient amplifying cell progenies will migrate across the cornea and differentiate into basal cells, and then into wing and apical epithelial cells.

As the most richly innervated tissue in the body, with receptors that number approximately 6000 sensory terminals per square millimeter, the cornea is designed to monitor and provide feedback for changes in the environment, including to the protective tear film.[2,3] The majority of these corneal receptors are mechanoreceptors, which detect touch or pain; but approximately 10% to 15% respond to temperature and osmolarity changes, which may help detect evaporation and provide a means to regulate basal secretion.[4]



Corneal staining shows advanced loss of epithelial barrier in severe dry eye with loss of the mucoadhesive layer and poor wettability of the tear film.

Healthy Tear Film

In a healthy eye, the tear film is stable and provides a sufficient refracting surface for good vision. It supports the ocular surface by providing oxygen and nutrients and protects it from dessicating environments, such as wind, and from toxins, microbes and particulate matter.

A healthy tear film contains a variety of constituent parts. It has a complex set and balanced number of electrolytes.[5] It is pH neutral to slightly acidic.[5] The tear film contains lysozyme and lacritin as defense mediators, as well as hundreds of proteins and proteolytic enzymes that support normal cellular function of the corneal epithelium and provide a protective barrier to the environment.[5]

Several glands on and around the ocular surface produce the constituent parts of the tear film, primarily the lacrimal and accessory glands, meibomian glands and conjunctival goblet cells.

Despite all of its important functions, the tear film in a healthy eye is extraordinarily thin, averaging between 2µm and 5.5µm in thickness over the cornea.[6]

Homeostasis

This entire system is designed to monitor the environment and maintain homeostasis by compensating for alterations in temperature and humidity and protecting exposed tissue from bacteria and other offenders.

A normal eye maintains its homeostatic environment via this monitoring and compensatory actions. For example, the lacrimal functional unit's ability to compensate and regulate tear production and volume is a hallmark of a healthy ocular surface system. Tearing is a compensatory reflex mechanism designed to increase or restore volume, to restore osmotic balance or to flush out toxins or irritants.

In the dry eye, patients suffer a loss of homeostasis, and the mechanisms normally designed to defend the eye—such as engagement of chronic inflammatory response—may turn against it and lead to DED progression. Returning to the example of tearing, it's common for mild dry eye patients to experience tearing as a response to stress (e.g., when reading or exposed to a cold, drafty environment). In contrast, more severe dry eye patients, particularly those diagnosed with autoimmune conditions such as Sjögren's syndrome, may have damaged glands and neurosensory systems due to chronic inflammation, preventing the ocular system from compensating to the stressors of increased evaporative demand.[7]

Corneal Impact

The loss of homeostasis has a multitude of sequelae on the cornea, including visual complaints, increased risk for infection, keratitis and microerosions and, of course, inflammation.

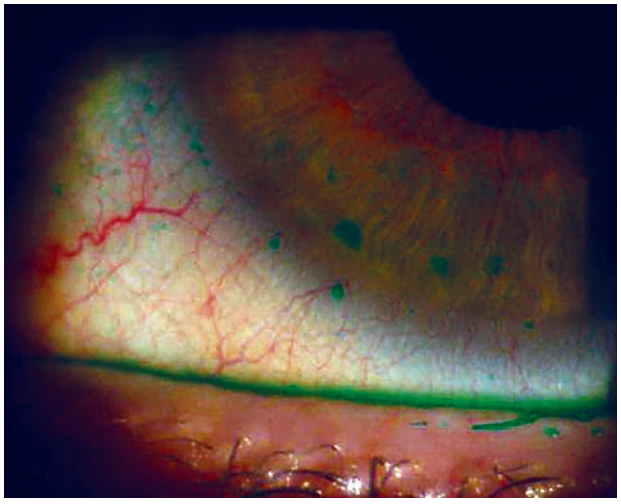
Blurry vision. Because the cornea is dependent on the function of the thinnest portion of the tear film, blurry and inconsistent vision may be one of the earliest clues to a dry eye diagnosis. The Progression of Ocular Findings Study (PROOF), a five year, prospective, multicenter study, reveals one of the primary differences between individuals with mild DED and those without dry eye is how they perceive their quality of vision. In both groups, baseline distance best-corrected visual acuity (BCVA) was 20/20. However,

58.5% of those who had level two dry eye as defined by the International Task Force guidelines expressed moderate, severe or very severe dissatisfaction with their vision, vs. only 13.7% of those in the control group.[8,9]

Inflammation. Hyperosmolarity of the tear film is one of the key mechanisms that drives inflammation and the progression of DED. In addition, evaporative stress may be at the center of hyperosmolarity.

Studies examining osmolarity show that a difference in the osmolarity levels between the tear menisci and the precorneal tear film likely exists, with the precorneal tear film experiencing higher osmolarity.[10] In patients with dry eye, this difference may be even greater. Mathematical models of osmolarity in the precorneal tear film show rapid increases due to evaporation and decreased tear break-up time. This may drive up the osmolarity of the precorneal tear film to levels that are quite high (e.g., 1,900mOsml) compared with normal (i.e., 300mOsml), especially where the tear film separates or collapses.[11] In contrast, the highest readings in the tear meniscus measure well below 500mOsml.

On a cellular level, increased osmolarity triggers inflammation via cell signaling. Cell membrane receptors such as toll-like receptors (TLR) initiate the internal cell signaling processes, driven primarily by NF-kB and mitogen-activated protein kinase (MAPK) activation.[12] These two cytoplasmic signaling pathways upregulate transcription of cytokines (primarily IL-1) and matrix metalloproteinases (MMPs). MMPs are substrate-specific proteolytic enzymes that regulate extracellular matrix deposition as well as its degradation.[12]



In this patient, conjunctival epithelial compromise extends onto the cornea in macropunctate erosions, caused by dry eye.

Keratitis. During periods of high evaporative stress, increases in tear film osmolarity trigger inflammation, beginning within the corneal apical cells. Increased tear film osmolarity alters the normal internal/external osmotic gradient, moving water and internal cell ionic content into the extracellular space. These result in cell volume losses, which cause gaps to form between adjacent epithelial cells, resulting in the appearance of "fine" superficial punctate keratitis (SPK) and increased penetration of fluorescein into the deeper layers of the corneal epithelium and then into the anterior stroma.

Recent measurements of SPK lesions seen in dry eye patients show that the mean diameters are smaller than a healthy epithelial cell. These are likely "deflated" or shrunken cells, which are in the process of apoptosis and have taken up dye.[2]

In more advanced forms of the condition, chronic epithelial compromise may also lead to mucin upregulation and formation of filamentary keratitis, where mucous

DED Testing

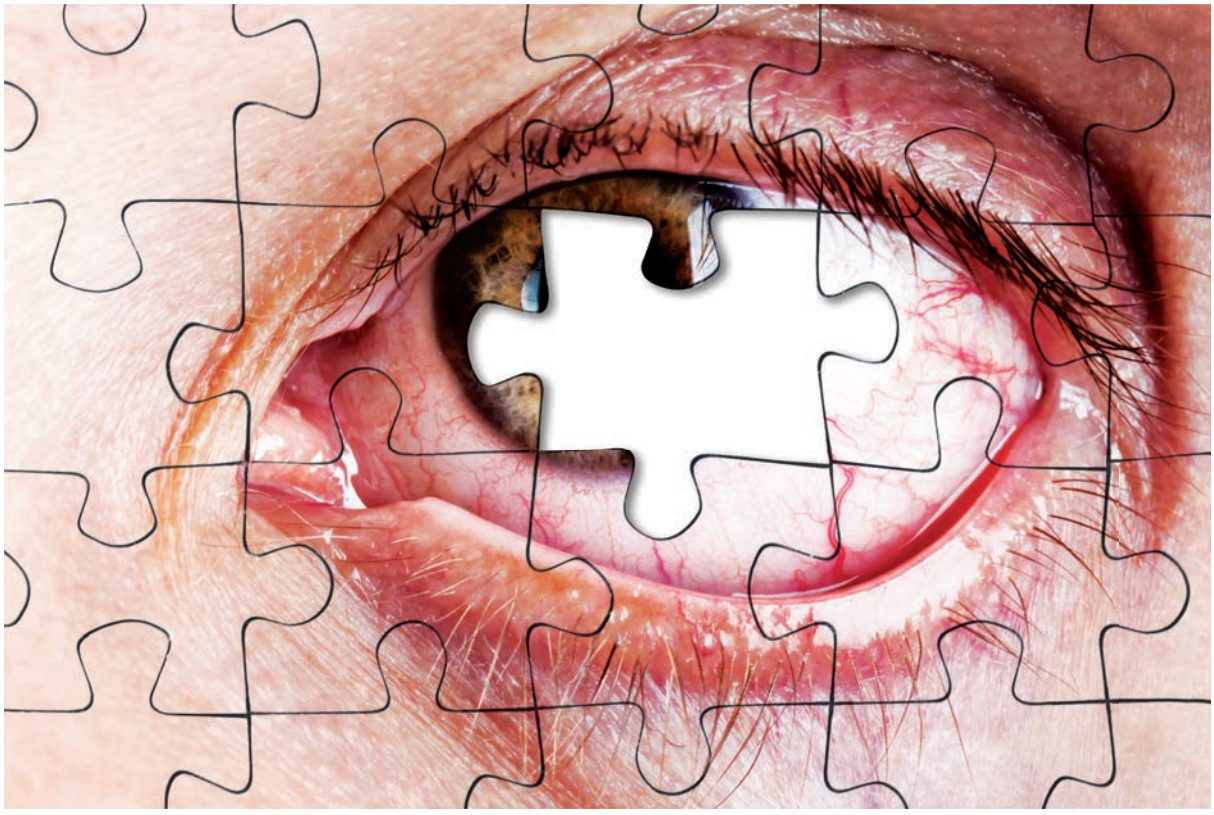
Several tests can help you quantify the severity of dry eye, including vital dye staining of the cornea and conjunctiva, and point-of-care testing for the presence or degree of inflammatory involvement. Corneal and conjunctival staining is perhaps one of the most accessible and easily quantifiable methods of assessing damage to the ocular surface.

Grading severity of corneal involvement is a key feature in determining DED severity. Several grading systems exist to help classify dry eye, such as the Oxford scheme, the Van Bjisterveld system and the NEI/Industry Workshop guidelines.[19]

Instillation of sodium fluorescein is a helpful diagnostic tool for grading damage to the ocular surface. Fluorescein staining will be present in cells with defective tight junctions, or a compromised glycocalyx.[20] Remember, some mild background uptake of fluorescein dye is considered normal, so there is a weaker correlation between disease severity and stain uptake in mild forms of dry eye.[21] Lissamine green, another vital dye well-tolerated by patients, will be taken up by epithelial cells with a damaged cell membrane and provides a means of assessing both the cornea and conjunctiva.

While a number of testing options exist to provide a systematic means to assess the presence of staining on the cornea, no one particular method seems to have higher accuracy or better correlation to disease severity, so the testing method is entirely up to the clinician.

MANAGING BIOBURDEN



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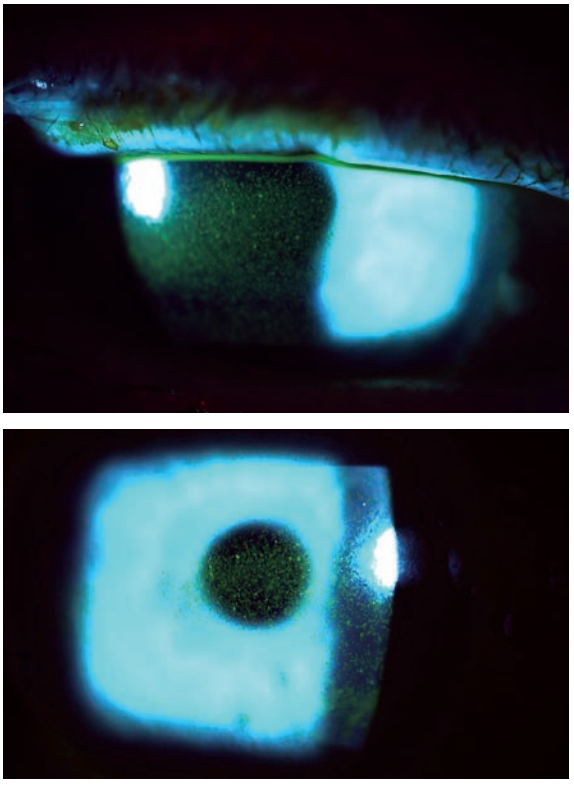
adhesions cling to areas of chronic epithelial irregularity or compromise.

Infections. Dry eye continually arises as one of the top three risk factors for bacterial keratitis.[13,14] Corneal integrity is necessary as an innate defense against bacteria. Chronic breaks in the surface of the cornea, in conjunction with decreases in lysozyme and lactoferrin, which provide a second defense against bacteria, predispose the dry eye to a higher risk of corneal infection. This becomes even more important for contact lens wearers, who are exposed to bacterial biofilms, as well as contact lens matrices that may become contaminated and populated over time by a number of bacteria, fungi and parasites.



This patient's punctate epithelial keratopathy involves the central cornea in a case of Sjögren's-related dry eye.

On a cellular level, lymphocytic activation, recruitment and infiltration of tissues by T-lymphocytes, all hallmarks of DED, can ultimately decrease resistance to infection. Activation and recruitment of TH1/TH17 via the nuclear factor kappa beta (Nf-KB) signaling pathway is a critical part of the mechanism that drives the conversion from an acute response to chronic inflammation and seems to play a key role in disease progression.[15,16] Infiltration of the lacrimal gland leads to damage and dysfunction of secretory acini. Ultimately, this alters the tear film composition.

Decreased corneal epithelial barrier molecules. While at least 30 known MMPs exist in the human body, MMP-3 and -9 appear particularly critical to maintaining the epithelial barrier of the cornea. For example, increased MMP-9 is correlated with increased corneal staining in dry eye patients, but is also increased in corneal infection, recurrent erosion and other pathologies where the corneal epithelial barrier is compromised.[17] MMP-9 is normally found on the ocular surface in low amounts, below 41ng/mL in healthy corneas. Levels above 41ng/mL are associated with epithelial compromise. MMP-9 affects the junctions between epithelial cells by breaking down the molecule occludin, a critical component of the tight junctions.

As concentrations of pro-inflammatory molecules increase, compounds that maintain the corneal epithelium may decrease. The molecule extracellular matrix metalloproteinase inducer (EMMPRIN), a type-1 cornea epithelial cell receptor that may have an important role in the maintenance of the corneal epithelial barrier, increases in proportion with MMP-9 levels.[18] Studies show an inverse relationship between EMMPRIN amounts and occludin in the cornea. Because occludin is critical to maintaining the tight junctions between adjacent epithelial cells, the overall barrier of the cornea is compromised.

Basal secretion, neurological changes and symptoms. In the presence of inflammation, damage to corneal nociceptors and associated neurologic pathways may decrease basal tear secretion as well as contribute to morphologic changes in nerve structure that may lead to sensations of pain or, conversely, to hypoesthesia and neurotrophia despite worsening disease.[4,7]

Mechanical epithelial desquamation. In a normal eye, the tear film provides a cushion and lubrication to help the lids move over the ocular surface with minimal friction. In a dry eye, however, both volume and content of the tear film is reduced, exposing the glycocalyx and apical epithelium to the frictional forces of the blink. This results in increased epithelial desquamation compared with normal eyes.

Dry eye disease has a number of negative effects on the ocular system, beginning with the breakdown of the homeostatic mechanisms designed to protect the health of the ocular surface. We can use the cornea as a window to assess the severity of DED, and once these systems are compromised, inflammatory

insult to corneal and conjunctival tissues make it difficult to return to baseline homeostatic function. Processes that direct corneal wound healing and tight junction formation are compromised. Ongoing injury to the corneal barrier and reduced corneal integrity results in the appearance of reduced wettability due to glycocalyx disruption or loss, punctate keratopathy, microerosions, development of filaments and increased risk for infection.

By identifying issues early, we can make the task of restoring homeostasis of the ocular surface and preventing progression of the disease less daunting. ■

Dr. Hauswirth is an assistant professor in the Department of Ophthalmology at the University of Colorado School of Medicine, in Denver, CO.

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PEER • REVIEWED • RRA • ARTICLE •

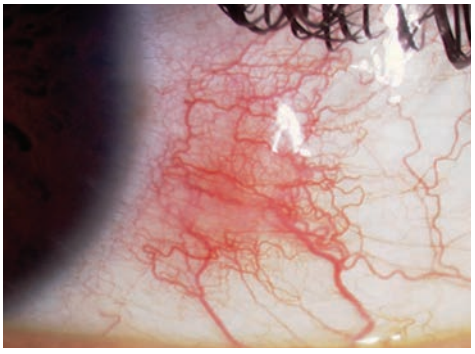
A Red Eye: Scleritis or Episcleritis?

Differentiating between the two is crucial to ensure you initiate the right treatment.

By Jim Williamson, OD

When differentiating episcleritis from scleritis, clinicians often use the phenylephrine blanching technique: blanching congested conjunctival and superficial episcleral blood vessels with either the 2.5% or the 10% concentration.[1-4] When the deep episcleral plexus does not blanch, the diagnosis is usually scleritis. If the redness does disappear, it's episcleritis.

But sometimes the answer is not that simple. For example, overlapping clinical features or variations in perceived patient pain may cloud the decision-making process. But a prompt and precise diagnosis is critical, as treatment and potential sequelae differ between the two clinical presentations.[5] Here, we discuss the differences between episcleritis and scleritis—and how you can identify each of them accurately.



Simple episcleritis is the most common presentation.[1,11]

Episcleritis

The episclera, the outermost layer, is composed of loose connective tissue with two vascular plexi (superficial and deep) derived from the anterior ciliary arteries.[6] Normally, these vessels—which run forward from the insertions of the recti muscles—are not visible because they run deep to the conjunctiva. However, inflammation can make them observable, and the superficial plexus anastomoses with the conjunctival and deep episcleral plexus at the limbus. The superficial vessels are mobile, while the deeper ones are more firmly attached to the sclera.[7]

Episcleritis, also known as subconjunctivitis, phlegmatous conjunctivitis and episcleritis periodica fugax, is a benign inflammation of the conjunctival and superficial episcleral vascular plexi.[8,9] Simple episcleritis is diffuse inflammation, while nodular episcleritis indicates a localized process with a well-defined area of elevation.[1,11]

Episcleritis is often a self-limiting condition with a proposed incidence of 21.7 per 100,000 person-years.[12-14] While rare in children, roughly two-thirds of cases occur in females with a peak incidence in the fourth decade.[1,2,8,15]

Scleritis

The sclera consists of a collagen scaffold, glycoproteins, proteoglycans and protein fibrils.[2,9] It is anteriorly contiguous with the cornea and posteriorly with the optic nerve's dural and arachnoid sheaths. The sclera is weakened in this area due to perforations by the axons of the optic nerve (lamina cribrosa).[9] This anatomical relationship explains why optic nerve edema may occur with inflammation of the surrounding posterior sclera.

Although the sclera is essentially

avascular, it does have a rich supply of sensory nerves.[6] Nutrient delivery comes from the choroid and episcleral vacular complexes.[2,16] This, combined with the sclera's web-like organization, slows the removal of antigens and other materials, providing an ideal environment for persistent inflammation.[2]

Normally, the fibrous sclera appears opaque, but in children it may look bluish due to the visibility of the underlying choroid. As patients age, it may appear more yellow due to fat deposition. The sclera measures roughly 0.45mm at the recti insertions and is thickest at the posterior pole (1.1mm to 1.3mm), which is important to remember when assessing for posterior scleritis using B-scan ultrasonography.[17]

Scleritis is separated into anterior or posterior, based on the inflammation's location in relation to the extraocular muscle insertion sites.[3,11,18] Anterior scleritis is further categorized into diffuse, nodular and necrotizing forms.[11] Necrotizing scleritis may result in scleral perforation, which can occur without inflammation and is termed scleromalacia perforans.[18]

Most practitioners judge the severity of scleritis on a numerical scale based on their clinical experience. However, researchers fostered an eight-component, subjective scoring scale to grade scleritis.[19] Because this scale did not assess inflammation, others established a system of standardized images for grading.[20] While helpful, limitations to this study include the instillation of 10% phenylephrine up to 20 minutes prior to photography and the documentation of only one quadrant.[20]

Scleritis, however, is considered a chronic inflammatory response that involves the superficial and deep episcleral plexus.[9,21] The exact mechanism of inflammation in scleritis remains unclear, as some report a variety of immunopathological findings, while others point to granulomatous inflammation and collagen disruption, which can lead to loss of tissue and subsequent thinning.[8,9,16,21]

Table 1. Systemic Disease Workup

Diagnostic Test	Remarks
Complete blood count	Elevated white cell count in infections
Basic metabolic panel	Evaluate for vasculitis-related renal disease
Erythrocyte sedimentation rate	Nonspecific inflammation
C-reactive protein	Nonspecific inflammation, acute
HLA B27	Possible posterior scleritis association[36]
Antineutrophil cytoplasmic antibodies	Granulomatosis with polyangiitis
Rheumatoid factor	Rheumatoid arthritis
Anti-cyclic citrullinated peptide	Prognostic indicator for RA severity
Antinuclear antibody	Systemic lupus erythematosus
Angiotensin-converting enzyme	Sarcoidosis
Chest x-ray	Sarcoidosis
Fluorescent treponemal antibody absorption	Syphilis
Rapid plasma reagin	Syphilis
Tuberculosis testing	Mantoux skin or Quantiferon Gold blood
Lyme serology	Lyme disease

Scleritis has a proposed incidence of 4.1 cases per 100,000 person-years and can be idiopathic, associated with a systemic autoimmune disease, surgically induced or infectious, although only 4% to 10% of all cases are deemed infectious.[2,14,22] Potential pathogens include bacteria, fungi, parasites and viruses.

Ocular surgery and trauma account for almost half of all bacterial infectious scleritis, and most others result secondarily from a severe corneal infection.[21,23] Pterygium excision and scleral buckling represent 75% of surgical causes, and *Pseudomonas aeruginosa* is the most likely causative agent.[2,9,24] Researchers speculate tissue and blood vessel destruction during ophthalmic procedures may increase susceptibility to infection and explain the late onset of scleritis.[9,24] Fungal and parasitic etiologies are rare.

The most common infectious cause overall is the herpes zoster virus (HZV), which is consistent with the greater-than-fourfold increase in HZV incidence over the last 60 years.[22,25] Though uncommon, scleritis has been reported with bisphosphonate use—a class of drugs used to treat osteoporosis.[12,21]

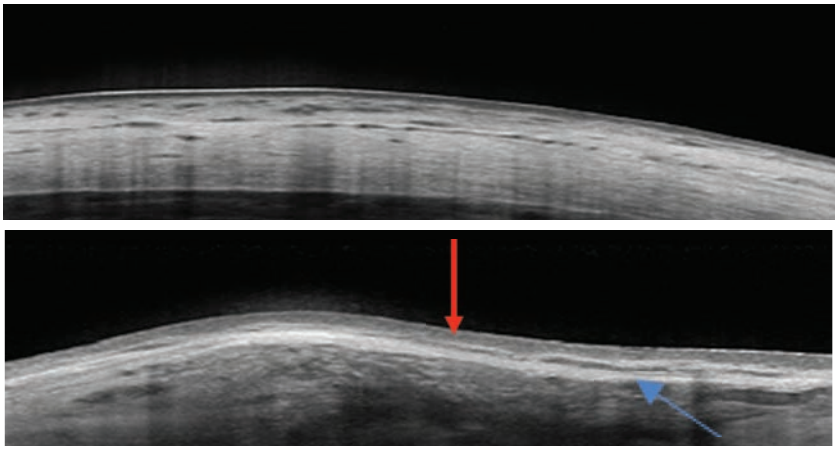
Many ocular procedures may trigger surgically-induced necrotizing scleritis (SINS)—most commonly after limbal-incision cataract surgery—and 75% of patients who develop SINS have undergone two or more procedures.[9]

Symptoms

Here are the symptoms to look out for that can help you differentiate between episcleritis and scleritis:

Episcleritis. Generally, this does not result in significant pain, and usually patients only complain of mild discomfort or irritation.[4,12] Episcleritis may present with epiphora but does not result in decreased acuity.[2,3,12]

Scleritis. This has the potential for sight-threatening sequelae.[26,27] Because of the anatomical relationship of the optic nerve's dural and



These images show a normal sclera, above, vs. nodular episcleritis, below. Note the increased thickness of the episclera (red arrow) while the scleral thickness is unaffected. The elongated hyporeflective area (blue arrow) could indicate edema in the presence of a thickened sclera. In this case, it was due to a scleral plaque.

arachnoid sheaths, decreased visual acuity may occur with inflammation around this area. One study found that, initially, poor vision was the most important risk factor for a negative visual outcome.[24] Other symptoms include photophobia and increased lacrimation.[9]

Scleritis is a more painful condition than episcleritis, and the pain may appear disproportionate to clinical findings.[12] Patients describe it as a deep, boring pain that may radiate to the face, cheek and jaw.[2,9,12,16] Often, it is worse at night and is exacerbated with eye movement.[2,9,21] Investigators discovered a significant increase in pain severity with HZV scleritis cases vs. those with idiopathic etiologies.[22]

Though more agonizing, scleritis may ironically reduce corneal sensation.[26] Researchers cite a decrease in conjunctival sensation in areas of previous inflammation, with the exception of HZV scleritis, which blunted sensation in both active and inactive states. This occurred due to the cornea and conjunctiva sharing the same classes of sensory receptors and the increased likelihood of corneal involvement with HZV.[26]

Clinical Presentation

Each of these conditions have slightly different presentations:

Episcleritis. This is usually diffuse or simple with benign, mild inflammation that resolves within days to weeks.[2,4] Nodular episcleritis, frequently located between the palpebral fissures, is more painful and lasts longer.[1,4] Epiphora may also be present. Because epislceritis involves the conjunctival and superficial episcleral plexi, the affected area appears bright red, unlike the characteristic bluish-violet hue associated with the deep episcleral plexus involvement in scleritis.[9,21] Additionally, intraocular pressure (IOP) may be elevated due to increased episcleral venous pressure (EVP).[27]

Scleritis. This varies depending on the location and nature of involvement. Uveitis occurs in up to 40% of all scleritis patients and is usually seen with the necrotizing type.[9] Keratitis is present in 14% to 37% of scleritis patients and usually targets the adjacent peripheral cornea and may include thinning, infiltrates and interstitial keratitis.[3,21] Increased IOP from elevated EVP or trabeculitis leads to glaucoma in 9% to 13% of scleritis patients.[2,9,21] Less than 10% progress from one type of scleritis to another.[3]

Vascular congestion and a tender globe follow the insidious onset of diffuse anterior scleritis, the most common and the least severe form.[1,3,9,21] A firm, immobile focal area of inflammation denotes nodular anterior scleritis. As with nodular episcleritis, it usually presents within the palpebral fissure and can be single or multiple.[1,9,21]

Necrotizing anterior scleritis marks the most severe form and the greatest threat to the integrity of the eye.[9] Intense vasculitis with closure of the deep episcleral vascular plexus leads to necrosis, tenderness and extreme pain.[1,2,9] The translucently thin sclera highlights the choroid's bluish hue. Necrotizing anterior scleritis is most likely associated with systemic disease and peripheral ulcerative keratitis.[1,3,16,21]

Although now considered rare due to improved therapies for RA, scleromalacia perforans lacks surrounding inflammation and stems from obliterative arteritis involving the deep episcleral plexus.[9,16] Necrotic scleral plaques may appear near the limbus, and severe thinning yields a brown color, along with a high amount of astigmatism.[1,2,9]

Diagnostic Tools

In addition to the clinical exam, clinicians can use optical coherence tomography (OCT), ultrasound biomicroscopy and B-scan ultrasound to help differentiate between episcleritis and scleritis. OCT, for example, can provide objective cross-sectional images and help to describe characteristic findings with anterior scleritis.[19] Using spectral-domain (SD) OCT, researchers note consistent findings of hyporeflective spaces secondary to edema and blood vessels, variations in reflectivity of tissues

The leading cause of ocular discomfort and contact lens dropout is dryness.

Meibomian Gland Function, the foundation of a healthy tear film.

Gland structure captured with Dynamic Meibomian Imaging (DMI).

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and dilated deep episcleral vessels.[19] OCT further shows treatment results in normalization of scleral tissue.[19]

Other researchers noted superficial layer involvement in episcleritis, but dilated vessels in the deeper vascular network with scleritis.[7] Another study found the scleral thickness in episcleritis and scleritis averages 825µm and 882µm, respectively (the normal sclera is roughly 750µm with a standard deviation of nearly 70µm).[5] Clinicians should be cautious about basing a diagnosis solely on thickness, however, as nodular cases will skew the measurements. The key is looking for pockets of edema in the sclera.[5]

High-frequency ultrasound biomicroscopy can be a useful tool in distinguishing between episcleritis and scleritis. Tissue penetration is better with this modality, but it comes at the expense of decreased resolution compared with OCT.[5] Early adopters found that episcleral thickening could be differentiated from scleral involvement.[28]

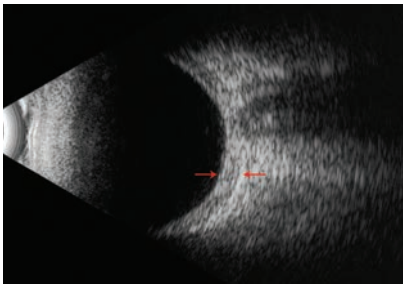
Unlike with other scleritis forms, the observable eye in posterior disease may be nonerythematous.[18] Other dissimilarities include its twice-as-often unilateral presentation and pain that does not correlate with the severity of inflammation.[1,2,29,30] Because it is not visible, clinicians must depend on other procedures when assessing posterior scleritis. A dilated fundus exam may reveal choroidal folds, serous retinal detachments, choroidal detachments, macular or optic disc edema and vitreous cells.[3,21,29] B-scan ultrasound demonstrates posterior thickening with fluid collecting in the sub-Tenon's space, producing the pathognomonic 'T-sign.'[31] Roughly 40% of posterior scleritis patients exhibited this finding and more than half had posterior scleral wall thickness greater than 2mm.[29]

Treatment

Once the proper diagnosis is clear, clinicians can initiate the proper treatment for the patient:

Episcleritis. Because episcleritis is usually a self-limiting condition with a nearly 20% resolution rate without treatment, patient education or topical lubricants may suffice.[1,2] Research suggests topical non-steroidal anti-inflammatory drugs (NSAIDs) provide no benefit over artificial tears.[32] Although this condition can be self-limiting, many clinicians initially treat with a topical steroid. If the inflammation continues, the dosing frequency may be increased or the patient can be switched to a more potent topical steroid.[1,2,33] Only with the failure of these regimens should practitioners resort to oral NSAID therapy, which occurs mainly in patients with a known systemic association.[1,33]

Scleritis. Before initiating any treatment, clinicians should first determine if the scleritis is infectious, as drugs such as oral steroids may worsen the condition. A thorough history into any ocular surgery or trauma should be obtained as well. Clinically, a mucopurulent discharge or scleral abscess may be sufficient signs to signal infection in the absence of a tissue culture and sensitivity test.[23] A complete blood count may reveal elevated white blood cells. HZV, as the most common infectious cause, responds well to oral acyclovir or famciclovir and should resolve the symptoms within several weeks or less.[22]



This B-scan ultrasound shows a thickened posterior sclera (arrows) with an absent 'T' sign.

Unlike with episcleritis, NSAIDs may be a first-line treatment for diffuse or nodular, idiopathic and non-necrotizing anterior scleritis.[3,4,9] If the patient sees no improvement, clinicians should prescribe a different NSAID before advancing to the next therapeutic level.[2] The selective COX-2 inhibitors such as celecoxib are good options when adverse gastrointestinal side effects are a concern. While some research suggests steroids provide no benefits, a study of a series of non-necrotizing anterior scleritis cases showed topical steroids resolved nearly half of the cases, but often they require additional treatment.[2-4,34] Durezol (difluprednate, Alcon/Novartis), the topical ophthalmic steroid emulsion that exhibits enhanced penetration and bioavailability, has not been studied for scleritis use.

Oral corticosteroids are the next therapeutic step for refractory cases, those with necrotizing signs or posterior scleritis.[9,33] Typical oral dosages range from 1mg/kg/day to 1.5mg/kg/day until the inflammation is controlled.[1,4] Given the nocturnal pain associated with scleritis, it may be wise to spread the dose over the day vs. a morning-only delivery.[1] Tapering depends on dosage, duration of use and practitioner discretion. Most practitioners use the lowest possible dose for the shortest possible time, as long-term steroid treatment should be avoided due to the deleterious side effects.

Other routes of steroid introduction include intravenous (IV) and periocular injection. Necrotizing scleritis, for example, may warrant IV methylprednisolone.[3,4] Though not routinely employed, periocular injection of steroids can be effective

in controlling inflammation in non-necrotizing anterior scleritis without the systemic side effects.[3]

Those with an associated systemic condition or the necrotizing type typically need immunosuppressive therapy or biological agents.[35] Examples include methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, infliximab and rituximab.

There are several concerns to remember regarding treatment:

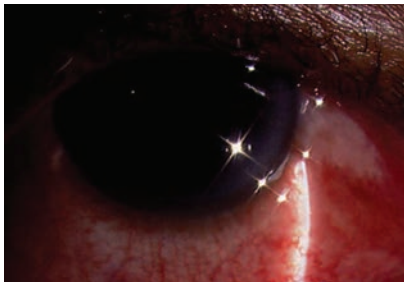
Recurrence is not uncommon. For example, research shows younger patients tend to have recurrence sooner and more frequently.[29] Diffuse anterior scleritis is least likely to recur, followed by the nodular version of the same process.[8] Drug tapering may initiate recurrence.

Immunosuppressive drugs increase the risk for a secondary infection. What starts out as an idiopathic condition could turn infectious, which should be considered in patients who respond well initially but then worsen.

Malignancy may mimic treatment-resistant scleritis.[2,18] This could include intraocular tumors such as melanomas or, rarely, conjunctival tumors and lymphoma.[9]

The chronic use of NSAIDs is not benign. Clinicians should regularly monitor liver and kidney function, as well as blood pressure in hypertensives.[2] Gastric irritation may require additional medications.

Nearly 50% of patients with scleritis, and more than 30% of those with episcleritis, have an underlying systemic disease.[2,4,9,21,33] Therefore, treatment must include a suitable workup with the understanding that scleritis is the first manifestation of systemic disease in only 15% of patients (*Table 1*).[3] Many clinicians defer this testing in episcleritis cases unless it is refractory or has a high rate of recurrence. Once discovering



This 58-year-old male with diffuse anterior scleritis was placed on naproxen 500mg BID, but continued symptoms warranted an increase to TID. The inflammation persisted, and we chose to change from naproxen to indomethacin 50mg TID. The patient responded well and the condition resolved.

systemic disease, clinicians should consult the proper specialist for management. Some state RA is the most common systemic condition associated with scleritis, while others found RA with vasculitis—particularly granulomatosis with polyangiitis (GPA)—was the number one cause.[12,33] Still others recorded GPA and relapsing polychondritis as top offenders.[3]

A thorough case history, a review of patient symptomatology, comparative clinical findings and further diagnostic tools are keys to helping clinicians successfully differentiate between episcleritis and scleritis. The right diagnosis and prompt treatment leads to improved outcomes, as does adhering to a multidisciplinary approach when applicable. ■

Dr. Williamson is the residency supervisor at the Memphis VA Medical Center and is adjunct faculty at multiple optometry schools.

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Glaucoma Therapy:
Don't Forget the Ocular Surface

Following the mantra "do no harm" can be a challenge when prescribing topical glaucoma medications. These tips can help minimize damage.

By Leslie O'Dell, OD, and Ben Gaddie, OD

An estimated 2.2 million Americans have glaucoma and 20 million have dry eye disease (DED)—odds are, practitioners are bound to see patients diagnosed with both.[1,2] Research suggests the comorbidity of DED in patients treated topically for ocular hypertension and glaucoma could be as high as 20% to 59%.[3] But few step back to consider the association between these two chronic and progressive diseases.

Often, it's nearly impossible to decipher which disease came first and how much of the DED is iatrogenic—caused inadvertently by a medical treatment or procedure.

DED may stem from the medical treatment of glaucoma, for example. Studies show 38% of glaucoma patients are using a tear substitute, and the mainstay topical medications for glaucoma management come with side effects such as allergy, toxicity, immuno-inflammatory effects, punctate keratitis, conjunctival inflammation and disruption of the tear film.[4,5] These all result in reduction of the lipid and aqueous layers, damage to the goblet cells and neurotoxicity to corneal nerves.[4,5] With each additional medication involved in the treatment of glaucoma, the risk of an adverse event or possible exacerbation of dry eye multiplies.[6-8] Here's a look at the ocular surface in patients being treated for glaucoma—and how you can help protect it.

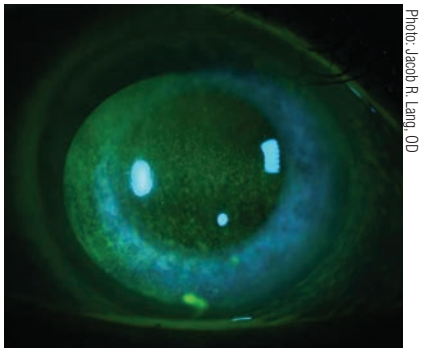

Photo: Jacob R. Lang, OD

Fig. 1. Corneal staining in the form of punctate epitheliopathy is a diagnostic finding for DED. Many BAK-containing glaucoma medications can cause this presentation, so ask glaucoma patients about ocular comfort during follow-up, as duration of use and multiple medication use increases the risk.

Treatment-related DED

Topical intraocular pressure (IOP)-lowering medication is often the first-line treatment for glaucoma patients. These agents not only contain their active ingredients for IOP lowering, but also excipients, including buffers, preservatives, drug vehicle and viscosity agents—all of which may negatively impact the ocular surface (*Table 1*). Some risk factors for iatrogenic DED as a result of topical glaucoma treatment include the duration of treatment, concentration of preservatives in the medication, the number of medications being used, a higher baseline IOP and disease severity.[6,9,10]

While randomized clinical trials of contemporary glaucoma drugs show decent tolerability, studies fail to depict their effects on the ocular surface because patients at risk for ocular surface disease are excluded, the study durations are short and they don't evaluate the effects of multiple meds on the ocular surface.[5]

Researchers now know the negative effects of glaucoma medications on the ocular surface are

dose-dependent.[7,8,11] In addition, studies show the prevalence of DED increases with multiple medication use.[6-8] In one study, 11% of patients using one medication reported dry eye symptoms, while 39% on two medications and more than 43% on three medications reported symptoms such as irritation, foreign body sensation, transiently blurred vision and increased blinking.[12]

The very pharmacokinetics of glaucoma medications can cause tear film alterations.[5] Medication administration onto the ocular surface for 15 to 20 seconds provides a low bioavailability of less than 5%, and absorption is affected by the medication's pH level and viscosity.[11,13] Absorption is also influenced by the drug's tear solubility and ocular surface permeability. For example, prostaglandin analogs (PGAs) require corneal esterases to convert the drug to the free acid form, which has the actual therapeutic effect as a prodrug.[14] The retention time is longer for more viscous solutions, allowing for increased absorption. This influences the drug's bioavailability and thus efficacy, but also increases the risk of an adverse effects (*Figure 1*).

The pH of a medication is also important for corneal penetration and absorption of the therapeutic agent. A healthy tear film has a pH ranging from 7.3 to 7.7 and is at the lowest (more acidic) in the morning upon awakening.[15] For a glaucoma medication to be comfortable with instillation, the pH should be between 6 and 8.[15] A topical glaucoma medication within this range allows for better drug absorption due to decreased lacrimation from discomfort, as well as less risk for tissue damage.

Some drugs, such as Trusopt (dorzolamide, Merck), Cosopt (dorzolamide hydrochloride-timolol maleate, Akorn) and Zioptan (tafluprost ophthalmic solution, Akorn) have a lower pH at 5.6, 5.65 and 5.5, respectively, making them less tolerable with increase symptoms of instillation irritation and lacrimation with instillation (*Table 2*).

Many glaucoma drugs contain preservatives, namely benzalkonium chloride (BAK). This quaternium ammonia is necessary to prevent microbial contamination and prevent breakdown of the active ingredient in multidose formulations. While good for bioavailability of the medication, they are not ideal for corneal health. BAK, for example, disrupts tear film homeostasis by stripping away the lipid layer, leading to increased evaporation and entry into the vicious circle of tear film instability.[15] Once in the vicious circle, hyperosmolarity of the tear film is followed by inflammation to the ocular surface, release of an inflammatory cascade of cytokines and damage to goblet cells and corneal and conjunctival tissues; if left untreated, the cycle perpetutes.[16]

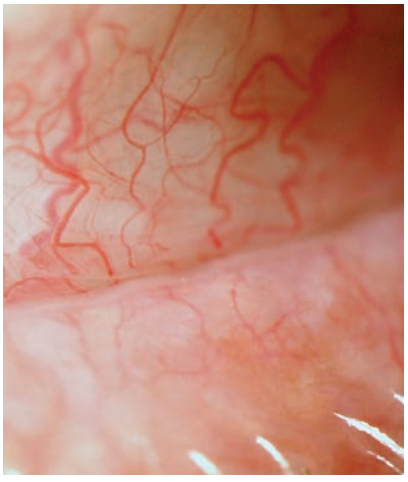

Fig. 2. Inflammation is present in all forms of DED. Conjunctival hyperemia to the meibomian gland orifice can be seen clinically, as pictured here.

One survey of 9,658 glaucoma patients found a significant difference in patient experience between preservative-free and preserved medications.[17] Eliminating preservatives led to a decrease in dry eye sensations from 34.9% to 16%, and simply by removing BAK, the clinical finding of corneal staining, a diagnostic criteria for DED, was reduced by 35%.[16] Another study found switching to preservative-free formulations reduced discomfort upon instillation, foreign body sensation, dry eye symptoms, tearing and

Table 1. Known Ocular Side Effects From Glaucoma Medications

Medication	Ocular Side Effects
Carbonic anhydrase inhibitor	Allergic reaction, blepharitis, blurred vision, burning/stinging, conjunctival edema, conjunctivitis, discharge, dryness, hyperemia, keratitis, photophobia, tearing
Alpha-agonist	Burning/stinging, blepharitis, blurred vision, conjunctival blanching, conjunctival follicles, conjunctival hyperemia, conjunctivitis, dry eye, keratitis, eyelid erythema, foreign body sensation, lid edema, pain, photophobia, tearing
Beta-blocker	Burning/stinging, blurred vision, conjunctivitis, contact dermatitis, eyelid erythema, photophobia, punctate keratitis
Prostaglandin analogs	Allergic reaction, burning/stinging, blepharitits, blurred vision, cataract, conjunctivitis, cystoid macular edema, dry eye, eyelash growth, eyelid skin darkening, foreign body sensation, hyperemia, iris color changes, iritis, pain, punctate keratitis
Cholinergic agents	Burning/stinging, blurred vision, conjunctival injection, decreased night vision, decreased vision due to ciliary spasm, myopia and retinal detatchment (rare), keratitis, periorbital headache (brow ache), tearing

eyelid itching.[18] The newer PGAs with preservative-free formulations and alternative preservatives show similar improvement of symptoms.[19] Researchers also found ocular surface improvement occurred as early as one month after removing the offending agent.[20]

Stay Proactive: Evaluate

When examining a patient using at least one glaucoma drug, clinicians should always pay close attention to the ocular surface, ask about dry eye symptoms and evaluate for signs of DED. The five-item Dry Eye Questionnaire (DEQ-5) or the Ocular Surface Disease Index (OSDI) should be repeated at every patient encounter, as the effects of topical glaucoma medications can be cumulative. DED is suspected if DEQ-5 is greater than six and if the OSDI staging of severity is mild (13 to 22), moderate (23 to 32) or severe (greater than 32). To evaluate for clinical signs of DED, clinicians can use one of three TFOS DEWS II recommended tools: noninvasive tear break-up time (NTBUT) or TBUT with fluorescein dye; tear film osmolarity; or corneal, conjunctival and lid staining with fluorescein and lissamine green vital dyes.[21] The dry eye testing sequence is important and should be performed from least to most invasive.

Osmolarity provides a measure of the tear chemistry including tear film stability and homeostasis. TearLab's osmolarity system collects and analyzes a 50nL sample of tears obtained from the inferior lateral meniscus and lid margin. Normal osmolarity ranges from 290mOsms/L to 300mOsms/L. An osmolarity of 309mOSms/L to 328mOSms/L is categorized as mild to moderate, and higher than 328mOsms/L is considered severe.[22] An inter-eye difference of 8mOsms/L or greater also indicates tear film instability and may be more diagnostic of DED than the level of osmolarity in each eye.[23]

NTBUT measures, as well as TBUT with fluorescein dye, should always be taken after tear osmolarity. A TBUT reading of 10 or less indicates DED.[21]

Another point-of-care test currently available in the United States includes the InflammaDry test (Quidel) for the detection of elevated levels of matrix metalloproteinase (MMP-9) in tears (*Figure 2*).

Table 2. Glaucoma Medication pH Values

Medication	pH Value
Beta-blockers	
Betagan (levobunolol 0.25%, 0.5%, Allergan)	5.5 to 7.5
Betimol (timolol hemihydrate 0.25%, 0.5%, Santen)	6.5 to 7.5
Betoptic S (betaxolol 0.5%, Alcon)	7.6
Carteolol 1.0%	6.2 to 7.2
Istalol (timolol maleate 0.5%, Bausch + Lomb)	6.5 to 7.5
Timoptic, Timoptic XE (gel) (timolol maleate 0.25%,	7.0
Prostaglandin Analogs	
BAK-free latanoprost	7.0
Lumigan (bimatoprost, Allergan)	6.8 to 7.8
Travatan Z (travoprost, Alcon)	5.7
Xalatan (latanoprost, Pfizer)	6.7
Zioptan (tafluprost, Akorn)	5.5 to 6.7
Alpha-agonist	
Alphagan P (brimonidine 0.1%, Allergan)	7.4 to 8.0
Alphagan P (brimonidine 0.15%, Allergan)	6.6 to 7.4
Alphagan (brimonidine 0.2%, Allergan)	5.6 to 6.6
Carbonic Anhydrase Inhibitors	
Azopt (brinzolamide, Alcon)	7.5
Trusopt (dorzolamide, Merck)	5.6
Combination Therapy	
Combigan (brimolidine/timolol, Allergan)	6.5 to 7.3
Cosopt (dorzolamide/timolol, Akorn)	5.65
Simbrinza (brinzolamide/brimonidine, Alcon)	6.5

Protect the Ocular Surface

When left undetected or untreated, DED can significantly impact glaucoma management, as increased symptoms of ocular discomfort can lead to decreased medication compliance—a known risk factor for disease progression.[23]

In addition, tear film disruption can affect the reliability and reproducibility of diagnostic testing such as visual fields and OCT. One study found artificial tears QID for one week prior to visual field testing for patients with DED and glaucoma improved test time and results.[24]

When it comes to surgical management of glaucoma, a healthy ocular surface is even more important. Conjunctival inflammation from prolonged exposure to BAK can result in poor surgical outcomes due to conjunctival scarring.[25] Research also shows an association between long-term topical glaucoma medication use and fibroblast proliferation of Tenon's capsule and elevated MMP-9 levels, which can contribute to filtering bleb scarring following trabeculectomy.[26] Another study shows inferior fornix shortening with topical glaucoma therapy for three or more years.[26]

The Meibomian Glands

While the many adverse events to the tear film and ocular surface associated with topical glaucoma treatments are well known, the impact on the meibomian glands is not. One study looked at the effects of beta-blockers and PGAs on meibomian gland function and morphology and found a positive correlation between topical treatments and decreased gland structure and function.[27]

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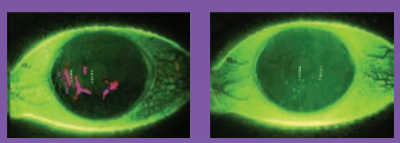

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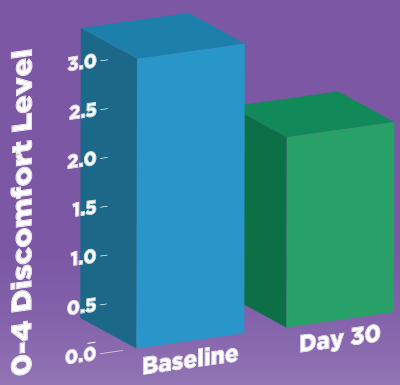


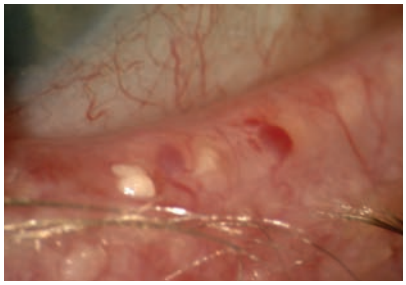


Fig. 3. MGD is a common cause of evaporative dry eye. Examining the lid for structural and functional gland changes—such as thickened meibomian gland secretions, as seen here—should be routine.

Another study of meibomian gland epithelial cell survival rates when exposed to pilocarpine and timolol found a dose-dependent survival rate on cell culture, but not with the drug levels accumulating near the glands during instillation.[28]

Much is unknown about the meibomain glands and their function, but clinical practice suggests PGAs have an inflammatory effect on the meibomian glands, evidenced by the thickened and red eyelid margin and tissue surrounding the meibomian glands (*Figure 3*). Meibomian gland assessment should remain an integral part of the comprehensive dry eye exam for glaucoma patients.

Treatment: Choose Wisely

Many choices exist when managing glaucoma patients, and clinicians should try to reduce the risk of iatrogenic DED whenever possible, especially in patients with multiple factors associated with dry eye. PGAs are often the first-line choice, as they offer great IOP reduction and convenient dosing. However, PGAs can lead to meibomian gland obstruction, which makes it less than ideal for patients with pre-existing MGD. Topical beta-blockers, however, can reduce aqueous secretions and may not be ideal for patients with autoimmune conditions such as Sjögren's syndrome, where aqueous secretions are already reduced.

A number of preservative-free and BAK-free glaucoma medications exist. Clinicians should consider starting patients with a BAK-free medication if possible. If a medication with BAK is unavoidable, a medication with the lowest concentration is the best option to start with. Before adding a second medication, clinicians should consider changing to a combination therapy to reduce the BAK load on the ocular surface, Cosopt PF is the only combination medication offering combination therapy with a BAK-free formulation (*Table 3*). ImprimisRx, a new concept in the pharmaceutical industry, uses compounding pharmacies to formulate preservative-free medication options (*Table 4*). While promising, these drugs should be used with caution, as they do not undergo the same FDA screening for safety, and contamination is a concern.

Alternative therapies such as selective laser trabeculoplasty (SLT) or minimally invasive glaucoma surgery (MIGS) may eliminate medication-induced effects, which should reduce the risk for dry eye symptoms. Research shows SLT is effective for both primary and adjunctive glaucoma treatment with a mean IOP reduction of 3.8mm Hg to 8.0mm Hg after six months to one year and a mean success rate of 55% to 82 % in the same time frame.[29] MIGS surgery can also be effective at lowering IOP, and lowers patients' dependency on topical therapies by increasing outflow through Schlemm's canal.[30]

Restore the Tear Film

Despite rigorous follow up and scrutiny, glaucoma patients often end up with iatrogenic DED from topical therapy. When treating the ocular surface, the main focus should be on restoring homeostasis and reducing the inflammatory response to the topical medications. Therapies such as Restasis (cyclosporine, Allergan) or Xiidra (lifitegrast, Shire) are often the first choice therapy for DED. As these add to a patient's daily list of drops, proper education is paramount to ensure they wait between drop for proper clearance of each medication.

Patient education on the side effects of DED therapy, including burning with instillation, blurred vision and dysgeusia, will improve medication compliance rates. It is possible that as the ocular surface heals, some of the side effects could diminish. Treatments for MGD include heat with at-home heat masks, as well as in-office LipiFlow (TearScience) and manual expression—an often necessary step,

Table 3. BAK Concentrations in Glaucoma Medications

Medication	BAK (%)
Alphagan P (brimonidine, Allergan)	BAK-free
Cosopt PF (dorzolamide/timolol, Akorn)	BAK-free
Timoptic XE (timolol maleate, Bausch + Lomb)	BAK-free
Travatan Z (travoprost, Alcon)	BAK-free
Zioptan (talfluprost, Akorn)	BAK-free
Simbrinza (brinzolamide/brimonidine, Alcon)	0.003
Alphagan (brimonidine, Allergan)	0.005
Betagan (levobunolol, Allergan)	0.005
Combigan (brimolidine/timolol, Allergan)	0.005
Lumigan (bimatoprost, Allergan)	0.005
Cosopt (dorzolamide/timolol, Akorn)	0.0075
Trusopt (dorzolamide, Merck)	0.0075
Azopt (brinzolamide, Alcon)	0.01
Betoptic S (betaxolol, Alcon)	0.01
Timoptic (timolol maleate, Bausch + Lomb)	0.01
Xalatan (latanoprost, Pfizer)	0.02

though it adds to your patient's treatment burden.

As with all patients, follow up is key. Patients with DED and glaucoma are often juggling multiple medications, and return visits are important to continue to monitor the ocular surface to ensure both treatments remain effective.

Identifying dry eye in patients undergoing glaucoma treatment is integral to comprehensive care. Often, we are so busy attending to the first disease that we ignore the fact that its remedy may adversely affect the ocular surface. But identifying DED in our glaucoma patient population may allow for earlier intervention, including a chance in glaucoma management and initiation of DED therapies. ■

Dr. O'Dell is the director of the Dry Eye Center of Pennsylvania at Wheatlyn Eye Care in Manchester, Pa.

Dr. Gaddie is owner and director of Gaddie Eye Centers in Louisville, Ky.

Table 4. ImprimisRx Glaucoma Combination Drop Therapy

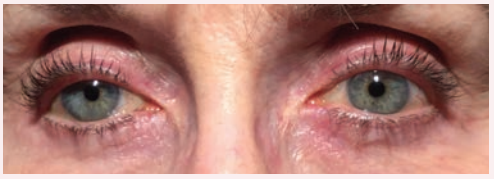
Medication	Concentration	Unit
LAT (latanoprost)	0.005%	5mL
TIM-LAT (timolol/latanoprost)	0.5/0.005%	5mL
BRIM-DOR (brimonidine/dorzolamide)	0.15/2%	10mL
TIM-BRIM-DOR (timolol/brimonidine/dorzolamide)	0.5/0.15/2%	10mL
TIM-DOR-LAT (timolol/dorzolamide/latanoprost)	0.5/2/0.005%	5mL
TIM-BRIM-DOR-LAT (timolol/brimonidine/dorzolamide/latanoprost)	0.5/0.15/2/0.005%	5mL
Triple/quad kit: • TIM-BRIM-DOR (timolol/brimonidine/dorzolamide) • TIM-BRIM-DOR-LAT (timolol/brimonidine/dorzolamide/latanoprost)	 0.5/0.15/2% 0.5/0.15/2/0.005%	 10mL 5mL

ImprimisRx. Compounded ophthalmic formulations. September 2017. www.imprimisrx.com/assets/IMPO0114-Rev6_Fold-out-Product-List_pgs.pdf. Accessed October 4, 2017.

Pitfalls of PGA Treatment

Glaucoma patients using PGAs may be at risk for prostaglandin-associated periorbitopathy, a condition that includes:

- Ptosis
- Relative enophthalmos
- Inferior scleral show
- Periorbital fat atrophy
- Involution of dermatochalasis
- Hypertrichosis



This patient has prostaglandin-associated periorbitopathy with deepened sulci bilaterally due to periorbital fat atrophy and ptosis. After topical treatment with a PGA for more than 10 years, she also has a relative endophthalmos with a sunken globe appearance.

Many of these side effects are irreversible, and clinicians should be cautious when initiating treatment with PGA medications, especially for patients treated monocularly. Patients should also be educated on the possible cosmetic side effects.

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THE ORIGINS AND MANAGEMENT OF CONTACT LENS DISCOMFORT

Understanding how this irritating nuisance develops is the first step toward fighting its deleterious effects. **By Dan Fuller, OD**

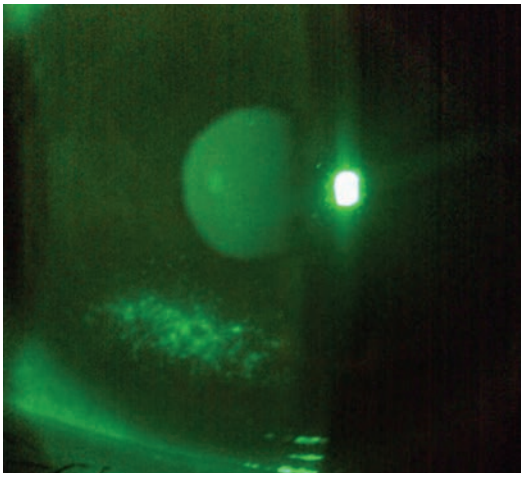

Fig. 1. Example of corneal staining representative of desiccation while wearing a Group IV lens in patient with severe ocular surface disease.

Contact lens discomfort (CLD) is a distinctly different entity than dry eye disease (DED), whose prevalence is estimated at 30%.[1-4] Numerous studies identify CLD (prevalence 30%) as a major contributing factor to contact lens dropout rates with best estimates placing it between 12% and 51%.[2,5-8] The broad range of values is a function of varying definitions of what constitutes a dropout (e.g., reduced wearing time, temporary or permanent discontinuance).

CLD creates significant burdens on patients and dramatically affects industry profitability. Identifying these patients and the factors contributing the condition will inform management decisions.

The TFOS Workshop classifies CLD by contributory factors into two large baskets: contact lens-related and environmental etiologies (each with four individual subcategories).[1] This article focuses on soft lenses and reviews what we believe we know about contact lens-related factors, the contribution from environmental factors second and offers a rational, evidence-based management approach.

Release Date: November 2017
Expiration Date: November 15, 2020
Goal Statement: Contact lens discomfort can develop because of a number of issues, including poor lens wettability, low oxygen permeability or a host of environmental factors. Optometrists should be skilled at delineating these causes and the available contact lens materials so they can best target treatment and fit patients with the most approriate option.
Faculty/Editorial Board: Dan Fuller, OD

Credit Statement: This course is COPE approved for 2 hours of CE credit. Course ID is **55368-CL**. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.

Disclosure Statements:
Author: The author has no relationships to disclose.

Editorial staff: Jack Persico, Rebecca Hepp, William Kekevian, Michael Riviello and Michael Iannucci all have no relationships to disclose.

The Material World

Within the contact lens-related category of CLD are four subcategories:

(1) Surface and bulk material differences.

(2) Design differences.

(3) Fit and wear differences.

(4) Lens care factors.

Materials vary widely in both surface and bulk properties. Designs vary from rigid to hydrogel to silicone hydrogel and hybrids. Rigid gas permeable lenses represented 7% of all fits worldwide in 2016 while soft lens fits/refits constituted 91% of all fits (55% of which were silicone hydrogels).[9] Substantial differences in modulus, wettability and oxygen permeability prevent direct comfort comparisons between silicone hydrogels and data from hydrogel studies.[10,11] Lens attributes commonly considered potential influences on comfort include polymer composition, lubricity, water content and wettability.[12-20]

Various modifications to early hydrogel polymers increased their water content and hydrophilic nature. The objective was to improve wettability and oxygen permeability in an attempt to improve comfort.[21] Several studies demonstrate increasing water content can lead to increased dehydration, corneal desiccation and decreased end-of-day comfort by as much as threefold in FDA Group II and IV lenses.[22-25] However, these studies failed to consider the contributions from differences in lens design, leading to the conclusion on-eye bulk dehydration of materials is likely neither associated or causative of discomfort.[21,25] The higher the water content, the more moisture is essentially wicked away from the ocular surface to replace moisture lost from the lens polymer through dehydration, resulting in corneal desiccation and corneal staining (*Figure 1*).[26] Silicone hydrogel lenses tend to have water contents lower than 50%, and are classified as "low" water content by the FDA, though at least four silicone hydrogel lenses have water contents above this threshold.[27]

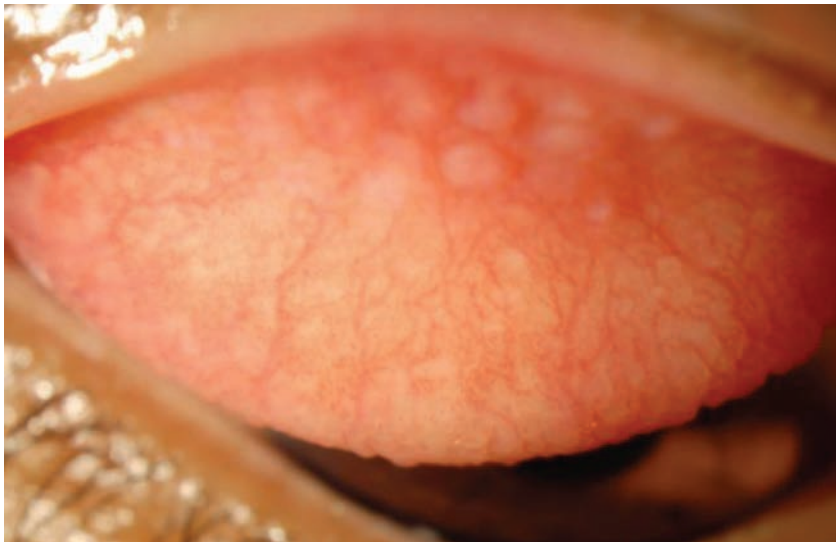

Photo: Christina Newman, OD

Fig. 2. Contact lens-related papillary conjunctivitis while wearing silicone hydrogel.

Increasing water content generally increases water and sodium chloride permeability more for ionic than non-ionic soft lenses.[28] This process is an order of magnitude less for silicone hydrogels than hydrogels since it appears to be more restricted by channels in the polymer.[28] The impact of ionicity on comfort has not been demonstrated conclusively.[21]

Research shows oxygen permeability increases with water content for hydrogel lenses, but the reverse is true for silicone hydrogel, owing to these fundamental differences.[21,29,30]

Not long after the introduction of modern silicone hydrogels late in the 1990s, interest in the contribution of modulus or stiffness to CLD began. "Stiffness" is a function of more than the material properties such as modulus, including water content, relative thickness and geometry of the lens.[12,31-33] The first generation silicone hydrogel lenses were high-modulus, low-water content designs with plasma coatings and contributed to higher rates of contact lens papillary conjunctivitis, superior arcuate epithelial lesions (SEAL) and corneal erosions and mucin balls (*Figures 2 and 3*).[12,31,33-38] Second and third generation designs reduced the incidence of these adverse events by eliminating plasma coatings in favor of internal wetting agents such as polyvinylpyrolidone (PVP) and by increasing water contents by altering the constituent polymers, resulting in more mechanical flexibility.[12] Notwithstanding some of the more prevalent adverse events associated with earlier high-modulus, low-water content designs, the Workshop on CLD concluded little difference in comfort between hydrogels and silicone hydrogels and when differences have been found, it is highly likely it resulted from methodological flaws in the study.[21,39]

The Workshop on CLD considered surface properties of contact lenses including friction, lubricity and surface wear (collectively referred to as tribology) and wettability.[21] Studies relating these surface properties to comfort are similarly plagued by confounding lens characteristics (e.g., sag and edge profile) or methodological challenges in

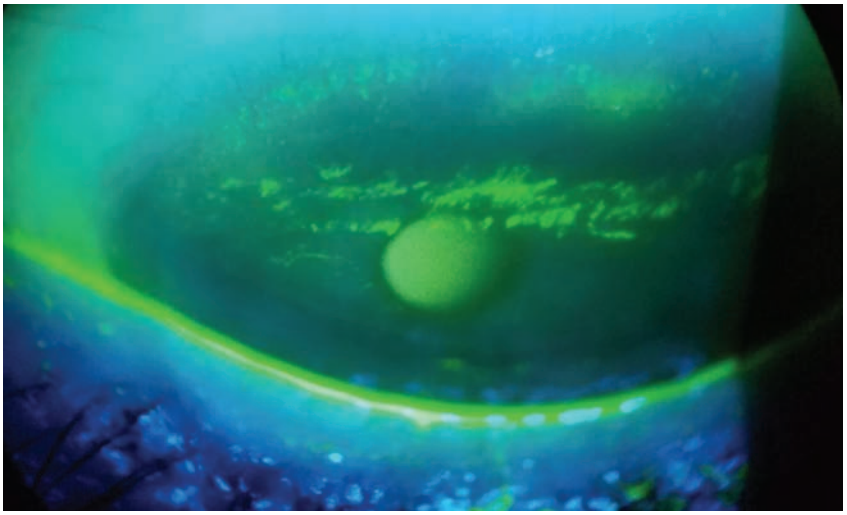

Fig. 3. Corneal erosions in high modulus silicone hydrogel in superior epithelial arcuate region.

attempting to model on-eye performance.[21,40] Notwithstanding, manufacturers have attempted to decrease friction and increase wettability at the lens surface by incorporating agents commonly used in over-the-counter wetting agents such as polyvinyl alcohol (PVA) and hyaluronic acid (HA) into their polymers.[41-43] Some of these are slowly eluted or activated while blinking and over the wear cycle. More recent designs such as deleficon A and nesofilcon A possess unique surface properties which have either not shown, or not tested, comfort differences over other lenses.[44,45] Interest in lid-wiper epitheliopathy and lid parallel conjunctival folds is growing as a possible predictor of CLD and may be related to studies investigating the role of frictional forces.[40,46-51]

Lens Design and Fit

Consideration of comfort must also include a review of fitting characteristics and lens design. Fitting characteristics are familiar to all clinicians and include coverage, movement and centration. Design attributes include edge profile, sphere, toric and multifocal parameters. Studies demonstrate a larger lens diameter can be a significant predictor of comfort.[52] Most spherical soft lenses typically fall within a range of 13.8mm to 14.2mm.[21] These values are above the largest diameter of 13.5mm used to study, which may explain why diameter (corneal coverage by extension) has not been shown to be associated with comfort in more recent studies.[40,52-55]

Lens movement contributes to tear exchange but the contribution of lens movement (or lack thereof) to comfort is somewhat murky. Two large retrospective studies demonstrate "loose" fitting lenses are associated with discomfort and "tighter" lenses are not, but no clear consensus exists on the minimum difference between base curves which elicit awareness.[21,40,55,56]

Centration has not been studied in relation to comfort independent of looseness/tightness of fit and researchers suggest small amounts of decentration (<0.3mm) are unlikely to affect comfort.[21,40] A well-centered lens, with coverage and minimal amounts of movement (about 0.5mm to 1.0mm) in primary gaze, is associated with better comfort.[40,55]

Additionally, edge profiles appear to matter, with thin knife edges consistently demonstrating better comfort than chisel or rounded edges even though they have a higher association with paralimbal conjunctival staining (*Figure 4*).[57-59] Chisel edge profiles are associated with higher frequencies of conjunctival indentation, which is associated with discomfort (*Figure 5*).[60]

Regarding lens designs, prism ballasted toric lenses may be more likely to elicit symptoms of discomfort confused with dryness and may represent lid-lens interactions, but direct comparisons with spherical lenses are rare to absent.[21,61-63] Multifocal contact lens comparisons with spherical lenses are similarly rare but have shown no difference in comfort.[64]

Modality and Wear Schedules

Research does not show that daily wear is any more comfortable than extended wear (except upon waking), but that may be due to a shortage of robust clinical studies.[21] Though duration of lens wearing experience has a role in adaptation, it is difficult to separate the impact of duration from frequency of replacement or age.[21] Multiple circumstantial studies demonstrate improved comfort with increasing frequency of lens replacement, but it is difficult to separate out the findings from confounding variables of differences in lens material or care systems in comparison studies.[21] Masked, randomized, controlled studies are lacking. End-of-day comfort is clearly differentially worse for all contact lens wearers compared with non-wearers, with increasing symptoms in both groups.[65–67]

Lens Care

It may seem counterintuitive, but regardless of the nature of deposits, they have not directly been implicated in decreasing comfort.[21] However, the subject of lens care solution inter-

actions and their impact (positive or negative) on comfort is a subject of ongoing debates. It remains very difficult to assess individual impacts of constituent agents due to the confounding influences of their interactions, compliance methods and conflicts between *in vitro* and *in vivo* performance differences. Comparison studies exist, but are limited by the number of possible lens-solution combinations tested. Biocides include hydrogen peroxide-based, polyhexamethylene biguanide PHMB-based, Polyquad-based, and dual disinfection systems. The reality is that all FDA-approved systems have met current standards for biocidal efficacy against the challenge panel of organisms.

Peroxide-based systems begin at 3% concentration (30,000 ppm) and must be neutralized to 100 ppm, though threshold sensitivity is between 50 to 300 ppm or discomfort will be reported.[21] As previously mentioned, there are few direct comparison studies that control for potential confounding variables. Nonetheless, there is a "suggestion" peroxide-based systems provide better comfort with the limited data available.[68,69] Comparisons of comfort using PHMB- and Polyquad-based systems have occasionally favored Polyquad- based systems but the majority view is there is no difference in comfort.[70-75] Preservative uptake/release and induction of corneal staining with possible CLD is unique to each lens-solution combination, making it relatively unpredictable. Modern multipurpose solutions incorporate surfactants as both detergents and wetting agents. There is compelling evidence these can contribute to patient comfort by increasing the hydrophilicity of the lens surface, particularly in silicone hydrogels.[21] Similar findings exist for the surfactants and wetting agents commonly added to blister pack solutions.

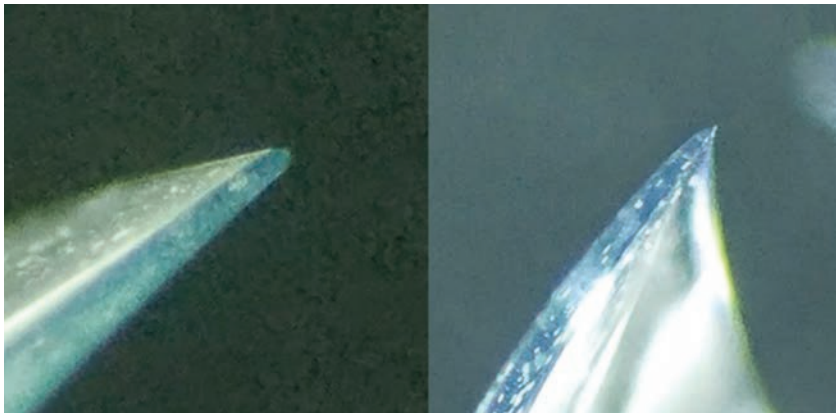

Fig. 4. Example of difference in edge profiles on -3.00D sphrerical lens designs, demonstrating a rounded, thicker edge in comifilcon A (left) and knife edge in senofilcon A (right).

Other Factors

We have summarized broadly the evidence supporting contact lens-related factors that may contribute to CLD. It may be unsatisfying, but nonetheless true, that there is no one factor most responsible for CLD. Rather, multiple lens and solution factors contribute to CLD. Factors such as discussion of wearing times, replacement intervals and modality must include consideration of environmental factors, controllable or uncontrollable. This section will summarize some of the more salient take-aways.

Non-modifiable patient factors surveyed in the Workshop on CLD included sex, age, ethnicity, tear film, blink characteristics, comorbidities and allergies.[2] The authors found females may have higher rates of CLD, but this does not appear to predicative of dropout. Younger patients report CLD more often than presbyopia patients do, particularly in hydrogels. Assessments of tear film volume and stability including phenol thread test, tear meniscus, noninvasive TBUT, and pattern of breakup correlate with CLD. Little evidence exists supporting an association between changes in blink rate and CLD, but stability of the tear film in the interblink interval may be related to CLD. Seasonal allergies may be associated with CLD. Ethnicity appears not to be associated with CLD, with little evidence supporting a relationship between systemic disease and CLD.[2]

Modifiable patient factors included medications, dietary habits, smoking, cosmetics, compliance and psychological factors. Use of oral contraceptives and isotretinoin have been associated with CLD but no other agents are conclusively documented as contributing to CLD. Poor compliance with replacement intervals is associated with CLD. There is little evidence to support the notion that dietary intake and fluids influence CLD. The influence of smoking on CLD lacks evidence. Little evidence supports an association between cosmetic use and CLD. Psychological factors have not been found to be associated with CLD.[2]

Ocular enviromental factors. Contact lens wear alters multiple aspects of the ocular anatomy and physiology, including: thinning and destabilization of the tear film; increasing tear osmolarity; loss or shortening of the meibomian glands; alterations to corneal sensitivity; cellular changes in the corneal and conjunctival epithelium.[2] Among these, the presence of lid-parallel conjunctival folds,

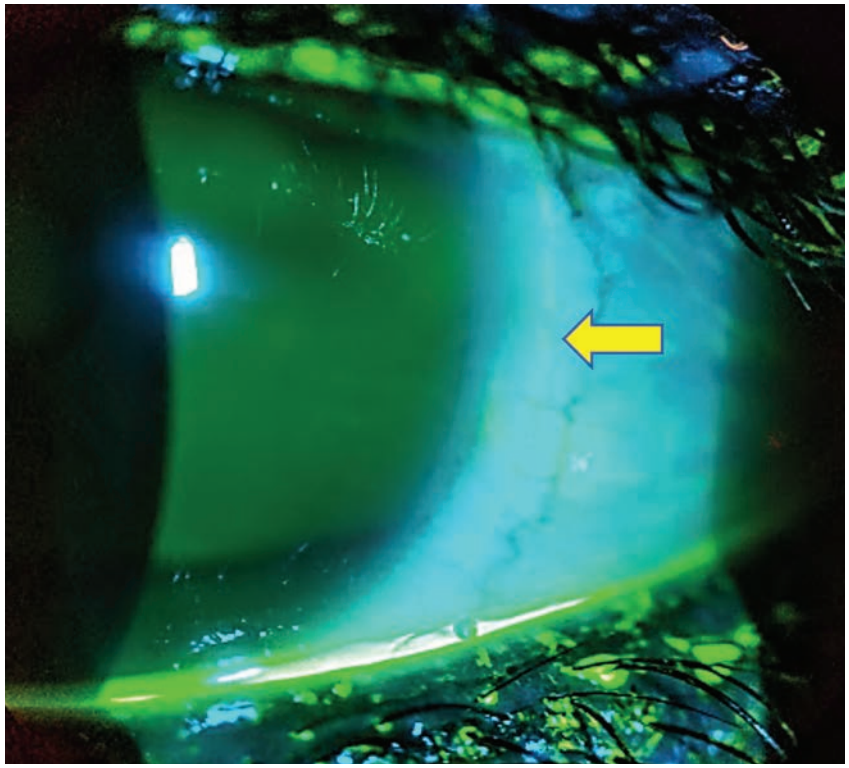

Fig. 5. Partial arcuate indentation of the nasal bulbar conjunctiva related to edge profile (yellow arrow).

Table 1. Management Strategies Based on 2013 TFOS Workshop on Contact Lens Discomfort[76]

Treatment strategy	Specific intervention
Replacement frequency	Increase
Material	No clear rule; switch to from higher to lower modulus within silicone hydrogel; switch from silicone hydrogel to hydrogel (or reverse); consider lower water content hydrogels
Add internal wetting agents	Consider silicone hydrogels lenses with PVP, PVA, hyaluronic acid.
Add external wetting agents	Preservative-free rewetting drops; modern MPS and peroxide disinfection systems offer surfactants and wetting agents
Elimination of the care system	Daily disposables
Change lens parameters	Steeper base curves; aspheric base curves; larger diameter; knife edge
Nutritional supplementation	Omega-6 in evening primrose oil
Punctal occlusion	Occlude upper and lower
Topical agents	Cyclosporin-A; lifitegrast
Digital device use and occupational exposure	Avoidance
Consider changing from GP to soft or vice versa	Consider in relationship to needs
Reduce wearing time	Adjust to find optimum level
Other	Orthokeratology; refractive surgery; spectacles

conjunctival metaplasia, decreased goblet cell density, meibomian gland dysfunction and lid-wiper epitheliopathy have been shown to be associated with CLD.[2]

External environmental factors reviewed included relative humidity, temperature, climate, air quality, atmospheric pressure and occupation. Among these, reductions in relative humidity, increased air movement and activities which reduce blink rates such as digital device use may all contribute to CLD.[2] The remaining factors lack evidence or are equivocal.

Management of CLD

History-taking continues to be the foundation of all patient encounters. Certain risk factors help identify wearers at risk for CLD. Younger patients are at increased risk; end-of-day discomfort or discomfort upon insertion; specifics on lens parameters; wearing time; replacement interval; care system; use of adjunctive wetting agents; compliance; occupation and vision demands; coexisting disease; allergies; and current medications.[76]

Strategically manage all underlying non-lens factors contributing to CLD, including diseases that contribute to ocular surface disease. Identify instances of inappropriate medication use, overuse or abuse, which may destabilize the tear film. Treat coexisting lid, tear film, cornea or conjunctival disease. Manage lens-related issues, including condition, fit and interactions with the eye. This approach is basic to all contact lens examinations.[76]

When confronted with lens wearers symptomatic for discomfort, one or more of the recommendations from the Workshop on CLD cited in *Table 1* may be employed based on your clinical assessment of the patient.[76] Not all strategies are supported by "level I" evidence and

a combination approach is often necessary. Implementing too many strategies at once and failing to manage underlying conditions may confuse your management plan. Be judicious and methodical.

CLD is ubiquitous, but we have never had more sophisticated lens and solution options. As our understanding continues to grow so, will our ability to provide wearers with lifelong comfortable, clear vision. Identify patients at risk and those with contributory conditions. Apply evidence-based management strategies in a methodical manner, increasing the probability for long-term success. ■

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

1. Which percentage best represents the number of contact lens wearers affected by contact lens discomfort worldwide?
a. 25%.
b. 50%.
c. 75%.
d. 100%.

2. Which percentage best represents the number of patients experiencing dry eye in the general population?
a. 10%.
b. 20%.
c. 30%.
d. 40%.

3. Which of the following definitions is responsible for the overly broad range of dropout rates?
a. Reduction in wearing time.
b. Temporary discontinuance of lens wear.
c. Permanent discontinuance of lens wear.
d. All the above.

4. Which TFOS workshop best summarizes what is known about contact lens discomfort?
a. DEWS I and II.
b. MGD.
c. CLD.
d. Delphi panel.

5. _____ is NOT a contact lens-related factor considered as a contributing factor to contact lens discomfort?
a. Materials.
b. Lens design and fit.
c. Modality and wear schedule.
d. Relative humidity.

6. Which percentage best represents the number of soft lens fits worldwide?
a. 7%.
b. 55%.
c. 80%.
d. 91%.

7. Which figure best represents the number of soft lens fits using silicone hydrogels?
a. 7%.
b. 55%.
c. 80%.
d. 91%.

8. Why are direct comparisons between hydrogels and silicone hydrogels are nearly impossible?
a. Inherent differences in surface and bulk properties unique to each lens.
b. Difficulty in controlling for differences in lens design.
c. Failure to mask investigators and/or subjects.
d. All the above.

9. Which statement regarding water content of hydrogel lenses is FALSE?
a. Higher water content is less likely to be associated with corneal staining.
b. Increasing water content increases dehydration rates.
c. Dehydration has been associated with corneal desiccation.
d. Bulk dehydration is neither associated or causative of discomfort.

10. Which statement is most accurate regarding silicone hydrogels?
a. Most have water contents less than 50%.
b. Permeability to sodium chloride and water is an order of magnitude less than hydrogels.
c. Increasing water content in silicone hydrogels does not increase oxygen permeability.
d. All the above are true.

11. Which of the following statements regarding comfort comparisons between hydrogels and silicone hydrogels is true?
a. Hydrogels are more comfortable.
b. Silicone hydrogels are more comfortable.
c. High water content lenses are most comfortable.
d. The question remains open due to confounding variables.

12. Which of the following adverse events is known to be associated with high modulus, first generation silicone hydrogels?
a. Contact lens papillary conjunctivitis.
b. Superior epithelial arcuate lesions.
c. Corneal erosions.
d. All the above are associated with first generation silicone hydrogels.

13. Which of the following is NOT a technique employed in second/third generation silicone hydrogels to reduce the frequency of adverse events?
a. Addition of plasma coatings.
b. Inclusion of internal wetting agents.
c. Increasing water content.
d. None of the above reduce adverse events.

14. Which of the following terms describes the study of friction, lubricity and wettability issues?
a. Troglodyteology.
b. Tribology.
c. Tribbleology.
d. Technology.

15. Which of these clinical signs is LEAST useful for identifying patients at risk for contact lens discomfort?
a. Corneal staining.
b. Lid-wiper epitheliopathy.
c. Lid parallel conjunctival folds.

OSC QUIZ

d. Lens movement in primary gaze greater than 1mm.

16. Which of the following lens design/fitting characteristics is LEAST likely to promote a comfortable fit?
a. Decentration less than 0.3mm.
b. Lens diameters greater than 13.5mm.
c. Lens design with a "knife" edge.
d. Prism ballasted toric designs.

17. Which of the following statements is LEAST accurate?
a. End-of-day comfort is worse for all individuals, regardless of lens wear.
b. Extended wear is less comfortable than daily wear at the end of the day.
c. More frequent lens replacement may be more comfortable.
d. There is a shortage of masked, randomized, controlled studies comparing modalities.

18. Which statement is MOST accurate regarding lens solutions?
a. Solutions preserved with PHMB are more comfortable.
b. Solutions preserved with Polyquad are more comfortable.
c. Peroxide systems are least comfortable.
d. Preservative uptake/release and impact on comfort is unique to each lens.

19. Which of the following non-modifiable factors has been shown to be positively associated with contact lens comfort?
a. Male gender.
b. Younger age.
c. Ethnicity.
d. Increased blink rates.

20. Which of the following modifiable or environmental factors has NOT shown to contribute to contact lens discomfort?
a. Oral contraceptive or isotretinoin use.
b. High relative humidity.
c. Decreased goblet cell density.
d. Digital device use.

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Examination Answer Sheet

The Origins and Management of Contact Lens Discomfort

Valid for credit through November 15, 2020

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Answers to CE exam:

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
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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. Improve my background in the development of contact lens discomfort. ① ② ③ ④ ⑤
22. Become familiar the oxygen permeability issues associated with different lens materials. ① ② ③ ④ ⑤
23. Better understand how to recognize adverse events related to contact lens discomfort. ① ② ③ ④ ⑤
24. Teach me to recognize and delineate the different types of environmental factors. ① ② ③ ④ ⑤
25. Better manage patients suffering from contact lens related discomfort. ① ② ③ ④ ⑤
26. Inform me of lens material options for CLD patients. ① ② ③ ④ ⑤

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

27. The content was evidence-based. ① ② ③ ④ ⑤
28. The content was balanced and free of bias. ① ② ③ ④ ⑤
29. The presentation was clear and effective. ① ② ③ ④ ⑤
30. Additional comments on this course:

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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 115667 RO-OSC-1117

Graft-vs.-host Disease: How, Why and What Next

Dry eye is rampant in this population, and other complications abound.

By Heather Spampinato, OD, and Matthew Hochwalt, OD

Graft-vs.-host disease (GVHD)—an abnormal immune response to healthy host tissue following stem cell transplantation for the treatment of hematologic diseases—can be a complex condition for eye care practitioners to manage. It can lead to a host of ocular complications, the most significant of which is dry eye—seen in 40% to 76% of patients with GVHD.[1] In particular, ocular GVHD can cause permanent severe aqueous-deficient dry eye (ADDE), as well as other dry eye etiologies, which can be visually debilitating. It is critical that practitioners correctly identify dry eye caused by GVHD and treat accordingly.

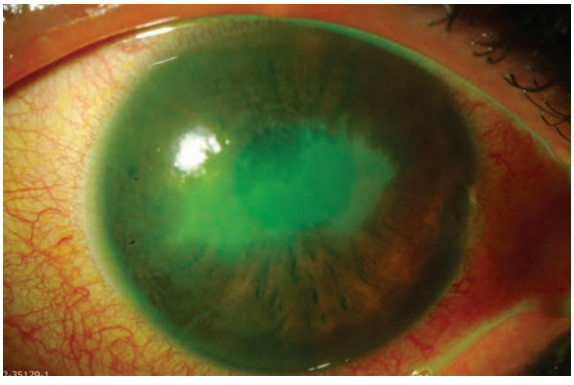


Photo: Christine W. Sindt, OD

Keratoconjunctivitis sicca is one manifestation that can help clinicians diagnose chronic GVHD.

Disease Presentation

The onset of GVHD typically follows allogeneic hematopoietic stem cell transplantation (HCT), a therapy commonly used for patients suffering from a range of malignant and non-malignant hematologic diseases such as anemia, leukemia and thrombocytopenia.[2]

HCT most often follows the eradication of malignancies with chemotherapy, radiation or both, to replace stem cells lost from the blood and prevent patient mortality.[3] GVHD occurs when the donor immune system attacks healthy recipient cells as foreign.[2] Incidence of GVHD varies from 25% to 80% after allogeneic HCT, although most studies put it close to 50%.[4]

Human leukocyte antigen (HLA) disparity is by far the most powerful risk factor for the development of GVHD.[5,6] Matching the donor HLA as close as possible to the recipient is critical before transplantation, as donor T-cells will view the host's cells as foreign and attack if a large enough discrepancy is present.[5] Other risk factors for GVHD include implantation of donor cells in a recipient of the opposite gender, advanced age of the recipient and significant damage during the conditioning process, a necessary step that serves to eradicate the host's diseased cells and prevent rejection of the graft.[7] However, it can also activate the host's antigen presenting cells, in turn stimulating proliferation of donor T-cells.[8]

Forms of GVHD

GVHD can present as either acute or chronic. Most clinicians classify the disease based on the pathologic nature of the inflammation (*Table 1*). Acute GVHD, most commonly seen within the first 100 days after transplantation, resembles a toxic-like syndrome, which is typically seen in response to bacterial toxins. When acute GVHD affects the eyes, it usually responds well to steroids or other immunosuppressants.[9,10]

Table 1. Acute vs. Chronic GVHD[11,13-15]

	Acute	Chronic
Timing	Less than 100 days after transplant	More than 100 days after transplant
Pathophysiology	Direct donor T-cell response towards recipient cells	Loss of regulation of central tolerance causing indirect activation of the host's T-cells against self
Tissues typically affected	Skin, bile duct and gastrointestinal system	Skin, lungs and mucous membranes

Chronic GVHD can have more dramatic ocular side effects and can cause significant long-term damage to the anterior segment of the eye. It is commonly seen more than 100 days after transplantation and has a relatively unknown pathophysiology. Successfully diagnosing chronic GVHD requires distinguishing from acute GVHD and other possible diagnoses, as well as identifying at least one distinctive manifestation of the disease, such as keratoconjunctivitis sicca, confirmed with diagnostic testing such as the Schirmer test.[11,12] More recently, NaFl corneal staining is the preferred method for diagnosing keratoconjunctivitis.

Ocular Effects

GVHD can affect many ocular structures, including:

Lacrimal and meibomian glands. Chronic GVHD can affect several tissues of the eyes, the most common and most significant of which are the lacrimal glands. Research shows CD4+ and CD8+ T-cells cause cytotoxic effects on the periductal epithelial cells of the lacrimal gland.[16,17] This damage causes permanent stenosis of the duct, resulting in moderate to severe ADDE similar to Sjögren's syndrome (SS). One study found the tear turnover rate in GVHD patients is similar to that of patients with SS.[18] The same study found the evaporation rate was highest in GVHD patients, and their lipid layer was the most unstable.[18] Although the signs of ocular GVHD are similar to those with SS, ocular GVHD shows prominent fibrosis and an increase in activated T-cells and stromal fibroblasts in the glandular ducts, while SS shows the fibrosis and inflammation distributed through lesions in the acinar region of the lacrimal gland.[16]

Severe meibomian gland dysfunction (MGD) is also common in patients with GVHD. Interferometry confirms a decrease in the tear lipid layer in patients with ocular GVHD.[19] However, research has yet to determine if the lipids are directly affected by the GVHD inflammation or due to the radiation during the conditioning process, which can destabilize the lipid layer.[20,21] Regardless, it can cause further evaporation of the already-depleted aqueous of the tears.

Conjunctiva. Researchers estimate 12% of patients with acute GVHD and 11% of patients with chronic GVHD exhibit some form of conjunctival involvement.[22] Inflammation can result in changes ranging from mild erythema to cicatrizing conjunctivitis similar to ocular cicatricial pemphigoid.[22] Conjunctival inflammation tends to be more significant in acute GVHD and is more commonly hemorrhagic in presentation.[23] Investigators have also linked GVHD patients to an increased incidence of conjunctival carcinoma.[24]

Cornea. Typically, this structure is not directly targeted in this disease process; however, significant secondary effects from lacrimal gland damage and altered tear makeup are often evident. This manifests as

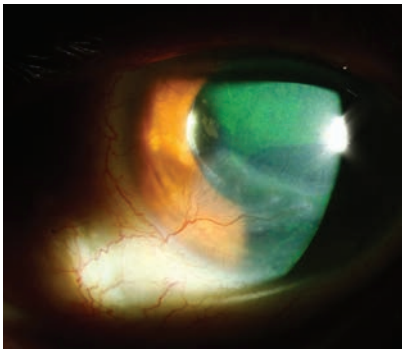


Photo: Christine W. Sindt, OD

Corneal neovascularization and scarring as a complication of GVHD.

keratoconjunctivitis sicca, which, when severe, can lead to filamentary keratitis, corneal ulceration and corneal perforation.[25,26] In rare cases, an immune-mediated limbitis can result in progressive neovascularization.[27]

Lenticular. Cataracts are a common ocular complication, with one study finding lens opacity in 39.4% of patients with GVHD.[28] However, researchers note the lenticular changes were likely secondary to steroid use, radiation or both, as opposed to the disease itself.[29]

Posterior segment. When this is involved, which is rare, researchers speculate it may be secondary to the radiation or high-dose steroid treatments and not a direct complication of ocular GVHD.[30]

Dry Eye Diagnosis

In ocular GVHD, performing a diagnostic evaluation for dry eye is essential to determine the severity of the disease and monitor for improvement. Clinicians should use sodium fluorescein, rose bengal or lissamine green staining to determine both corneal and conjunctival involvement. Additional diagnostic tests include tear break-up time (TBUT), Schirmer scoring, meibomian gland evaluation, corneal sensitivity and tear osmolarity.[31,32] A Schirmer score of less than 5mm at five minutes or new-onset dryness with a Schirmer score of 6mm to 10mm is sufficient for a diagnosis of chronic GVHD if distinctive manifestations are also seen in at least one other organ.[11,31,32]

In general, dry eye disease is characterized by hyperosmolarity of the tear film, which can lead to surface epithelium impairment by activation of proinflammatory cytokines released into tears.[33] Research indicates a statistically significant correlation between tear hyperosmolarity and TBUT with osmolarity testing, but the same correlation is not seen with Schirmer testing or vital dye staining.[33] Therefore, TBUT is an important measure of dry eye severity for patients with GVHD.

Numerous grading systems exist to assess the severity of ocular surface disease in these patients. The National Institutes of Health (NIH) research group developed one specifically for diagnosing and staging GVHD, which takes into consideration the severity of dry eye along with its effect on activities of daily living (*Table 2*).[11] However, the NIH scoring system does not take into account the degree of corneal staining or other dry eye findings, instead focusing on the frequency of topical lubricant use. Because of this, some researchers and clinicians use the Dry Eye Workshop score, which is based on patient symptomatology, Schirmer score, TBUT, corneal and conjunctival involvement, as well as MGD.[34]

Ocular Treatment

Treating GVHD actually begins with prevention, which is accomplished through T-cell depletion. Prophylactic treatment is not without risks, which can include increased rates of graft failure, relapse of malignancy and infection.[32] If preventative therapy fails, systemic immunosuppression is the mainstay for both acute and chronic GVHD. However, despite adequate systemic therapy, ocular complications may still arise. Ocular GVHD treatment focuses on increasing ocular surface moisture and decreasing ocular surface inflammation.[26,31]

Lubricants. Treatment typically begins conservatively with the use of preservative-free artificial tears and ointments, which are less likely to cause epithelial toxicity.[35] Research also suggests hydroxypropyl cellulose ophthalmic inserts can improve dry eye symptoms and decrease the frequency of artificial tear use.[26]

Punctal Plugs. As lubricants alone are rarely adequate for the severe dryness seen in GVHD, punctal plugs may be a useful therapeutic option. Patients can show significant subjective improvement in symptoms and decrease in corneal staining with the use of punctal plugs over the course of twelve months. Also, there does not appear to be an increase in ocular inflammation, infection or other adverse events with the use of punctal plugs in patients with ocular GVHD.[36]

Topical corticosteroids. Local topical treatment with corticosteroids decreases the overall risk associated

Table 2. NIH Ocular Scoring in Chronic GVHD[11]

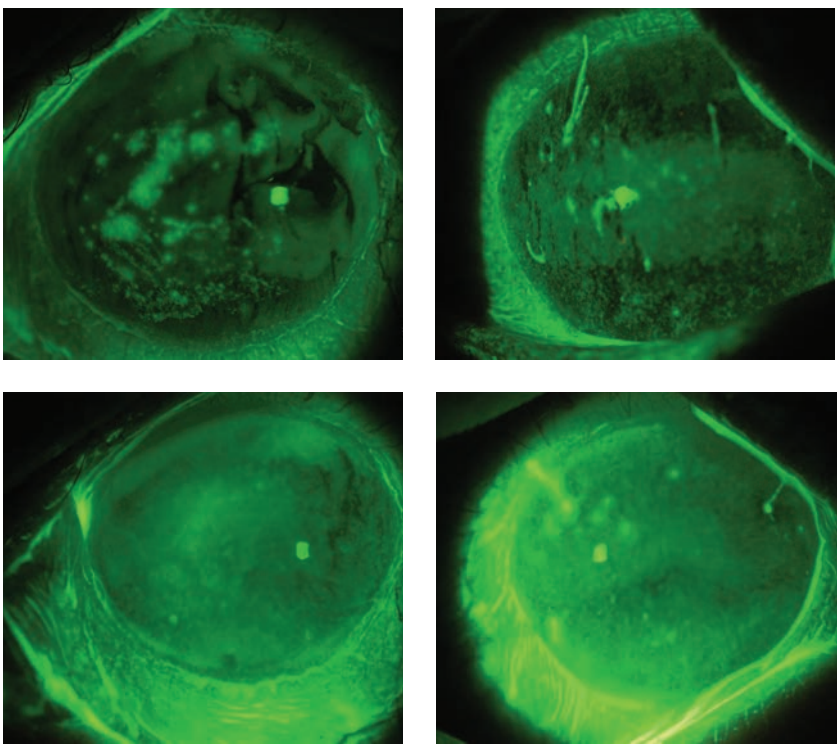
Score	Definition
0	No dry eye symptoms.
1	Mild dry eye symptoms not affecting daily activities (requiring eye drops ≤3x/day) or asymptomatic signs of keratoconjunctivitis sicca.
2	Moderate dry eye symptoms partially affecting daily activities (requiring drops >3x/day or punctal plugs), without vision impairment.
3	Severe dry eye symptoms significantly affecting daily activities (special eyewear to relieve pain) or unable to work because of ocular symptoms or loss of vision caused by keratoconjunctivitis sicca.

with prolonged and intense systemic immunosuppression and more effectively targets the affected area.[26,37] In particular, ocular corticosteroid use promotes lymphocytic apoptosis and suppresses cell-mediated inflammation in the eye more directly than does systemic administration.[37] Because long-term use of topical steroids carries the risk of steroid-induced glaucoma, cataracts, infectious keratitis and corneal thinning, many clinicians recommend short-term use combined with additional supportive therapy.[26,31,37]

Topical cyclosporine. This agent is another therapeutic option that shows great promise in the treatment of ocular GVHD. It is an immunosuppressive drug that inhibits T-cell proliferation on the ocular surface, increases goblet cell density in the conjunctiva, decreases epithelial cell apoptosis and interferes with the activity of proinflammatory cytokines in the conjunctiva.[38,39] Several studies indicate statistically significant improvement in Schirmer basal secretion tests, TBUT, corneal fluorescein staining and patient symptoms after twice-daily cyclosporine 0.05% for at least three months.[38,39] For refractory cases, compounding topical cyclosporine to 1% to 2% and increasing dosage to six to eight times per day may help promote healing during the early stages of ocular GVHD.[40]

Autologous serum. These eye drops contain epidermal growth factor, vitamin A, cytokines, nerve growth factors and fibronectin, all of which are essential for the proliferation, differentiation, maturation and integrity of the corneal and conjunctival epithelial surfaces.[32,41-43] Studies show autologous serum is effective in treating severe dry eye, and one

Photos: Alan Kwok, OD



These images depict a GVHD patient's eyes before (top) and after scleral lens wear, showing an improved ocular surface, including a reduction in filaments, after just a few hours of wearing time.

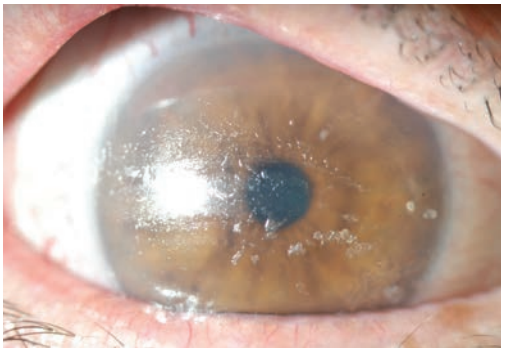


Photo: C. Kelly Olson, OD, MBA

Extreme poor wetting and lipid deposits in a GVHD patient.

demonstrated 20% autologous serum dosed two to three drops ten times a day is effective in improving fluorescein and rose bengal staining, TBUT, corneal sensitivity and patient symptoms in ocular GVHD patients resistant to conventional artificial tear therapy.[32,41-43]

Tacrolimus. Another potential treatment option in the management of ocular surface inflammation from chronic GVHD is topical 0.03% tacrolimus ointment. This medication is FDA approved for the dermatological treatment of atopic eczema but has been used off-label to treat eczematous eyelid disease, atopic keratoconjunctivitis and other anterior segment inflammation.[44] The mechanism of action is thought to be similar to that of cyclosporine, though the immunosuppressive potency of tacrolimus in vitro is 50 to 200 times greater than that of cyclosporine.[31,45] Although beneficial effects of systemic tacrolimus in GVHD have been well documented, data regarding its use topically is limited.[31,32,45]

Contact Lens Wear

Several contact lens types are often used to treat ocular GVHD, including bandage silicone hydrogel lenses and gas permeable scleral lenses. Research suggests contact lenses reduce friction pain and control evaporation from the inflamed ocular surface.[26] In one study, patients were fit in a monthly extended wear silicone hydrogel lens after failing to maintain adequate symptom control with topical lubricants and punctal plugs after three months.[35,46] Investigators showed statistically significant improvement in patient symptoms in as little as two weeks with the use of these lenses, but little to no improvement in clinical signs of ocular surface disease and no significant changes to the tear film.[35,46] Despite the absence of significant improvements in ocular surface disease, these lenses can still be considered in patients whose symptoms are not adequately controlled with conventional treatment. Patients fit in extended-wear contact lenses should be closely monitored due to the increased the risk of corneal edema, infiltrates, neovascularization and microbial keratitis.[47]

Scleral lenses may be the best option for treating ocular GVHD because the liquid reservoir beneath the lens allows for continuous hydration of the ocular surface, protecting against evaporation and aiding in resurfacing the damaged corneal epithelium, possibly by reducing the hyperosmolarity of the tear film.[48,49] The liquid reservoir also helps to mask corneal irregularity secondary to dry eye and can significantly improve visual acuity in these patients. Patients with ocular GVHD successfully fit in scleral lenses often report substantial improvement in pain and photophobia associated with the disease.[35,48]

Surgical Treatment

Patients with severe dry eye refractory to other treatment options can consider surgical management with tarsorrhaphy, amniotic membrane transplantation or punctal occlusion.[26] Amniotic membranes can aid in epithelialization and prevention of fibrosis and inflammation.[50,51] Research shows using sutureless amniotic membranes to treat moderate to severe dry eye significantly improves symptoms and ocular health for up to four months after treatment.[51]

Patients who do well with punctal plugs but experience recurrent extrusion may be good candidates for permanent occlusion with punctal cautery. In those with severe dry eye secondary to chronic GVHD, researchers found significant improvements in subjective symptom scores, Schirmer values, fluorescein and rose bengal scores and TBUT after thermal cauterization.[52]

Ocular GVHD is a complex and challenging condition to diagnose and manage. Because it can affect many ocular tissues, clinicians must properly identify all the ocular signs to determine the best treatment modality. Furthermore, early intervention is essential to reduce, or even prevent, the severe complications often associated with GVHD. A multidisciplinary approach is useful to determine when systemic, topical or other therapy options are best. These patients rarely return to a fully normal state due to lacrimal gland fibrosis and will need long-term treatment and follow up. ■

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Go Deep on Corneal Abrasions

Understanding the physiology of rupture and repair will improve your management decisions. **By Bisant A. Labib, OD**

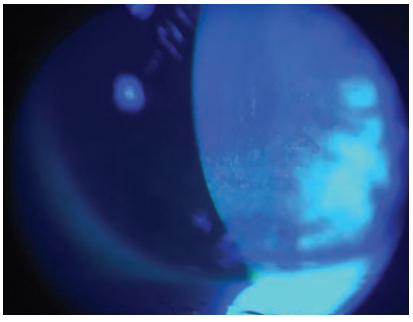
In daily practice, we tend to focus more on clinical signs and symptoms than pathophysiology, especially in corneal abrasion cases—the patient is in pain, infection risk is high and time is tight. The way we treat these patients prioritizes pain relief over a more holistic approach to the cornea's status and risk profile. But gaining a greater awareness of how such conditions progress can help inform our treatment choices. This month we do so by looking more deeply at the mechanisms of corneal trauma and wound repair.

Why the Cornea is Unique

The cornea contains the highest concentration of sensory nerves and nociceptors in the body, making pain management a primary concern.[1] Because the cornea is an avascular and immune-privileged site, wound repair involves several unique mechanisms, including epithelial cell proliferation, differentiation, migration and adhesion to the basement membrane.[2,3]

An intact corneal epithelium plays a vital role as a physical and mechanical barrier against infection, as well as in sustaining the necessary biochemical properties required for optical clarity.[4] Several mechanisms can compromise an intact cornea and manifest clinically as abrasions, dystrophies or degenerations, as well as refractive problems.

The corneal epithelium is made up primarily of three distinct cell layers: an outermost layer of squamous cells, a wing cell middle layer and finally the basal cells. In corneal abrasion, the basal layer—the only epithelial component capable of regeneration—begins to proliferate. Basal cells migrate and spread over the wounded lesion, and then differentiate into wing cells, which then differentiate further into the squamous cells that comprise the superficial corneal epithelium.[5]



Fluorescein stain under a cobalt blue filter depicts a diffuse breakdown of an otherwise intact corneal epithelium.

Keys to Corneal Wound Repair

Following injury, which appears clinically as a defect in the corneal epithelial surface that stains with fluorescein dye, several processes bring the cornea back to its normal state.

Epithelial cell migration. In the early stages of wound healing, migration and proliferation of epithelial cells are necessary for closure. The process of epithelial cell migration is highly metabolic, depending heavily on glucose from the aqueous humor, and occurs in two ways. First, transient amplifying cells (TAC) travel centrally to the abrasion site within the basal layer, where they then differentiate into the post-mitotic cells that comprise the more superficial epithelial layers. Concurrently, epithelial cells also migrate peripherally around the limbus until the wound is fully closed.[6] These migrating epithelial cells briefly express matrix metalloproteinase (MMP) and tissue inhibitor of metalloproteinase (TIMP) enzymes, which regulate the adherence between the injured epithelium and underlying basement membrane.[7] Fibronectin, an extracellular structural protein in the basement membrane that binds to cells and collagen, provides a provisional matrix with which epithelial cells can migrate. Along with collagen I and IV, fibronectin also increases cell motility and migration.[8] Systemic diseases, such as diabetes, may delay these metabolic processes and prevent the proper adherence of the epithelium to the basement membrane.[2]

Keratocyte release of matrix proteins. Corneal abrasions induce an acute inflammatory response and also result in the death of underlying keratocytes.[9,10] While diseases that cause chronic inflammation to the cornea are typically detrimental, it is the acute inflammation following abrasion that is necessary for the ocular system to initiate and complete the repair process, and, as such, treatment in this acute phase with a topical steroids may delay healing time.[9] This response is characterized primarily by neutrophil recruitment and migration from the

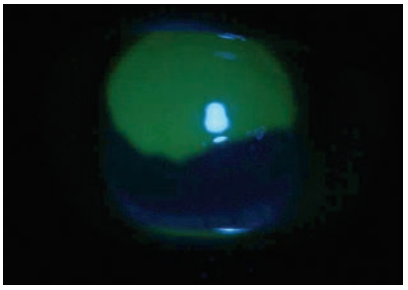
limbal vessels to the wounded area. The accumulation of neutrophils at the wound site is vital to the repair effort; studies that investigated the effects of reducing neutrophil concentrations to the injured area show a significant delay in wound closure occurs.[11]

Corneal keratocytes, found in the stroma, produce extracellular matrix components such as collagen, proteoglycans and crystallins—all essential in maintaining corneal structure and clarity. Studies have concluded that keratocytes are depleted for several years following corneal injury, which may lead to complications such as ectasia following refractive procedures.[9]

Platelet build-up. Accumulation of these cells at the limbus happens in concert with neutrophil migration; both are critical for successful corneal wound healing. During the first 24 hours following injury, platelet recruitment aids in epithelial cell division. Platelets attach to neutrophils and augment migration. Studies report that platelets also aid in efficient keratocyte recovery.[9] Platelets reach copious levels around the limbal blood vessels approximately 12 hours following injury, a crucial time when many of the cellular repair processes are underway. Research also shows reducing platelet levels also reduces neutrophil accumulation, and vice-versa.[12] Following the commencement of this stage, the size of the epithelial defect is noticeably diminished or, in some instances, completely closed.

Patches vs. Lenses

Since corneal healing mechanisms are unique compared to that of other ocular tissues, which carry a blood supply and lack immune privilege, the treatment approach initiated by the practitioner will "make or break it." As our understanding of the cornea advances, so do our protocols. As a result, one historically popular therapy has been phased out and another has emerged as the staple modality.



This corneal abrasion with large epithelial defect is stained with fluorescein dye under cobalt blue light.

Pressure patching. Once the mainstay of abrasion treatment, this protects the cornea from the shearing force of the eyelid secondary to blinking. Prior to patching, topical antibiotics and a cycloplegic are often instilled into the affected eye.

Today, however, pressure patching is somewhat controversial. It reduces the amount of oxygen reaching the cornea and raises its temperature, both of which increase the risk of microbial infection and may even delay healing. As such, exercise caution with this approach.[11] Studies question its value, noting that it does not demonstrate a faster healing time than observation alone, or even additional pain alleviation. In fact, the patch itself was the main cause of pain in 48% of cases.[12] The occlusive effect from patching also prevents the patient from functioning binocularly.[11] Cases where pressure patching may be used include large abrasions in young children or special populations where the patient may risk rubbing their eye and worsen the injury.

Bandage contact lens. This option supersedes pressure patching in that it not only alleviates pain, but also promotes wound healing.[11] The bandage lens also provides lubrication, which aids in healing by providing a smooth surface for the migration of cells, and mitigates pain by shielding the cornea from external forces such as blinking. Its barrier function also adds microbial protection.[13] Lastly, a bandage contact lens allows antimicrobial drops to remain on the corneal surface for an extended period, extending the their duration of action.[13]

Adjuvant Therapies

Though a bandage lens will be the workhorse therapy, other efforts that can accompany it include:

Artificial Tears. Topical lubricants, such as artificial tears or gels, help accelerate the healing process by smoothing out ocular surface abnormalities. The lubrication reduces friction from the patient's eyelid and prevents desiccation.[11]

Topical NSAIDs. Systematic reviews conclude that topical NSAIDs are effective in reducing pain, as well as in reducing the need for oral analgesic therapy. Due to pain control, patients were able to return to work earlier without jeopardizing the healing process.[12] Note that long-term use of topical NSAIDs may increase the risk of corneal melt and toxicity.[5]

Topical Antibiotics. Due to the risk of microbial superinfection from an open epithelial defect, topical antibiotics are frequently used as prophylaxis. Studies report a reduced risk of infection or ulceration with, particularly when antibiotic is implemented within the critical period of 12 to 18 hours following injury, a time where the many cellular processes discussed above are in play.[12] Gel formulations of antibiotics offer additional lubrication as well. However, patients must be educated regarding the transient blurring effect due to viscosity.

Topical antibiotic coverage should especially be considered in abrasions secondary to contact lenses, foreign body or vegetative matter, as there is an increased risk of infection. Antibiotic-steroid combination drops should be used with caution, as the steroidal component may suppress the necessary inflammatory processes and retard wound healing. These agents are typically used for 24 hours, or until full resolution of symptoms and signs.[5]

Clycloplegics. While commonly used for pain management because they minimize ciliary body spasm and reduce pain, the literature does not suggest a substantial benefit in uncomplicated corneal abrasions.[14]

Topical gel. Though unavailable in the US, a combination of xanthan gum, sodium hyaluronate and netilmicin may increase healing time and provide antimicrobial coverage.[11] The hyaluronate incites epithelial migration; studies report adequate prophylaxis and faster resolution of abrasions.[11] It is available in Europe under the trade name Xanternet.

Acacia honey. Honey's antimicrobial, anti-inflammatory and antioxidative properties promotes healing on the skin surface.[15] Epithelial cell migration was enhanced in a small, *in vitro* rabbit study, possibly because of its high sugar content, which is necessary for metabolic cell activity. Though it remains far from clinical deployment, its novel mechanism of action makes acacia worthy of future exploration.[15]

Corneal wound healing possible through a number of complex cellular processes. Informed treatment choices promote repair and prevent delay or complication. ■

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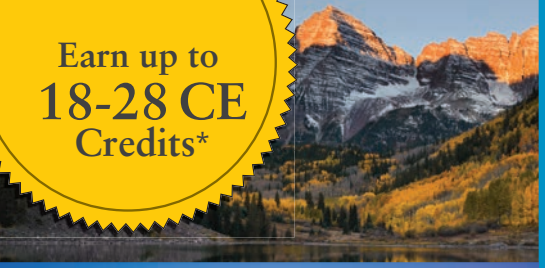

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Jaundice and the Eyes

Optometrists may be the first to notice icterus, a harbinger of systemic concerns.

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

An important element of the review of systems (ROS) specific to the gastrointestinal system is to investigate for jaundice—a yellowish staining of the skin, conjunctiva/episclera/sclera (termed *icterus*), other mucous membranes and excretions.[1]

While not a disease itself, jaundice is a sign of a number of underlying conditions that cause the bile ducts, gallbladder, liver or pancreas to malfunction. The color is caused by subsequent hyperbilirubinemia, an excess amount of bilirubin in the blood. Jaundice is often reported in infants and newborns, as well as in children and adults with medical complications (*Table 1*).[1,2]

Jaundice is a clinical sign optometrists should be on the lookout for, as it is usually first noticeable in the eyes.[1] However, its onset may be so gradual that even those in frequent contact with the affected person may not notice it.[1] In addition to its ocular features for diagnostics, jaundice may result from conditions that have significant ocular complications, such as sarcoidosis, sickle cell disease and various infections.[1]

How and Why

Bile is produced and released by the liver and stored in the gallbladder. Eventually delivered directly to the intestinal lumen, it helps with digestion by breaking down fats into fatty acids to be taken into the body by the digestive tract. The primary constituents in bile are cholesterol, acids (also called bile salts) and bilirubin.

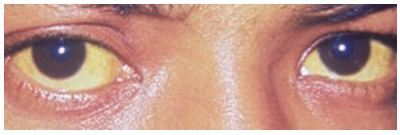


Photo: CDC/Dr. Thomas F. Sellers

Hepatitis A may manifest as jaundice of the conjunctiva and facial skin.

It also contains water, potassium, sodium, copper and other metals.[3]

Bilirubin is a yellow/brownish chemical in bile, formed by the breakdown of heme rings, usually from metabolized red blood cells. Bilirubin is normally excreted in bile, giving feces the normal yellow-brown coloration. As senescent hemoglobin-containing erythrocytes break down, the body builds new cells to replace them, and the liver processes the old red blood cells. If the liver cannot handle the blood cells as they break down, bilirubin builds up in the body and jaundice results. Jaundice is detected clinically once the serum bilirubin level rises above 2.5 mg/dL to 3mg/dL.[1,3]

The amount of bilirubin manufactured (0.5 to 2.0 grams per day) relates directly to the quantity of red blood cells destroyed. Bilirubin has no known function and can be toxic in the fetal brain. Bilirubin in the bloodstream is usually in an unconjugated (free) state. Once transported to the liver, it is attached to the protein albumin and becomes conjugated with glucuronic acid. Bilirubin is then concentrated to about 1,000 times the strength found in blood and transferred to the gallbladder, where it mixes with other bile components.[1,3]

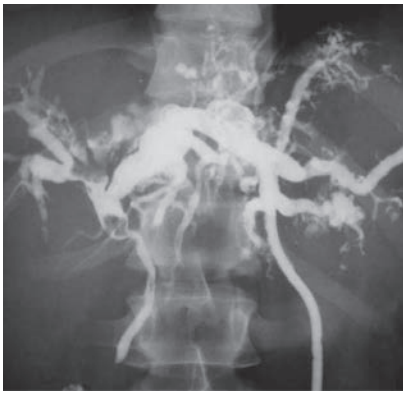
Jaundice may result from an overproduction of bile or from an inability of the liver to remove bile pigments from the blood due to hepatic disease, regurgitation of bilirubin back into the bloodstream or obstruction of the bile ducts.[1-3]

Classification

Clinicians generally describe three types of jaundice, classified according to what is disrupting the normal removal of bilirubin from the body:[1]

Prehepatic (hemolytic) jaundice. Here, the disruption happens before bilirubin has been transported from the blood to the liver. It is caused by conditions such as sickle cell anemia and hemolytic anemia. Hemolysis is an accelerated breakdown of red blood cells, leading to an increase in bilirubin production.[1]

Intrahepatic (hepatocellular) jaundice. The disruption happens inside the liver and is caused by conditions such cirrhosis or other liver damage, including injury.[1]



Cholangiography shows dilated bile ducts with extensive abscesses and stones.

Post-hepatic (obstructive) jaundice. With this form, the disruption prevents bile (and thus bilirubin) from draining out of the gallbladder and into the digestive system. This can be caused by conditions such as gallstones, biliary tract infection, pancreatitis or neoplastic disease.[1]

Gallstones are solid particles that form from bile cholesterol and bilirubin in the gallbladder. They are known as bile duct stones or choledocholithiasis when located in the bile duct. Certain bacteria can infect the gallbladder and change the conjugated bilirubin back to free bilirubin and acid. The calcium from the freed bilirubin can settle out as pigment stones, which may eventually block the common bile duct between the liver, gallbladder and small intestine. When blockage occurs, conjugated bilirubin is absorbed into the bloodstream and becomes clinically evident as jaundice and icterus.

Jaundice in Infants

A healthy newborn may acquire jaundice because the liver has not fully matured.[2] Unconjugated hyperbilirubinemia is a normal physiologic event that occurs in approximately 60% of normal full-term infants and in 80% of preterm infants.[2,3] The bilirubin level normally increases after two to three days and peaks by five to seven days, reaching as high as 12mg/dL in normal full-term babies and up to 14mg/dL in normal premature infants by the end of the first week of life.[2] Breast-fed babies may normally have an elevated bilirubin level until the end of the second week of life. In infants two weeks of age or older, however, the onset of jaundice within the first 24 hours of life, rate of rise of serum bilirubin levels greater than 5mg/dL in 24 hours, direct bilirubin level greater than 1mg/dL at any time, or the persistence or new onset of jaundice may no longer be physiologic.[2,3]

Table 1. Common Causes of Jaundice by Age[1,2]

Age	Conditions
Neonates younger than 2 weeks	Neonatal jaundice (physiologic)
Neonates older than 2 weeks	Hepatitis, biliary atresia, choledochalcyst, obstructive congenital anomalies of the biliary tract, total parenteral nutrition, furosemide treatment, phototherapy, dehydration, infection, hemolytic anemia and short-gut syndrome
Infants and young children (two months to four years of age)	Cirrhosis, benign strictures and neoplastic disease
Children and adolescents (four to 18 years of age)	Sickle cell disease, bowel resection, hemolytic anemia and choledochal cyst
Adults	Viral infections (hepatitis A, B and C), chronic alcohol use, autoimmune disorders, drugs, pregnancy, parenteral nutrition, sarcoidosis, primary biliary cirrhosis, primary sclerosing cholangitis, gallstones, surgical strictures, infection (e.g., cytomegalovirus and Cryptosporidium infection in patients with acquired immunodeficiency syndrome), intrahepatic malignancy, cholangiocarcinoma, extrahepatic malignancy (pancreas, lymphoma) and pancreatitis

Investigating the Cause

Organizing the differential diagnosis of jaundice by prehepatic, intrahepatic and post-hepatic helps make the workup straightforward. Lab work should begin with a urine test for bilirubin, which indicates that conjugated hyperbilirubinemia is present. If the complete blood count and initial tests for liver function and hepatitis are unrevealing, the workup typically proceeds to abdominal imaging by CT or ultrasonography.[1,3] More invasive procedures such as cholangiography or liver biopsy may occasionally be necessary to arrive at a diagnosis.

Jaundice in Your Chair

One of the first things an optometrist should do during a patient encounter is to take a step back and observe the patient. Whether it is a shuffling gait as a result of advanced glaucomatous field loss, a head tilt indicating a high vertical phoria or changes in coloration such as flushing or jaundice, the optometrist must be keenly aware of these signs and the potential underlying causes.

A thorough review of systems and comprehensive history are key, as they may point to a specific cause, such as cirrhosis or pancreatitis. In addition to icterus, your ophthalmic workup may uncover such signs as uveitis or metastatic choroidal carcinoma. These ocular complications can guide your lab workup as you rule out various causes of jaundice. As always, the patient's primary care physician should be promptly made aware of your findings.

Timely and appropriate testing, as well as comanagement with and referral to the appropriate subspecialist (e.g., pediatrics, gastroenterology, infectious disease) are typically required. Physicians do not treat jaundice; they treat the condition that causes this telltale sign. ■

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Could Eyelids Be the Key to DED?

A new theory finds the two linked by a familiar foe: bacterial biofilm.

By Paul M. Karpecki, OD

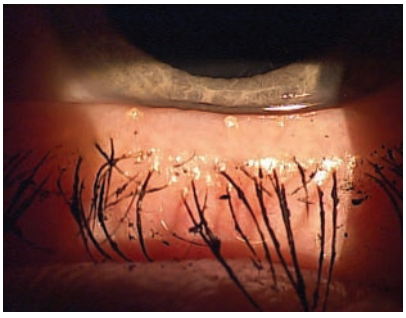
For many years, blepharitis and dry eye disease (DED) were considered two completely independent diseases. But the Ryner-son theory of dry eye blepharitis syndrome (DEBS), recently published in *Clinical Ophthalmology*, suggests dry eye may be the result of decades of chronic blepharitis.[1] Let's take a closer look at what this might mean for clinical practice.

The Biofilm Bridge

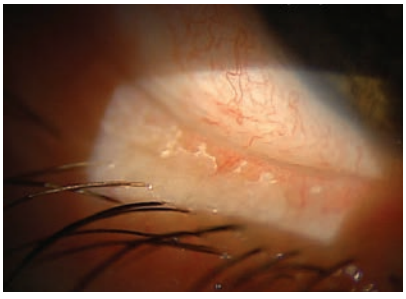
We've heard a lot about biofilms lately, especially with overused contact lens cases, for example. Although a biofilm can accumulate on an inert structure such as a stent or contact lens case, it can also exist on a living structure.[2] For instance, plaque on your teeth is essentially biofilm formation.[3]

Depending on the age of the patient, contact lens use, *Demodex* and other factors, various manifestations of blepharitis may demonstrate various degrees of lid margin "scurf" or debris—biofilm. But the key factor is inflammation, and if it exists, blepharitis is present and should probably be considered as the underlying disease process.[1]

The diagnosis of blepharitis and DED has been difficult in the past because both of these conditions have significant overlap, hence the theory of causation. As an example, multiple symptoms of blepharitits can overlap with those of DED, ranging from dry, gritty, irritated and itching eyes to tearing and blurred vision.[4] In addition to multiple similar symptoms, both conditions can be slowly progressive and chronic with various manifestations depending on the stage of the disease.[4,5] However, examining the eyelid margins more closely for biofilm formation may serve as a bridge of understanding between these two poorly understood diseases.



Expression showing thickened meibum and the 'volcano' sign along the lashes.



You can see significant biofilm on this patient's lid margin, a common site for biofilm adherence.

From Lid Margin Disease to DED

According to the new theory, lid margin disease progresses to inflammation through six steps: (1) bacterial survival, (2) biofilm formation, (3) over-colonization, (4) quorum-sensing gene activation, (5) virulence factor production and (6) inflammation that affects the lash follicles, meibomian glands and lacrimal glands.[1] To begin the process, bacteria must survive enzymes such as lactoferrin, tear flow, natural cleaning activities of the eyelids with each blink and the protective mechanism of mucin secreted by goblet cells.[6] When a patient's blink rate decreases due to surgery, extensive digital device use, the use of eye drops containing preservatives, systemic medications that decrease tear volume, presence of various comorbidities and a host of multifactorial contributors, bacteria can survive longer.

Next is biofilm formation, described as "the prevailing microbial lifestyle."[7,8] Biofilm formation is a survival tactic allowing the bacteria to avoid desiccation and host responses, produce virulence facts and communicate with other bacterial species (as quorum-sensing). Biofilm adherence exists in many bacteria, but *Staphylococcus* in particular produces a protein known as adhesin that ensures a tight adherence to the surface.[9] The lid margin is a common a site of adherence, considering one study shows 32 of the isolates cultured from eyes immediately after cataract surgery had the ability to form biofilms.[10]

Furthermore, although we wash and shower often, we don't naturally wash or clean our eyelid margins—particularly the inner

eyelid margins. In fact, most people tightly close their eyes when washing their face to prevent access to the eyelid margins. This leads to the slow, progressive, chronic destruction that occurs via inflammation over decades, eventually resulting in dry eye and even damage to the lid structure itself.

The Four Stages of DEBS

The Rynerson theory also suggests stages of DEBS progression.

Stage 1 involves the lash follicles, where a biofilm can establish itself. This can often be assessed under high magnification for a 'volcano sign' when the base of the lash appears edematous. Scurf, or cylindrical dandruff in cases of *Demodex* blepharitis, is a sign of progression; however, these descriptions are misnomers and likely represent biofilm that has accumulated around the lash that pulled off as the lash grew.[1]

Stage 2 DEBS involves both the lash follicles and the meibomian glands and may explain obvious vs. non-obvious meibominan gland dysfunction (MGD). Because the biofilm blocks the large meibomian gland orifices (a combination of biofilm and poor or altered meibum), stage 2 takes longer to achieve.[1]

Stage 3 involves the follicles, meibomian glands and the accessory lacrimal glands of Krause and Wolfring. The distance, narrow ducts and constant tear flushing serve to protect these glands for decades, making them the last glands affected by biofilm formation.[1]

Stage 4 occurs when the structural integrity of the eyelid finally breaks down due to the chronic inflammation, which can manifest clinically as lid laxity, floppy eyelid syndrome, ectropion and entropion, for example.[11,12]

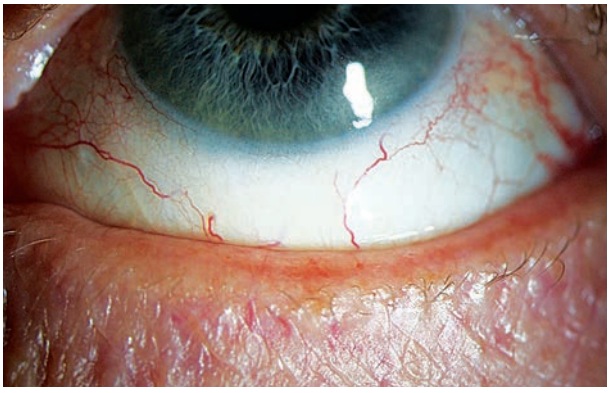
This DEBS theory may help explain any number of factors, including how bacteria can survive a Betadine prep prior to surgical procedures, resulting in endophthalmitis—the bacteria is at the stage of biofilm formation when it is resistant to an antiseptic.[10]

Putting Theory Into Practice

I can't prove or disprove this theory, but I have seen a significant positive impact when treating the biofilm mechanically for my DED patients, in addition to anti-inflammatory treatment and managing the obstructed meibomian glands. Furthermore, mechanical removal of the biofilm from the lid margin shows a profound impact on symptoms, quality of tears and quality of life.[13]

This theory affects so much of the optometric practice from a pathology perspective, including contact lens wearers who are more prone to early MGD/blepharitis and DED.[14-16] With this knowledge, we may help patients remain in contact lenses longer by consciously focusing on and managing the biofilm component of ocular surface disease. Dentistry has mastered this important aspect of prevention by addressed biofilm formation with regular cleanings, brushing and flossing; this new theory suggests a similar model that could be even more critical in eye care. ■

Dr. Karpecki is a consultant to Blephex, OcuSoft, Bruder Healthcare, Paragon Biotech, TearScience and Akorn.



This 65-year-old woman presented with frequent dryness and irritation, and she reported a "dry eye diagnosis" from a previous practitioner. A closer look at her lid margin suggests blepharitis is at play here as well.

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The Role of Toric Peripheries

They provide one last refinement to the fit, improving comfort and vision.

Edited by Joseph P. Shovlin, OD

Q I just started fitting scleral lenses but haven't yet ordered any toric peripheral curve lenses. My lab consultant mentioned that a majority of the orders she gets are for toric peripheries. Most of my patients seem happy and I rarely see much difference in lens edge appearance, but am I missing the point by not ordering toric peripheral curve lenses?

A "Following the rebirth of scleral lenses, symmetric landing of the lenses was the norm," says Randy Kojima, a research scientist and clinical instructor at the Pacific University College of Optometry. "Most if not all designs came as a standard symmetric landing. At the same time, anterior segment OCT was being used to better understand the shape of the scleral 360 degrees around."

According to Mr. Kojima, numerous studies performed at Pacific University have found the sclera to exhibit a toricity at 15mm of approximately 125µm. "When constructing sclerals with toricities of between 100µm and 150µm, the lenses appear rotationally stable in most eyes, suggesting we have improved alignment," says Mr. Kojima. "Additionally, when patients are given the choice between the symmetric in one eye and the toric in the other, they will usually choose the toric as being more comfortable."

Findings from both Europe and the United States have suggested that comfort, fit and physiologic response is improved when using sclerals with a toric landing, Mr. Kojima says.[1-3] "Numerous larger lens designs greater than or equal to 16mm in diameter have made a toric back surface standard in their trial sets."

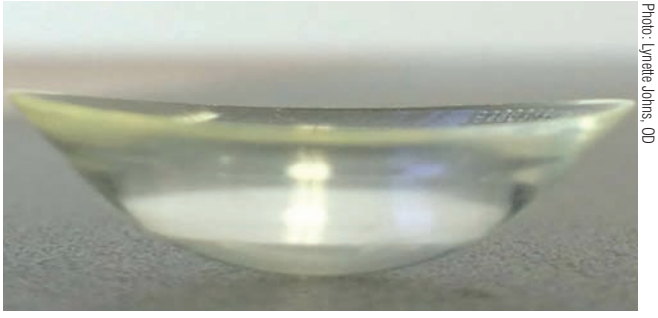

Photo: Lynette Johns, OD

Toric sclerals could help improve end-of-day comfort for your scleral lens patients.

Also citing scleral shape studies, Melissa Barnett, OD, immediate past president of the Scleral Lens Education Society, concurs.[2-4] "There may be toricity in the sclera, irrespective of corneal toricity," she says. "For lens diameters greater than approximately 16mm, back surface toricity may have certain advantages, including improved alignment on all meridians, reduced post-lens reservoir debris, better centration, less movement and improved comfort."

To get a better idea of whether toric peripheral curve lenses would be beneficial for a patient, it may help "to evaluate the scleral lens fit outside of the slit lamp and using dim illumination and then with the slit lamp to look for areas of compression and impingement," says Dr. Barnett. At the follow-up appointment, the cornea and conjunctiva should be evaluated for areas of staining after removing the scleral lens, Dr. Barnett adds. "Ask patients about their comfort with sceral lenses, especially end-of-day comfort. If any aspect of scleral lens wear could be improved, consider back surface toricity."

"It appears the industry is moving from symmetric to toric as the lens of first choice in the larger diameter," says Mr. Kojima. "However, studies show the closer to the limbus we land, the more symmetric the eye surface, so symmetric landing in scleral lens diameters of less than or equal to 15mm may be advisable."

According to Mr. Kojima, researchers should further explore asymmetric scleral lenses, which may be "the way of the future." ■

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Next Time, Order Well Done

A young man returned from an overseas trip with more than just memories.

By Faten Edriskhalaf, OD, and Mark T. Dunbar, OD

A 16-year-old Hispanic male presented with a sudden and painless onset of blurred vision in the right eye for the past two weeks. His social history was remarkable for recent travel to Nicaragua, but his medical history was unremarkable. An examination revealed his best-corrected vision was 20/25 OD and 20/20 OS. His extraocular motility was normal, and confrontation visual fields were full-to-careful finger counting. The pupils were equally round and reactive; there was no afferent pupillary defect. An exam of the anterior segment was remarkable for keratic precipitates (KP) on the endothelium in the right eye and 1+ cell in the anterior chamber. The left eye was unremarkable.

A dilated fundus exam of the right eye showed 1-2+ vitreous cells. The optic nerve and macula appeared healthy. Of interest was an elevated lesion superior to the nerve as seen in the fundus photo (*Figure 1*). A spectral-domain optical coherence tomography (SD-OCT) is available for review (*Figure 2*).

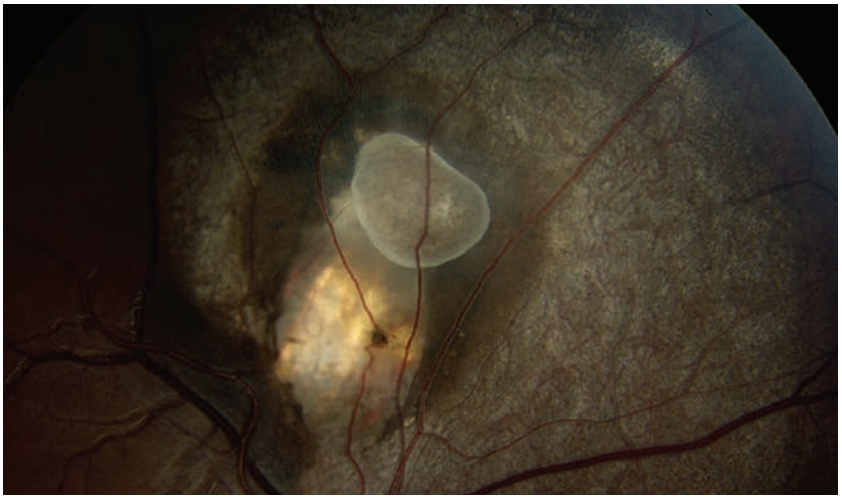

Fig. 1. Fundus photo of the right eye showing the area of interest. What does this represent?

Take the Retina Quiz

1. How would you characterize the OCT image of this patient?
a. Intraretinal cyst.
b. Hemorrhagic RPE detachment.
c. Sub-retinal pigment epithelium (RPE) hyperreflective lesion with fluid.
d. Exudative retinal detachment.

2. How would you best characterize the fundus changes seen in this patient?
a. Inflammatory.
b. Infectious.
c. Congenital.
d. Traumatic.

3. What is this patient's most likely diagnosis?
a. Toxocariasis.
b. Toxoplasmosis.
c. Cysticercosis.
d. Treponema pallidum (syphilis).

4. How should this patient be managed?
a. Placed on Bactrim and monitored.
b. Referred for surgical removal.
c. Panretinal photocoagulation.
d. Penicillin.

For answers, see page 98.

Diagnosis

The lesion superior to the nasal appeared to be a subretinal cyst with adjacent subretinal fluid surrounding it. We also observed chorioretinal scaring and atrophy surrounding the cyst. This was confirmed on the SD-OCT, which shows well delineation of the cystic lesion in the subretinal space along with fluid and exudates.

The patient admitted to having recently traveled to Nicaragua. He also admitted to eating uncooked pork. Given this history, the anterior chamber and vitreous cells, and OCT findings, we made a tentative diagnosis of cysticercosis.

Discussion

Cysticercosis is the most common parasitic disease of the central nervous system, affecting the eye, mus-

cle and subcutaneous tissue.[1] It is caused by encystment of the tapeworm *Taenia solium* from uncooked pork meat.[1,2] It is believed that the larvae travels from the choroid through the RPE and either encysts in the vitreous or subretinal space.[2]

In the ocular form, it typically presents unilaterally, affects young individuals in the second to fourth decade of life and is endemic in developing countries.[1] In severe cases, anterior and posterior inflammation is present and vision is greatly reduced due to exudative retinal detachment.[2] Rarely, vitreous hemorrhage can occur if the cyst migrates through the retina into the vitreous.[2] Systemically, neurocysticercosis is the most serious of this condition's sequela.[2] Neurological findings are most commonly seizures and hydrocephalus.[2]

Upon close comparison of our high-definition OCT with histopathological slides of cysticercosis, we were able to definitively characterize that the double-layered cyst wall is evident (*Figure 3a*). The scolex, which represents the knoblike anterior end of the tapeworm, can also be seen but is more difficult to visualize. We suspect our imaging captured the outline of the cyst (*Figure 3b*). The honeycomb invagination within the cyst is the intestine of the larvae.(*Figure 3c*).[3,4]

Fig. 2. The above SD-OCT image shows the lesion.

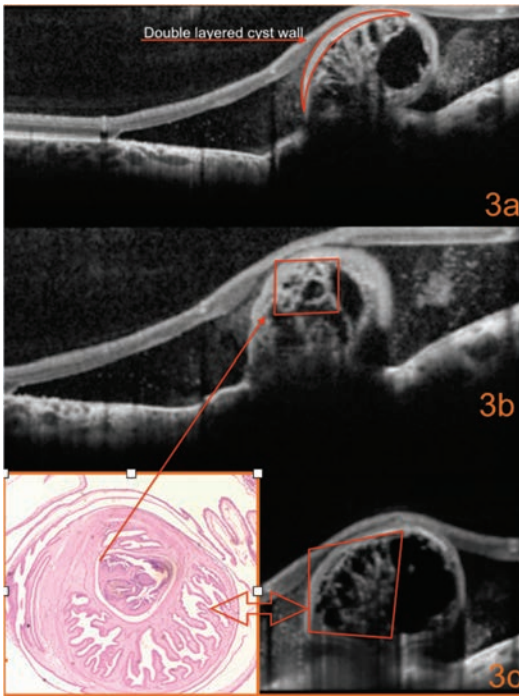

Fig. 3. What can this detailed look at the SD-OCT image reveal?

Treatment

The management of ocular cysticercosis consists of prompt referral to a retina specialist for consideration of surgical removal of the cyst and treatment of the retinal detachment, if present. All patients we suspect have this condition should undergo a serology work up for toxocariasis and toxoplasmosis, as well as a full blood panel to rule out systemic involvement. Serologic testing for our patient was obtained and was negative for active cysticercosis infection and also negative for toxoplasmosis infection. The negative testing likely indicates the patient may have had this for some time even though he only recently became symptomatic. Some of the clinical findings such as RPE mottling and atrophy also suggest this has been present longer than his symptoms would have indicated.

Systemic treatment for neurocysticercosis involves anthelminthic therapy; however, this treatment may be contraindicated if an active ocular infection is present.[4] Our patient underwent magnetic resonance imaging to rule out neurological involvement prior to coming in for his retinal exam, and the results were normal.

Visual prognosis for these patients is good if it does not involve the macula, and is typically restored to normal once the cyst is removed and the patient's condition is treated systemically. Recurrence is uncommon.

Proper follow up is warranted postoperatively, as with any surgery. Lastly, the best method of prevention is to thoroughly cook pork and use proper hygiene when handling meat.

Our patient underwent pars plana vitrectomy, removal of the cyst and was treated for retinal detachment. One month post-surgery, his vision returned to baseline of 20/25 without correction. The pathology report confirmed the presence of the cyst in the specimen removed. He did not require anthelminthics, as he was not affected systemically. ■

Dr. Edriskhalaf is a former optometric resident at the Bascom Palmer Eye Institute in Miami, FL.

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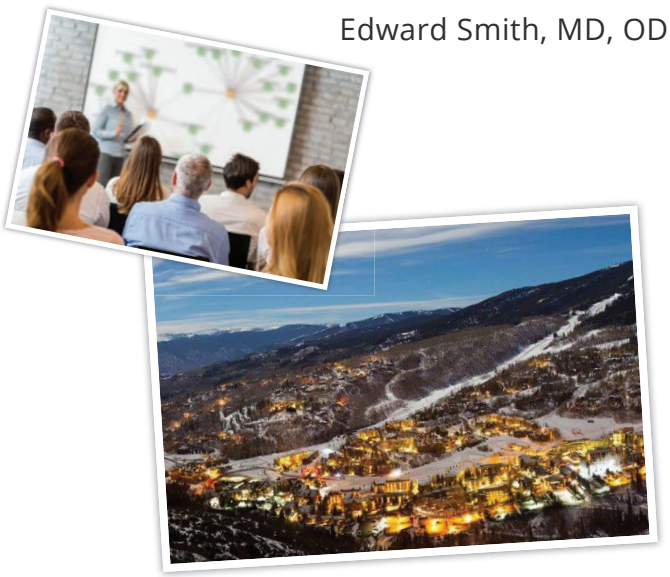

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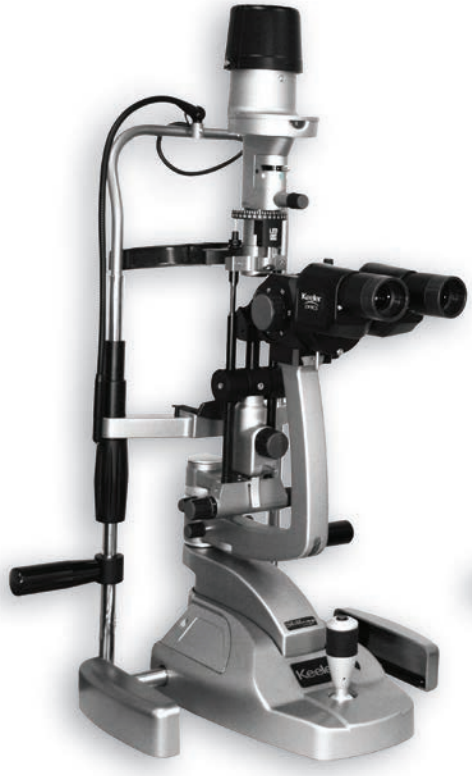

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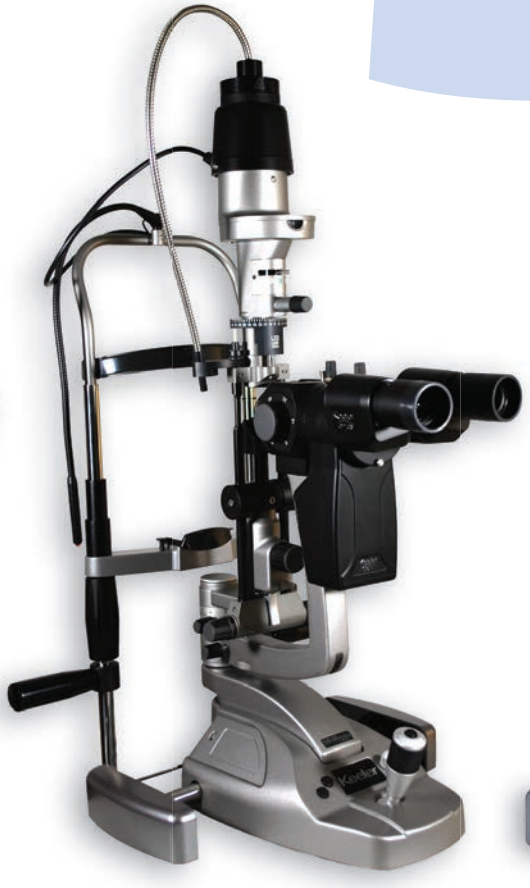

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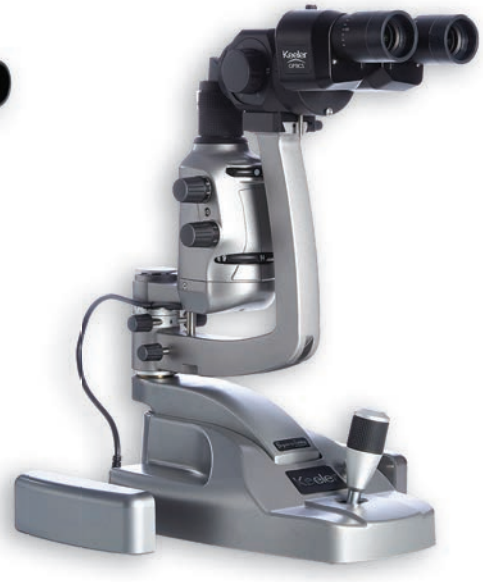

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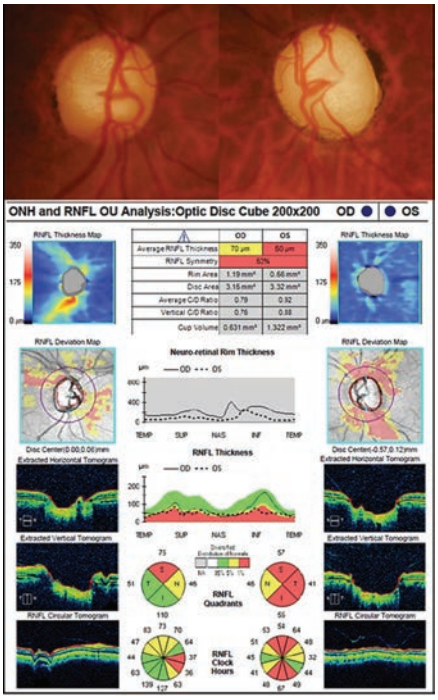
Stemming the Tide

Cycloablation lowers IOP at its source: the ciliary body. Once considered a last resort, it may be warranted earlier. **By Alan G. Kabat, OD, and Joseph W. Sowka, OD**

A 56-year-old black woman presented for a comprehensive ocular examination. Prior to a relocation, her long-time ophthalmologist had been treating her for glaucoma. The patient reported using latanoprost 0.005% QHS OU, dorzolamide/timolol maleate fixed combination BID OU and brimonidine 0.2% solution TID OU. She further reported having had laser treatment for glaucoma in both eyes (most likely laser trabeculoplasty) within the past two years.

Examination

Her best-corrected visual acuity was 20/20 OD and 20/40-1 OS. Confrontation visual fields were full in the right eye but severely constricted in the left. Consistently, the left eye displayed a 3+ relative afferent defect on pupil testing. Intraocular pressure (IOP) was measured at 20mm Hg OD and 28mm Hg OS. Gonioscopy revealed open angles to the ciliary body in all four quadrants, with moderate pigment and no sign of angle recession in either eye. Central corneal thickness measured 517µm in the right eye and 504µm in left. Upon dilated examination, the optic nerves were markedly cupped, measuring approximately 0.8/0.8 OD and 0.9/0.95 OS. OCT evaluation showed notable retinal nerve fiber layer (RNFL) damage superiorly in the right eye and extensive RNFL damage both superiorly and inferiorly in the left eye. Since the patient was already on maximum tolerable medications and reported excellent compliance, we ordered a consultation with a glaucoma specialist. After examining her and reviewing the testing, he recommended proceeding with transscleral cyclophotocoagulation (TS-CPC) in the left eye using the Cyclo G6 system (Iridex).



Fundus photos and OCT images of our 56-year-old glaucoma patient.

Procedural Process

Cyclodestruction procedures aim to decrease IOP by diminishing the ciliary body's capacity to produce aqueous. The earliest cyclodestructive techniques involved the use of extreme cold (-80° C) applied to the conjunctival surface circumferentially around the cornea, approximately 4mm beyond the limbus; this procedure is referred to as cyclocryotherapy.[1]

Limitations of cyclocryotherapy include a variable response, in which patients may experience no IOP lowering effect or extreme lowering to the point of hypotony.[2,3] Moreover, a host of complications may be seen, including intraocular hemorrhage, secondary cataract, retinal detachment and phthisis bulbi, any of which can lead to further loss of vision and even enucleation.[2,3] Today, cyclocryotherapy is rarely used, but similar techniques that employ ophthalmic lasers (collectively referred to as cycloablative procedures) remain an option for some glaucoma patients.

Endoscopic cyclophotocoagulation is invasive and uses a laser endoscope to allow direct visualization and treatment of the ciliary processes by means of a semiconductor diode laser.[4] The procedure is typically performed in conjunction with cataract surgery for patients with moderate to severe glaucoma.[5] TS-CPC is a noninvasive procedure that uses a diode laser attached to a specialized contact probe which is applied to the conjunctival surface around the limbus. Like cyclocryotherapy, TS-CPC has been criticized for its lack of predictability and propensity toward complications, which include hypotony, early postoperative inflammation and pain, cystoid macular edema, persistent flare and loss of vision.[6]

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Therapeutic Review

An Updated Approach

Most glaucoma surgeons today view TS-CPC as an option only for those patients who have failed more invasive surgeries (i.e., trabeculectomy or tube shunt procedures) or those who have minimal or no useful vision, but experience chronic pain associated with uncontrolled IOP.[7] The procedure is generally frowned upon for patients with good vision and those who have only been previously managed with topical meds. However, those attitudes appear to be changing, and some have even suggested that this procedure may be a viable first-line surgical treatment.[8,9]

This potential paradigm shift can be attributed to new technology and a modified treatment approach. The Cyclo G6, when coupled with the MP3 glaucoma probe, employs micropulse technology; this differs substantially from the continuous wave laser that was used in prior versions of TS-CPC. As its name implies, the micropulse platform produces short bursts of laser energy with intervening rest periods, permitting for tissue cooling and rebound.[8] This ensures cellular disruption without total cell destruction, and while the mechanism of action is not completely understood, researchers theorize that the thermal insult may activate a cellular biochemical cascade, resulting in an IOP-lowering effect.[10]

As experts explain, this unique platform offers some distinct advantages over other surgical techniques. Unlike invasive procedures such as trabeculectomy or tube-shunt surgery, micropulse TS-CPC is theoretically repeatable (much like SLT). Moreover, it has the capacity to be performed as an in-office procedure, although some surgeons still recommend it be done in an outpatient facility for greater safety.[11] TS-CPC appears to provide significant results that can be tailored to the patient's needs. Studies show IOP reduction ranging from 30% to 45% among populations with varied types and severity of glaucoma.[12-16] They also show a diminished need for multiple medications following treatment.[12-16] In one trial, the average number of glaucoma medications fell from 3.3 down to 1.8 after the procedure.[16]

Micropulse TS-CPC can be associated with a significant amount of discomfort, to the point that it requires a retrobulbar block, often with the adjunctive use of oral anxiolytics or intravenous sedatives.[16] Physicians can also anticipate substantial inflammation after the procedure, necessitating the use of strong topical corticosteroids during the immediate postoperative period. Of course, the greatest concern with this technique has been the potential for vision

loss, particularly the "snuffing out" of central fields in sighted patients with advanced disease.

In a 2010 study involving 49 glaucomatous eyes with best-corrected visual acuity of 20/60 or better, 18.3% experienced a loss of greater than or equal to two Snellen lines within 12 months of the procedure.[6] After five years, 30.6% of the eyes showed a similar loss of vision.[6] The authors found this outcome "concerning," but also concluded that much of the visual deterioration was likely due to the natural course of the disease rather than the intervention itself. They cited a 2007 study in which the same magnitude of vision loss was seen in approximately 33% of eyes undergoing trabeculectomy or tube-shunt surgery after one year of follow-up.[17]

Advocates of this new technology argue that any surgical intervention places the patient at risk for complications and progression, particularly in advanced glaucoma. But they insist micropulse TS-CPC is more predictable and efficacious in the hands of a well-trained surgeon than laser trabeculoplasty, minimally invasive glaucoma surgery or filtration surgery, while maintaining an acceptable safety profile and the potential for repeatability. Advocates also point to the rising cost of medications, declining insurance coverage and diminishing physician reimbursement for more invasive glaucoma surgeries as a rationale to consider TS-CPC earlier in the disease course.[8] ■

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Pharmaceuticals

Glaucoma Drug Now Approved

Vyzulta (latanoprostene bunod ophthalmic solution, 0.024%), by Bausch + Lomb and Nicox, is now FDA approved. A prostaglandin analog, it is indicated for open-angle glaucoma and ocular hypertension, and will be available by the end of year, according to B+L.

The once-daily monotherapy agent metabolizes into latanoprost acid, which primarily works within the uveoscleral pathway, and butanediol mononitrate, which releases nitric oxide to increase outflow through the trabecular meshwork and Schlemm's canal, B+L says.

Visit ir.valeant.com.

Diagnostic Technology

New Ultrasound System

DGH Technology's Scanmate Flex ultrasound system is notable for the flexibility it gives clinicians, the company says. The device can be equipped with any combination of three probe types: UBM, A-scan and B-scan. Desktop or wall-mounted, its internal battery allows it to operate for hours without being plugged in, according to DGH.

Visit dghtechnology.com.

Camera for Retinal Video

Heine recently upgraded the imaging resolution of its Omega 500 BIO. The camera now provides five-megapixel resolution with no disturbing picture noise, due to the camera's increased light sensitivity, according to the company. Practitioners can easily connect to a projector to display the video imaging. The company is offering institutional discounts for the Omega 500.

Visit www.heine.com.

Accutome by Keeler

Keeler has acquired the Accutome clinical and diagnostic lines of products. The new "Accutome by Keeler" brand offers a full complement of clinical pharmaceuticals and supplies, according to the company. Devices for pachymetry, tonometry and ultrasound imaging add to Keeler's established line of ophthalmic products.

Visit www.accutome.com.

Patient-use Devices

Low Vision Aid

Practitioners interested in adding low vision have a new device to consider. IrisVision uses Samsung's Galaxy S7 phone and GearVR virtual reality headset to magnify, brighten and sharpen text or objects seen through the device. It enables a 70-degree visual range, wider than other low vision devices, the company says. Users can zoom in and out as needed for different visual tasks and can adjust screen brightness and contrast, interpupillary distance and magnifier position and shape. Black and white and inverted text modes allow for easier reading.

Visit irisvision.com.

In-home Vision Therapy

Vivid Vision has launched a home-use version of its virtual reality vision therapy system, called Vivid Vision Home. Patients first see a doctor for an evaluation and prescription, then can use the device (in conjunction with the Oculus Rift, HTC Vive or Samsung GearVR) to conduct vision therapy at home. Vivid Vision Home includes tools to assess and track changes in vision, as well as exercises designed to take advantage of room-scale VR and positional controls, according to the company. Doctors can track treatment and response remotely.

Visit www.seevividly.com.

Scleral Lenses

New Design for Irregular Corneas

The Onefit Med scleral lens from Blanchard simplifies fitting for keratoconic patients with nipple and oval cones, as well as post-RK and post-LASIK patients. Practitioners set the parameters for central, mid-peripheral, limbal and edge zones, then customize the final design with an online fitting tool. Multifocal, oblate and front toric geometries are possible, the company says, and the design minimizes lens thickness and tear layer to maximize oxygen transmission.

Visit blanchardlab.com.

Quadrant-specific Control

BostonSight has introduced a new quadrant-specific toric lens design that comes with built-in scleral shape and right- and left-eye anatomical designs. Available in 18.0mm, 18.5mm and 19.0mm, the BostonSight Scleral is the first of its kind to provide front-surface eccentricity options for aberration control, the company says. BostonSight used six years of data from approximately 7,000 eyes to develop the lens. The incorporated scleral shape allows clinicians to use the same starting point for every patient regardless of their condition, according to the company.

Visit www.bostonsight.org. ■

Meetings + Conferences

December 2017

■ **1-2.** *Retina Update 2017*. Sheraton Park Hotel, Anaheim, CA. Hosted by: *Review of Optometry*. Key faculty: Mohammad Rafieetary, Steven Ferrucci, Leo Semes, Mark Dunbar, Jeff Gerson, Rishi Singh. CE hours: 11. For more information, email reviewmeetings@jobson.com, call (800) 999-0975 or go to www.reviewofoptometry.com/orsretupdate2017.

■ **2-3.** *34th Annual Cornea, Contact Lens & Contemporary Vision Care Symposium*. Westin Memorial City, Houston, TX. Hosted by: University of Houston College of Optometry. Key faculty: Jan Bergmanson. CE hours: 16. For more information, email University of Houston College of Optometry at optce@central.uh.edu, call (713) 743-1900 or go to http://ce.opt.uh.edu.

■ **3.** *Clinical Topics in Optometry*. Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. CE hours: 8. For more information, email Antoinette Smith at asmith@ketchum.edu, call (714) 872-5684 or go to www.ketchum.edu/ce.

■ **7.** *UABSO Evening of Education*. University of Alabama Birmingham School of Optometry, Birmingham, AL. Hosted by: University of Alabama Birmingham School of Optometry. CE hours: 2. For more information, email Katherine Clore at kclore@uab.edu, call (205) 934-5700 or go to www.uab.edu/optometry/home/uabso-ce.

■ **7-11.** *VT/Learning Related Visual Problems*. Southern College of Optometry, Memphis, TN. 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.

■ **15-16.** *West Coast Optometric Glaucoma Symposium*. Hilton Hotel, Huntington Beach, CA. Hosted by: *Review of Optometry*. Key faculty: Murray Fingeret, Robert Weinreb, Ben Gaddie, Alex Huang, Richard Madonna, Sameh Mosaed. CE hours: 12. For more information, email reviewmeetings@jobson.com, call (800) 999-0975 or go to www.reviewofoptometry.com/wcogs2017.

■ **23-30.** *Considerations in Ocular Disease Management and Treatment*. Norwegian Cruise Line's Norwegian Epic, Western Caribbean Cruise, round-trip Orlando (Port Canaveral), FL. Hosted by: Dr. Travel Seminars and the New Jersey Society of Optometric Physicians. Key faculty: Mark Dunbar. CE hours: 16. For more information, email Dr. Travel Seminars at info@drtravel.com, call (800) 436-1028 or go to www.drtravel.com.

January 2018

■ **6.** *Glaucoma Symposium*. Willows Lodge, Woodinville, WA. Hosted by: Pacific University College of Optometry. Key faculty: Howard Barnebey, Murray Fingeret. CE hours: 7. For more information, email Michelena Buckingham at mikibuckingham@pacificu.edu, call (503) 352-2985 or go to www.pacificu.edu/future-graduate-professional/colleges/college-optometry/continuing-education.

■ **12-14.** *AZOA 2018 Bronstein Contact Lens & Cornea Seminar*. Hilton Scottsdale Resort & Villas, Scottsdale, AZ. Hosted by: Arizona Optometric Association. Key faculty: Melissa Barnett, Patrick Caroline, Thomas Quinn, Roy Wesley. CE hours: 15.5. For more information, email Kate Diedrickson at kate@azoa.org or go to www.azoa.org/Connect.

■ **13-15.** *Kraskin Invitational Skeffington Symposium on Vision*. Embassy Suites Hotel at the Chevy Chase Pavilion, Washington D.C. Hosted by: Optometric Extension Program Foundation and the Institute for Behavioral Optometry. Key faculty: Multiple presenters. CE hours: 19. For more information, email Jeffrey Kraskin at jlkraskin@rcn.com, call (202) 363-4450 or go to www.skeffingtonsymposium.org.

■ **13, 14, 20, 21.** *Coding and Compliance Seminars*. Various locations, CA. Hosted by: Primary Eyecare Network. Key faculty: John McGreal. CE hours: 4. For more information, email education@primaryeye.net or go to www.primaryeye.net.

■ **14-20.** *2018 Island Eyes Conference*. Ritz-Carlton Kapalua, Kapalua (Maui), Hawaii. Hosted by: Pacific University College of Optometry. Key facutly: Mark Andre, Carlo Pelino, Alan Reichow, Tracy Doll, Walt Whitley, Fraser Horn. CE hours: 29. For more information, email Jeanne Oliver at jeanne@pacificu.edu, call (503) 352-2740 or go to www.pacificu.edu/future-graduate-professional/colleges/college-optometry/continuing-education/conferences-events/island-eyes-conference.

■ **22.** *Day at the Capitol & Winter CE*. Boise Centre, Boise, ID. Hosted by: Idaho Optometric Physicians. CE hours: 4. For more information, email Randy Andregg at execdir@iopinc.org, call (208) 461-0001 or go to idaho.aoa.org.

■ **25-28.** *Global Specialty Lens Symposium*. Tropicana Hotel, Las Vegas, NV. Hosted by: Pentavision. Key faculty: Melissa Barnett, Lyndon Jones, Pauline Cho, Philip Morgan. CE hours: 55 total, 19 per OD. For more information, email Maureen Trusky at maureen.trusky@pentavisionmedia.com or call (215) 628-7754.

■ **28.** *VOA One-Day CE Conference*. Omni Charlottesville, Charlottesville, VA. Hosted by: Virginia Optometric Association. Key faculty: Leo Semes. CE hours: 4. For more information, email Bo Keeney at office@thevoa.org, call (804) 643-0309 or go to www.thevoa.org/voa/89-events.

To list your meeting, please send the details to:
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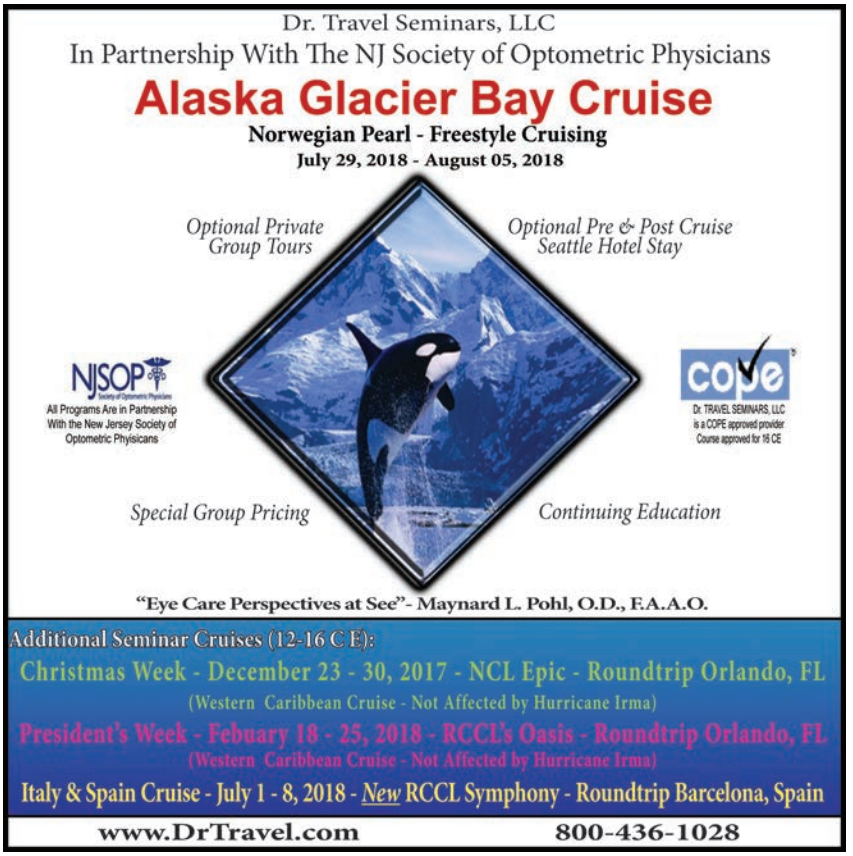

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- Participating in leadership roles in state, regional, and national optometry organizations;
- Participating on College and University committees, as assigned;
- Participating in College and University service activities.

c) **Scholarly activity**

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CONTACT INFORMATION: 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. Inquiries may be directed to Dr. Melissa Suckow, Associate Dean; Midwestern University: msucko@midwestern.edu.

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Diagnostic **Quiz**

Like Sunglasses at Night

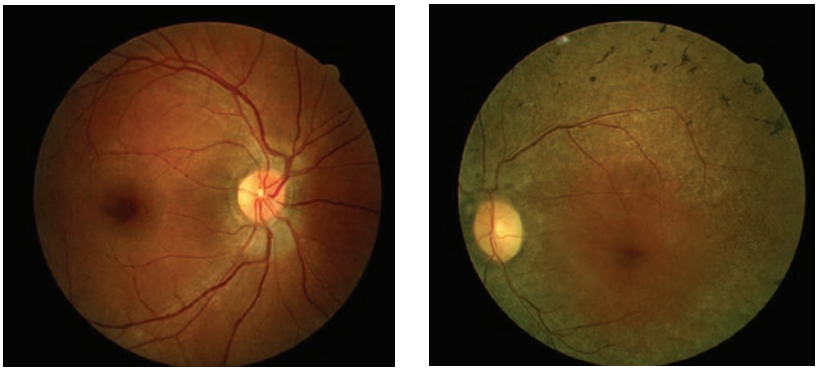
By Andrew S. Gurwood, OD

History

A 44-year-old Caucasian male reported to the office with a chief complaint of poor night vision. He explained that he had been seen by other eye doctors who had told him he had some "freckles" in his left eye. His systemic and ocular histories were unremarkable and he denied allergies of any kind.

Diagnostic Data

His best-corrected entering visual acuities were 20/20 OU at distance and near. His external examination was normal with evidence of sluggish pupil on the left side. His peripheral confrontation visual field was distorted and constricted in the left eye. The biomicroscopic examination of the anterior segments found normal structures with Goldmann applanation pressures measuring 15mm Hg OU. The pertinent dilated fundus findings are demonstrated in the photographs.



Can these fundus images help point to a diagnosis for this 44-year-old patient suffering from poor night vision?

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 would be your diagnosis? What do you believe is the patient's most likely prognosis? To find the answers, please visit *Review of Optometry* online at www.reviewofoptometry.com. ■

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

Next Month in the Mag

Coming in December, *Review of Optometry* will proudly celebrate its 23rd Annual Surgery Report.

Topics include:

- *Is it the Lens, Retina or Tear Film? Knowing When to Refer a Cataract Patient*
- *Postoperative Cataract Care: The Optometrist's Role in Prescribing NSAIDs, Steroids and Antibiotics*
- *Intraocular Lens Choices: How to Find the Best Match For Each Patient*
- *Will SMILE be the Game Changer for Refractive Surgery Has Been Waiting For?*

Also in this issue:

- *Hey Good Lookin', It's Our 2017 Office Design Contest Winners*
- *Review of Optometry's Annual Income Survey Results*

REVIEW OF OPTOMETRY (ISSN 0147-7633) IS PUBLISHED MONTHLY, 12 TIMES A YEAR BY JOBSON MEDICAL INFORMATION LLC, 440 9TH AVENUE, 14TH FLOOR, NEW YORK, NY 10013-1678. 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.

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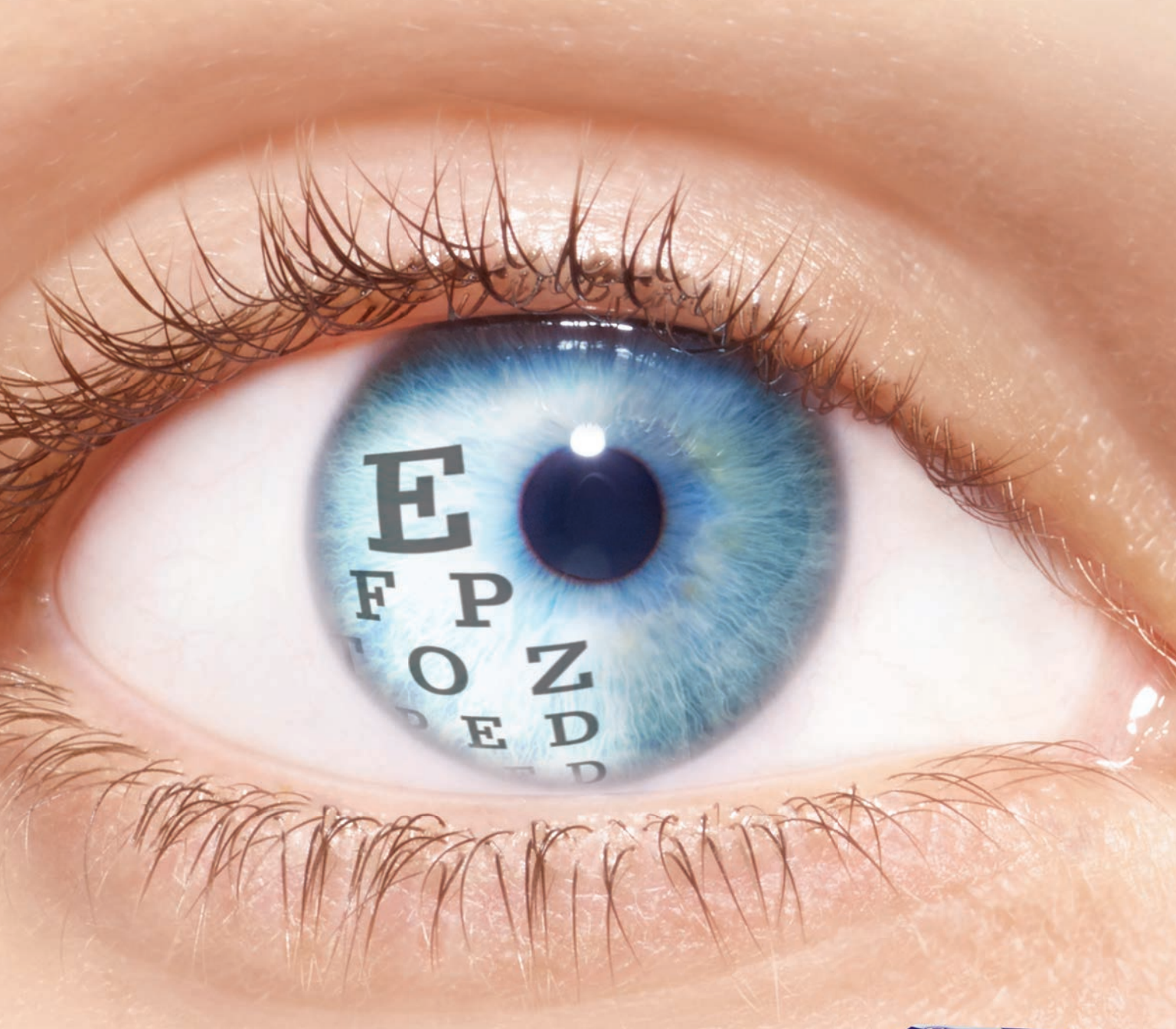

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1. Korb D, et al. Evaluation of extended tear stability by two emulsion based artificial tears. Poster presented at: 6th International Conference on the Tear Film and Ocular Surface: Basic Science and Clinical Relevance; September 22-25, 2010; Florence, Italy.

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