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DEVELOPING TAILORED MANAGEMENT STRATEGIES FOR DED:

A Comprehensive Treatment Approach



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A Comprehensive Treatment Approach

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Content Source

This continuing education (CE) activity captures content from a synchronous in-person symposium.

Activity Description

This supplement summarizes a discussion on the importance of a healthy ocular surface, especially prior to cataract surgery, as well as the relationship between dry eye disease and meibomian gland dysfunction and how to recognize the signs even when patients do not mention symptoms.

Target Audience

This certified CE activity is designed for optometrists.

Learning Objectives

Upon completion of this activity, participant should be able to:

- **Diagnose** patients with dry eye disease (DED) using an algorithmic approach that considers the signs and symptoms as well as individual factors that increase the risk for disease
- **Relate** the clinical manifestations of DED/meibomian gland dysfunction to the underlying pathophysiology
- **Perform** comprehensive diagnostic evaluations for patients suspected to have DED, integrating point-of-care diagnostics where appropriate and beneficial
- **Explain** how the composition and mechanism of action of artificial tears and DED treatments may influence clinical outcomes
- **Develop** a personalized treatment plan that uses complementary treatment approaches, where appropriate, to improve the signs and symptoms of DED

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PRETEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation/Satisfaction Measures for credit.

- 1. Please rate your confidence in your ability to develop a personalized treatment plan that uses complementary treatment approaches, where appropriate, to improve the signs and symptoms of dry eye disease (DED) (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).
 - a. 1
 - b. 2
 - c. 3
 - d. 4
 - e. 5
- 2. A 22-year-old patient presents with redness in both eyes. She has an ocular history of contact lens wear and intermittent allergies. Her medications include sertraline and an oral antihistamine. What is the best next clinical step for this patient?
 - a. Perform corneal sensitivity testing
 - b. Perform meibography
 - c. Perform ocular surface staining
 - d. Measure tear meniscus height
- 3. Meibomian gland blockage, inflammation, or dropout causes _____ meibum production, which triggers the _____ of bacteria leading to alterations in meibum lipid composition.
 - a. Excessive, death
 - b. Excessive, growth
 - c. Insufficient, death
 - d. Insufficient, growth
- 4. A 63-year-old patient presents with a history of chronic DED. Her ocular history includes refractive surgery. She has used multiple artificial tears without symptomatic relief. What is the best next step in diagnostic testing?
 - a. Meibomian gland expression
 - b. Ocular surface staining
 - c. Osmolarity
 - d. Tear film break-up time (TBUT)
- 5. Patients with aqueous-deficient DED may benefit from ______, which increases the production of basal tears by activating the trigeminal parasympathetic pathway.
 - a. Loteprednol etabonate ophthalmic suspension 0.25%
 - b. Lotilaner ophthalmic solution 0.25%
 - c. Perfluorohexyloctane ophthalmic solution
 - d. Varenicline solution 0.03 mg
- 6. A 56-year-old patient presents with intermittent blurriness of 6 months at her computer. She uses a low viscosity artificial tear. She has a TBUT of 5 sec, and her meibography imaging shows mild gland atrophy and tortuosity. What is the MOST appropriate treatment approach?
 - a. Recommend punctal plugs and cyclosporine 0.09%
 - b. Recommend punctal plugs and loteprednol etabonate ophthalmic suspension 0.25%
 - c. Recommend thermal pulsation and loteprednol etabonate ophthalmic suspension 0.25%
 - d. Recommend thermal pulsation and cyclosporine 0.09%

- 7. Meibomian gland disease (MGD) is prevalent in which of the following populations?
 - a. Patients who are male
 - b. Patients who wear contact lenses
 - c. Patients with aqueous-deficient DED
 - d. Patients with glaucoma using short-term topical medications
- 8. The cycle of MGD within DED comprises dysfunction of the _____ and the release of toxins by lipases and esterases.
 - a. Goblet cells
 - b. Corneal epithelium
 - c. Eyelid
 - d. Tear film
- 9. A 32-year-old patient presents with contact lens intolerance, itchiness, and symptoms of dryness for 3 months. His TBUT is 12 seconds. Which of the following is the best next step in diagnostic testing?
 - a. Evaluate corneal sensitivity
 - b. Evaluate for dry eye inflammatory markers
 - c. Express the meibomian glands
 - d. Observe for eyelash collarettes
- 10. A new patient who is a 66-year-old female presents with burning, irritated eyes of 1 month. Her medical history includes hypertension with a change in systemic medications 4 months ago. She has significant corneal staining. What is the MOST appropriate dry eye therapy?
 - a. Cyclosporine 0.01%
 - b. Loteprednol etabonate ophthalmic suspension 0.25%
 - c. Omega-3 supplementation
 - d. Thermal pulsation of eyelids
- 11. A 45-year-old patient presents with red, irritated eyes. His SPEED questionnaire indicates dry eye. His TBUT and osmolarity testing results are normal. What is the best next step in diagnostic testing for DED according to TFOS DEWS II?
 - a. Express the meibomian glands
 - b. Measure corneal sensitivity
 - c. Measure tear meniscus height
 - d. Stain the ocular surface

Developing Tailored Management Strategies for DED: A Comprehensive Treatment Approach

ry eye disease (DED) is a self-perpetuating multifactorial disorder that affects a large proportion of the population.^{1,2} Prevalence rates have been reported to be anywhere from 5% to 50%, but may be as high as 75%, affecting patient populations such as those with glaucoma, contact lens wears, and patients with certain systemic conditions.^{3,4} Many patients with DED experience a decreased quality of life and are unable to perform activities of daily living.^{5,6} Although there is no "cure" for DED, we now have a numerous treatment options that have been shown to better manage the condition when tailored for specific patient needs. In the following activity, leading experts will discuss how to diagnose DED using an algorithmic approach that considers the signs and symptoms as well as individual factors that increase the risk for disease. We'll also review how to differentiate between DED types and develop a personalized treatment plan that uses complementary treatment approaches, where appropriate, to improve DED signs and symptoms.

-Kelly K. Nichols, OD, MPH, PhD, FAAO, Program Chair

UNDERSTANDING THE PATHOPHYSIOLOGY AND RISK FACTORS FOR DED

Dr. Nichols: Are DED and meibomian gland dysfunction (MGD) the same? DED is certainly very common.^{7,8} Studies have shown that 86% of dry eye patients have some component of MGD.9 MGD is a risk factor for dry eye and a leading cause of dry eye across the globe. 10

When you're in clinical practice, once you begin looking for DED, you'll find it, whether it's in patients with glaucoma, patients undergoing cataract surgery evaluation, or in patients who wear contacts. 11 Several studies have assessed dry eye prevalence in different patient populations. For example, 80% of patients with glaucoma on long-term topical medications have MGD.¹² Studies indicate that 60% of contact lens wearers have DED or MGD, but the prevalence may actually be higher.¹³ Importantly, 63% of pre-cataract patients have dry eye, and that only includes patients presenting for cataract evaluation.¹⁴

Dry eye is often referred to as a vicious cycle (Figure 1). 15 You can enter the cycle at any place. It often starts with tear film instability, which leads to hyperosmolarity, cell damage, apoptosis, or death of the cells on the cornea and conjunctiva. This



Figure 1. The vicious cycle of dry eye disease. 15

further stimulates an inflammatory response, leading to cytokine release and upregulation of the inflammatory pathway and goblet cell loss.

At the center of the cycle (Figure 1), we see MGD and its impacts on the lids, esterase/lipase release toxins, changes to the lipids, and changes in flora. MGD is extremely complex, and there are many ways we can address these issues.

Walter O. Whitley, OD, MBA, FAAO: Is MGD the inner circle or the outer circle of that diagram? Does MGD start with the lids and then affect the surface?

Dr. Nichols: It's both. Certainly if you have issues with your lids, that will create lipid abnormalities, which will then create an abnormal loss of homeostasis of the tear film that starts the cycle. You can have inflammation from systemic conditions such as Sjögren syndrome, which will start the cycle as well. For example,

it's unusual to see a patient with Sjögren who doesn't also have MGD. Sjögren likely came first, but MGD is making it worse.

Other factors associated with MGD include age, sex, contact lens wear, ocular surgery, the environment, smoking, certain anterior segment diseases, and digital devices. 16,17 We're on digital devices all the time. Studies have shown that we're not blinking as frequently as we need to while using these devices, which is negatively impacting our tear film. 18,19

Patient questionnaires such as the Ocular Surface Disease Index (OSDI), Standardized Patient Evaluation of Eye Dryness (SPEED), Symptom Assessment In Dry Eye (SANDE), and others, are helpful in identifying patients who have DED risk factors. 20,21 Which of these questionnaires do you use?

Jaclyn Garlich, OD, FAAO: I use the SPEED questionnaire in my practice. It is a simple way to measure patient symptoms.

Dr. Whitley: I use the SPEED questionnaire as well to help screen and monitor treatment, but you don't need a questionnaire to assess patient symptoms. The important point is to ask the questions. Do you feel like you have dry eyes? Are you bothered by red eyes? Do you feel the need to use artificial tears? Does your vision fluctuate throughout the day? If they say yes to any of those questions, you need to assess them for DED and MGD.

Dr. Nichols: Other causes of MGD include proliferation such as Staphylococcus epidermidis, Staphylococcus aureus, Propionibacterium acnes, Bacillus oleronius, and Demodex. 15,22 Collarettes are the hallmark of Demodex blepharitis.²³ You can't see them in straight-ahead view, and some patients are good at cleaning their eyelids. Therefore, sometimes when a patient comes to you, you may not see collarettes because they were removed mechanically.

DIAGNOSING DED

Dr. Nichols: The Tear Film & Ocular Surface Society Dry Eye Workshop (TFOS DEWS) II report and diagnosis recommendations have been out for several years.²⁴ There's a TFOS DEWS III in development, which will provide us a refined dry eye definition, diagnostic recommendations, and a summary of management plan options. TFOS DEWS II has several triaging questions you should ask patients to identify risk factors for dry eye (Table). You're looking to rule out some masquerading conditions.

TFOS DEWS II suggests two questionnaires that have been validated: the 5-Item Dry Eye Questionnaire (DEQ-5) and ODSI.20 Many clinicians, us included, like the SPEED questionnaire, but OSDI is also a good one that has been used in clinical trials. DEQ-5 is a short version that has been validated as well. In addition to assessing symptomology through a validated questionnaire, you can screen with simple homeostasis marker tests, or a combination. If more than one homeostasis marker test is performed and is abnormal, the patient screens positive for dry eye. The tests should be performed in the following order: noninvasive tear

TABLE. TFOS DEWS II DIAGNOSTIC QUESTIONS²⁰

- 1. How severe is the eye discomfort?
- 2. Do you have any mouth dryness or swollen glands?
- 3. How long have your symptoms lasted and was there any triggering event?
- 4. Is your vision affected and does it clear on blinking?
- 5. Are the symptoms or redness much worse in one eye than the other?
- 6. Do the eyes itch, appear swollen or crusty, or have given off any discharge?
- 7. Do you wear contact lenses?
- 8. Have you been diagnosed with any general health conditions (including recent respiratory infections) or are you taking any medications?

break-up time (TBUT), osmolarity, fluorescein TBUT (if noninvasive TBUT isn't available), and ocular surface staining.

Signs of dry eye include a fluorescein TBUT of <10 seconds, osmolarity ≥308 m0sm/L in either eye (or interocular difference >8 m0sm/L), and ocular surface staining >5 corneal spots, >9 conjunctival spots, or lid margin (≥2 mm length and ≥25% width).20 You can observe staining on the conjunctiva with fluorescein as long as you look carefully and use enough dye. A yellow Wratten filter can aid viewing.

If the patient has one or more positive symptoms for DED, the next step is to determine the type, whether it's evaporative, aqueous, diffusion, or a combination. MGD is the underlying cause of evaporative dry eye. You can assess the patients' meibomian glands using the "look, lift, push, and pull" exam, which is part of the American Society of Cataract and Refractive Surgery preoperative ocular surface disease algorithm.²⁵ It requires no special equipment, only a cotton swab. When you push on the meibomian glands, the oil expressed should be clear, not cloudy or thick.

Aqueous-deficient dry eye is caused by dysfunctional lacrimal glands and/or mucin-producing goblet cells that produce a low volume of aqueous. Their tear meniscus height can be assessed at the slit lamp. To assess for Sjögren, ask a few pointed questions. Patients with Sjögren are most likely women in their 40s with extremely dry eyes.26 Do they have a dry mouth? If they do, you may want to screen them for Sjögren dry eye and refer them for a rheumatology consult.

You should also check corneal sensitivity. We now have treatments for patients with neurotrophic keratitis (NK), but you have to proactively test.²⁷ Patients are often unaware of their NK condition because they don't experience pain. Dry eye and NK often coexist. NK may resemble dry eye, especially in the early

stages, complicating diagnosis.^{28,29} I use a cotton wisp to check corneal sensitivity, but you can also use unflavored dental floss to lightly touch all five corneal zones and classify sensitivity as normal, hypoesthesia, or anesthesia for each zone.²⁷

Dr. Whitley: You should also look for an incomplete lid seal. I ask patients when their eyes feel worse. If it's in the morning, is it due to Demodex blepharitis? Is it due to incomplete lid closure? Using the Korb-Blackie lid light test, do you see any illumination when the patient closes their eyes? If you do, they have an exposure problem. The patient could use drops on their eyes all day long, but unless we address the anatomy, they will continue to be symptomatic.

SELECTING THE OPTIMAL TREATMENT

Dr. Garlich: There are many factors that contribute to someone's dry eye status: inflammation, environmental issues, anatomy, and others. We have a variety of treatment options for patients, which is wonderful. But it can also be confusing to determine which person is right for which treatment in which situation. For example, when selecting a treatment for a patient with moderate dry eye, you need to determine which outcome you're prioritizing. Is it rapid symptom relief, long-term efficacy, improvements in tear film stability, a reduction in ocular surface inflammation, minimizing side effects, or a combination?

Dr. Nichols: These are all important, but some may be more important than others. Rapid symptom relief is very important to patients.

Dr. Garlich: Yes. If a patient comes back and they clinically look better but they don't feel better, that is a problem.

EMPLOYING A STEPWISE TREATMENT APPROACH

Dr. Garlich: I take a stepwise approach to treatment and break it into 4 phases.^{30,31} I start simply with phase 1, which includes behavior modifications such as reducing screen time. They can try preservative-free drops, loteprednol etabonate 0.25%, omega-3 supplements, warm compresses, and lid hygiene with a tea-tree oil pad. If those home interventions don't help after 3 weeks and clinical signs and symptoms are still present, we move to phase 2. This includes topical cyclosporine or lifitegrast, continuing preservative-free tears but stopping loteprednol etabonate 0.25%, temporary plugs in the lower lids, and thermal expression if the patient has MGD. Phase 3 includes lubricating gels, oral doxycycline or metronidazole, intense pulsed light (IPL), and extended punctal plugs. Finally, phase 4 is the most significant treatment and includes serum tears, amniotic membranes, and topical vitamin A therapy.

Dr. Nichols: A stepwise approach is best, because you don't want to throw everything at them at once. Sometimes you get patients who have been dealing with dry eye for years, and they do need a multipronged approach. Those are the most difficult cases to treat.

Dr. Whitley: Lifestyle changes are the hardest to manage. It's difficult to change someone's diet, digital habits, and environment.

Dr. Garlich: You make a good point about lifestyle because it is difficult to change, and it is a lot of information for the patient to absorb. I have a handout available for patients with tips for success that they can take with them.

TOPICAL TREATMENTS

Dr. Garlich: Regarding artificial tears, this is what most patients reach for first when their eyes start to bother them. Patients with aqueous-deficient DED are the most frequent users of artificial tears. As clinicians, it's our job to give the patient a specific recommendation for artificial tears and be very intentional about that recommendation.

Many of us have learned that patients with evaporative DED due to MGD benefit from a combination of emollient-containing tears, warm compresses, environmental management, and a review of systemic medications that may be exacerbating the condition. Patients with mild DED may have success with a lower viscosity drop. However, if they are using something at night before bed, especially if they have an incomplete lid seal, a gel or ointment may be more effective. How do you work artificial tears into your treatment?

Dr. Whitley: It's critical that if a patient is using artificial tears, that they use a preservative-free option. I haven't had much success with artificial tears alone for symptomatic dry eye patients. As you mentioned, most often the patient has tried several, so suggesting another doesn't have much benefit. Evidence suggests that omega and nutraceutical supplements can improve tear osmolarity, TBUT, MMP-9, and OSDI symptom scores. 32,33 It's working on the dryness from the inside.

Dr. Nichols: Many times the patient has already tried artificial tears, but it can be a nice adjunct, depending on what they have tried and failed otherwise.

Dr. Whitley: I ask the patient how long they have had dry eye. If it's 1 or 2 months, that is likely a dry eye flare. In this case, 2 weeks of steroids may help, but you need to carefully monitor their intraocular pressure (IOP). I'd also check their nerves for glaucoma. Now, if you ask the patient how long they've had dry eye and they say years, we need to minimize their symptoms and improve their quality of life while also setting the expectation that improvement may take time.

Dr. Garlich: Yes, I agree. If a patient has been suffering for years, I explain that we won't reverse it in a month. Dr. Whitley mentioned this, but if a patient has drop fatigue and there is

significant staining on the cornea, you can recommend a stronger therapy like a steroid to quiet that inflammation. They need the full 2 weeks or longer, depending on the case. When I first started treating patients with ocular surface disease, my downfall was not prescribing the steroid for long enough. A week is sometimes not enough time. Loteprednol etabonate 0.25%, which is now approved by the US Food and Drug Administration (FDA), improved ocular discomfort scores at day 15 with a rapid onset of action; improvement was seen at day 8 in all phase 3 trials and as early as day 2 in one trial.³⁴ The most common treatmentemergent adverse event (AE) was instillation site pain (5%). As Dr. Whitley mentioned, corticosteroids are known to increase IOP, and prolonged use may lead to glaucoma. However, IOP elevation in patients receiving loteprednol etabonate 0.25% in the clinical trials was low. I prescribe it to patients who are highly inflamed.

Dr. Nichols: How many times a day do you recommend we prescribe the steroid?

Dr. Whitley: The only FDA approved steroid for short-term relief of the signs and symptoms of dry eye is loteprednol etabonate 0.25%. It can be prescribed for up to four times a day for 2 weeks. When you're prescribing a steroid, it's important to check their IOP and their nerves. If anyone will respond, it will most likely be a patient with glaucoma.

Dr. Nichols: When prescribing loteprednol etabonate 0.25%, do you provide refills?

Dr. Garlich: No, I don't. If someone needs a steroid all the time, they likely need an immunomodulator or inflammation suppression. Until 2016, we had one option, cyclosporine 0.05%. It worked by suppressing the activation of T-lymphocytes and inhibiting cell death. It was thought to enhance tear production and increase goblet cell density while decreasing cell apoptosis. In the clinical trials, it increased Schirmer score and decreased conjunctival staining scores. The most common AE was ocular burning (17%).35 But it can take more than 3 months to experience improvements, which was frustrating for the patient.

In 2016, lifitegrast 5% was approved by the FDA. This has a different mechanism of action from cyclosporine. It blocks LFA-1 on T cells from binding with ICAM-1, which inhibits T-cell activation and migration of activated T cells to the ocular surface, and reduces cytokine release.³⁶ LFA-1 is something that lives on a T cell, and ICAM-1 is thought to be overexpressed in DED. Lifitegrast works by blocking that interaction, which will then inhibit the inflammatory cascade that we see in a patient with dry eye. Patients experience improvements in eye dryness in as few as 14 days.³⁷ The most common AEs in 5% to 25% of patients were instillation-site irritation, dysgeusia, and reduced visual acuity. There was a low discontinuation rate overall.

We now have two additional cyclosporines: cyclosporine 0.09% and cyclosporine 0.1%. The difference between them is the vehicle in which the medication is delivered to the eye. Cyclosporine 0.09% uses NCELL technology. Nanomicelles encapsulates cyclosporine through a hydrophobic core and hydrophilic shell, which allows penetration through the aqueous layer.³⁸ That's why we see improvement in corneal and conjunctival staining as soon as 4 weeks. The most common AEs are pain on drop instillation (22%) and conjunctival hyperemia (6%).³⁸

Cyclosporine 0.1% uses a novel water-free vehicle (perfluorobutylpentane), which allows cyclosporine to spread evenly over the ocular surface with longer residual time and increased penetration. In the phase 2/3 ESSENCE-1 and phase 3 ESSENCE-2 trials, 66% of patients had three or more grades of total corneal fluorescein staining (tCFS) improvement by day 29, and 57% of patients showed at least three grades of improvement in tCFS at day 15.39,40 The most common AEs were instillation-site reactions (8%) and temporary decreases in visual acuity (3%), but 99.8% of patients experienced no or mild instillation-site irritation. We now have three cyclosporine options. How do you determine which one you prescribe?

Dr. Whitley: Insurance coverage is an important factor because our preferred drop may not be covered. It's important to understand the differences with the various dry eye treatments, too. In the past several years, we have seen innovations in drug delivery. One example is cyclosporine 0.09%. Patients who have been on cyclosporine 0.05% for years saw improvements in the signs and symptoms of dry eye when they switched to cyclosporine 0.09%. 41 The data for cyclosporine 0.1% is impressive, too. We should prescribe it to our patients, regardless of insurance issues, to see how it performs. If it's covered, that's great; if not, we can adjust as needed.

Dr. Nichols: For me, it depends on what I'm observing clinically. For example, if the patient has a small amount of staining and I know they have MGD, I may treat the MGD first. But if they have MGD and significant staining, I may treat both at once. If they have staining and confirmed inflammation, then you'll have to manage the inflammation as well.

Dr. Garlich: We're also seeing patients with evaporation issues driven by our digital devices. With that in mind, we have now FDA approval for 100% perfluorohexyloctane. This is the only drop that targets tear evaporation. It forms a monolayer at the air liquid interface of tear film that prevents tears from evaporating. The MOHAVE and GOBI trials demonstrated a 32% improvement in tCFS at day 57, 36% in cCFS, and 43% improvement in eye dryness at day 57. Improvements were noted as early as day 15. The most common AE was blurred vision (2.1%).42 To me, it feels like an oil slick on the eye, which reduces friction. What patients are you considering for this drop?

Dr. Nichols: This is good for patients with MGD and a small amount of staining. Patients do need to be coached on the

amount of drop to instill. It's so smooth and silky, they don't necessarily feel it, and they end up using half the bottle. They should tap the bottle to release the drop.

Dr. Garlich: Patient education on the small drop size is important because, unfortunately, patients are used to drops running out of their eye. If they do that with 100% perfluorohexyloctane, they'll run out of it very quickly.

We talked a little bit earlier about Demodex blepharitis. We now have a treatment for that that was approved by the FDA last year, lotilaner 0.25%. This is a lipophilic agent in an aqueous drop that acts via glutamate- and GABA-gated chloride channels to target, paralyze, and kill Demodex. The clinical trial results speak for themselves. SATURN-1 and SATURN-2 included more than 800 patients. Investigators found that 60% of patients had total eradication of the mites. 43,44 There was a 50% reduction of collarettes to two or fewer, 85% reduction to 10 or fewer, and a 25% erythema cure rate, which is important to patients. Patients are often frustrated with their eye redness, and this drug works to improve it by eliminating the inflammation from the mites. AEs included stinging and burning (10%) and chalazia/punctate keratitis (2%).

Dr. Nichols: If Demodex is not eradicated in 6 to 8 weeks, do you repeat treatment?

Dr. Garlich: I would yes, but that is a very rare occurrence. I also want to mention that patients with severe dry eye may benefit from autologous serum drops. These contain natural growth factors, proteins, antioxidants, and anti-inflammatory properties that can help tremendously.⁴⁵ After blood draw, it is allowed time to clot, then put into a centrifuge, filtered, and finally diluted to the prescribed concentration. Common concentrations are 20% to 40%. It's usually ready in 48 hours. There are companies that will help facilitate serum tears for your patient. Depending on the clinical case, maximum benefit is seen within 6 to 8 weeks. The caveat is that the vials have to be refrigerated, and they must be used within 1 week. Unopened vials must stay frozen (up to 3 months) until time for use.

VARENICLINE NASAL SPRAY

Dr. Garlich: If the patient is tired of eye drops, we have varenicline 0.03 mg, which is a nasal spray that activates the trigeminal parasympathetic pathway to increase the production of basal tears. It's a completely different approach. Varenicline works on the lacrimal functioning unit, which includes the lacrimal gland, goblet cells, and meibomian glands. In the ONSET-1 trial, 52% of patients experienced ≥10 mm increase in Schirmer score from baseline.⁴⁶ In ONSET-2, 47% experienced that Schirmer score increase by day 28.47 The downside is it makes you sneeze, however, it's not common for patients to discontinue use because of it. The most common AEs include sneezing (82%), cough, throat irritation, and instillation-site (nose) irritation (5% to 16%).

Dr. Nichols: Varenicline 0.03 mg is a great option for patients with glaucoma who are already on multiple drops. It's also ideal for contact lens wearers who don't want to remove their contacts in the middle of the day to use eye drops.

IN-OFFICE TREATMENTS FOR MGD

Dr. Garlich: For a patient with MGD, sometimes the at-home warm compresses are not enough. They require a more powerful therapy to remove that obstruction in the meibomian gland. That's where thermal expression comes into play. There are three well-known ways to do this. The first to the market was LipiFlow, which uses vectored thermal pulsation to apply heat and a peristaltic motion to the eyelid to remove gland obstructions and stagnant gland content. In clinical trials, it increased gland secretion three-fold, on average, with just one treatment. 48

Dr. Nichols: How often do you recommend LipiFlow treatments for your typical patient with MGD?

Dr. Whitley: In my practice, about 5% of patients who have had LipiFlow have a repeated treatment, however, that number would be much higher if it were covered by insurance. MGD requires lifetime management, and we'll repeat the treatment when they need it again.

Dr. Garlich: We also have TearCare, which uses localized heat, applied using SmartLids technology, to the upper and lower eyelids. It heats the glands to 113° F for 15 minutes. The clinician then takes the patient to the slit lamp and expresses the thick oil out of the glands. Studies found significant improvements in mean TBUT and meibomian gland secretion score 1 month post-treatment.⁴⁹ Patients need TearCare treatment once a year on average. Some patients receive this treatment every 6 months.

The Systane iLux² is a similar concept. This is light-based heat and gland expression under visualization. A single treatment can result in an increase in meibomian gland secretion, improvement in tear film stability, and reduction in dry eye symptoms as early as 1 week.50

We also have IPL, which is different from thermal expression. IPL uses selective photothermolysis to destroy blood vessels by targeting chromophores (hemoglobin, melanin, and water). It's a combination of pulse duration, wavelength, pulse interval, and fluences that treats many skin conditions.51-53 I use IPL in patients with significant lid inflammation. It reduces the presence of Demodex mites by attacking their pigmented exoskeleton and also improves TBUT by 87%.52

I find these treatments very helpful for patients who are not compliant with warm compresses. If they have any level of obstruction, warm compresses are not effective, so other therapies are required. Patients love these treatments and they work, but the downside is these are not covered by insurance. If your patients are unable to pay the out-of-pocket costs, that can be a hurdle.





Figure 2. Baseline meibography.

Dr. Nichols: How do you present some of the more expensive out-of-pocket treatments to your patients?

Dr. Garlich: I prefer a collaborative approach with my patients. I'm honest and upfront about the costs. I will tell them what I think is best for them, but if it's not in their budget, I will recommend other therapy. There are ways to get some of the more expensive treatments to patients, such as payment plans, care credit, and FSAs or HSAs.

PUNCTAL PLUGS

Dr. Garlich: Punctal plugs work by raising the tear lake. They are a great option for patients who are noncompliant. Some patients do not want at-home therapy, and this is one way that you can improve symptoms with no work from the patient. They are also a good option for patients with inferior corneal staining, lagophthalmos, patients who are neurotrophic, and patients who have Sjögren syndrome. 54,55 Punctal plugs are not for everyone. If a patient has allergies or significant inflammation, you will trap that inflammation on the eye. Inflammation must be quiet before I consider a plug. It's also not appropriate for patients with active infections or severe blepharitis.

CASE 1: 45-YEAR-OLD ATTORNEY WITH MEIBOMIAN GLAND DROPOUT

Dr. Garlich: Our first case is a 45-year-old white female. She is an attorney, and complains that her eyes are burning and gritty during the day, which worsens in the winter. She is frustrated with how her eyes feel during the day.

She rates her dryness a 3 out of 10. She's very healthy, has a negative medical history, and takes no medications. She doesn't use eye drops. Her SPEED score is 9, and her VA is 20/20 OU. She is a very low hyperope (OD: +0.50sph; OS: plano; add: +1.25). Her MMP-9 is trace positive OU. MMP-9 is a biomarker of inflammation in the tear film. Sometimes the positive pink line is faint, and other times it's dark pink.

The color density of the line tells you if there is a lot or a little inflammation.

I check her glands at the slit lamp and note that she has some turbid expression. Her TBUT is 7 to 8 seconds OU. She does have mild inferior superficial punctate keratitis (SPK). The Korb-Blackie lid light test was positive. Figure 2 shows her meibography images. What are your initial impressions?

Dr. Whitley: She's lost 40% of her glands in the right and left eyes. These are vital to producing good quality tears, so this must be addressed.

Dr. Nichols: Typically, superior and inferior glands are not both checked clinically, but with loss like this, examining the superior lid can be useful. If the upper glands look good, then that may change how aggressive I am with treatment.

Dr. Garlich: This patient has mild keratitis, and her MGD is exacerbated by all-day computer use. I prescribed an over-thecounter gel at night because of her incomplete lid seal. I also recommended lid tape, but she was not interested. She doesn't want to use drops because she has a high-profile job and wears makeup. I talked to her about varenicline. I recommended omega-3 supplements, and we discussed at-home warm compresses. I offered thermal expression as well.

Dr. Nichols: Of note, she uses computers all day. The location of her computer monitor is important. For example, a vent or space heater may be blowing on her eyes. It's important to ask patients about their air environment because you may discover an easy adjustment.

Dr. Garlich: Would you have done anything differently?

Dr. Whitley: No, I agree with your approach. I would provide them education on thermal pulsation and IPL and send them home with some information for consideration.

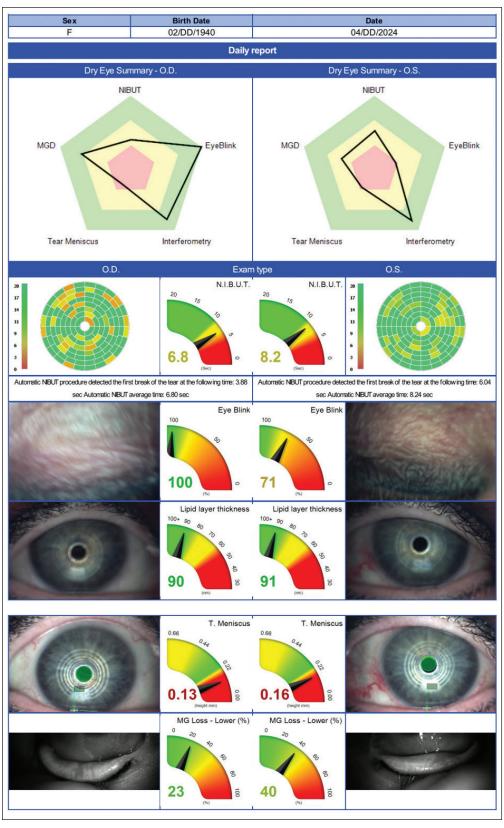


Figure 3. Examination.

CASE 2: ELDERLY WOMAN WITH CHRONIC DRY EYES AND POAG

Dr. Whitley: Our second case is an 84-year-old white female who presents with chronic dry eyes. She has a foreign body sensation in the left eye and a small tender bump on the left upper lid. She reports occasional use of artificial tears and heat mask. She uses cyclosporine 0.05% OU twice a day. She has a varied ocular history, including phaco OU, yag laser capsulotomy OU, mild primary open-angle glaucoma OU, and s/p selective laser trabeculoplasty OU. She has diabetes, hyperlipidemia, and takes atorvastatin. Her SPEED score is 10. Her BCVA is 20/25 OD and 20/30 -2 OS. Figure 3 shows some tear deficiency, decreased tear meniscus, and meibomian gland loss. This patient clearly has both evaporative and aqueousdeficient dry eye.

The look, lift, push, pull exam revealed some thickening of the oil, indicating MGD. Our final assessment of this patient was dry syndrome OU and external hordeolum in the left upper lid. Our treatment plan included a heat mask for 10 minutes, four times a day. We also prescribed azithromycin and twice daily cyclosporine 0.09%. Finally, we recommended omega-6 and omega-3 supplements to help with her dry eyes from the inside out.

Dr. Nichols: Thank you, Drs. Whitley and Garlich, for your thoughts and expertise.

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DEMOGRAPHIC INFORM	MATION					
Profession	Years in Practice	Patients Seen Per Week	Region			
MD/DO	>20	(with the disease targeted	Midwest			
OD	11-20	in this educational activity)	Northeast			
NP Nurse/APN	6-10	0 1-15	Northwest Southeast			
PA	1-5 <1	16-30	Southeast Southwest			
Other	<1	31-50	Southwest			
Other		>50				
LEARNING OBJECTIVES						
Did the program meet the	following educational objectives?	Agre	e Neutral	Disagree		
Diagnose patients with dry	eye disease (DED) using an algorithmic ap	oproach that				
· ,	ptoms as well as individual factors that in	•				
disease						
Dalata the clinical manifesta	tions of DED/maihamian aland durfunct	ion to the underlying				
pathophysiology	tions of DED/meibomian gland dysfunct	ion to the underlying				
	gnostic evaluations for patients suspecte gnostics where appropriate and beneficia					
Explain how the composition	on and mechanism of action of artificial to	ears and DED				
treatments may influence cl			_			
•	tment plan that uses complementary tre	atment approaches				
	ove the signs and symptoms of DED	аннен арргоаснез,				

PRETEST QUESTIONS

Please complete at the conclusion of the program.

- 1. Based on this activity, please rate your confidence in your ability to develop a personalized treatment plan that uses complementary treatment approaches, where appropriate, to improve the signs and symptoms of dry eve disease (DED) (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).
 - a. 1
 - b. 2
 - c. 3
 - d. 4
 - e. 5
- 2. A 22-year-old patient presents with redness in both eyes. She has an ocular history of contact lens wear and intermittent allergies. Her medications include sertraline and an oral antihistamine. What is the best next clinical step for this patient?
 - a. Perform corneal sensitivity testing
 - b. Perform meibography
 - c. Perform ocular surface staining
 - d. Measure tear meniscus height
- 3. Meibomian gland blockage, inflammation, or dropout causes meibum production, which triggers the _____ of bacteria leading to alterations in meibum lipid composition.
 - a. Excessive, death
 - b. Excessive, growth
 - c. Insufficient, death
 - d. Insufficient, growth
- 4. A 63-year-old patient presents with a history of chronic DED. Her ocular history includes refractive surgery. She has used multiple artificial tears without symptomatic relief. What is the best next step in diagnostic testing?
 - a. Meibomian gland expression
 - b. Ocular surface staining
 - c. Osmolarity
 - d. Tear film break-up time (TBUT)
- 5. Patients with aqueous-deficient DED may benefit from _ which increases the production of basal tears by activating the trigeminal parasympathetic pathway.
 - a. Loteprednol etabonate ophthalmic suspension 0.25%
 - b. Lotilaner ophthalmic solution 0.25%
 - c. Perfluorohexyloctane ophthalmic solution
 - d. Varenicline solution 0.03 mg
- 6. A 56-year-old patient presents with intermittent blurriness of 6 months at her computer. She uses a low viscosity artificial tear. She has a TBUT of 5 sec, and her meibography imaging shows mild gland atrophy and tortuosity. What is the MOST appropriate treatment approach?
 - a. Recommend punctal plugs and cyclosporine 0.09%
 - b. Recommend punctal plugs and loteprednol etabonate ophthalmic suspension 0.25%
 - c. Recommend thermal pulsation and loteprednol etabonate ophthalmic suspension 0.25%
 - d. Recommend thermal pulsation and cyclosporine 0.09%

- 7. Meibomian gland disease (MGD) is prevalent in which of the following populations?
 - a. Patients who are male
 - b. Patients who wear contact lenses
 - c. Patients with aqueous-deficient DED
 - d. Patients with glaucoma using short-term topical medications
- 8. The cycle of MGD within DED comprises dysfunction of the _____ and the release of toxins by lipases and esterases.
 - a. Goblet cells
 - b. Corneal epithelium
 - c. Evelid
 - d. Tear film
- 9. A 32-year-old patient presents with contact lens intolerance, itchiness, and symptoms of dryness for 3 months. His TBUT is 12 seconds. Which of the following is the best next step in diagnostic testing?
 - a. Evaluate corneal sensitivity
 - b. Evaluate for dry eye inflammatory markers
 - c. Express the meibomian glands
 - d. Observe for eyelash collarettes
- 10. A new patient who is a 66-year-old female presents with burning, irritated eyes of 1 month. Her medical history includes hypertension with a change in systemic medications 4 months ago. She has significant corneal staining. What is the MOST appropriate dry eye therapy?
 - a. Cyclosporine 0.01%
 - b. Loteprednol etabonate ophthalmic suspension 0.25%
 - c. Omega-3 supplementation
 - d. Thermal pulsation of eyelids
- 11. A 45-year-old patient presents with red, irritated eyes. His SPEED questionnaire indicates dry eye. His TBUT and osmolarity testing results are normal. What is the best next step in diagnostic testing for DED according to TFOS DEWS II?
 - a. Express the meibomian glands
 - b. Measure corneal sensitivity
 - c. Measure tear meniscus height
 - d. Stain the ocular surface

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to partici	pating in this cou	rse: 5 = High, 1	= Low				
Rate your knowledge/skill level after participat	ing in this course	: 5 = High, 1 = L	_OW				
This activity improved my competence in mar	naging patients wi	th this disease/	condition/sympto	om Yes	No		
Probability of changing practice behavior base	d on this activity:	High	_ LowNo cha	ange needed			
If you plan to change your practice behavior, w	what type of chan	ges do you plar	n to implement? (d	check all that appl	y)		
Change in pharmaceutical therapy	Change in nonpharmaceutical therapy						
Change in diagnostic testing	Choice of treati	Choice of treatment/management approach					
Change in current practice for referral	Change in differ	s					
My practice has been reinforced	I do not plan to implement any new changes in practice						
Please identify any barriers to change (check all th	at apply):						
Cost	Lack of consensus or professional guidelines						
Lack of administrative support	Lack of ex	Lack of experience					
Lack of time to assess/counsel patients	Lack of op	Lack of opportunity (patients)					
Reimbursement/insurance issues	Lack of res	Lack of resources (equipment)					
Patient compliance issues N		No barriers					
Other. Please specify:							
The design of the program was effective for the co	ontent conveyed	Yes	No				
The content supported the identified learning obj	Yes	No					
The content was free of commercial bias		Yes	No				
The content was relative to your practice		Yes	No				
The faculty was effective		Yes	No				
You were satisfied overall with the activity	Yes	No					
You would recommend this program to your coll	Yes	No					
Please check the Core Competencies (as defined by	by the Accreditation	n Council for Gra	aduate Medical Edu	ıcation) that were e	nhanced through your par-		
ticipation in this activity:	•			,	0 / 1		
Patient Care							
Practice-Based Learning and Improvement							
Professionalism							
Medical Knowledge							
Interpersonal and Communication Skills							
System-Based Practice							
Additional comments:							
This information will help evaluate this activity; m on this activity? If so, please provide your email ac		by email in 3 mo	onths to inquire if y	ou have made chan	ges to your practice based		





