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UPDATES IN DRY EYE DISEASE:

Diagnosing and Treating Patients with Ocular Surface Disease

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Updates in Dry Eye Disease:
Diagnosing and Treating Patients with Ocular Surface Disease

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CONTENT SOURCE

This continuing education (CE) activity captures content from a round table discussion that occurred on March 21, 2019.

ACTIVITY DESCRIPTION

Nearly 33% of patients in eye care clinics present with complaints about dry eye signs and symptoms. Clinicians remain challenged with both the diagnosis and best treatment options for dry eye disease (DED) because, to date, multiple causes of the disorder has been identified. Yet the proportion of US adults who reported having symptoms of DED seemed to plateau from 2015-2018, with about 41% noting occasional DED and 12% noting frequent DED. Extrapolating those figures to the US population equates to more than 135 million people with DED.

TARGET AUDIENCE

This certified CE activity is designed for optometrists managing ocular surface disorder patients and other health care providers involved in the management of ocular surface disorders.

LEARNING OBJECTIVES

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

- **Identify** the prevalence of dry eye disease and the related signs and symptoms of patients.
- **Explain** the importance of taking a thorough patient history and evaluation in creating an accurate diagnosis.
- **Recognize** the need for constant maintenance and ongoing care related to the various dry eye disease treatments.
- **Develop** an individualized treatment plan for patients with dry eye disease.

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PRETEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation.

1. **PLEASE RATE YOUR CONFIDENCE ON YOUR ABILITY TO APPLY UPDATES IN THE TREATMENT OF DRY EYE IN THE CLINIC. (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. **PLEASE RATE HOW OFTEN YOU INTEND TO APPLY ADVANCES IN THE MANAGEMENT OF DRY EYE IN THE CLINIC. (BASED ON A SCALE OF 1 TO 5, WITH 1 BEING NEVER AND 5 BEING ALWAYS.)**
   a. 1
   b. 2
   c. 3
   d. 4
   e. 5

3. **ALL BUT WHICH OF THE FOLLOWING IS ASSOCIATED WITH A RISK FOR DEVELOPING DRY EYE DISEASE?**
   a. Contact lens wear
   b. Use of digital handheld devices
   c. Allergies
   d. Male sex

4. **WHICH SYMPTOM MAY BE INDICATIVE OF DRY EYE?**
   a. Red eyes
   b. Gritty sensation
   c. Fluctuating vision
   d. Contact lens intolerance
   e. All of the above
   f. A, b, d
   g. B, c, d

5. **IN THE TFOS DEWS II REPORT, AN INITIAL SCREENING EVALUATION FOR MILD DED SHOULD INCLUDE ANY OF THE FOLLOWING DIAGNOSTIC TESTS EXCEPT:**
   a. Corneal aesthesiometer
   b. DED questionnaire such as SPEED or OSDI
   c. Meibography
   d. Tear film osmolarity

6. **WHAT IS THE MOST COMMON ENVIRONMENTAL FACTOR FOR THE DEVELOPMENT OF DRY EYE?**
   a. Rapid change in altitude (ie, mountain hiking)
   b. High humidity
   c. Low humidity
   d. Fluctuating outdoor temperatures

7. **WHICH IMMUNOMODULATOR MAY BE PRESCRIBED FOR RAPID-ONSET ACTION IN REDUCING DED SYMPTOMS?**
   a. Lifitegrast
   b. Cyclosporine 0.05%
   c. Prednisolone
   d. Loteprednol

8. **A STUDY BY SULLIVAN ET AL FOUND WHAT PERCENTAGE OF PATIENTS WITH DRY EYE HAD CLINICAL SYMPTOMS OF THE DISEASE AS WELL?**
   a. 36%
   b. 42%
   c. 57%
   d. 73%

9. **THE THRESHOLD FOR A POSITIVE (ABNORMAL) MMP-9 TEST IS _____.**
   a. ≥ 20 ng/mL
   b. ≥ 30 ng/mL
   c. ≥ 40 ng/mL
   d. ≥ 50 ng/mL

10. **A TEAR BREAK-UP TIME OF _____ IS CONSIDERED NORMAL; TBUT TIMES UNDER THAT ARE CONSIDERED ABNORMAL.**
    a. ≥10 seconds
    b. ≥12 seconds
    c. ≥27 seconds
    d. ≥15 seconds

11. **ACCORDING TO TO A RETROSPECTIVE STUDY BY LEMP ET AL, APPROXIMATELY 86% OF PATIENTS WITH DED ALSO HAVE _____.**
    a. A history of smoking
    b. Increased age (older than 80 years)
    c. Meibomian gland dysfunction
    d. Hypertension

12. **MRS. SMITH PRESENTS FOR HER ANNUAL SPRING EYE EXAM ASKING FOR A STRONGER PRESCRIPTION FOR HER GLASSES AND CONTACTS; HER VISION IS RECENTLY FREQUENTLY BLURRY, AND SHE'S NOTICED A REDUCTION IN THE NUMBER OF HOURS SHE CAN WEAR HER CONTACTS PLUS ITCHING. SHE HAS A HISTORY OF ALLERGIES TO POLLEN, BUT NO HISTORY OF AUTOIMMUNE DISEASE. SHE FILLS OUT THE SPEED QUESTIONNAIRE AND SCORES GREATER THAN 6. HER TEAR BREAK-UP TIME IS 8 SECONDS. MRS. SMITH'S BLURRY VISION AND CONTACT LENS INTOLERANCE MAY BE DUE TO:**
    a. Seasonal allergies
    b. Aqueous-deficient dry eye
    c. Cataract
    d. Both A and B
    e. Both B and C
    f. None of the above

Updates in Dry Eye Disease:
Diagnosing and Treating Patients with Ocular Surface Disease

Dry eye disease (DED) impacts upwards of 16 million Americans.[1] The traditional profile of a patient with DED is changing, as is our understanding of the underlying mechanisms driving the disease state. Once thought to be a disease of middle-aged women with autoimmune disorders,[2] we now know DED impacts younger patients across both sexes, possibly due to the rise of handheld digital devices and other environmental impacts.[1] Further, DED is commonly underdiagnosed because patients believe the symptoms they experience are normal or routine and don't report them to their eye care physician. The following roundtable discussion provides clinicians with tools to better diagnose and manage DED, even when clinical signs and symptoms don't align.

—Kelly K. Nichols, OD, MPH, PhD, FAAO, Moderator

PREVALENCE OF DRY EYE DISEASE

Q | KELLY K. NICHOLS, OD, MPH, PHD, FAAO: Many questions remain about the prevalence of DED. Studies show that 25% of patients aged 65 and older suffer from some form of DED, although prevalence may be as high as 75%.3-6 We also know it disproportionally affects more women than men.[7,8] The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II, which was released in 2017, listed female sex as a significant risk factor for DED. Not only are women diagnosed at a younger age, they also experience more severe symptoms than men.[2]

But recent studies have shown an uptick of DED in patients aged 18 to 34[1]; Farrand et al found a 2.7% prevalence of diagnosed DED among this demographic.[1] Based on your recent experiences treating DED patients, describe the types of patients you are diagnosing with DED. Are you seeing any changes in your practice regarding prevalence of DED?

MILTON HOM, OD, FAAO: One problem that we have in defining prevalence is that we tend to profile the middle-aged female, and I think dry eye impacts patients beyond this demographic.

We base many of our demographic assumptions on the epidemiological studies that were conducted before 2007.[3] Those studies don't consider the impact digital devices are having on dry eye prevalence. Although there is sparse evidence in the literature linking the use of handheld digital devices to DED, reduced blink rate and digital eye strain is consistently reported with computer use and may negatively impact tear stability.[9-12] As many as 90% of digital device users experience symptoms of digital eye strain such as tired, burning, and itchy eyes.[10,13,14] In my opinion, digital devices have changed our patient profile, and I'm now seeing millennials with DED. I honestly think the younger Generation Z will be even worse.

WALTER O. WHITLEY, OD, MBA, FAAO: I'm also seeing that trend in my practice. Identifying a patient profile can be challenging because most patients don't realize they have dry eye; they think their symptoms—including stinging, redness, a gritty sensation, and eye watering—are normal. It's easy to miss a DED diagnosis unless you're actively looking for it because patients don't report the symptoms.

DOUGLAS K. DEVRIES, OD: One of the most overlooked symptoms of DED is fluctuation and blurred vision caused by an unstable tear film.[15] Dry eye is a visual disorder that leads to difficulty performing common tasks such as driving, reading, and watching television,[15] and patients and physicians don't always recognize this. We need to include vision fluctuation within our surveys because, although patients tend to downplay how their eyes feel, they certainly know when their vision fluctuates or when they can't sustain a task.

There's no question that digital devices are changing the demographics of dry eye. The referrals I receive are for younger and younger patients. I'm also seeing contact lens intolerance at earlier ages. Like Dr. Hom, I believe digital devices are acting as an accelerator and physiologically advancing dry eye development.

DED is also impacting our surgical outcomes. The PHACO study by Trattler et al sought to the determine the incidence and severity of dry eye in patients being screened for cataract surgery.[16] It found the majority of patients (62.9%) had a tear break-up time (TBUT) of less than 5 seconds, 77% of eyes had positive corneal staining, and 50% of the eyes had positive central corneal staining.[16] Clearly, even in older patient populations, dry eye frequently goes undiagnosed, and that's certainly what we find in our practice. The overall prevalence of DED is understated.

MARC R. BLOOMENSTEIN, OD, FAAO: I completely agree. Dry eye is a vision-driven, symptom-related disease state. Patients make an

appointment to see an optometrist because they perceive something is not right about their vision. We need to encourage younger clinicians to look at the ocular surface, the quality of the tears, the tear meniscus, and the meibomian glands. We need to look for any signs of inflammation that may be affecting patients' vision before we write a prescription for glasses or contacts. In this day and age, when evaluating patients, you should assume they have dry eye until proven otherwise. Dry eye is the most underdiagnosed condition in our practices.

DIAGNOSING DRY EYE DISEASE

Questionnaires for symptom assessment

Q | DR. NICHOLS: How do you assess dry eye symptoms in your practice? Do you have patients complete a questionnaire or do you have a verbal discussion? Has dry eye symptom assessment become more routine in a dry eye algorithm?

DR. HOM: One thing that's missing in dry eye is a clear algorithm on how to approach, diagnose, and manage the disease. We're more confused than ever.

DR. BLOOMENSTEIN: One reason we don't see an algorithm is because there's no good definition of the disease state at the clinical level. TFOS-DEWS II defined DED as "a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[5]

That's a high-level definition. At the clinical level, I don't think patients understand what dry eye is and clinicians don't understand how to convey this to patients. There's a lot of confusion for both patients and providers.

DR. WHITLEY: In my practice, all patients take the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire, which scores patients from zero to 28 (Figure 1). If a patient scores 6 or higher, we either evaluate and treat them right away or reappoint them for a dry eye evaluation. There are several other questionnaires that can be used as well, including the Ocular Surface Disease Index (OSDI), Dry Eye Questionnaire 5 (DEQ-5), and McMonnies dry eye questionnaire. A study by Ngo et al found SPEED to be both repeatable and valid compared with the other surveys available.[17-19] Regardless of the questionnaire used, it's very important to ask patients specific questions such as: Do your eyes ever feel dry or uncomfortable? Are you bothered by red eyes? Do you suffer from blurry, fluctuating vision? Do you feel the need to use eye drops?

DR. HOM: SPEED was actually designed to assess meibomian gland dysfunction (MGD).[15] OSDI is also more for aqueous deficiency. If you think most dry eye is caused by MGD, then SPEED would work for you. I prefer to keep my questions as simple as possible. I ask the patient, "How often do you have dryness?"

SPEED™ QUESTIONNAIRE

Name: _____ Date: ___/___/___ Sex: M F (Circle) DOB: ___/___/___

For the Standardized Patient Evaluation of Eye Dryness (SPEED) Questionnaire, please answer the following questions by checking the box that best represents your answer. Select only one answer per question.

1. Report the type of SYMPTOMS you experience and when they occur:

Symptoms	At this visit		Within past 72 hours		Within past 3 months	
	Yes	No	Yes	No	Yes	No
Dryness, Grittiness or Scratchiness						
Soreness or Irritation						
Burning or Watering						
Eye Fatigue						

2. Report the FREQUENCY of your symptoms using the rating list below:

Symptoms	0	1	2	3
Dryness, Grittiness or Scratchiness				
Soreness or Irritation				
Burning or Watering				
Eye Fatigue				

0 = Never **1** = Sometimes **2** = Often **3** = Constant

3. Report the SEVERITY of your symptoms using the rating list below:

Symptoms	0	1	2	3	4
Dryness, Grittiness or Scratchiness					
Soreness or Irritation					
Burning or Watering					
Eye Fatigue					

0 = No Problems
1 = Tolerable - not perfect, but not uncomfortable
2 = Uncomfortable - irritating, but does not interfere with my day
3 = Bothersome - irritating and interferes with my day
4 = Intolerable - unable to perform my daily tasks

4. Do you use eye drops for lubrication? ☐ YES ☐ NO **If yes, how often?** _____

Cornea. 2013 Sep;32(9):1204-10

13-ADY-123 A

For office use only
Total SPEED score (Frequency + Severity) = ___/28

Figure 1. Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire.[17]

DR. BLOOMENSTEIN: We use a modified version of this. When patients come in and fill out their medical history, those questions are on the form. For me, one of the most important questions for a patient I ask is, "Do you feel a desire to use drops? Do you feel a need to lubricate your eyes?" Many patients are self-medicating with over-the-counter drops before seeing a doctor. I tend to judge their dry eye severity based off those answers. The frequency of drop administration is a better indicator to me. The literature indicates this as well. When DEQ-5 was developed, Begley et al found the measurement of dry eye symptom frequency to be an incredibly useful clinical tool in determining which patients had Sjögren syndrome versus keratoconjunctivitis sicca.[20]

DR. WHITLEY: We also know from International Task Force guidelines for the treatment of dysfunctional tear syndrome that if a patient is using artificial tears more than twice a day, they need some type of prescription dry eye treatment.[21]

Clinical assessment and diagnosis algorithms

DR. NICHOLS: One challenge clinicians have is managing patient expectations around their eye exam. Many patients come in with an expectation of the visit and don't understand a dry eye evaluation may be a separate part of their eye exam that assesses their vision.

DR. BLOOMENSTEIN: When you ask a patient what prompted them to have an eye exam, it's usually dry eye symptoms, most notably blurry vision. This is especially notable in patients who do not have persistent changes to their refractive error, but feel they are not seeing well. You can't prescribe them glasses or contacts if they have a significant amount of dry eye because their prescription won't be accurate. I manage their expectations by telling them we're going to hold on their glasses and contacts and convert the appointment to a medical exam. Then, after the tear film is stable, we'll use their vision plan and evaluate them for glasses and contacts. Patients seem to understand that approach.

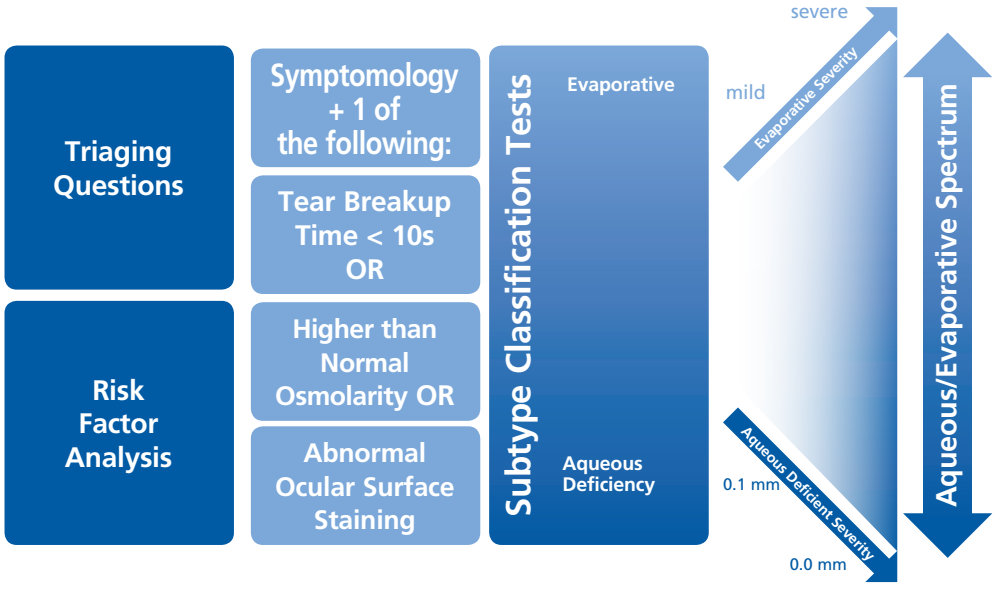

Figure 2. Basic components of the TFOS DEWS II Diagnostic Algoritm.[7]

DR. HOM: We do the same thing in my clinical practice. Many patients have contact lens dryness,[22,23] so we delay the prescribing of the contacts until their ocular surface has improved. It's well known that contact lenses exacerbate dry eye, and about 75% of contact lens wears will discontinue use at some point because of discomfort.[24,25]

DR. WHITLEY: We know with the Canada Dry Eye Epidemiology Study (CANDEES) study that 50% of contact lens wearers had dry eye, compared with non-contact lens wearers, which was about 27%.[26] Contact lens wear is a known risk factor for the development of DED.

DR. NICHOLS: Do you have any tips to manage patient expectations when they want to walk out of the appointment with a contact lens prescription?

DR. HOM: Patients already know that their lenses are uncomfortable. I tell them we are going to work on some treatments so they can wear the lenses longer. I explain that DED will be much easier to manage if we intervene early. That's a great motivating factor for the patient.

We know that if we wait to treat DED, the disease will progress and get worse. This is validated in the literature. For example, Ong et al conducted a longitudinal study in veterans with dry eye signs and symptoms between Oct.1, 2013, and April 30, 2015.[27] One hundred and twenty patients had no symptoms or mild to moderate symptoms at baseline. Of those, 44.8% progressed to more severe symptoms at 1 year, while 74.2% with severe symptoms at baseline had those symptoms persist at 1 year.

DR. NICHOLS: The TFOS DEWS II report provided a dry eye diagnosis algorithm that can confuse or overwhelm clinicians, but can be simple if you step through (Figure 2). It starts out with triaging questions such as, "Do you use artificial tears? Do you ever have dry mouth?" and "Do you have itching or burning eyes?"[5] Then you get into risk-factor profiling, which identifies some groups you want to target such as contact lens wearers, smokers, and people on certain medications, such as antidepressants. As a screening, it includes abnormal results on at least one questionnaire, including Dry Eye Questionnaire-5 (<6) or OSDI (≥13). That then moves you into doing three additional tests looking for abnormalities, such as assessing TBUT (<10 seconds), ocular surface staining (>5 corneal spots, >9 conjunctival spots, or lid margin [≥2 mm length and ≥25% width]), or osmolarity (≥308 mOsm/L in either eye).

Abnormal screening for dry eye includes an abnormal survey result and at least one abnormal result on one of the screening tests. What are your thoughts on this algorithm? Is it too complicated?

DR. DEVRIES: There are some complicated areas, but they are essential to the diagnosis of dry eye. You have to have an established, standardized protocol. For example, in our practice, it has become standard that technicians do osmolarity on all patients who score 6 or higher on SPEED. They check for inflammation and they do meibography on those patients as well. We diagnose the patient with DED if any of those tests are abnormal.

DR. BLOOMENSTEIN: Meibography should be included in an initial test. Systems in widespread use include the LipiScan (Johnson & Johnson Vision), the Keratograph 5M (Oculus), and the HD Analyzer (Visiometrics). TFOS DEWS II identified MGD as the most common cause of dry eye,[7] and a retrospective study by Lemp et al found that 86% of patients with DED have MGD.[28] MGD is driving a lot of this dryness and inflammation.

DR. DEVRIES: I also express the meibomian glands, and look at the results under the slit lamp. Clinicians often think MGD is nonobvious, but it's only not obvious if you don't look for it.

DR. WHITLEY: I agree; we need to express the glands and look at the lid margins for disease. Look for any signs of blepharitis, rosacea, seborrheic dermatitis, and psoriasis.[29,30] Examine the lashes as well, as they may include clues if there are changes in their color, length, shape, or position. You want to use corneal and conjunctival staining, whether it's with lissamine green or fluorescein, and evaluate tear film stability. TBUT is the most frequently used diagnostic test for tear film instability. Patients without dry eye have an average TBUT of 27 seconds. A TBUT of 10 seconds or less is considered abnormal.[31]

Tools for Differentiating DED Diagnosis

DR. NICHOLS: The Schirmer test and Phenol Red Thread are two common tests to assess aqueous production. There have been head-to-head comparisons between the two tests in the literature, and there are conflicting data on their agreement.[32-34] How do you use these tests in your clinic?

DR. BLOOMENSTEIN: I think where we confuse our colleagues and patients is this differentiation between aqueous deficient and evaporative dry eye. Aqueous deficient dry eye can be caused by a number of factors including age, contact lens wear, hormonal changes, medications, diabetes, Sjögren syndrome, and other autoimmune diseases.[5] Evaporative dry eye can be mucin-related, lid-related (including MGD and incomplete blink), and ocular surface-related (mucin and contact lens wear).[5] Yes, we have tests to help tell us what symptoms are associated with which type of dry eye (such as TBUT, ocular surface staining, and Schirmer) but it's more complicated than that.

For example, if a patient has high osmolarity, that means homeostasis is not being reached. In that case, we could have the meibomian glands not working as well, which will create inflammation and lead to a decrease in goblet cell density. The complexity of this disease state is such that it is very difficult to differentiate between the types. TFOS DEWS II acknowledged that aqueous and evaporative dry eye exist on a continuum and recommended that elements of each type need to be considered for proper DED management.[5] We need to look at the disease more broadly. From a treatment perspective, we need to minimize the environmental aspects (including dry, windy, or smoky environments and extended computer use) and globally reduce the problems.

DR. WHITLEY: According to TFOS DEWS II, 80% of dry eye cases are both combined aqueous and evaporative.[5] I agree that we need a comprehensive approach that addresses the meibomian glands, inflammation, and tear stability. I do a Schirmer test on all new patients that come in for dry eye. I'll follow up with tests if they have a low Schirmer score, including a test for Sjogren syndrome. I'll work closely with their primary care provider and rheumatologist because the more information we have for the patient, the better we can care for them.

Knowing the Triggers

Triggers of dry eye, allergic conjunctivitis and asthma are very similar. For many patients, the disease can be underlying and not offer any signs or symptoms. Sometimes, environment can trigger an inflammatory condition such as dry eye. The subclinical dry eye becomes a flare-up. Typical triggers can be high temperature, high pollen counts or low humidity (Table).[1-3]

-Milton M. Hom, OD, FAAO

TABLE. TRIGGERS OF COMMON OCULAR SURFACE DISEASES[1-3]

Weather	Asthma	Dry Eye	Allergic Conjunctivitis
Temperature	High (or very cold)	High	High
Pollen	High	High	High
Humidity	High (or very dry)	Low	High (dust mites)

1.Harthan JS, Hom MM, O'Dell L, Halleran C. Impact of Humidity Levels, Temperature, Breathing and Heat Indices on Dry Eye Symptom Scores. Available at: www.aaopt.org/detail/knowledge-base-article/impact-of-humidity-levels-temperature-breathing-and-heat-indices-on-dry-eye-symptom-scores. Presented at: American Academy of Optometry; Oct. 11-14, 2017; Chicago.
2. Symptoms of ocular surface disease. www.aaopt.org/detail/knowledge-base-article/the-role-of-pollen-counts-on-the-signs-and-symptoms-of-ocular-surface-disease. Presented at: American Academy of Optometry; Oct. 11-14, 2017; Chicago.
3. Hedhly A, Hormaza JI, Herrero M. The effect of temperature on pollen germination, pollen tube growth, and stigmatic receptivity in peach. *Plant Biol (Stuttg).* 2005;7(5):476-483.

DR. DEVRIES: It's about gathering as many data points as you can. It's Schirmer, inflammation, osmolarity, and TBUT. We need to gather information and look for a correlation because if you look at the sensitivity and specificity of any single test, it's pretty low.

DR. NICHOLS: When do you do staining, and what dyes do you use?

DR. BLOOMENSTEIN: I use lissamine green more than anything else. I don't necessarily do fluorescein staining unless the patient isn't responding well to treatment, and I don't know why. I ask patients not to use drops for a minimum of 2 hours before they come in for their appointment because I want to evaluate their eyes in a virgin state.

DR. DEVRIES: I agree. We also tell patients not to use drops for 2 hours before their appointment.

DR. BLOOMENSTEIN: Twenty or 30 years ago, the philosophy was very black and white: if you see staining, the patient has dry eye, if there's no staining, there's no dry eye. There's been so much innovation in this space during the past few years that I reserve staining for the end game, not the beginning. It's no longer a good diagnostic test to differentiate disease, it tells you how far along their disease is and how well you have or haven't treated them.

DR. HOM: I agree. Corneal staining is one of the last things you'll see in patients with DED. It won't appear with patients who have mild dry eye. It may show up if a patient has moderate dry eye, but it will always appear in severe cases. I rely more on conjunctival staining; it's an earlier indicator of dry eye than corneal staining.

DR. NICHOLS: That is a point to drive home to our colleagues—you should be looking at staining of the cornea and conjunctiva to determine if someone is at risk for dry eye.

DR. NICHOLS: InflammaDry (Quidel) is a rapid-onset, in-office test that detects elevated levels of matrix metalloproteinase-9 (MMP-9). MMP-9 plays a pathogenic role in inflammatory disease, and elevated MMP-9 levels have been detected in patients with DED.[35] A positive test is considered ≥ 40 ng/ML.[36] Does anyone use this test to diagnose DED? How are you incorporating technology into your practices to diagnose dry eye?

DR. DEVRIES: InflammaDry provides helpful information, but it is highly dependent on the technician's skill level to get accurate results.[35] Technicians have to press the sampling fleece in multiple locations under the patient's lower lid, and it is as not as comfortable as the TearLab Osmolarity System (TearLab), which only requires one quick press in each eye. Both tools have similar positive predictive values (85% for InflammaDry and 89% for TearLab), according to company materials.[36,37] InflammaDry affects the patient a little bit more, and technicians are often hesitant to gather the sample in the way that's needed to identify inflammation. However, when done correctly it really does guide me; I know that there is fluctuation in MMP-9s just like there's fluctuation in osmolarity. It helps in initial diagnoses, and I also use it during treatment to tell if I am lowering the inflammation. I also use MMP-9 as a second metric because it's a great patient motivator; it's a call to action. It correlates with their symptoms.

DR. BLOOMENSTEIN: What do you do when the MMP-9 numbers don't correlate with the patient's symptoms? That's always been the concern for me. It's like with staining. Many clinicians believe that if there's no staining, there's no dryness. What do you do if the InflammaDry results are normal? We can't look at these test results in isolation.

DR. DEVRIES: MMP-9 helps guide me into looking in other areas, as well. It's all about gathering information. If I see that the inflammation is up and the osmolarity is down, I look for something else. In those situations, the diagnosis is often epithelial basement membrane dystrophy. I think InflammaDry helps the detective work a little bit.

DR. WHITLEY: We also use InflammaDry within our practice. Dry eye may seem complex but doesn't have to be however there are times when the signs and symptoms don't correlate. However, there are times when the signs and symptoms do not correlate.[38] A patient may not have staining, but they still have significant symptoms. We still have to treat it accordingly.

Case Study: Evaluating the Cataract Patient

By Walter O. Whitley, OD, MBA, FAAO

A 72-year-old woman presents for evaluation of blurry vision in both eyes. She notes her symptoms are constant and affect both eyes, but are mild in nature. She presents for a cataract evaluation. She states her vision has decreased since she underwent chemotherapy (initial 12-week course of treatment started in July 2018). Since then, vision is blurry at all ranges with and without correction. She denies flashes of light, but notices floaters bilaterally in her field of vision (which she has noticed for "quite some time"). She notes her eyes are sometimes dry, but she does not use artificial tears. The figure shows her irregular corneal topography.

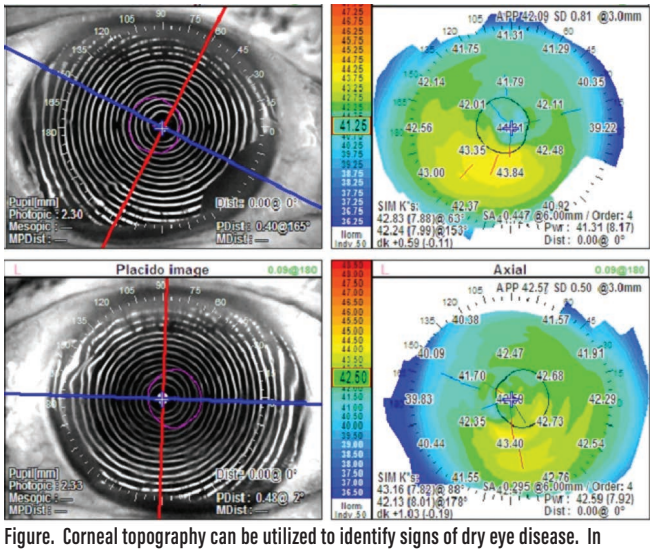

Figure. Corneal topography can be utilized to identify signs of dry eye disease. In this example, the irregular mires on the placido disks demonstrates a poor tear film in addition to irregular topographies.

On exam:

- VA is 20/40 OU with NI on pinhole
- Slit lamp exam shows 2+ diffuse superficial punctate keratitis OU/3+ nuclear sclerotic and 2+ cortical cataract OU

Assessment:
This patient has visually significant cataracts bilaterally, as well as dry eye syndrome bilaterally.

Treatment plan:

1. Refer patient for dry eye evaluation. Once stable, repeat cataract measurements. Discuss the importance of improving her ocular surface to maximize surgical outcomes and to minimize symptoms of dry eye.
2. Start artificial tears to be instilled 3 times daily in each eye; follow-up in 2 to 3 weeks for subsequent dry eye evaluation.

"...Allergy is undertreated in dry eye patients, and patients with allergies are more susceptible to dry eye."

—Dr. Devries

MANAGING DED FLARES

Q | DR. NICHOLS: Signs and symptoms of DED don't always align. Sullivan et al examined 263 patients with DED and found that only 57% of those patients had symptoms consistent with DED.[39] Could this be due to flare? Sometimes you will have a patient with a lot of symptoms, but they don't manifest signs on the day you see them. Or maybe there is not an abnormal test. How does the concept of flare fit into the timing of a dry eye patients' life?

DR. HOM: We all know that dry eye is an inflammatory disease. Sometimes we can miss inflammation, but it still can be present. It could be subclinical inflammation that's not detectable by any signs or any symptoms. Just like with allergy triggers, there are dry eye triggers, and they are usually environmental. That's when you'll get a flare up. To me, a flare up is a manifestation of a more likely subclinical inflammation that has gone undetected.

DR. DEVRIES: I agree. I think there's certain episodic flare-ups that occur, and they're probably environmentally induced. Environmental factors include hot, dry, windy climates; tobacco smoke; dust; low humidity; and air travel.[40] I've seen these in some patients who drive into clinic from a number of miles away in the cold with the defroster on. They'll say their eyes have done well recently, but are bothering them today. Environmental factors caused a flare-up on that particular day.

DR. HOM: We've conducted studies looking at how temperature and pollen impacts dry eye symptoms. We found that patients who have dry eyes have more severe symptoms when pollen counts are high.[41,42] Low humidity is a known trigger for dry eye.[43] The literature indicates that environmental triggers are extremely important in the management of dry eye disease.[44-46]

DR. NICHOLS: I think you're right, and this is something we haven't done a good job of studying or classifying. In the south, where I live, you can have triggers during pollen season even with high humidity.

DR. BLOOMENSTEIN: In Arizona, where I practice, we tend to see more flare-ups during the winter. We have an inversion layer, and the air quality tends to be worse. A number of international studies have attempted to understand how poor air quality impacts the ocular surface. A Korean study found that higher ozone levels and lower humidity levels were associated with DED,[47] whereas a Chinese study found an increase in outpatient visits for conjunctivitis when air pollution levels were higher.[48] Increased nitrogen dioxide levels are also associated with eye irritation.[49] In my experience, I see more dry eye flare-ups and MGD in the spring and the fall, and there seems to be a correlation.

DR. DEVRIES: Allergies are a large component of this. Overall, allergy is undertreated in dry eye patients, and patients with allergies are more susceptible to dry eye. I was involved in a study looking at the overlap of allergic conjunctivitis and dry eye syndrome. Using the validated questionnaire Subjective Evaluation of Symptom of Dryness, we studied self-reported itchiness, dryness, and redness in 689 patients treated from Jan. 1, 2007, to Jan. 1, 2011. Clinically significant itchiness was found in 28.2%, dry eyes in 35.8%, and redness in 8.2%. Symptom overlap was demonstrated in many of the patients.[50]

DR. BLOOMENSTEIN: The end result of both allergy and dry eye is inflammation.

STEP-WISE APPROACH TO DED MANAGEMENT

Q | DR. NICHOLS: Do you have specific treatment algorithms that you use for your patients?

DR. HOM: I like to keep my treatment algorithm as simple as possible. I divide patients into two categories: mechanical therapy/obstruction, or antiinflammatory. I like to take a treatment from the obstruction camp and a treatment from the antiinflammatory camp to increase the efficacy of the dry eye treatment. Having said that, I like to start with an antiinflammatory because the patient may have subclinical inflammation. To me, the backbone of treatment is the antiinflammatory agent.[51] You add things from there.

DR. DEVRIES: I address the inflammation first, and we begin with mild treatment to see how they respond. I recommend patients take omega-3 fatty acids, as they have known antiinflammatory effects and have been shown to improve TBUT and Schirmer results in patients with DED.[52,53] I prescribe one of the antiinflammatory medications for dry eye: corticosteroids, cyclosporine, or lifitegrast. Each comes with pros and cons. Corticosteroids have a broad mechanism of action, but they are not recommended for long-term use due to side effects such as cataracts and increased intraocular pressure.[54,55] Topical cyclosporine 0.05% has been shown to increase goblet cell density and conjunctival production of immunomodulatory TGF-ß2 in patients with DED, but it's antiinflammatory effects don't typically take hold for at least 4 to 6 weeks.[56,57]

"I always companion lifitegrast or cyclosporine with an antihistamine like olopatadine. I've found that resolves 80% of the dry eye problems in my practice."

—Dr. Hom

Restasis (Allergan) was approved by the FDA to increase tear production in patients with keratoconjunctivitis sicca, and Cequa (Sun Pharma) was approved by the FDA in 2018.[58,59] At 0.09%, Cequa currently has the highest concentration of cyclosporine A on the market, and it is the only topical cyclosporine product that incorporates nanomicellar technology.[60] Lifitegrast was approved by the FDA in 2016 for DED. OPUS-1 established improvement in signs of DED such as corneal staining, by not in symptoms.[61] OPUS-2 and OPUS-3 illustrated improvement in eye dryness score, and symptom relief has been shown to occur as soon as 2 weeks in patients with moderate DED.[62] Finally, I recommend warm compresses to heat the lids and melt any obstruction in the glands.

On the return visit, unless the mild treatment approach has generated the exact result we want, I explain we need to elevate the treatment and address the lids. I also explain that we can't cure the dry eye, and that the process is a marathon not a sprint. We're going to control the disease, but not cure it.

DR. NICHOLS: What other differences have you noticed between the antiinflammatory agents?

DR. HOM: In my opinion, if you want rapid-onset action, lifitegrast is the best choice.[62] We've used topical cyclosporine 0.05% for years, and it does work to calm that inflammatory response if it's used properly. You'll achieve the same effect with a cyclosporine, but it will take longer.[51]

DR. WHITLEY: I also use lifitegrast because of its response time. I'll also add a steroid, such as loteprednol etabonate or fluorometholone, 4 times a day to treat flare. Anytime you prescribe a steroid, you must check the patients' pressure every 2 weeks.[54,55] Once they start responding, taper down the steroid to twice a day, add in the cyclosporine or lifitegrast, and then bring the patient in 6 weeks later. If that helped the symptoms, we continue the therapy with cyclosporine or lifitegrast alone.

DR. BLOOMENSTEIN: I tend to be more aggressive and proactive; I don't wait for my patients to become truly symptomatic. I've had great results with cyclosporine 0.05%. When lifitegrast came out, there were some challenges with patient acceptance. Some of the ancillary side effects made it harder for patients to stay on it. In my patients, most notably those were the dysgeusia and initial burn that the patients encountered upon instillation. A patient who has more mild symptoms is more likely to avoid using the drops if the side effects are more severe. I have found that patients with more pronounced symptoms are more willing to tolerate these issues as long as the drops work.

DR. HOM: I think the most efficacious antiinflammatory is a steroid, mainly loteprednol. However, like other steroids, it does increase intraocular pressure with extended use.[63] I always companion lifitegrast or cyclosporine with an aantihistamine like bepotastine or olopatadine. I've found that resolves 80% of the dry eye problems in my practice.

DR. NICHOLS: How do you piggyback medical management into your best practices for contact lens wear?

DR. HOM: It depends on what's causing the contact lens dryness.[13] There are two categories of treatment for contact lens dryness: lens-based treatments and disease-based treatments. For lens-based treatments and to extend wearing time, I first increase the replacement schedule (like daily disposables) and/or peroxide-based solutions. For ocular surface disease, we're talking about obstruction/mechanical therapy or antiinflammatories such as cyclosporine, lifitegrast, and loteprednol. I've found that using both lens-based and disease-based treatments together are the most efficacious ways to minimize contact lens discomfort.

TAKE-HOME MESSAGES

Q | **DR. NICHOLS:** What would be your best advice to the practitioner who is starting out or wanting to enhance their dry eye expertise?

DR. WHITLEY: Ask questions, either through a conversation or one of the questionnaires. We all have an abundance of patients already in our practice who have undiagnosed DED. You don't need to externally market. The patients are already there; just look for it and treat it.

DR. BLOOMENSTEIN: Everything we've discussed is predicated on evaluating the quality of the tear film and the quality of the ocular surface. From a surgical aspect, it's important to ramp up the treatment for dry eye symptoms preoperatively before they go in for testing. Starting them on an antiinflammatory preoperative will get you the best quality measurements.

DR. DEVRIES: I echo that. Many patients who go in for LASIK or cataract surgery are on the cusp of developing profound dry eye, and no one is aware of it.[16] The patient goes in for surgery, it exacerbates the dry eye disease, and then they blame their dry eye symptoms on the procedure.

I now pretreat every patient with an antiinflammatory who is referred for cataract surgery. We also take a look at the meibomian glands to see if we can rule out patients in the hopes of avoiding that situation down the road.

DR. BLOOMENSTEIN: As clinicians, we are not meant to be passive observers; we're supposed to be disruptors. We're supposed to insert ourselves into our patients' lives to make their lives better. We need to tell patients they have dry eye instead of waiting for them to mention it. Are we doing everything possible for the patient to maintain good quality of tears? If not, it will keep getting worse as they get older.

DR. NICHOLS: Thank you all for your input on diagnosing and managing DED. It was an honor working with you. ■

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UPDATES IN DRY EYE DISEASE:
Diagnosing and Treating Patients with Ocular Surface Disease

Release Date: May 15, 2019
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INSTRUCTIONS FOR CME CREDIT

To receive credit, you must complete the attached Post Test/Activity Evaluation/Satisfaction Measures Form and mail or fax to Evolve Medical Education LLC; 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please visit evolvemeded.com and click http://evolvemeded.com/online-courses/1913. If you are experiencing problems with the online test, please email us at support@evolvemeded.com. Certificates are issued electronically; please be certain to provide your email address below.

Please type or print clearly, or we will be unable to issue your certificate.

Name _____ ❑ OD ❑ non-OD participant

Phone (required) _____ ❑ Email (required) _____

Address _____

City _____ State _____ Zip _____

License Number _____

OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ > 20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week (with the disease targeted in this educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
___ 50+

Region
___ Northeast
___ Northwest
___ Midwest
___ Southeast
___ Southwest

Setting
___ Solo Practice
___ Community Hospital
___ Government or VA
___ Group Practice
___ Other
___ I do not actively practice

Models of Care
___ Fee for Service
___ ACO
___ Patient-Centered Medical Home
___ Capitation
___ Bundled Payments
___ Other

LEARNING OBJECTIVES

DID THE PROGRAM MEET THE FOLLOWING EDUCATIONAL OBJECTIVES?	AGREE	NEUTRAL	DISAGREE
Identify the prevalence of dry eye disease and the related signs and symptoms of patients.	_____	_____	_____
Explain the importance of taking a thorough patient history and evaluation in creating an accurate diagnosis.	_____	_____	_____
Recognize the need for constant maintenance and ongoing care related to the various dry eye disease treatments.	_____	_____	_____
Develop an individualized treatment plan for patients with dry eye disease.	_____	_____	_____

POSTTEST QUESTIONS

1. **PLEASE RATE YOUR CONFIDENCE ON YOUR ABILITY TO APPLY UPDATES IN THE TREATMENT OF DRY EYE IN THE CLINIC BASED ON THIS ACTIVITY. (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. **PLEASE RATE HOW OFTEN YOU INTEND TO APPLY ADVANCES IN THE MANAGEMENT OF DRY EYE IN THE CLINIC. (BASED ON A SCALE OF 1 TO 5, WITH 1 BEING NEVER AND 5 BEING ALWAYS.)**
   a. 1
   b. 2
   c. 3
   d. 4
   e. 5

3. **ALL BUT WHICH OF THE FOLLOWING IS ASSOCIATED WITH A RISK FOR DEVELOPING DRY EYE DISEASE?**
   a. Contact lens wear
   b. Use of digital handheld devices
   c. Allergies
   d. Male sex

4. **WHICH SYMPTOM MAY BE INDICATIVE OF DRY EYE?**
   a. Red eyes
   b. Gritty sensation
   c. Fluctuating vision
   d. Contact lens intolerance
   e. All of the above
   f. A, b, d
   g. B, c, d

5. **IN THE TFOS DEWS II REPORT, AN INITIAL SCREENING EVALUATION FOR MILD DED SHOULD INCLUDE ANY OF THE FOLLOWING DIAGNOSTIC TESTS EXCEPT:**
   a. Corneal aesthesiometer
   b. DED questionnaire such as SPEED or OSDI
   c. Meibography
   d. Tear film osmolarity

6. **WHAT IS THE MOST COMMON ENVIRONMENTAL FACTOR FOR THE DEVELOPMENT OF DRY EYE?**
   a. Rapid change in altitude (ie, mountain hiking)
   b. High humidity
   c. Low humidity
   d. Fluctuating outdoor temperatures

7. **WHICH IMMUNOMODULATOR MAY BE PRESCRIBED FOR RAPID-ONSET ACTION IN REDUCING DED SYMPTOMS?**
   a. Lifitegrast
   b. Cyclosporine 0.05%
   c. Prednisolone
   d. Loteprednol

8. **A STUDY BY SULLIVAN ET AL FOUND WHAT PERCENTAGE OF PATIENTS WITH DRY EYE HAD CLINICAL SYMPTOMS OF THE DISEASE AS WELL?**
   a. 36%
   b. 42%
   c. 57%
   d. 73%

9. **THE THRESHOLD FOR A POSITIVE (ABNORMAL) MMP-9 TEST IS _____.**
   a. ≥ 20 ng/mL
   b. ≥ 30 ng/mL
   c. ≥ 40 ng/mL
   d. ≥ 50 ng/mL

10. **A TEAR BREAK-UP TIME OF _____ IS CONSIDERED NORMAL; TBUT TIMES UNDER THAT ARE CONSIDERED ABNORMAL.**
    a. ≥10 seconds
    b. ≥12 seconds
    c. ≥27 seconds
    d. ≥15 seconds

11. **ACCORDING TO TO A RETROSPECTIVE STUDY BY LEMP ET AL, APPROXIMATELY 86% OF PATIENTS WITH DED ALSO HAVE _____.**
    a. A history of smoking
    b. Increased age (older than 80 years)
    c. Meibomian gland dysfunction
    d. Hypertension

12. **MRS. SMITH PRESENTS FOR HER ANNUAL SPRING EYE EXAM ASKING FOR A STRONGER PRESCRIPTION FOR HER GLASSES AND CONTACTS; HER VISION IS RECENTLY FREQUENTLY BLURRY, AND SHE'S NOTICED A REDUCTION IN THE NUMBER OF HOURS SHE CAN WEAR HER CONTACTS PLUS ITCHING. SHE HAS A HISTORY OF ALLERGIES TO POLLEN, BUT NO HISTORY OF AUTOIMMUNE DISEASE. SHE FILLS OUT THE SPEED QUESTIONNAIRE AND SCORES GREATER THAN 6. HER TEAR BREAK-UP TIME IS 8 SECONDS. MRS. SMITH'S BLURRY VISION AND CONTACT LENS INTOLERANCE MAY BE DUE TO:**
    a. Seasonal allergies
    b. Aqueous-deficient dry eye
    c. Cataract
    d. Both A and B
    e. Both B and C
    f. None of the above

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this CE 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 participating in this course: 5 = High, 1 = Low _____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low _____

This activity improved my competence in managing patients with this disease/condition/symptom. _____ Yes _____ No

I plan to make changes to my practice based on this activity. _____ Yes _____ No

Please identify any barriers to change (check all that apply):

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
Other. Please specify: _____
_____
_____

The design of the program was effective for the content conveyed. ___ Yes ___ No

The content supported the identified learning objectives. ___ 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

Would you recommend this program to your colleagues? ___ Yes ___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____ I certify that I have participated in this entire activity.

This information will help evaluate this CE activity; may we contact you by email in 3 months to see if you have made this change? If so, please provide your email address below.

_____

MODERN**OPTOMETRY**