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CHRONIC VERSUS ACUTE: RETHINKING DRY EYE DISEASE

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Chronic Versus Acute: Rethinking Dry Eye Disease

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CONTENT SOURCE

This continuing education activity (CE) captures content from a virtual roundtable discussion.

ACTIVITY DESCRIPTION

Dry eye disease (DED) is a significant public health issue that threatens patient economic productivity and quality of life. About 16 million Americans have a formal DED diagnosis, but the true incidence is likely much higher because many who are symptomatic may not seek medical care. This supplement addresses this issue and others related to managing DED and providing the best care possible for patients.

TARGET AUDIENCE

This certified CE activity is designed for optometrists who manage patients with ocular surface diseases.

LEARNING OBJECTIVES

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

- **Describe** how DED symptoms can impact patient quality of life
- **Explain** how inflammation is a key driver of DED pathogenesis and symptomatology
- **Describe** how episodic flares are part of the inflammatory disease process
- **Formulate** an individualized treatment plan for patients experiencing DED flares
- **Compare** available data on agents in the pipeline and their potential significance for DED management

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DIGITAL EDITION

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PRETEST QUESTIONS

PLEASE COMPLETE PRIOR TO ACCESSING THE MATERIAL AND SUBMIT WITH POSTTEST/ ACTIVITY EVALUATION/SATISFACTION MEASURES FOR CE CREDIT.

1. Please rate your confidence in your ability to formulate an individualized treatment plan for patients experiencing dry eye disease (DED) flares (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 discuss with patients the impact of DED symptoms on their quality of life (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. What is a 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

4. According to the TFOS DEWS II study, more than 80% of patients with DED also have _____.

a. A history of smoking
b. Younger age (less than 30 years)
c. Meibomian gland dysfunction
d. Hypertension
e. Ocular allergies

5. Ms. Smith is a 22-year-old female who presents for her annual spring eye exam asking for a stronger prescription for her glasses and contacts. Her vision has recently become frequently blurry, and she's noticed a reduction in the number of hours she can wear her contacts without dryness and 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 (TBUT) is 5 seconds. Mrs. Smith's blurry vision and contact lens intolerance may be due to:

a. Seasonal allergies
b. Evaporative dry eye
c. Cataract
d. Both A and B
e. Both B and C

6. The more topical drops a patient takes (regardless for what condition), the more likely there is concomitant _____.

a. Ocular surface disease
b. Ocular hypertension
c. Neurotrophic keratitis
d. Allergic conjunctivitis

7. Which of the following is not recommended to solely identify asymptomatic DED patients?

a. Lid margin evaluation
b. Vital dyes
c. Questionnaires
d. Meibography
e. Family history

8. Based on the current literature, all but which of the following may adversely impact ocular surface health?

a. Elevated cholesterol levels
b. Diabetes
c. Autoimmune disorders
d. Sleep apnea

9. What is a dry eye flare?

a. A spike in Standardized Patient Evaluation of Eye Dryness scores
b. A lengthy amount of time with elevated matrix metallopeptidase 9 (MMP-9) levels
c. A spike in symptoms directly related to medication compliance
d. A spike in symptoms even while being compliant on current therapy

10. Which diagnostic symptom/result should lead to treatment with an antiinflammatory agent?

a. Schirmer test result of 11 mm
b. Positive MMP-9 test result
c. Low osmolarity score
d. TBUT of 7 seconds

11. For patients with neurotrophic keratitis, _____.

a. Photobiomodulation is a viable option.
b. Cenegermin 0.002% has been recently approved
c. TP-03 is still in the pipeline, but looks promising
d. There still remains an unmet need as there are no approved treatments

12. Mr. Smith is a 27-year-old computer programmer who complains of "sore eyes" at the end of the day, after he's worked and then played online games in the evening. He is presenting to your office because he wants refractive surgery as he notes his contact lenses are bothersome and "don't work" after hours of wear. What is the best option?

a. Evaluate the corneal surface with vital dyes and the lid margins and refer to a surgeon.
b. Change the contact lens prescription (ie, from soft lenses to rigid lenses), and recommend against refractive surgery.
c. Assess the ocular surface and if damage is present, recommend delaying refractive surgery until the ocular health has improved.
d. Rely on patient questionnaires and vital dyes to determine whether refractive surgery would benefit the patient.

Chronic Versus Acute: Rethinking Dry Eye Disease

Dry eye disease (DED) impacts upwards of 16 million Americans.[1] The traditional profile of a patient with DED is changing, as we now recognize that flares are more common than once thought. Whereas DED was 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, increased overall screen time due to COVID-19, and other environmental factors.[1] Further, DED is commonly underdiagnosed because patients believe the symptoms they experience are normal or routine and don't think to report them unless specifically asked.

The following roundtable discussion brings together experts in DED who share their clinical and research expertise and have come to a consensus on important topics related to dry eye. This is intended to provide 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 IN CLINIC SETTINGS

Q | Kelly K. Nichols, OD, MPH, PhD: How do you think both the prevalence and the different types of dry eye—aqueous deficient, evaporative—have changed over the years?

Douglas Devries, OD: We tried to silo dry eye, whether it was evaporative or aqueous deficient, but the more patients I see, the more I realize that the pathophysiology patients experience are unique and they're somewhere along the continuum. For example, someone with Sjögren disease should be the consummate definition of aqueous deficiency, but how often does that patient have healthy meibomian glands?

Years ago, we might not have correlated the two, but in today's clinic, I see more patients with combinations of aqueous-deficiency and evaporative.

The prevalence is much higher than we thought. Trattler et al[3] found that nearly 80% of patients presenting for cataract surgery had clinical signs of dry eye, and that's reflective of what we're seeing in our own practices.

More of our colleagues are looking for the various signs and learning more about the subtleties of presentation. For some of our patients, it will be a minor annoyance, but for others, it's debilitating. When we tell patients we're concerned about some of the potential DED signs they're showing, it's because we want to avoid that extreme end where the disease adversely affects their occupations and evocations.

Q | Dr. Nichols: Dr. McGee, your practice is predominantly dry eye—do you see mostly dry eye patients through referrals?

Selina R. McGee, OD, FAAO, Dipl ABO: Most of my patients have DED, but they're not from referrals. They're patients who come in for their annual eye exam. To Dr. Devries' point, DED is everywhere. I go in with the mindset that this patient has dry eye, and they're going to prove to me that they don't. That mindset switch allowed us to have an ocular disease capture rate. In our practice, it's how many patients did we see that day, how many underwent DED testing, and how many are being treated? Those numbers range from 40 to 90%; if it's lower than that, we reevaluate our system to uncover why we aren't recognizing patients with DED.

DED affects every aspect of our practices. I see a lot of contact lens wearers, many of whom want to wear contact lenses longer or more comfortably; I've been able to help most patients with DED who wear contact lenses. Most of my referrals are for patients whose DED is severe; but I want to educate all patients about preventive measures so they can potentially avoid reaching such a severe level.

Walter O. Whitley, OD, MBA, FAAO: As mentioned by Dr. McGee, every patient has dry eye until proven otherwise. Various studies have shown the more topical drops patients take, the more likely there is ocular surface disease (OSD); this has certainly borne itself out in our glaucoma patients.[4-15] Fechtner et al showed about 50% of patients with glaucoma have abnormal Ocular Surface Disease Index (OSDI) scores.[6] It's one of those things—where there's glaucoma, there's dry eye. Other studies show more than 50% of patients with diabetes have DED.[14,16-18] As practitioners, we have to make sure we're asking the right questions.

Dr. Nichols: There may be 17 million patients with diagnosed dry eye,[19] but there are even more who have not yet been diagnosed or are not seeking treatment. How do you focus on those patients from the others who may know they have DED?

Justin Schweitzer, OD, FAAO: Those who know they have DED or who we identify after they fill out a patient

CONSENSUS PANEL FINDING #1

The prevalence of DED may be much higher than estimated in clinical studies. Presume every patient has dry eye until proven otherwise.

questionnaire are the easy ones. The challenge is identifying those who are asymptomatic, and we must rely on clinical exam.[20] Every patient I see I now evaluate the lid by looking, lifting, pushing, and pulling; I examine the lid margin, look at meibum. I look for staining, whether that's on the conjunctiva with lissamine green or sodium fluorescein on the cornea (Figure 1). Asymptomatic patients are the hardest to convince they have an issue, but if we're not looking, many patients are going to slip by and develop significant dry eye issues.

Dr. McGee: I do the same exploration as Dr. Schweitzer, and it has helped me uncover patients with DED. Dr. Schweitzer touched on meibum; I added meibography to my overall testing. Patients can visualize it—they can see there's a problem and they become engaged and concerned. For our practice, that's been a huge clinical turning point. We still don't know what we don't know about meibography because we haven't been analyzing it for years, but it is a great way to open the conversation about DED and OSD with patients.

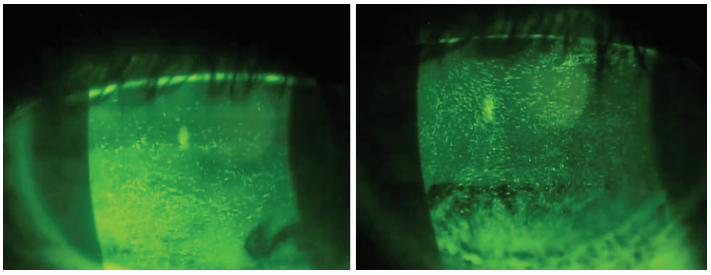
Dr. Devries: We often overlook one of the diagnostic tools in our clinics: the phoropter. DED is a vision-related condition that makes many of these patients difficult to refract, which is where the phoropter can be invaluable. Patients who may be asymptomatic may have fluctuations in vision.

Dr. Whitley: Just think about the patients who call in for emergencies because of blurred vision or foreign body sensation. It's most often the case that emergency phone calls are a result of DED symptoms.

Dr. Nichols: For the longest time, we were specific in our questions as they directly related to symptoms, but now we've moved somewhat into more quality-of-life questions. We've done some research showing patients are at least 30% less productive at work if they have DED.[21] This is called "presenteeism." They're physically at work, but not performing at their peak levels. Asbell et al backed this up in the DREAM study.[22]

Q | What are some of the questions you're now asking patients about the impact of DED on their daily lives, or even the economic burden they may face?

Dr. Devries: We've certainly all seen a tremendous environmental impact with masking because of COVID-19. Before that, we were looking at screen time. We've really started talking to our patients about how much time they spend on light-emitting displays. That issue, combined with the mask phenomenon, and we've really had to switch gears and start looking at those environmental factors in a grander light.



Images courtesy of M. Brujic, OD, FAAO

Figure 1. In these images, the patient presented with dry eye, as seen with fluorescein staining while viewing the eye with a cobalt blue light and wratten #12 filter (left image). The eye is much improved after 2 weeks following 0.25% loteprednol etabonate QID.

Mile Brujic, OD, FAAO: When we talk about the impact on the quality of life, we should be thinking outside of the exam room, too. How many times do we hear from our patients that there's something changing with their vision that they maybe can't verbalize or explain very well in the absence of what we would think of as classic dry eye symptoms? Patients who may be using artificial tears 2 to 5 times daily may not necessarily know that's not what we would consider normal and healthy. But it's "their normal," so they may not express it or tell the technicians.

Oftentimes, I ask about artificial tear use based on what I see on the ocular surface. All of these things are going to impact quality of life, not only how Dr. Devries described the destruction of their visual quality, but also in terms of the inconvenience of instilling drops. Anecdotally, if someone is using artificial tears 2 to 3 times a day, they usually want to use them twice as often. There is a clear-cut relationship between dry eye and quality of life.[23,24]

Q | Dr. Nichols: How might other systemic conditions and comorbidities impact patients' quality of life and dry eye status?

Dr. Schweitzer: To Dr. Devries' earlier point, since the COVID pandemic began, I have noticed substantially more dry eye in my practice in a lot of younger patients. This is particularly true in certain professions—a lot more teachers, students, people working from home—all of which are related to screen time.[25,26]

Patients who take antihistamines or multiple systemic medications can cause dry eye issues. We need to consider this and review in the electronic medical records (EMR) or when you're taking an oral history. We need to identify those patients who don't realize their long-term autoimmune disorder may adversely impact their ocular health and their vision.[27-31] We need to ask about thyroid disease, Grave disease, or rheumatoid arthritis, and have an open channel of communication with the primary care provider (PCP) to determine if those are contributory factors to the DED. My patient base is a heavy Medicare popula-

tion, with a significant number of underlying conditions when they present to us for surgery, but their ocular surfaces are not healthy enough for surgery.

Dr. Devries: Often, we're the sleuths who are identifying DED as a downstream manifestation or ramification of a systemic autoimmune condition. I've seen patients who are taking 600 or 800 mg of ibuprofen multiple times a day for unknown reasons, who have these vague symptoms and we're the ones who link those symptoms and their medication regimens to systemic conditions. To me, as important as appreciating what systemic conditions can do to the ocular surface, thinking in the reverse order is important as well.

Q | Dr. Nichols: Sjögren syndome was mentioned earlier. Dr. McGee, have you ever been the one to diagnose a patient with Sjögren through your exam? What was that patient's response?

Dr. McGee: That's really where I got started in this years ago, because once you diagnose a few patients, word-of-mouth starts in their circle of recognizing an eye care specialist who can actually help.

We know there is a median delay of 4 years between onset and diagnosis, and the average diagnosis time is around 6 years.[32] Once these patients find you, they're never going to leave. It's so gratifying to be able to help them, and help them on a long-term basis. Sjögren symptoms can flare, just like so many other autoimmune diseases and I tell my patients I'll be on that journey with them for the duration. To Dr. Brujic's point, we're conversing with their PCP, the rheumatologist, or the endocrinologist to inform them the systemic disease is not being well managed because of the ocular surface issues.

The troubling component for me is that these patients reset their normal. They think this is how their life is supposed to be, and we can help reset it.

Dr. Nichols: I've seen that in my own studies. The very first dry eye clinical trial for which I was an investigator, I had a patient whose corneas were just a train wreck. When I asked her about her symptoms, she would always report them as "very mild-ish." It could have been her cornea was anesthetized. She couldn't feel anything, but when she started treatment, she kept coming back and saying, 'I didn't really realize that my eyes felt as bad as they did until they started getting better.'

Dr. McGee is right about these patients setting a new normal, and we do need to communicate that we can work through it and be their partner until their eyes are comfortable again. Luckily, we have the tools to diagnose these patients, and we have the tools to properly treat them. Within the past few years, we have a new classification scheme and definition from the TFOS DEWS II workshop.[33] We've talked about some of those diagnostic tools, but what are you seeing our colleagues do?

Dr. Devries: I still feel the biggest missed opportunity is under-

CONSENSUS PANEL FINDING #2

Autoimmune conditions have a strong association with DED. Patient communication and education about the long-term nature of DED is important.

using questionnaires. Those aren't going to catch the neurotrophic types of cases that have down-regulated, but those questionnaires are going to catch some of the more common DED symptoms. I think these questionnaires should be a starting point, and followed up with meibography, osmolarity, and inflammatory diagnostic tests.[34-37] Some colleagues may think these are time-consuming to administer, but we don't find that in our clinic.

Q | Dr. Nichols: Which questionnaire do you use and who administers it?

Dr. Devries: We use the Standardized Patient Evaluation of Eye Dryness (SPEED) Questionnaire[34] within our practice just to start the conversation. In so many cases, patient responses lead to additional testing. We've also found that even though it's not a point-of-care test, meibography has become more common in our clinic. We don't charge for that, and I consider it part of the information we're gathering to allow us a more in-depth look at the patient's ocular surface.

Dr. McGee: We also use questionnaires. Vital dye is a critical component to every patient encounter. I'm often asked what equipment a colleague should buy to enhance their practice. I encourage practitioners to incorporate the basics first: questionnaires, vital dye, and pushing on glands. I love that we have all the technology, but I think it can be a little overwhelming. We should start by sticking to the basics and uncover opportunity there, and then we can enhance beyond the basics.

In our clinic, we use a short questionnaire derived from TearLab and have added questions on sleep apnea[38,39] and rosacea,[40] and neurotoxins because that may change the blink reflex.[41] If patients answer two or more questions on the dry eye component, then we do a point-of-care testing with matrix metalloproteinase 9 (MMP-9) and osmolarity.[20,42,43] That's all completed before I come into the room; once the patient has been diagnosed, we switch and give them the SPEED questionnaire.

Dr. Whitley: That questionnaire gives us a baseline; it gives us a place to start. Based on the TFOS DEWS II diagnostic recommendations, noting 80% of people will have both MGD and DED, we have to treat both, and MGD may be the root cause.[20,43]

CONSENSUS PANEL FINDING #3

Dry eye questionnaires are useful diagnostic tools.

INFLAMMATION AND FLARES

Q | Dr. Nichols: How are we treating and thinking about inflammation (innate versus adaptive immunity) in today's clinical settings?

Dr. Schweitzer: The overarching view for me is that every patient who has dry eye probably has some inflammation.[33,44] Managing the inflammation is really the key factor in treating our dry eye patients and how long we have to manage that inflammation. It's frustrating when patients are doing well, but 3 to 9 months later the inflammation returns. That's a key point to understand—DED equals inflammation somewhere.

Dr. Brujic: Patients oftentimes initially symptomatically peak with innate immunity, triggered by an immune response.[45-47] With DED, there's an adaptive immunity,[47] a snowball effect of inflammation on the ocular surface. What we're attempting to do is to control that inflammation because we know that adaptive immune responses lower threshold for activation over time. That may also explain why these patients have flares once or twice a year, and then those symptoms start occurring more frequently.

It's why we've embraced the MMP-9 rapid test as one of the key components in our dry eye work up, but also in managing these patients over time.[42,48-50] We presented a poster[51] that indicated stronger or weaker signals on the MMP-9 rapid test and suggested a grading system for that specific reason—the MMP-9 rapid test isn't just a positive or negative result.

Dr. Whitley: As Dr. Brujic mentioned, for patients with chronic DED, we need to have a lower threshold for future flare or flare response. That's something we've been monitoring with our patients, just as we would with our glaucoma patients, or any other chronic disease. We need to ask about triggers—especially for the patient who comes in with a SPEED score or osmolarity that has changed from the previous few visits. That tells me to treat with something different since an inflammatory response has been triggered. For me, that's usually a situation in which antiinflammatory agents will be successful.

Dr. Nichols: With inflammation, we don't always know if it's the cause or the effect, but we know that once you have any irritation on the ocular surface, that chronic exposure leads to an inflammatory response. The concept of dry eye flares[52,53] has been interesting for me, because I think of it as something that has always been a part of clinical dry eye, and now we are naming it. For me, there are really two scenarios. First, the chronic dry eye patient who's doing well on your current management plan, who has these episodes when they're suddenly feeling bad. The other is the patient with episodic flares, like from being on an airplane and their eyes are bothersome the next morning, or those who experience symptoms with other triggers, like allergy season.

Q | What are your thoughts on flares and how to manage them?

Dr. Devries: I don't think many of us considered flares—we just presumed a patient wasn't being treated at that particular point. Patients have been identifying flares long before we called them that. How often have you seen a patient who said they weren't doing well 6 weeks earlier, but when you evaluate, the surface looks healthy. If they come in during that flare-up, we'd adjust by using a different adjunctive therapy.

The eye doesn't care about the source of inflammation, whether it's allergy or environmental, including with screen time/masks like we've seen during the pandemic. It's going to react in that adaptive fashion, and need to get it under control. I like the concept now that flare is really a beginning point and it's a continuum even for patients with maximal treatment.

Dr. McGee: As you're saying that, I'm thinking through the conversations I have with my patients about the chronicity of the disease and that it will wax and wane. I love the word flare. It makes this conversation much easier to understand and now I can take it one more step and say, 'When you have a flare, then there's more we can do at that point when that happens.' I never connected that, or thought to be more aggressive by letting patients know we can address that flare as it's occurring. Now I can help patients make that connection and do something about it.

Dr. Nichols: I agree that flare gets a bit lost when the patient is not in your chair. They may say they had it once or twice a year. Making the connection between that time period 6 months earlier when they were not with you is a challenge.

Dr. Devries: The MMP-9 rapid test can be a great indicator of flares, and where on the spectrum the patient is at that point (mild, moderate). It gives us an opportunity to ask about other occurrences and recognize those greater adaptive responses.

Dr. Whitley: That's part of the education. As Dr. McGee just mentioned, we're not typically talking to our patient about triggers and what those symptoms are, or that we have treatments for it. Data suggests 80% of patients suffer from flares,[54,55] but most clinicians think it's about 40%. There's definitely some disconnect there.

Dr. Schweitzer: What we still do not know is what untreated flares will do over the long-term to the already-treated DED. What if, over time, treating and managing flares results in better overall ocular health and allows the patient to maintain that level of ocular surface health? What if flares are the dip points, the recognition of DED progression? As more treatments come to market and we can use them for flares, we'll have a better understanding of their implications for long-term DED prognosis.

Dr. Brujic: When I had a patient at a good spot with the right treatment plan who would come in and was not doing well, my knee-jerk response was to think they weren't compliant with their treatments. I find that's often the case with my glaucoma patients.

CONSENSUS PANEL FINDING #4

It's important to recognize and appropropriately treat dry eye flares because flares can occur throughout the year, with or without chronic DED.

But with DED, they've been doing everything I've told them to, and they're just having these episodic flares and they need additional treatment, or I need to reevaluate what should be the next steps. Although poor compliance used to be higher on my differential for these patients, dry eye flares are important to understand and appropriately treat for patients experiencing them.

DIAGNOSIS AND TREATMENT ALGORITHMS

Dr. Nichols: Even though there have been a number of dry eye definitions and diagnostic algorithms over the years, adaptation into clinical practice has been a challenge. Recently a group of international experts reviewed definitions around the world and recommended the following definition: "Dry eye is a multifactorial disease characterized by a persistently unstable and/or deficient tear film causing discomfort and/or visual impairment, accompanied by variable degrees of ocular surface epitheliopathy, inflammation and neurosensory abnormalities."[52] The new definition is similar to the TFOS DEWS II definition, but focuses on key clinical criteria for diagnosis, including unstable tear film, inflammation, ocular discomfort and visual impairment. This definition also recommends the assessment of ocular surface epitheliopathy and neurosensory abnormalities in each patient with suspected DED.

Q | Does this change your current thinking about diagnosis?

Dr. Brujic: I think this paper highlights the most contemporary body of knowledge on dry eye. It truly emulates the fact that dry eye disease is much more than simply a lack of tear production. It is complex, involving a myriad of signs and symptoms of which the clinician needs to be aware. It does solidify the inflammatory nature of the condition and the importance of incorporating diagnostic tests to help assess for inflammation, along with treatments directed at reducing inflammation.

Dr. Whitley: As we mentioned earlier, asking patients about their dry eye symptoms or utilizing dry eye questionnaires are slam dunks to identify sufferers and make an initial diagnosis. Nonetheless, we still have to use our various diagnostic tests to evaluate the ocular surface. We often talk about the various advanced diagnostic technologies, which we do believe in (tear osmolarity, MMP-9, tear film analyzers, etc.), yet we can use standard tests everyone should have, which include vital dyes to identify epitheliopathy, tear stability, and lid evaluation and expression, which is a great starting point (Figure 2).

Q | **Dr. Nichols:** We all know there are also numerous treatment algorithms that suggest how to best manage our patients, beginning with better lid hygiene, artificial tears, immunomodulatory and anti-inflammatory medications, in-office treatments, and even more advanced therapies such as autologous serum. What are your general approaches?

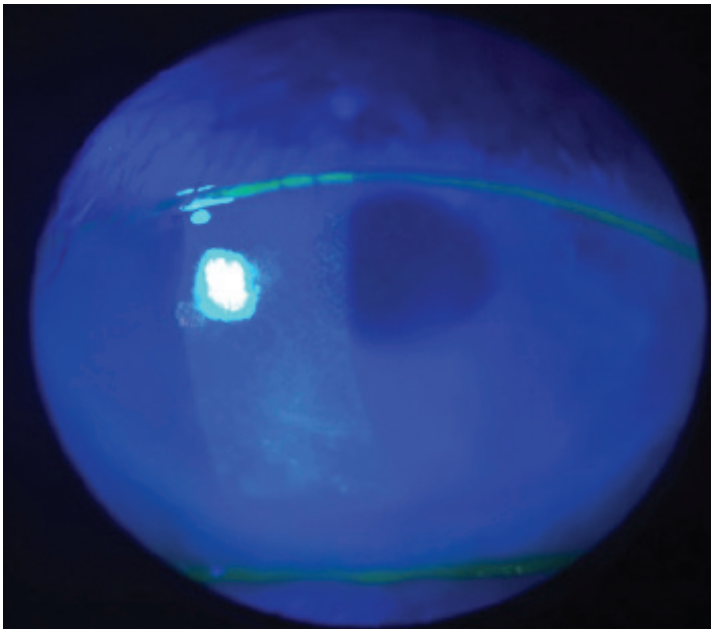


Image courtesy of J. Schweitzer, OD, FAAO.

Figure 2. Vital dyes can be an important tool for clinicians to identify dry eye disease.

Dr. Devries: If someone presents with moderate or severe disease, I'll start with an immunomodulatory drug and maybe a supplement to help address some of the inflammation, but I'm also going to look at the lid margins and treat for that. I tend to look at the acute nature first and then plant the seeds for doing more of the procedural aspects of treating the lids 4 to 6 weeks down the road.

Dr. Brujic: The more we learn about the immune system and how it affects the ocular surface, the more my treatment approach has changed. I used to develop a plan and implement it. Now I develop a plan but note there are going to be times when patients are not going to respond. When that happens, we arm them with the appropriate pharmaceuticals. I tell them the goal is to get to a point where the symptomatic episodes decrease, but when they do happen we can manage them appropriately. Fortunately, we have good FDA-approved pharmaceuticals that we can readily prescribe.

Dr. Schweitzer: I want my patients to feel better as quickly as possible. I also try to address that acute phase immediately. I commonly start patients on a steroid to address that inflammatory component. But I'm also looking very carefully at the lids and lashes. I do a lot of same-day meibomian gland treatment. I won't let them go home if there's a meibomian gland issue; we'll treat right there. My personal algorithm is to control the inflammation and treat the MGD. At follow-up, I'll move along to an immunomodulatory therapy (lifitegrast 5% or cyclosporine 0.05% or 0.1%).[56-58]

Dr. Whitley: I used steroids for years just to address the acute inflammation, and added in topical cyclosporine or lifitegrast later. We now prescribe the heat mask, nutraceuticals, some type of lid cleanser, and an antiinflammatory because most of our patients are already using artificial tears. When the patient returns for the next visit, I'll do more, if needed, or I'll add an MGD treatment.

Dr. McGee: There are certainly algorithms to help guide us with identification and treatments. Most recently a new definition that includes tear film instability as a primary endpoint. This further reiterates the importance of vital dye testing for identification of patients—adding a questionnaire and measuring TBUT can simplify identification.

As for treatments, my preference is a blend of what everyone has said based on current algorithms, and the key piece is bringing patients back in 4 to 6 weeks. I will start a patient on a steroid with either cyclosporine or lifitegrast accompanied by moist heat therapy, nutraceuticals, and hygiene. We talk about all of their cosmetics during the exam and what ingredients are in the products they're utilizing on their faces and around their eyes. At that next visit, I set the stage that this is where we're starting and we're going to continue to step up the therapy until they're where they need to be.

Q | **Dr. Nichols:** Do your patients bring their artificial tears with them? How are you incorporating them, how do you address preservatives in artificial tears, and how are you reconciling what patients see in the store or pharmacy?

Dr. Devries: I'm shocked how often the patients will be on such inappropriate artificial tears, and using them at such a high level that they're causing toxicity to their surface. So we try to redirect them. Most of my patients have been on that palliative treatment and have been overdoing it for a long time before they come in.

Dr. McGee: And it's not just artificial tears. They're typically on some sort of redness-reducing drop, and patients are sometimes shocked that using artificial tears could actually be making the problem worse. There's a huge disconnect. I explain that their eyes are red because there's inflammation that needs to be treated. I do recommend and prescribe artificial tears, but it's always in conjunction with a prescription medication or in-office treatment.

Dr. Brujic: I'm surprised at how infrequently people will admit they're using artificial tears. It's part of their normal routine and they don't believe they need to share that with us. Sometimes I'm surprised at what people actually use on their eyes—the power of marketing is strong, and it's obvious when you see what patients have in their medicine cabinets. I think artificial tears have their place, but it's important to realize they're not treating the underlying issues. They make people feel better temporarily, but they don't necessarily do anything to help rehabilitate the ocular surface and improve the quality of tears the eye is producing.

CONSENSUS PANEL FINDING #5

Educate patients about the proper use of artificial tears in dry eye management.

Dr. McGee: When I ask about their artificial tear use and whether it helps, most say their eyes only feel better for a little while, and the dryness returns. That one simple question changes the entire conversation.

Dr. Nichols: Exactly, because they've just admitted they're failing on artificial tears, and their DED management plan should be revisited.

NEW TREATMENTS ON THE HORIZON

Q | **Dr. Nichols:** What current treatments are you most excited about and what are you most looking forward to seeing come to market?

Dr. Devries: Some of the more exciting work is in nasal neurostimulation. A steroid was also recently approved for dry eye flares,[59] which is very exciting because that's going to create more awareness for our colleagues about flares.

Being able to reduce MGD and reaching greater efficacy out of thermal pulsation[60,61] is equally exciting.

Dr. Brujic: What's interesting to me is the drug delivery mechanism—some of the more intelligent and sophisticated ways that molecules are being repackaged, redesigned, reengineered to really get to the target tissues more effectively and more intelligently. I think we're going to see a lot of innovation here, particularly in new pharmaceuticals to treat DED and MGD.

Dr. Schweitzer: In addition to all those, I'm excited that we have cenegermin 0.002%, for the treatment of neurotrophic keratitis.[62,63] Also in the pipeline, but hopefully coming soon, is a *Demodex* treatment called TP-03. Those are two conditions that have traditionally been difficult to manage.

Dr. McGee: It wasn't that long ago we had only steroids, artificial tears, and punctal plugs. Those treatments compared to what we have today, along with newer diagnostics and what's coming in the next 5 years, is incredible and shows how quickly this field is moving. I've been very impressed with what my intense pulsed light device can do for patients.

What really excites me, however, is how we're able to better educate our patients and help them fully understand this disease and what they can do to alleviate symptoms and possibly prevent progression.

Dr. Whitley: Another exciting thing on our radar is photobiomodulation (LLLT) and using low light therapy to address the

meibomian glands, but it can also address aesthetics.[64,65]

We also know through experience that neurostimulation works, and a product coming down the pipeline is OC-01 (varenicline) nasal spray, which is a trigeminal nerve stimulator. The advantage to OC-01 is that patients are familiar with nasal sprays and generally know how to use them. This product will be slightly different because of the angle of the spray and how it needs to be applied into the nasal cavity, but it's something patients are more accustomed to compared with eye drops.

There are extranasal, sonic stimulation devices that I've had great success with. These types of products (either intranasal or extranasal) would be extremely helpful to glaucoma patients, so they don't have to use additional topical medications. I'm excited about these products and to have more tools in the armamentarium once they're available.

Regarding regenerative treatments, when thinking about using autologous serums or amniotic membranes, it comes down to severity. These typically are used in the worst-case scenarios but can be used much earlier with great success. Some of these are not covered by insurance and that does play a role.

Another treatment I think that is underutilized is punctal plugs. We know these are in early studies using cyclosporin and with steroids for short-term use in patients with dry eye. These could address the compliance aspect of treatment and these agents have been shown to work for our patients.

Dr. Nichols: OC-01 will be an interesting approach to dry eye considering it's not an ocular application. Should this come to market, it will be something novel to add to the dry eye toolbox and will likely be promising because it could potentially hit all three elements of the tear film, including the mucin, lipid, and the aqueous component.

There's also a place for regenerative treatments in dry eye management of severe cases. These orphan drugs, if they make it to market, would be best for those types of cases. It would be nice to have additional options across the spectrum of DED. Fortunately for our patients, the pipeline is certainly much bigger and more promising now than it was 5 to 10 years ago.

CASE EXAMPLES

Q | Dr. Nichols: Our first case is a 58-year-old female with chronic dry eye who has been treated successfully, but she has "break-through" symptoms each winter. How would you diagnose the patient? How do patients with these symptoms typically come to you, and how do you manage their ocular health?

Dr. Schweitzer: It's currently winter in South Dakota, so this really resonates with me and my typical patient. I recently had a patient whose DED has been well-controlled for years and she does everything I ask her to do. She takes artificial tears when needed, is on lifitegrast, and we've also treated her MGD. She presented with what is essentially a flare and she was struggling. She's a classic example of someone who is bothered by the dry winter environment.

For this flare event, we prescribed steroids for about a month, and then I reevaluated.

Dr. Nichols: Our next patient is a 42-year-old male business executive with nonstop screen time. He describes his symptoms during airplane travel, and he has difficulty with late night work hours and dry environments. He has never been diagnosed with DED.

Dr. McGee: I have a 42-year-old patient who is a pilot. He teaches flight simulation and publishes several studies every year. He has an enormous amount of screen time, and he has very distinct visual needs. He didn't have any symptoms, but upon imaging, his meibomian glands were nubs and he had zero expression.

He was shocked when I showed him those images. To look at someone that age, I wouldn't have come up with an MGD plan that would have resonated with the patient without imaging, no matter what I said.

These two cases represent what we see every day. This is a patient who could have easily fallen through the cracks. He is someone I will watch much closer now, educate on what a flare could feel like, and develop a comprehensive plan for that.

Dr. Nichols: The last patient is a 47-year-old part-time contact lens wearer. She sometimes doesn't wear her lenses because of dryness. She takes lifitegrast "off and on," mostly in the spring and late fall.

Dr. Brujic: It is interesting that whenever you look at any chronic medication, the compliance rate is approximately 50% with a lot of these medications. Some people are just good at taking their medications every day and some patients are not. This case resonates with me because I just saw a patient exactly like this. As clinicians, it's frustrating because we have to wonder how often are we going to have these conversations? Or we end up just managing the flare periods.

Dr. Whitley: In all these cases, adding the questionnaires would help identify some of these symptoms. I just had a patient who has tried both cyclosporine and lifitegrast and nothing worked successfully; she's still having symptoms. We're now using steroids, and I've got her initial SPEED score. Using the steroid to hit the heart of the inflammation should improve her scores. We'll see what her scores are when I next see her.

Dr. Schweitzer: I had four refractive consults today. All of these patients were younger than 30 years, and in three out of the four we are delaying refractive surgery so we can manage their OSD. Two of them had fairly significant MGD that we need to manage and treat. The other one has good glands but is suffering from some corneal staining, indicating some inflammatory event is occurring. All of these patients can be managed, but the point is that DED is affecting younger patients. All three of them were surprised we had to put off any type of refractive procedure to manage their DED, but that's becoming a really common occurrence.

FINAL COMMENTS

Q | Dr. Nichols: What one piece of advice would you give to practitioners who are trying to ramp up their dry eye practice?

Dr. Whitley: Use questionnaires. Presume everyone has dry eye until proven otherwise. I'd challenge these practitioners to give a questionnaire to their patients for a week, and they'll see they already have a high percentage of patients with DED within their practice.

Dr. McGee: I agree with Dr. Whitley about presuming every patient has dry eye until proven otherwise. I would empower your staff to think the same way. Do not do this in a vacuum. Realize that you already have all the tools you need to successfully ramp up your dry eye practice. Incorporate your staff to help, whether it's with vital dyes or administering a questionnaire.

Dr. Brujic: I would say utilize the tools that you have. In my opinion, the slit lamp and the vital dyes are the most valuable tools, and make sure you're using your vital dyes on a regular basis. By incorporating vital dyes into every patient visit, you'll be surprised at what fluorescein will expose, not only on the cornea, but in the tear film as well.

Dr. Devries: Press on every lid of every patient you see, so you can judge what abnormal is for each individual patient, and follow the stages of development. No purchases required.

Dr. Nichols: Just because you image, that doesn't mean you shouldn't express.

Dr. Schweitzer: Vital dyes are extremely useful. I recommend having the patient look down, so you can look at the upper lid and the upper lashes. It's an easy way to identify *Demodex* blepharitis, and blepharitis in general. Good lid hygiene makes such a difference for these patients.

Finally, if you help make your patients' lives better, the trust you're going to earn with them and the people they're going to talk to is only going to elevate your practice.

Dr. Nichols: It has been my extreme pleasure to work with you all. You are all experts in the field, and your patients are very lucky to have you. Thank you for your knowledge and expertise, and I look forward to working with you all again. ■

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Chronic Versus Acute: Rethinking Dry Eye Disease

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INSTRUCTIONS FOR CREDIT

To receive credit, you must complete the attached Pretest/Posttest/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 go to https://evolvemeded.com/2043-supplement. If you experience problems with the online test, please email us at info@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.

Full Name_____ ❑ MD/DO participant ❑ OD ❑ non-MD participant

Phone (required) _____ ❑ Email (required) _____

Address/P.O. Box _____

City _____ State/Country____ Zip/Postal Code_____

License Number _____ OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession
___ OD
___ Other

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

Patients Seen Per Week (with the disease targeted in this 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
Describe how dry eye disease (DED) symptoms can impact patient quality of life	_____	_____	_____
Explain how inflammation as a key driver of DED pathogenesis and symptomology	_____	_____	_____
Describe how episodic flares are part of the inflammatory disease process	_____	_____	_____
Formulate an individualized treatment plan for patients experiencing DED flares	_____	_____	_____
Compare available data on agents in the pipeline and their potential significance for DED management	_____	_____	_____

POSTTEST QUESTIONS

PLEASE COMPLETE PRIOR TO ACCESSING THE MATERIAL AND SUBMIT WITH POSTTEST/ ACTIVITY EVALUATION/SATISFACTION MEASURES FOR CE CREDIT.

1. Based on this activity, please rate your confidence in your ability to formulate an individualized treatment plan for patients experiencing dry eye disease (DED) flares (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. Based on this activity, please rate how often you plan to discuss with patients the impact of DED symptoms on their quality of life (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. What is a 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

4. According to the TFOS DEWS II study, more than 80% of patients with DED also have _____.

a. A history of smoking
b. Younger age (less than 30 years)
c. Meibomian gland dysfunction
d. Hypertension
e. Ocular allergies

5. Ms. Smith is a 22-year-old female who presents for her annual spring eye exam asking for a stronger prescription for her glasses and contacts. Her vision has recently become frequently blurry, and she's noticed a reduction in the number of hours she can wear her contacts without dryness and 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 (TBUT) is 5 seconds. Mrs. Smith's blurry vision and contact lens intolerance may be due to:

a. Seasonal allergies
b. Evaporative dry eye
c. Cataract
d. Both A and B
e. Both B and C

6. The more topical drops a patient takes (regardless for what condition), the more likely there is concomitant _____.

a. Ocular surface disease
b. Ocular hypertension
c. Neurotrophic keratitis
d. Allergic conjunctivitis

7. Which of the following is not recommended to solely identify asymptomatic DED patients?

a. Lid margin evaluation
b. Vital dyes
c. Questionnaires
d. Meibography
e. Family history

8. Based on the current literature, all but which of the following may adversely impact ocular surface health?

a. Elevated cholesterol levels
b. Diabetes
c. Autoimmune disorders
d. Sleep apnea

9. What is a dry eye flare?

a. A spike in SPEED scores
b. A lengthy amount of time with elevated matrix metallopeptidase 9 (MMP-9) levels
c. A spike in symptoms directly related to medication compliance
d. A spike in symptoms even while being compliant on current therapy

10. Which diagnostic symptom/result should lead to treatment with an antiinflammatory agent?

a. Schirmer test result of 11 mm
b. Positive MMP-9 test result
c. Low osmolarity score
d. TBUT of 7 seconds

11. For patients with neurotrophic keratitis, _____.

a. Photobiomodulation is a viable option.
b. Cenegermin 0.002% has been recently approved
c. TP-03 is still in the pipeline, but looks promising
d. There still remains an unmet need as there are no approved treatments

12. Mr. Smith is a 27-year-old computer programmer who complains of "sore eyes" at the end of the day, after he's worked and then played online games in the evening. He is presenting to your office because he wants refractive surgery as he notes his contact lenses are bothersome and "don't work" after hours of wear. What is the best option?

a. Evaluate the corneal surface with vital dyes and the lid margins and refer to a surgeon.
b. Change the contact lens prescription (ie, from soft lenses to rigid lenses), and recommend against refractive surgery.
c. Assess the ocular surface and if damage is present, recommend delaying refractive surgery until the ocular health has improved.
d. Rely on patient questionnaires and vital dyes to determine whether refractive surgery would benefit the patient.

ACTIVITY EVALUATION/SATISFACTION MEASURES

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

Probability of changing practice behavior based on this activity: _____ Yes _____ No _____No change needed

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

_____ Change in pharmaceutical therapy
_____ Change in diagnostic testing
_____ Change in current practice for referral
_____ My practice has been reinforced
_____ Change in nonpharmaceutical therapy
_____ Choice of treatment/management approach
_____ Change in differential diagnosis
_____ I do not plan to implement any new changes in practice

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 _____

MODERNOPTOMETRY