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THE LATEST IN COMPREHENSIVE CARE FOR PATIENTS WITH DRY EYE DISEASE

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The Latest in Comprehensive Care for Patients with Dry Eye Disease

Part 2 of 2

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from a virtual roundtable discussion held on April 24, 2019.

ACTIVITY DESCRIPTION

This activity focuses on providing ongoing and continuous education with up-to-date information and cases for anterior segment specialists and general ophthalmologists involved in the treatment and management of patients with dry eye disease (DED).

TARGET AUDIENCE

This certified CME activity is designed for anterior segment specialists, general ophthalmologists, and other eye care practitioners involved in the management of DED.

LEARNING OBJECTIVES

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

- **Discuss** the mechanism of action of DED.
- **Evaluate** the signs and symptoms in patients with dry eye complaints.
- **Discuss** the prevalence of DED.
- **Develop** a differential diagnosis for patients with complaints of dry eye.

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DIGITAL EDITION

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

1. PLEASE RATE YOUR CONFIDENCE IN YOUR ABILITY TO APPLY DRY EYE TREATMENTS IN YOUR PRACTICE (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 APPLY DRY EYE TREATMENTS TO PATIENTS IN YOUR PRACTICE (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. SIGNS AND SYMPTOMS OF DRY EYE DISEASE (DED) CAN BE FOUND IN AS MUCH AS _____ OF THE POPULATION:

a. 5%
b. 10%
c. 15%
d. 20%

4. AS PART OF THE VICIOUS CIRCLE, PATIENTS WITH DRY EYE OFTEN PRESENT WITH:

a. Evaporative dry eye
b. Aqueous-deficient dry eye
c. Meibomian gland dysfunction (MGD)
d. All of the above

5. COMPARED WITH THE GENERAL POPULATION, MGD IS MORE PREVALENT IN ALL OF THE FOLLOWING *EXCEPT*:

a. Patients with Sjogren syndrome
b. Patients without Sjogren syndrome
c. Patients with rosacea
d. Women

6. WHICH OF THE FOLLOWING CAN WORSEN SYMPTOMS OF DED?

a. Environment
b. Corneal subbasal nerve damage
c. Artificial tears with preservatives
d. Prolonged screen time
e. All of the above

7. ACCORDING TO THE PANEL MEMBERS, WHAT IS THE PREFERRED METHOD FOR DIAGNOSING SIGNS OF DED?

a. Fluorescein staining
b. Schirmer test
c. Dry eye questionnaire
d. All of the above

8. WHICH DED TREATMENTS HINDER THE T-CELL ACTIVATION, RELEASE OF INFLAMMATORY MEDIATORS, AND CONSEQUENTLY INHIBIT THE INFLAMMATORY PATHWAYS?

a. Cyclosporine A
b. Lifitegrast
c. Artificial tears
d. Corticosteroids
e. A & B
f. C & D

9. WHEN SHOULD YOU TREAT OCULAR SURFACE DISORDERS?

a. Prior to surgery
b. Following surgery
c. When signs and symptoms are present
d. All of the above

10. ACCORDING TO THE PANELISTS, WHAT SHOULD BE THE IDEAL BIOMARKER FOR DED?

a. Microbiological involvement
b. Inflammation
c. Environmental sensitivities (allergies)
d. Autoimmune disorders

The Latest in Comprehensive Care for Patients with Dry Eye Disease

Part 2

We bring together for this educational discussion about dry eye disease (DED) some of the most well-known experts from Europe. We will review the important issues we face in treating patients with DED, including varying degrees of prevalence in certain populations, the discordance between signs and symptoms, new treatment options, the effect of comorbid conditions on signs and symptoms of DED, and how best to manage DED in patients before and after surgery, among others. We hope this will help guide clinicians to achieving improved outcomes for their patients.

— Professor Christophe Baudouin, MD, PhD, FARVO, Moderator

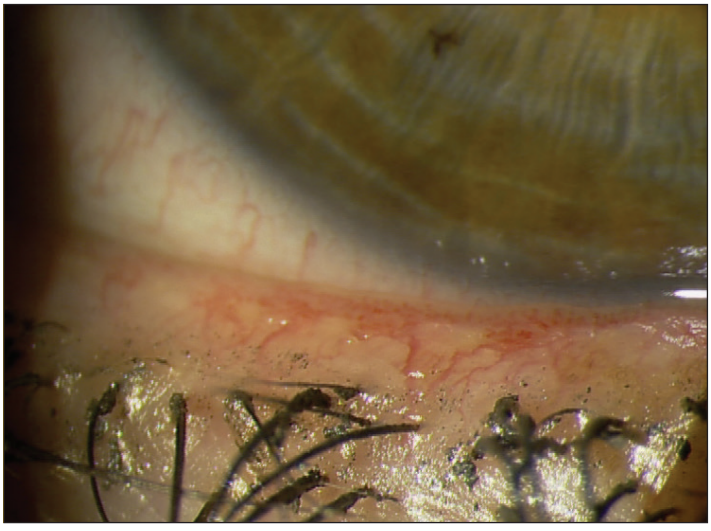
PREVALENCE OF DRY EYE

Q | PROFESSOR CHRISTOPHE BAUDOUIN, MD, PHD, FARVO: DED may be found according to signs and symptoms in approximately 5 to 20% of the general population. The condition presents more frequently in women than in men and especially in patients older than 60 years, but it may start very quickly and very early in the life.[1] Please share any data you have on the prevalence of DED.

PROFESSOR JOSE BENITEZ-DEL-CASTILLO, MD, PHD: Based on results of the follow-up from the Salnés Eye Study, the 11-year incidence of DED was 25.4% (95% confidence interval [CI], 19.5-31.3) and that of symptoms was 31.6% (CI, 25.4-37.8).[2] The incidence of symptoms was higher than that reported in similar studies, moreover, this population was from the northwest of Spain where it is very humid.

PROFESSOR ELISABETH MESSMER, MD, FEBO: Another study from Spain that investigated the relationship of meibomian gland dysfunction (MGD) and other prevalent ocular diseases with DED found that DED and MGD prevalence were 11.0% (95% CI, 8.6-13.3) and 30.5% (95% CI, 26.9-34.1), respectively.[3]

PROF. BAUDOUIN: We can confirm that dry eye prevalence is very high, higher in some regions and some populations than others. For example, we know that MGD is very common in Asia (Figure 1). Several studies in patients from Asia that are mentioned in the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshops (DEWS) II Epidemiology Report indicate the overall prevalence of disease ranged between14.4 and 24.4%.[1] Other studies show it may be up to 60% of the population which seems to be very huge. We know that in glaucoma patients it can be up to 50% of the patients.[4] So, we think there are different categories and regions where prevalence is even higher.[4]



Courtesy of Christophe Baudouin, MD, PhD, FARVO

Figure 1. A patient with meibomian gland dysfunction.

PROF. BENITEZ-DEL-CASTILLO: Speaking to certain populations, other studies have shown that MGD is related to rosacea and rosacea is very prevalent, mainly in whites.[1,5,6] Worldwide incidences of rosacea peak as high as 18%, particularly in populations with a predominant Celtic heritage, such as is observed in Ireland.[7] Worldwide, the prevalence is estimated to reach over 5%.[7] Females and males are affected equally.[7]

MECHANISMS OF DED

Q | PROF. BAUDOUIN: The different conditions are related to the different types of dry eye: aqueous-deficient dry eye versus evaporative, or MGD. So, the prevalence is different according to the two mechanisms.[1] Are there any differences in how they present in general, or in specific patients? Is one type

more prevalent than the other? Do you think these types of dry eye are very common in our areas of the world?

PROFESSOR MAURIZIO ROLANDO, MD: Sjogren syndrome dry eye falls under aqueous-deficient dry eye and represents 0.4% of the population.[8] So, it's not very frequent. And many years ago, it was the only DED population that was recognized. But now I think the mixed form of dry eye, evaporative and aqueous deficient, is the most common. I find that when a patient comes to me, they may start with pure, evaporative dry eye, but because of the vicious circle[9] that is formed by the disease, from time to time they become aqueous deficient. So, it can be difficult on initial evaluation to separate the types of dry eye patients until we can do specific tests based on the genetic essence of the disease. By far, the most common, I think, is evaporative dry eye, which is linked to MGD or instability or tear film instability because of epithelial damage, for example, following surgery.

We are also now realizing there can be nerve involvement in some patients with DED, which is very important.[10,11] I don't think I have a straight-forward way of separating the two forms, aqueous deficient and evaporative dry eye. A patient who is purely aqueous deficient or purely evaporative is very difficult to find.

PROF. MESSMER: I also find that in many cases in my practice, we have aqueous deficiency in addition to MGD in these patients. So, even in this very clear and straight-forward population of Sjogren disease patients, we do have a combination of the two very often.[8]

PROF. BENITEZ-DEL-CASTILLO: I have the same experience with my patients. We know that MGD is more prevalent in patients with Sjogren syndrome compared with non-Sjogren syndrome patients.[1] And what's also important is a patient can start with evaporative dry eye and can finish with a mix of aqueous-deficient dry eye. And vice versa. Refering to the prevalence of MGD, the 11-year follow-up study to the original Salnés Eye Study also revealed that the prevalence of asymptomatic MGD was 21.9% and the prevalence of symptomatic MGD was 8.6% among the general adult population in northwestern Spain.[2]

PROF. BAUDOUIN: It's common to discriminate between evaporative versus aqueous-deficient dry eye, but, in fact, this discrimination is a bit artificial because the disease is not separated that way. It's a vicious circle—the disease in which a biological cascade self-stimulates. Evaporative dry eye may be a very constant medical deficiency and in the end the disease has a mixture of the different mechanisms.[9,12,13]

RISK FACTORS FOR DEVELOPING DED

Q | **PROF. BAUDOUIN:** We know dry eye is prevalent, but let's discuss how the eyes become dry. It's a vicious circle, but how do the patients progressively or immediately move to a condition where they have DED? We mentioned rosacea and the Asian population, but are there other conditions that may also be risk factors for developing dry eye?

PROF. MESSMER: I think use of chronic medication, especially those with preservatives, is an important risk factor for developing DED.[8,14]

PROF. BAUDOUIN: To take that point one step further, the people working for hours on a computer are likely also exposed to air conditioning and probably inducing ocular fatigue. And dry eye will also cause poor functional visual acuity.[15,16,17]

PROF. BENITEZ-DEL-CASTILLO: Many eye care providers don't think visual problems are related with dry eye, but our corneal epithelium is rough, not smooth. We need the tears to maintain an optimal optical ocular surface, so tears are very important (Figure 2), and some patients complain of having poor vision while reading. This is because their blinking is impaired.[8]

The problem is that many eye care providers don't have the proper noninvasive instruments to evaluate tear break-up time. As corneal specialists we have them, but they are not usually found in general eye care practices. When we test visual acuity in a patient with DED, if he or she could blink whenever they want, visual acuity would be perfect. The problem is when blinking is impaired, visual acuity will drop very rapidly.[1] This is very important when the patients are asking for a premium IOL or refractive surgery. Ophthalmologists should be aware that poor vision is part of dry eye.

PROF. BAUDOUIN: Very good point. We have identified risk factors that may possibly cause dry eye, like long-term exposure to a computer or video screen. Dr. Rolando, can you discuss how surgical patients may experience dry eye and how this may be a major problem for the surgeon and the patient.

PROF. ROLANDO: If a patient has dry eye after cataract surgery, especially if he or she didn't recognize symptoms of dry eye before surgery, the patient may perceive the surgery as a failure and that the surgeon caused the dry eye. Without proper testing, it could be possible the surgeon didn't realize the patient had dry eye before surgery.

It is important to inform a corneal surgery patient that he or she must be tested before the surgery if they have risk factors for MGD—even without symptoms. This has to be recognized before, and it's very important to tell the patient before the surgery that they can have dry eye.[18]

Following surgery, some patients will have dry eye, possibly due to the drugs that we use during and before the surgery. For instance, the nerves will have some problems after the surgery, especially if you instill many drops of anesthetic. And most of the drugs that we use before the surgery are very toxic for the epithelium. We need to use them to prevent infection, but they can be very toxic.[1,8,14]

And, of course, during the surgery we use something to separate the lids and that can be very traumatic for the lids. So, after the

first days after the surgery, you have a very bad dispersion of the tears with blinking because the lids lose tension and they don't spread the mucins over the surface of the eye in the correct way. And the nerves are cut during surgery. When you measure the sensitivity of the cornea after cataract surgery, you have a reduced sensitivity in the cornea that is far away from the tunnel made to enter the cornea. So, it looks like there's a total reaction of the corneal nerves in depressing sensitivity and in this way depressing the tear production.[1,8,14]

There are a lot of things that can happen during surgery that can change the ocular surface, leaving the patient to suffer with dry eye.[1,8,14] Luckily, in most of cases, after 2 or 3 months, the problem goes away by itself. But, in a few patients it stays there. And the patient is very, very disappointed with surgery. So, it's a problem that should be considered before surgery and we have to inform the patient there is a risk of having some problem with dryness after the surgery.[14,19]

PROF. BAUDOUIN: We should also discuss the impact of blue light, screen time, and the visual function on dry eye.

PROF. MESSMER: We must consider the digital age in which we live.[15] I think working on a computer for many hours a day, then in the evening coming home, playing on our smart phones or tablets, watching television, doing all these visual tasks on a digital display, I think is a big inducer of dry eye. Because the break-up time is going down, the blink frequency is going down.[8]

PROF. BENITEZ-DEL-CASTILLO: I don't think blue light is related to dry eye, and I do not think blue light is what produces dry eye.[20] The problem is the reduced number of blinks a person takes when staring at a screen. When we use these computers or devices, we not only reduce the number of blinks, but we also have more partial, incomplete blinks. And this is also very important.[1,8] A lot of companies are producing lenses that filter out blue light and they are making money, but there's no real science behind this theory.[21]

PROF. BAUDOUIN: What about the natural history of dry eye? Will dry eye always follow a standard evolution, beginning as mild disease and progressing to severe? Are there other options for the evolution?

PROF. MESSMER: We don't have a lot of really good data on the natural cause of the disease. We have already discussed that most patients with DED will move onto a combined problem with aqueous deficiency and MGD with time. This seems to be some kind of progression.[9]

We do have some information from a study during which patients were asked for their symptoms over a time of 10 years, or from the time of diagnosis. Patients were asked after 10 years how much in their subjective views had their dry eye progressed. In about 20% of patients, they had the feeling that their dry eye was worse from subjective symptoms, but also from vision and from social components, their dry eye was worse. So, it seems that a certain subgroup of patients will progress with the disease, and it seems that it's mostly those patients who had very severe dry eye from the beginning. Or patients who have an autoimmune disease.[22,23]

We have, for example, some data for Sjogren's patients where it's completely clear that these patients progress over time. However, we're still waiting for the results of the PROOF study[24] that will hopefully answer in detail all these questions and look at progression in dry eyes over time. And we will expect the data in about 5 years. So, at the moment, we have the feeling that a certain group of patients progress, but not everyone.

DIAGNOSTIC TOOLS AND SEVERITY ASSESSMENT

Q | **PROF. BAUDOUIN:** Let's discuss severity and therapeutic strategy. What about severity assessment? If you follow the TFOS DEWS recommendations, you will follow a step-by-step approach in which, according to symptoms and the symptom intensity, are more or less severe. And it seems to follow a two-part evolution. The more symptomatic, the more severe, the more corneal thinning, the more severe. But in fact, we know that it's not true.[25] It is important we talk about the frequent discrepancy between signs and symptoms. In my experience, I have had some patients complain of dry eyes, yet they have poor corneal staining, and some patients don't complain at all despite severe corneal staining.

PROF. ROLANDO: This is really important. As ophthalmologists, we consider severe patients as those who complain a lot or those with damage of the cornea. But, for some patients, they may feel the symptoms even if the corneal staining isn't indicative of dry eye.[25] This is the problem, I think, because we may not understand completely the role of the nerves.

The more the superficial plexus is damaged in most of our patients with dry eye or at least is changed. But we cannot correlate perfectly the sensitivity with the morphology of the nerves. And I think this is the most important problem, because if we have nerve damage and a patient is going to have problematic dry eye because damage to the nerves will decrease the number of healthy cells of the epithelium and will decrease the tear production.[10,11]

The role of the nerves is something that we should try to better understand. The symptoms can disappear because of the damage to the nerves. We should ask the patient if he or she feels better or worse compared to last year. The patient may say the treatment has been very useful and they feel better. But we can see the surface of the eye is getting worse.

PROF. BAUDOUIN: The corneal nerves are important to understand the kind of discrepancy between signs and symptoms.[11] But the problem is that it is difficult for the clinician to precisely analyze the nerve. Prof. Benitez-del-Castillo, could you address the topic of confocal microscopy of the nerve and the inflammatory marker or inflammatory cells.

PROF. BENITEZ-DEL-CASTILLO: There are different studies showing that problems have developed in the nerves of patients with dry eye.[11,12] In a minority of patients, the progression of dry eye is indicated by the increasing nerve damage, but when DED is already present, the density of the basal nerves is decreased. This is important because these patients are having dry eye symptoms but also probably related with neuropathic pain. Because of low nerves, they are having problems at the level of the epithelium. And there is also a correlation because dry eye is an inflammatory disease.[26] It is important to consider the correlation between the density of the dendritic cell at the level of the central cornea, in comparison with nerves. In DED, with confocal microscopy we can find a higher density of dendritic cells in the center of the cornea and low density of nerves. So, this is the relation between inflammation and nerves and having also neuropathic inflammation.[8,27] I believe this will be an important target for treating dry eye in the future.

PROF. BAUDOUIN: Neuropathic pain, because it's very important emerging concept, should be considered when we have a patient who complains a lot and we don't understand why based on the patient's signs. So many patients seem to have neuropathic pain, but it's possible this is not accurate. We need better tools to understand the neuropathic symptoms. For example, through confocal microscopy, I have found inflammatory infiltrates and nerve abnormalities that show it's not really neuropathic pain. In fact, in patients with repeated nerve stimulation resulting from microvariations of temperature and osmolarity in case of major tear instability, we are unable to measure what level of stimulation really occurs at the nerve levels.[28]

What about biological biomarkers? Would it be useful for the clinician to have biological biomarkers, maybe in the tears?

PROF. MESSMER: Biomarkers would be great, especially for studies, to have some objective markers for inflammation, maybe for cell damage. I think if we had some numbers, we could much better analyze than what we have at the moment. I think biomarkers would also be very helpful for the practicing ophthalmologist. But it would need to be an easy test to be used at the chairside. At the moment, this is a big problem. We have HLA-DR.[29] But we need a laboratory to analyze HLA-DR. We need impressions to analyze HLA-DR. We have a test on the market to measure MMP-9.[30] But it's just a "yes" or "no" test. It's not a test that gives us any numbers or any details. We have the possibility to measure osmolarity as an indirect sign of inflammation. We have two instruments now on the market, but both of them have their problems.[31,32] So, yes, I think biomarkers might be very helpful.

PROF. BAUDOUIN: I agree completely. If we had to choose one specific biomarker, what would be the most important criteria to measure? For myself, I would say inflammation. I don't need to measure dryness. I know that the patient is dry. But, for example, the level of inflammation would be of interest.

PROF. MESSMER: I think MMP-9 is a good biomarker, but inflammation is not specific to dry eye. We can't, for example, discriminate from other causes of inflammation with this marker, such as allergy. So, even when we measure inflammation, we have to measure very specific inflammation associated with dry eye.

PROF. BAUDOUIN: I agree. The level of inflammation could be of interest because it could drive some treatment. But also, the origin of inflammation, allergy versus dry eye, MGD versus inflammation, etc.

PROF. BENITEZ-DEL-CASTILLO: I agree with both of you. The problem of DED is that it is not a simple disease. So, there's nothing pathognomonic of dry eye; we can find dry eye associated with allergy, after surgery, and many other situations.[1,8,10] So, nothing is specific of inflammation, nothing specific of dry eye except for osmolarity but I find osmolarity testing to be unreliable.[31]

PROF. ROLANDO: I think we should change our approach to dry eye because we don't have a clear understanding of what constitutes dry eye and how it correlates with specific levels of severity or inflammation. But I think we should address the five different pathogenic factors and ask more questions, including how unstable the tear film is by evaluating the tear breakup time and how much inflammation is present. We should select the best markers available to determine the level of inflammation and not only for the presence of inflammation. I think when diagnosing DED, the most important is the level of inflammation. We should also evaluate the epithelium with the level of staining, determine how much the nerves are functioning, and figure out how the lids are involved in the vicious cycle.[9] We should try to give a score to each of these five points.[33,34]

I see chronic dry eye as a failure of the ocular surface to maintain itself. If you have severe MGD, you're going to have a dry eye. Is that severe dry eye? I'm not sure. So, I think at the time being we should work to find available biomarkers for these five points. And this will give us an idea of the level of severity of dry eye.

PROF. BAUDOUIN: For the comprehensive ophthalmologist who may not have the extensive dry eye testing modalities that DED experts may have, what would be the best test to indicate a patient has dry eye? Is it Schirmer test, fluorescein staining, lissamine green? Or more sophisticated testing that measures tear film, etc.?

PROF. ROLANDO: To me, meniscus height, tear turnover, and staining are the most important diagnostic tools we currently have available, especially staining. I usually use fluorescein with a yellow filter. In Italy, we have a form of lissamine green in drops and I will sometimes use that. But mainly you can use fluorescein and have a very good idea of staining.[35,36]

PROF. BAUDOUIN: I know that lissamine green is not available everywhere. Are there other preferred methods?

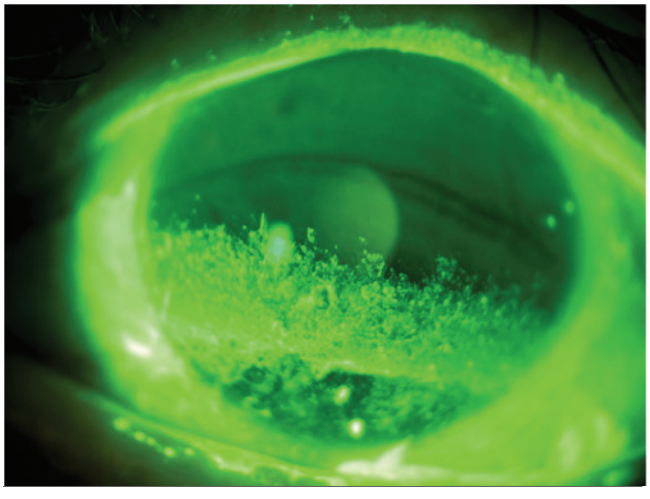
PROF. MESSMER: I agree with Dr. Rolando. I think you can diagnose DED with a drop of fluorescein (Figure 2). You can see the tear meniscus, you can do break-up time, and you can see the ocular surface staining.[35,36] The second test for me is indeed the Schirmer test. Because a Schirmer test result below 5 indicates severe DED and that the patient should be watched closely. This might be a patient that has more progression than others.[35-37]

PROF. ROLANDO: I agree.

PROF. BENITEZ-DEL-CASTILLO: I also agree. But I also believe a brief questionnaire is necessary to help quantify symptoms.[36] I also use the slit lamp for looking at the lid margin and I to press the eye lid to determine quality and quantity of the meibum.

PROF. BAUDOUIN: To summarize our opinions on DED diagnosis, I would say that for the general ophthalmologist the preferred basic test would be one drop of fluorescein staining, which is extremely useful for the cornea, for the conjunctiva, for the tear break-up time. Not only the time but also the way and the shape of the break-up. That may also indicate a different mechanism. We should also examine the eyelid, and a very good point raised by Prof. Benitez-del-Castillo, is that we should listen to our patients. A questionnaire is a way to collect information on their symptoms, but we should listen to our patients to learn from their comments how much they suffer and which type of symptoms they develop.

Adding to the diagnosis dilemma, there are several disorders that present with similar symptoms as dry eye, but are separate entities requiring either different or concomitant treatment, including MGD, conjunctivochalasis, lid wiper epitheliopathy, ocular allergy, and contact lens intolerance.[1,36]



Courtesy of Christophe Baudouin, MD, PhD, FARVO

Figure 2. A drop of fluorescein is the helpful in diagnosing DED.

THERAPEUTIC OPTIONS AND TREATMENT STRATEGIES

Q | PROF BAUDOUIN: Moving on to therapy, my first point is that I'm not comfortable with the algorithm proposed by the TFOS DEWS II because it's based on the severity assessment. As we have already discussed, you cannot really base your severity assessment on the severity of either the symptoms or the signs. The second point deals with treatment.[38] When you look at the different possibilities of treating the patient, it's a combination of many possibilities.

The first question is about the dry eye work shop and artificial tears. According to the TFOS DEWS II report management and therapy report,[38] it is considered acceptable in the mild phase of dry eye for patients to use artificial tears with preservatives. But we know that the preservatives worsen dry eye.[14]

If a patient with a moderate dry eye uses preservative-free artificial tears, it is possible for the condition to change to mild dry eye. In that case, the patient will be allowed to use preservative eye drops with preservatives, and will once again develop more moderate dry eye, and so on. My opinion is that all dry eye patients should avoid at least the most toxic preservatives, namely benzalkonium chloride.[38]

PROF. ROLANDO: We should also consider that if you have even a very low concentration of preservative in the bottle, because of the high level of evaporation and very low turnover of tears on the surface of the eye, the water will go away but the preservative will stay there. So, you increase the concentration of preservatives on the ocular surface.[14,39,40] I think it's another point that should be considered. All of my patients are instructed not to use formulations with preservatives on the surface of the eye.

PROF. BENITEZ-DEL-CASTILLO: I agree. Even in a patient with mild dry eye who only has symptoms when after prolonged exposure to digital devices should avoid drops with preservatives. Because when using computer, blinking aborts, so you will have decreased tear clearing. Anything with preservatives clings too long to the ocular surface, will last longer and will harm the ocular surface. So, even mild cases, preservatives should be avoided.[14]

PROF. MESSMER: I agree completely. I think this is an unfortunate recommendation by the TFOS DEWS II to allow preserved eye drops in the mild cases as a first step of dry eye treatment. In addition, I am surprised by the TFOS DEWS II recommendation on the use corticosteroids for the long-term considering the side effects of topical steroids. I would not even use a "soft" steroid as a long-term treatment.

PROF. ROLANDO: We have some data on short-term use of steroids,[38] but we do have data on prolonged treatments with a very low dosage of cortisol, which is a physiologic steroid actively secreted by the epithelium of the ocular surface. It's a very low level of secretion. We should try to use very low levels of steroids

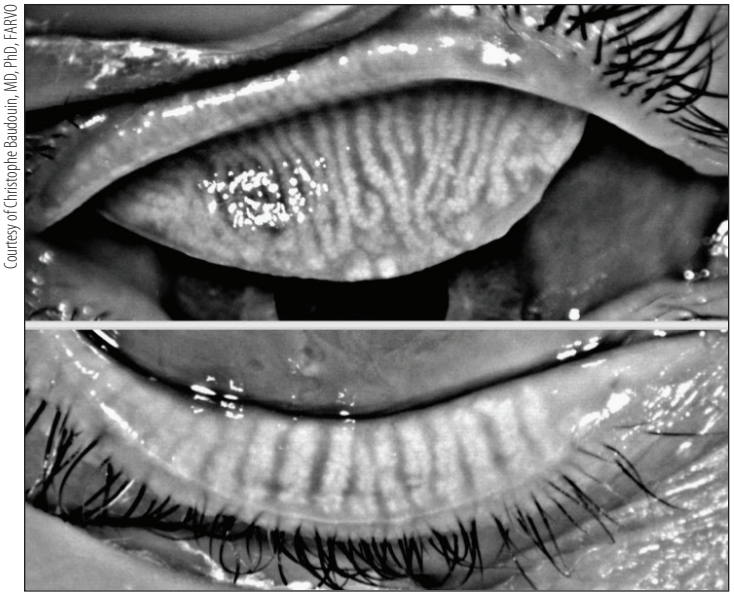

Courtesy of Christophe Baudouin, MD, PhD, FARVO

Figure 3. Images of meibomian glands.

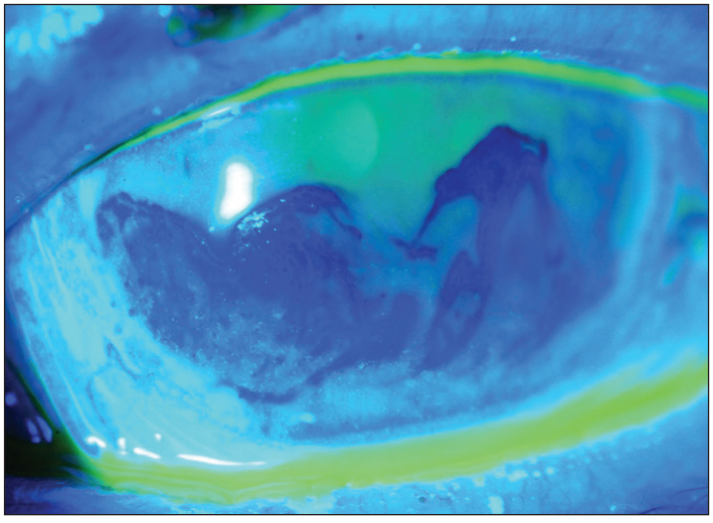

Courtesy of Christophe Baudouin, MD, PhD, FARVO

Figure 4. Image showing severe tear instability.

because we have learned, for example, that for the treatment of viral immune-mediated infections on the stroma that you can use low dosage of steroids and they are able to control the inflammation.[41]

It's possible we are using too high levels of steroids, which are the steroids currently on the market. I have some experience in diluting the steroids. I have been treating a patient for several months using a very low concentration of steroid. However, you are responsible for patients like this so you must closely follow them and be sure they come back for follow-up visits. Oftentimes with the steroid, they will feel a little better and so they tend to over use their steroids drops.

PROF. BAUDOUIN: As MGD is very common, what is your best strategy for lid hygiene and to fight against meibomian gland obstruction? Do you think that lid hygiene is important? If so, do you recommend the recently developed sophisticated tools on the market for massage with warming machine? Or do you propose warm and cold compresses? Describe what you propose for your patients?

PROF. MESSMER: For me, lid hygiene is very important, and it has to be as simple as possible for patients to comply. I always start with warming with hot compresses and then massaging with a cotton swab without any further emulsions or liquids. For me, the most important is that the patient understands why he/she should perform lid hygiene. If available, I show scans of the meibography or noninvasive tear film break-up time to the patient to demonstrate the problem (Figure 3). I can show the patient images of their meibomian glands and they can see that some glands are lost already or their tear film is of bad quality (Figure 4). So they understand that we have to work on the problem. I think this is very helpful in keeping the patient informed and aware. Most patients experience lid hygiene as something very nasty, very discomforting, or very disturbing. In my experience, they don't really like to do it.

PROF. BENITEZ-DEL-CASTILLO: I think patients should know this can be a chronic disease, although this term is not yet included in the TFOS DEWS II official definition.[42] There is no curative treatment at the moment so it's possible they will have to manage this condition all of their life. One important thing is also to teach patients what to do at home. When they come into your office, you have to ask them what they are doing because some treatments can be offensive for the ocular surface. I tell my patients to do the type of warming they find acceptable because they have to do it for all their life. I also tell patients about hygiene for the eye lashes, but not to do it every day because they contain detergents, and detergents can be harmful to the lipid layer of the tear film.[38,43] I tell my patients that it's best to use them at most 3 or 4 times a week.

I also explain to patients that it's like going to the dentist. You have to brush your teeth at home, and from time to time you have to go to the doctor in order to apply a new treatment. In my opinion, some of the sophisticated treatments are very effective in the well-chosen patient, but not for everybody. We will have to see if future studies show they are effective. But some machines, some intense pulsed light devices have some evidence that it's useful in the right patient.[38]

Q | PROF. BAUDOUIN: So, the consensus of the European experience is that lid hygiene is very important. This can be used with very simple methods but probably the future or the very near future, will give us more sophisticated techniques that are currently under evaluation.

According to the DEWS II, when the patient is developing severe dry eye, we are proposed to use an immunomodulating agent that can control inflammation differently from the steroid and with limited side effects. Do you consider immunomodulating agents as being restricted to the most severe patients, or can they be used earlier to prevent the development of severe condition? Describe your approach with these agents.

PROF. BENITEZ-DEL-CASTILLO: With immunomodulatory drugs, it's important to start early, even in mild cases, in order to stop the progression of the disease. But I think we have to start very early because we have safe medications, they are expensive, but they are safe.[44-46] And in those cases as the disease progresses, we can stop the disease very efficiently.[38]

PROF. ROLANDO: I think cyclosporine A is a very useful ophthalmic treatment and as an immunomodulator. Cyclosporine is a potent inhibitor of T-cell proliferation and thereby inhibits T-cell-mediated immune responses.[47] I think the earlier we treat the patient with cyclosporine, possibly the better the outcome for the patient. But there's a new class of treatment available that I think is theoretically very clever. We have learned that our body is able to make an inflammatory condition chronic by stimulating the adhesion molecules and allow the infiltration by lymphocytes in the area of inflammation, thereby maintaining the inflammatory condition. A new drug, lifitegrast, is now available in Europe that hinders the T-cell activation, release of inflammatory mediators, and consequently inhibits the inflammatory pathways.[48] So, it will be very interesting to have a drug to stop the chronicity of the disease. We don't have a large number of results, but I think that will be a good opportunity to stop the disease at the beginning.[35,49,50]

PROF. MESSMER: I agree with Prof. Benitez-del-Castillo's comment about disease progression. I also agree that we have to start with long-term treatment much earlier, not only in more severe case. And there's very good data available that when we stop cyclosporine and reduce our medications to only artificial tears again, there is much more progression in these patients than if they stayed on cyclosporine for a specified length of time. There's quite good data available documenting this.[38,44]

MANAGING HIGH-RISK PRESURGICAL PATIENTS

Q | PROF. BAUDOUIN: Some patients develop dry eye after cataract or LASIK surgery, even if the cataract was performed without complications.[14] What is the best advice we could give to surgeons to avoid dry eye symptoms following refractive surgery, cataract surgery, and glaucoma surgery?

PROF. ROLANDO: I tell patients before surgery that complications, like dry eye, are possible. For example, a patient may come into the office after surgery and say they feel some mild foreign-body sensation. But if you don't mention anything before surgery, the patient could say they feel something in their eye and suggest that you possibly left a stitch in the eye. Discussing potential complications with patients before surgery is also important from the legal point of view.

In addition, it is necessary to check the patient's ocular surface before surgery and correct any problems prior to surgery. Inflammation should be under control, the epithelium stable, and tear stability should be checked. If you will be putting in a premium lens, it's very important that you check the stability of the tears. Otherwise you are going to have troubles because the measurement of the lens will be not perfect.[51] There are other potential complications, but these are the most important.

PROF. BAUDOUIN: These are very important points. Examine the patient and identify those at high risk for postsurgical DED. Before refractive surgery, some patients, for example, want LASIK surgery because they are wearing contact lens and they develop dry eye and they stop wearing contact lens. They already have dry eye before refractive surgery, so the risk is very high for those patients.

One example that is common involves elderly patients following cataract surgery. When we observe the eye, we observe MGD in both eyes. But only the operated eye is symptomatic. It is likely the patient had meibomian gland dysfunction before surgery but was asymptomatic and he became, for some reason, symptomatic following surgery. It's possible the nerves were impaired because the surgeon used too many eye drops.[14]

PROF. MESSMER: I think we have to identify any dry eye problem and treat it before surgery. And only do surgery when the ocular surface is healthy and when the lids are in satisfying condition. The risk of infection is higher in MGD patients. You would want to treat their dry eye before surgery.[14,51]

PROF. BENITEZ-DEL-CASTILLO: I think patients become symptomatic mainly because of the eye lid. Depending on the size of the eye lid speculum, you can have more or less lid alteration, and because of this, you can have more symptomatic MGD. And studying the ocular surface before surgery is key. Mainly if you are implanting a premium IOL, not because of the IOL and the power calculation, but you will have low tear break-up time before surgery, and you will have patients unhappy and complaining. So, before surgery, assess tear break-up time.[13]

PROF. BAUDOUIN: I agree with the points about lid trauma made so far, but it's a common mistake for many surgeons to use nonsteroidal antiinflammatory agents just after surgery even if there is positive corneal staining or corneal ulceration. What should be done in a patient with a poor ocular surface after surgery?

PROF. MESSMER: You need steroids to reduce inflammation, but they should be without preservatives.[38] Unpreserved artificial tears can also be used. And I recommend that with some severe dry eye patients to keep them under cyclosporine A during the procedure.[38,52] Antibiotics should be used only for a very short time. You don't need them long-term after cataract surgery.[14]

PROF. BAUDOUIN: So, one important point to prevent further complication is to remove as early as possible any treatment that can be potentially toxic or that is not really necessary.

PROF. ROLANDO: Maybe it's not so important to instill such a large number of drops during the day.[41]

We prescribe an antibiotic for instillation sometimes 4 or 6 times a day after surgery. Overuse of drugs postoperatively may be a cause of toxicity.[14,53,54]

And whenever you have some kind of inflammation on the surface of the eye, it is very important for patients to wash the eye's surface in order to remove the inflammatory cytokines, the problematic cells from this surface of the eye.[55]

CONCLUSION

PROF. BAUDOUIN: We have covered some very important topics related to patient care of DED. We have discussed that dry eye is common, and that it is not a linear disease, but instead it is a mixture of different mechanisms—a mixture of different ways to enter the vicious circle. Some patients may have very severe corneal impairment, and sometimes there is a discrepancy between the examination findings and what patients are telling us. We know that more sophisticated techniques may be available soon and could be interesting for surgeons and patients with dry eye.

Finally, the key point is to listen to the patient, look at the ocular surface with a slit lamp using fluorescein or lissamine green staining (where available). Fluorescein staining is a very good tool, and the treatment could be adapted to each condition.

We must remember the most important points about preservative-free eye drops, and to use steroids carefully. We should also use the most recent antiinflammatory, antiimmunomodulating strategies available in patients other than those with severe symptoms. And to be ensure the patient's ocular surface is healthy before the patient has to undergo surgery.

I'd like to thank everyone for their participation in this lively and engaging discussion. ■

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THE LATEST IN COMPREHENSIVE CARE FOR PATIENTS WITH DRY EYE DISEASE

Release Date: August 2019
Expiration Date: August 2020

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DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ 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 activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
___ 51+

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

Training of Fellows ___ Yes ___ No

LEARNING OBJECTIVES

DID THE PROGRAM MEET THE FOLLOWING EDUCATIONAL OBJECTIVES?	AGREE	NEUTRAL	DISAGREE
Discuss the mechanism of action of dry eye disease	_____	_____	_____
Discuss the prevalence of dry eye disease	_____	_____	_____
Evaluate the signs and symptoms in patients with dry eye complaints	_____	_____	_____
Develop a differential diagnosis for patients with complaints of dry eye	_____	_____	_____

POSTTEST QUESTIONS

1. PLEASE RATE YOUR CONFIDENCE IN YOUR ABILITY TO APPLY DRY EYE TREATMENTS IN YOUR PRACTICE 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. BASED ON THIS ACTIVITY, PLEASE RATE HOW OFTEN YOU INTEND TO APPLY DRY EYE TREATMENTS TO PATIENTS IN YOUR PRACTICE (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. SIGNS AND SYMPTOMS OF DRY EYE DISEASE (DED) CAN BE FOUND IN AS MUCH AS _____ OF THE POPULATION:

a. 5%
b. 10%
c. 15%
d. 20%

4. AS PART OF THE VICIOUS CIRCLE, PATIENTS WITH DRY EYE OFTEN PRESENT WITH:

a. Evaporative dry eye
b. Aqueous-deficient dry eye
c. Meibomian gland dysfunction (MGD)
d. All of the above

5. COMPARED WITH THE GENERAL POPULATION, MGD IS MORE PREVALENT IN ALL OF THE FOLLOWING *EXCEPT*:

a. Patients with Sjogren syndrome
b. Patients without Sjogren syndrome
c. Patients with rosacea
d. Women

6. WHICH OF THE FOLLOWING CAN WORSEN SYMPTOMS OF DED?

a. Environment
b. Corneal subbasal nerve damage
c. Artificial tears with preservatives
d. Prolonged screen time
e. All of the above

7. ACCORDING TO THE PANEL MEMBERS, WHAT IS THE PREFERRED METHOD FOR DIAGNOSING SIGNS OF DED?

a. Fluorescein staining
b. Schirmer test
c. Dry eye questionnaire
d. All of the above

8. WHICH DED TREATMENTS HINDER THE T-CELL ACTIVATION, RELEASE OF INFLAMMATORY MEDIATORS, AND CONSEQUENTLY INHIBIT THE INFLAMMATORY PATHWAYS?

a. Cyclosporine A
b. Lifitegrast
c. Artificial tears
d. Corticosteroids
e. A & B
f. C & D

9. WHEN SHOULD YOU TREAT OCULAR SURFACE DISORDERS?

a. Prior to surgery
b. Following surgery
c. When signs and symptoms are present
d. All of the above

10. ACCORDING TO THE PANELISTS, WHAT SHOULD BE THE IDEAL BIOMARKER FOR DED?

a. Microbiological involvement
b. Inflammation
c. Environmental sensitivities (allergies)
d. Autoimmune disorders

ACTIVITY EVALUATION/SATISFACTION MEASURES

Your responses to the questions below will help us evaluate this continuing medical education (CME) activity. They will provide us with evidence that improvements were made in patient care as a result of this activity as required by the Accreditation Council for Continuing Medical Education (ACCME).

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

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.


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