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CME ACTIVITY

Ocular Surface Disease: How Earlier Diagnosis and Treatment May Control Disease Progression

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from a live roundtable discussion held in February 2015 in San Diego, California.

INTENDED AUDIENCE

This certified CME activity is designed for optometrists and ophthalmologists involved in the management of ocular surface disease.

LEARNING OBJECTIVES

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

- Diagnose acute dry eye conditions and chronic ocular surface disease
- Explain the importance of early diagnosis and treatment to optimize clinical outcomes
- Review the most recent dry eye management guidelines
- Discuss diagnostic tools and treatments in late-phase study or those new to market
- Enhance the management of the ocular surface in corneal and cataract surgical patients
- Review lid disease therapies and perioperative treatment strategies
- Address barriers to prescribing and monitoring patient compliance

STATEMENT OF NEED

As population changes lead to shifts in ocular disease prevalence, ophthalmic development in pharmaceuticals and new medical device technology continues to change the treatment strategies available to ophthalmologists. Shifts in population demographics, access to care, and the increasing number of aging patients will continue to have significant implications for the delivery of modern eye care for years to come.

There is currently no "gold standard" for the diagnosis of dry eye severity; many differing opinions exist as to which test or combination of tests is most accurate. As a result, providers tend to use the patient's description of symptoms to guide clinical decisions more than objective signs. Considering that dry eye disease symptoms often do not correlate with damage severity, many cases of severe disease are likely to be misdiagnosed and undertreated. Diagnosis in the early stages of dry eye disease is critical; if treatment is given early in the disease process, the eye is able to adapt and compensate. Delayed treatment or extensive damage is difficult to recover from; if insufficiently treated, dry eye disease can progress into what has been termed a "vicious cycle" of escalating inflammation that can result in permanent damage. As such, more anti-inflammatory compounds are being investigated for use in dry eye disease; the majority of treatments currently in phase III clinical trials are anti-inflammatories, steroids, non-steroids, and antibiotics. It is imperative to increase awareness of new diagnostic and treatment options as they come to market, as well as to emphasize timely, effective treatment of initial symptoms. Earlier diagnosis of patients (ie, those in their 30s and 40s) can reduce the need for aggressive procedures and improve overall outcomes.

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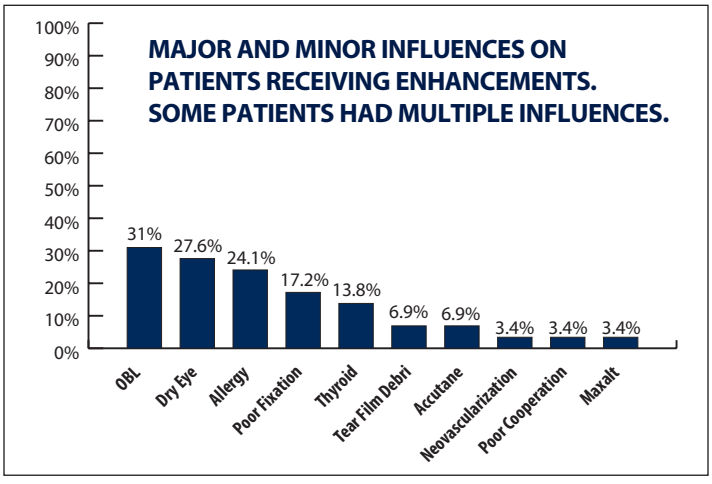
Ocular Surface Disease: How Earlier Diagnosis and Treatment May Control Disease Progression

Not only can ocular surface disease threaten vision and quality of life, it can also negatively affect surgical outcomes.

Kenneth A. Beckman, MD: Our discussion focuses on ocular surface disease and the importance of early diagnosis and treatment, particularly in the setting of cataract and refractive surgery. First, let us review who is at risk for dry eyes.

Jodi I. Luchs, MD: Anyone potentially is at risk for dry eyes, but the primary risk factors are advancing age, female sex, contact lens wear, extended periods of computer use, some systemic diseases, and some medications.[1] As eye surgeons, we know that dry eye disease (DED) is common in the older population, particularly in people presenting for cataract or refractive surgery. Studies have shown that ocular surface diseases, including dry eyes, are prevalent in 60% to 80% of people who present for these procedures.[1-3]

Neda Shamie, MD: Patients with autoimmune disease are at high risk for DED, as are those with glaucoma who are using topical drops to lower their intraocular pressure (IOP).[1,4]



(Courtesy of Karl G. Stonecipher, MD.)

Figure 1. Dry eyes and dry eye-associated factors are most frequently associated with LASIK enhancements.

DED's IMPACT ON OCULAR SURGERY

Dr. Beckman: We must take the time to optimize the ocular surface prior to cataract and refractive surgery for three key reasons:

1. to avoid perioperative infection
2. to obtain accurate preoperative measurements for intraocular lenses or refractive surgery
3. to minimize the potential for postoperative aberrations caused by a disrupted ocular surface.

Dr. Stonecipher, you recently reported some interesting statistics regarding enhancements. What did you find?

Karl G. Stonecipher, MD: In a recent study, I looked at 4,079 refractive cases treated at my practice and found that dry eyes and dry eye-associated conditions are some of the most frequent influences for patients to receive enhancements (Figure 1).[5]

Most concerning are the patients who do not report dry eye symptoms but who light up like a Christmas tree with lissamine green staining. One of the most amazing findings from the PHACO study[3] thus far was that patients did not complain of dry eyes, even though 60% to 80% of them showed conjunctival or corneal staining.

Refractive surgery is an elective procedure, and patients are paying for it out of pocket. If we miss the mark for any reason, we have a bit of a challenge when they are dissatisfied with their results.

Dr. Luchs: When we do uncover DED, it is important to address it preoperatively. Otherwise, despite a perfect surgery, the patient will have a visual deficit owing to the previously unrecognized dry eye problem.[6]

Dr. Shamie: Cataract surgery itself challenges the ocular surface. Therefore, if a patient is close to the threshold of developing symptomatic DED, and that is not recognized preoperatively, the surgery can push him or her over the threshold and cause worsening of the disease. We all want emmetropia for our patients. To achieve that, we must optimize the ocular surface before we can rely on our measurements.

Dr. Luchs: When patients have cataracts, we tend to blame every symptom on the cataracts. We need to step back and pay attention to the patient's history, particularly reports of fluctuating vision. For me, that raises the suspicion of an ocular surface disorder or tear-film instability, because, for the most part, fixed visual problems, such as a cataract, tend to produce fixed visual symptoms. Fluctuating symptoms and vision suggest a problem on the ocular surface, such as an unstable tear film or DED.

Dr. Luchs: We should not discount a history of dry eye symptoms, such as dry, gritty, foreign body sensation, and burning. Although many people report these symptoms, we must be particularly mindful of them when patients present for surgery.

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—Neda Shamie, MD

SCREENING/DIAGNOSTIC TESTS

Dr. Beckman: How do you screen for DED?

Dr. Shamie: In many practices, it is most efficient to train a technician—or whoever is the first person to interact with patients—to ask questions designed to reveal dry eye problems. For example, they can ask: Do your eyes burn in the morning or at the end of the day? Do you have problems with glare? Are your eyes sensitive to light? Do they have a gritty feeling? Do you feel discomfort when you blink?

Dr. Stonecipher: I use the Ocular Surface Disease Index (OSDI), but whatever your preference—the OSDI, the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire, or the University of North Carolina Dry Eye Management Scale—you can have patients complete the questionnaire along with your other intake forms.

In addition, if patients mention to the technician that their vision fluctuates from day to day and during the day, the technician documents staining. Therefore, when I walk into the examination room, all tests have been performed, and I can confirm the DED diagnosis and discuss how we will treat it.

Dr. Beckman: Specific to cataract surgery, I routinely perform certain tests or evaluations preoperatively to address any DED issues. I always carefully examine the lid margins and the tear film in general. I obtain multiple sets of measurements, including manual keratometry readings, corneal topography, and biometry with the IOLMaster (Carl Zeiss Meditec). I want to make sure these three measurements correspond with one another. If they do not, if the mires are irregular, I have the patient begin treatment for ocular surface disease and return at a later time to repeat the measurements. These may need to be repeated two or more times.

Dr. Stonecipher: When do you add a tear osmolarity test to the mix?

Dr. Beckman: I measure tear osmolarity with the TearLab Osmolarity System (TearLab Corporation) in anyone I consider a DED suspect (ie, if a patient reports any symptoms or shows any signs, such as irregular mires, staining, or rapid tear breakup times). Unlike other factors, tear osmolarity is dynamic, and test-to-test variation is not uncommon. Therefore, I repeat the measurements multiple times while managing a patient with DED.

Dr. Luchs: Do you routinely measure osmolarity on all patients who present for cataract or refractive surgery?

Dr. Beckman: Yes. I look extensively for DED, particularly in my preoperative cataract patients. The vast majority of them are elderly, and most have some sort of comorbidity, such as lid margin disease, and nearly all of them have DED. If a patient has a pristine-looking cornea and the other tests are normal, I may not measure osmolarity, but when I see lid margin disease, rapid tear breakup times, or when I hear complaints about vision, I have to consider the possibility that these factors stem from DED rather than cataracts.

Dr. Luchs: I take a similar approach. If a patient's history suggests DED, my technician includes tear osmolarity in the preoperative tests. I want to correlate all of the data, and I use that result as another piece of the puzzle. If tear osmolarity is low, I do not necessarily rule out DED, because the measurements fluctuate. If the measurement is very high and the patient has a history of symptoms, I consider that person a DED patient and address the disease preoperatively.

Dr. Shamie: The tear osmolarity test validates my clinical judgment and my assessment of the condition, and it facilitates communication with my patients. I also use it to monitor how patients respond to treatment.

Topography is also a critical tool. With all of the visual demands associated with premium lenses, we cannot perform cataract surgery without knowing what the ocular surface looks like—the tear film as well as the corneal surface.

I use the IOLMaster and corneal topography preoperatively for all of my cataract surgery patients. If the topography shows patchy areas of irregularity, I postpone the surgery to address the ocular surface issues.

INITIATING TREATMENT

Dr. Stonecipher: The PROOF Study is looking at patients over time to determine if DED worsens if it is untreated.[7] The Rao data showed that.[8,9]

Dr. Beckman, if a patient's tear osmolarity is 340 mOsm/L and your diagnosis is DED, what is your first-line treatment? Do you choose a modality directed toward inflammation?

Dr. Beckman: To follow up on Dr. Shamie's comment, I agree that inflammation causes damage, but we may not see a lot of damage on the eye at the time of diagnosis, so I am proactive. Evidence has shown that high osmolarity kills epithelial cells.[10] Therefore, patients with readings of 340 mOsm/L may not have staining initially, but inevitably they will. We also know high osmolarity affects ocular scatter.[11]

If a patient's eyes look healthy, but he or she complains of visual problems and the tear osmolarity reading is high, I am extremely aggressive with treatment. I immediately prescribe an anti-inflammatory, such as

OSMOLARITY: WHAT DO THE SCORES MEAN?

Dr. Beckman: Some clinicians become frustrated when trying to interpret osmolarity readings, because the readings vary. As I explain to patients, a random osmolarity measurement is analogous to a random blood sugar measurement in a person with diabetes. The blood sugar level may be 95 at one moment in time, but that does not mean it is controlled. That is why the A1c test, which calculates an average over time, is so valuable. We do not have that type of test for osmolarity. So, we need to run a series of tests to detect intra-eye variability and variability from test to test, as well as the overall severity indicated by the numerical score. I think the osmolarity test helps patients understand why they need multiple treatments. I use osmolarity to help me gauge improvement, and I repeat it multiple times.

Dr. Stonecipher: What are the ranges for osmolarity and what do the scores mean? What do you consider significant intra-eye variability?

Dr. Beckman: A normal osmolarity reading is below 300 mOsm/L. A reading in the 300 to 320 mOsm/L range is abnormal but in the mild category. From 320 to 340 mOsm/L is moderate, and over 340 mOsm/L is severe. The measurements for both eyes should be similar. If the difference between the two eyes is 8 mOsm/L or more, I consider that abnormal and indicative of tear-film instability.

Dr. Luchs: Occasionally, patients have some mild dry eye symptoms and their ocular surface looks good, but they have a high osmolarity number. I monitor those patients closely and explain that, even though everything looks good now, their numbers are somewhat high, and they may need to start therapy. I may have them increase their use of topical lubricants and return to the office in 4 to 6 weeks to repeat their measurements.

Dr. Shamie: Another approach is to just say the test results are normal or not normal, and we will treat the patient's disease until they are in the normal range, and then monitor them and maintain them there.

In my opinion, the InflammaDry test (Rapid Pathogen Screening) is a wonderful tool, particularly when I want to start anti-inflammatory therapy. I believe inflammation is at the core of dry eye disease. Some patients resist therapy, but if I can show test results that confirm they have inflammation in their tear film, then they comply with therapy.

In addition to helping us diagnose dry eye, all of these tools help us communicate with patients to ensure their compliance. By identifying elevated levels of the MMP-9 protein with the InflammaDry test and measuring tear osmolarity, we confirm our diagnosis, but also, importantly, convince patients to start treatment.

Dr. Stonecipher: Patients love to see a number, which is why I like the OSDI. If their score is 62, for example, they can see they have a severe problem that needs to be treated before their surgery. They know their therapy was successful when they see their score has decreased.

> "If a patient's eyes look healthy, but he or she complains of visual problems and the tear osmolarity reading is high, I am extremely aggressive with treatment."
> *—Kenneth A. Beckman, MD*

cyclosporine ophthalmic emulsion 0.05% (Restasis, Allergan) with or without a steroid. I add the steroid if inflammation is significant or if the patient is having noticeable discomfort. If the patient is fairly comfortable and surface staining is minimal, I may prescribe cyclosporine alone. I do not usually use a steroid alone. If I combine a steroid with cyclosporine, I typically start an agent such as loteprednol etabonate gel (Lotemax, Bausch + Lomb), twice daily. If a patient is using cyclosporine alone, I have him or her return for evaluation in 4 to 6 weeks. If a patient is using a steroid with the cyclosporine, I see him or her sooner to monitor intraocular pressures.

Dr. Luchs: I, too, start cyclosporine immediately in patients with high tear osmolarity, particularly if their InflammaDry test result is positive. I also prescribe a steroid and artificial tears.

Improving the ocular surface as quickly as possible is imperative for patients who are scheduled for surgery. Usually within a couple of weeks of initiating treatment, the ocular surface has improved enough for me to obtain accurate biometry measurements. Often, these measurements do not need to be repeated. Certainly, I continue to treat these patients postoperatively, but we can effect a change in a short period, which makes the patient happy, allows for more accurate measurements, and does not necessarily require postponing surgery.

Dr. Beckman: Dr. Shamie, at what point do you start thinking about your next step for therapy?

Dr. Shamie: In a typical scenario, I make the initial diagnosis of ocular surface disease and DED using the tools we have discussed (ie, a questionnaire, point-of-service diagnostics, ocular surface examination). I educate the patient about the chronic and progressive nature of the disease and obtain his or her buy-in for treatment. I then start anti-inflammatories in the form of cyclosporine, including a steroid for the short term in patients with any corneal staining or those who failed conservative treatment. We know that cyclosporine takes at least 3 to 6 months to cause a significant improvement in tear production, corneal staining, and conjunctival goblet cell density. If a patient agrees wholeheartedly to start treatment, I see him or her at 3 months to assess treatment response. If a patient is hesitant or

apprehensive, I see him or her in 6 weeks to reinforce our goals and reassure the patient.

One pearl is to not prescribe only 1 month of cyclosporine with refills, because that sends the message that 1 month is enough time to show us that it is working. I usually write the prescription for 3 months. If diagnostic tests or physical examination show absolutely no improvement after 3 months, then I consider other treatments, such as aggressively treating lid margin or meibomian gland disease when they are present using a combination of the LipiFlow Thermal Pulsation System (TearScience), oral omega-3 fatty acid supplementation, meibomian gland probing, oral doxycycline, or topical azithromycin. Amniotic membrane grafts can be a great option for temporizing severe ocular surface damage while waiting for the treatment to take effect, and autologous serum drops can be an excellent option for some refractory cases. If there is improvement with the cyclosporine, we know from studies by Rao and others that tear production and staining continue to improve over 2 years.[12] So, I reassure patients and ask them to continue with therapy for another 3 months. I may add another therapy, but I rarely, if ever, stop the cyclosporine sooner than 6 months.

COEXISTING CONDITIONS

Dr. Beckman: Not all dry eyes are alike. What else do you look for as far as different mechanisms for ocular dryness? What other treatments do you use for conditions such as lid margin disease?

Dr. Shamie: I first look at the patient's face for evidence of cutaneous rosacea. Then, I zoom in to examine the eyelashes, looking for waxy sleeves at the base or loss of lashes. I look for anterior blepharitis, posterior blepharitis, and meibomian gland disease. I press on the eyelid margin to express and examine the meibum. I look for telangiectasia and stenosis of the meibomian gland openings. Any of these findings indicates significant pathology around the eyelids, and the patient has at least evaporative tear dysfunction and some mechanical problems with the ocular surface.

I also examine the conjunctiva for significant conjunctivochalasis. I look for staining of the conjunctiva as well as the epithelium. If the corneal surface has punctate staining, the patient would benefit from a steroid together with cyclosporine.

Dr. Beckman: Dr. Stonecipher, what would you do if you performed an examination as Dr. Shamie described, and you found thickened secretions and telangiectasias, along with dry eyes and a rapid tear breakup time? What is your go-to therapy in that situation?

Dr. Stonecipher: When I see lid margin disease, I start long-term therapy. I am a fan of oral doxycycline, but I take care to review doxycycline's side effects with my patients. The list for side effects is quite long, but I discuss mainly its pregnancy category (D IV), potential phototoxic effects, and digestive issues with concomitant intake of calcium.

I also want to address the crusty lid debris in these patients. Some options include lid scrubs, LipiFlow Thermal Pulsation (TearScience), or intense pulsed-light therapy. Resolving lid margin disease is imperative, because I worry about endophthalmitis more than visual fluctuations in that group.

"When I see lid margin disease, I start long-term therapy. I am a fan of oral doxycycline, but I take care to review doxycycline's side effects with my patients."
—Karl G. Stonecipher, MD

Dr. Beckman: I also treat lid margin disease aggressively. I prefer topical medications, so I usually prescribe azithromycin ophthalmic solution 1% (AzaSite, Merck & Co.), which is not FDA-approved to treat lid disease, along with warm compresses, lid hygiene, and oral omega-3 supplements. If I do not see a response from the standard medications, which may also include erythromycin or bacitracin ointment, I may try certain compounded medications, such as doxycycline drops or metronidazole ointment. I may consider oral doxycycline at this point.

Dr. Luchs: I completely agree. In addition, I have recently started using the BlephEx procedure (RySurg) to cleanse the lid margins if I see clear signs of anterior blepharitis. It is important to not overlook that, because we do not want to increase the risk of postoperative infection. Of course, we must address the meibomian glands, as well.

Dr. Shamie: Rarely does meibomian gland disease exist in isolation. Inflammatory cells circulate in the tear film when meibomian gland disease is present. Therefore, patients can still benefit from topical anti-inflammatories. If a patient has blepharoconjunctivitis and cutaneous rosacea, I prescribe topical doxycycline, because it treats the skin in addition to the eyelids. If meibomian gland disease is isolated to the lids or if the patient is not concerned about the cosmesis of the cutaneous rosacea, then local azithromycin is best. In these cases, I also prescribe cyclosporine. I start with a steroid and add azithromycin and cyclosporine.

Finally, in patients with chronic severe rosacea who are unresponsive to treatment, I consider the presence of Demodex mites.

PATIENT EDUCATION

Dr. Beckman: Dr. Luchs, how do you explain DED—particularly the therapy and its duration—to patients?

Dr. Luchs: I explain at the outset that DED is a chronic disease that requires daily management. Just as people brush their teeth every day to keep them healthy, those with ocular surface disease must use prescription medications every day to keep the disease under control and maintain their quality of life. I explain their initial therapy—usually artificial tears and cyclosporine—and have them return in about 6 weeks. I explain that they may not be feeling better

at that time, because the therapy needs time to take effect, but I will evaluate their response to treatment at that visit. I tell patients this is a process, and I will assess how they are doing along the way and adjust their therapy as needed.

Dr. Shamie: I tell patients they have a chronic disease that can worsen over time, but it can be controlled and managed if caught early. I really emphasize the importance of early detection and treatment initiation, because patients tend to resist prescription medications.

I sometimes use the analogy of applying wrinkle cream for youthful-looking skin, which resonates with my female patients. The idea that we are treating a disease does not impress them as much as hearing that their DED therapy will help keep the surface of their eyes youthful.

Patients who are mildly to moderately symptomatic may tune out any discussion of a disease, and if they think treatment will delay their refractive surgery, they may seek another surgeon with the hope that a different surgeon will not require preoperative treatment. That is one of the reasons why I explain that the eye's surface is showing signs of damage as a result of aging, hormonal changes, or extended periods of computer use, and we want to reverse that damage and maintain the youthful nature of their eye's surface. I find patients are much more compliant when I give them something positive to hold on to.

Dr. Beckman: How do you counsel patients about cyclosporine, Dr. Stonecipher?

Dr. Stonecipher: I tell them we are instituting a therapy that will increase their tear volume. I also note that the effects of DED did not happen overnight; therefore, it will take time before we see an improvement.

Dr. Beckman: When I talk to patients, I do not cite statistics. I tell them studies have shown that untreated DED will worsen over time, but it is much less likely to progress when it is treated. In the Rao study, for example, about one-third of patients who used only artificial tears had their condition worsen by at least one International Task Force (ITF) level.[8] That is concerning, because DED that advances from level 1 to level 2 implies that corneal staining is present where it did not exist before, indicating epithelial breakdown.[13]

Rao also found that patients using cyclosporine had a dramatic increase in tear production at 1 year and continued improvement the second year.[8] The group that was not treated with cyclosporine until the second year eventually showed improvement, but those patients always lagged behind. I stress to my patients that the longer we wait to initiate treatment, the more difficult it is to catch up, and I want to start treatment early before the disease becomes severe.

Dr. Stonecipher: Tears alone will not solve the problem. We must get to the root of the problem, which is inflammation.

Dr. Luchs: One problem is that use of artificial tears often helps patients with mild symptoms feel better, and if they are feeling better, they think they must be controlling the problem. What they do not understand until we explain it to them is that the underlying inflammation still exists and so does the disease.

Dr. Shamie: I believe the only patients who can potentially be managed appropriately with artificial tears are those at severity level 1. These are patients who have no evidence of ocular surface damage and no staining. Their tear lake may be somewhat less than normal, their tear breakup times may be slightly faster than normal, and they may be symptomatic occasionally. A patient who feels the need to use artificial tears on a daily basis, even just one drop a day, is responding to changes in the ocular surface that are indicative of advancing disease. I think it is critical to talk about disease and the aging process, stressing that you cannot stop it unless you treat it early. I am sure we all agree, the patients who respond best to treatment are those whose disease is not yet too severe. So the earlier we catch the disease, the better the response. Patients who do not have severe symptoms may not have that "wow!" effect when therapy is started early. Nevertheless, we can have the most impact on slowing the disease progression when we catch it early.

Dr. Stonecipher: Patients must own their disease. We all know

SYSTEMIC CAUSES OF DRY EYE

Dr. Beckman: At what point do you suspect systemic issues may be associated with a patient's dry eyes, and what do you do?

Dr. Luchs: When patients are recalcitrant to dry eye therapy, particularly if they have other symptoms of dryness, I look closely at their history. Dry mouth, for example, raises my index of suspicion for a systemic health problem. I also look at their medication regimen to see if anything is particularly problematic in terms of causing dryness and if anything can be modified.

I am very quick to test for Sjögren syndrome, particularly when a patient reports a dry mouth. My technicians perform the *Sjö* test (Bausch + Lomb [Valeant]) in the office, and we receive a report in a couple of weeks. Alternatively, if a patient's insurance provider designates LabCorp for diagnostic testing, I write a prescription for the *Sjö* test to be run as a blood draw.

We do a tremendous service for our patients when we diagnose Sjögren syndrome. We empower them with the knowledge that they have an autoimmune disease. They can now be monitored closely by the appropriate medical professionals and treated properly at the earliest manifestations of disease, potentially limiting its severity. That benefit carries over to the eyes, as well.

Dr. Shamie: Sjögren syndrome is a serious systemic condition that can cause severe end-organ damage, but it is probably not as commonly associated with dry eyes as thyroid disease. Often, at the same time I order testing for Sjögren syndrome, I also order a thyroid-stimulating hormone test.

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>
> *—Jodi I. Luchs, MD*

glaucoma patients who only use their drops right before and after they see their eye doctor. Many people start flossing their teeth just before a cleaning and then stop right afterward. I think some patients have the same mindset with DED therapy. If we suspect that patients are not using the medicines we prescribe, and if we do not make them own the problem, we are just rowing against the tide.

Dr. Beckman: We have to take into account that some patients do not perceive a problem. They may not sense the dryness because they have neurotrophic corneas. Patients with diabetes, for example, may have low sensation and not perceive that their eyes are dry.[14] Post-LASIK patients, in particular, may experience this decreased corneal sensation.[15] Contact lens wearers may also be more vulnerable to DED, and at the same time be neurotrophic, because their corneas are somewhat hypoxic.[16] I monitor patients with compromised corneas more frequently, because they cannot feel the effects of DED.

We must educate patients that DED can be "silent" until the corneal surface starts to break down and show damage. That is one of the benefits of having a tear osmolarity number or a positive InflammaDry test result.

Dr. Luchs: If I detect something outside the norm, such as a high tear osmolarity reading, I monitor the patient as a DED suspect, even though he or she may not be aware of a problem. If a patient has some mild symptoms and is at ITF level 1, I may recommend artificial tears. Either way, I monitor these patients closely and institute therapy when necessary.

Dr. Stonecipher: Dr. Beckman, when do you use punctal plugs?

Dr. Beckman: I am more hesitant now to insert plugs than I used to be, because I am looking for more than just a palliative treatment. Therefore, initially, I do not use punctal plugs in anyone, unless I

DRY EYE MASQUERADERS

Dr. Beckman: What conditions may masquerade as DED?

Dr. Shamie: In my opinion, conjunctivochalasis is a common masquerader or, rather, one that often coexists and exacerbates dry eyes. Even in patients with conjunctivochalasis, I still treat ocular surface inflammation first. In about half of those cases, I have found improving the lubrication of the ocular surface lessens the friction between the eyelid and the loose overhanging conjunctiva, and the patient may become less symptomatic.

Dr. Stonecipher: Dr. Shamie, suppose you see a patient for a routine cataract evaluation, and you have treated the inflammation, but he or she still has tears draining off the eyelid. What do you do?

Dr. Shamie: At the time of the cataract surgery, I do a "nip and tuck," a technique I saw several years ago at a meeting of the American Society of Cataract and Refractive Surgery. Basically, I cut a tiny hole in the redundant conjunctiva about 2 mm posterior to the limbus. I dry the hole with a sterile sponge, inject fibrin glue into the hole, pull up the excess conjunctiva, let the seal dry, and then remove the excess. This maneuver takes about a minute and is performed at the end of the surgery.

Dr. Stonecipher: Another syndrome that masquerades as dry eye is lid wiper epitheliopathy, which is characterized by keratinization of the eyelid margin.[17] These patients often present with a mixed mechanism rather than with typical dry eye symptoms. This syndrome can be detected with lissamine green or fluorescein staining. For patients with lid wiper epitheliopathy, I typically prescribe long-term steroids, usually loteprednol, because it attaches to their eyelids at bedtime.

Dr. Beckman: Contact lens-related dry eye may not be true dry eye. It may result from contact lens intolerance. Whenever possible, I prescribe frequent-replacement contact lenses for these patients, preferably daily disposables. I also recommend that they rinse their lenses with plain saline solution before inserting them. Even though they may be using a multipurpose solution to clean and soak their lenses, those products contain disinfectants that can be problematic for some patients.

Dr. Luchs: We need to remember that patients who have any of these masquerading syndromes can also develop true DED. The chronic irritation can trigger an inflammatory cycle that ultimately leads to dry eye. It is important to identify masquerading syndromes and treat them appropriately, especially in patients who will undergo cataract or refractive surgery.

Dr. Shamie: Allergy can masquerade as DED, but it can also be concomitant with and exacerbate dry eyes. I have seen quite a few patients with concretions or giant papillary conjunctivitis as a result of chronic inflammatory ocular surface disease. Floppy eyelid syndrome is also a concern.

> "Electronic medical records enable us to communicate efficiently with our colleagues, whether they are retina specialists, internal medicine physicians, or rheumatologists."
>
> —*Karl G. Stonecipher, MD*

am sure the inflammation is under control. I typically do a Schirmer test before inserting punctal plugs, because I do not want to cause secondary epiphora. Typically, a patient has already been treated with cyclosporine with or without other anti-inflammatories before receiving punctal plugs.

Dr. Stonecipher: I would like to make one other point. I do not give samples of cyclosporine, because patients may use the samples, think the drug did not work, and not fill the prescription. I prescribe enough of the medicine to send the message that this is a long-term treatment for a chronic disease.

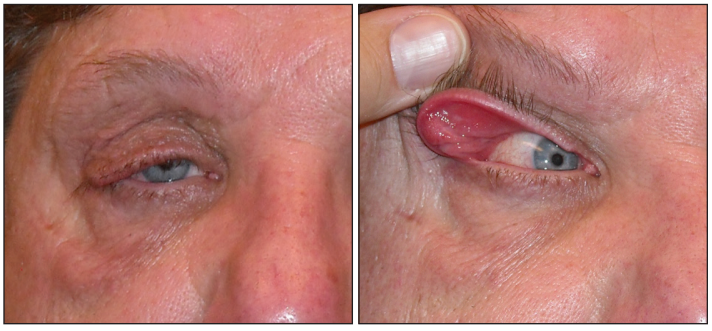
Dr. Beckman: I agree with Dr. Stonecipher. I explain to patients: "This is not like an infection where you receive an injection of an antibiotic, and you are cured. This is a chronic, progressive condition that we are trying to reverse."

I frequently tell patients, "If you ran marathons when you were 20 years old, and then you stopped, and now you are 50, you are not going to go out one day and be in shape to compete. You have to build up your strength and stamina. When you are being treated for DED, you are restoring health to your eyes, rejuvenating the ocular surface, and it is a slow process. The symptoms may lag behind the clinical signs."

Patients need frequent encouragement, and they need to understand the process.

Dr. Stonecipher: Most patients cannot get the diagnostic tests that we can provide from their internal medicine doctors. Often, they cannot get an appointment to see a rheumatologist for several months. That is why it is so important for us to own the disease processes we see in our patients, whether it is diabetes, a thyroid disease, or Sjögren syndrome. Patients with these diseases can get really sick very quickly.

Dr. Shamie: I have started conversations with rheumatologists in my community and in our university about the role of ophthalmology in the management of patients with certain systemic diseases. Many have agreed to place OSDI questionnaires in their waiting areas. If patients have DED, they can fill out a form while they wait to see the rheumatologist. I hope this will facilitate meaningful collaboration with our colleagues.



(Courtesy of Samuel Gallo, MD.)

Figure 2. This patient has a floppy eyelide; the photograph on the left shows the lid in its natural state. He sleeps on his right side, which results in the upper lid overriding the lower lid, loss of the lateral canthal ligament, and an easily everted upper lid, as seen on the right. He also has lid margin thickening from meibomian gland dysfunction and lash ptosis.

Dr. Beckman: I explain to patients the systemic relevance of Sjögren syndrome, particularly its association with lymphoma, and the importance of being monitored by their primary care physician and their rheumatologist. I often find that the tear film improves when patients are receiving systemic therapy for their autoimmune disease. I believe it is absolutely critical that we make these diagnoses and get patients in the hands of people who can manage them systemically.

Dr. Shamie: This is also an opportunity to communicate with potential referring doctors. Besides taking care of the whole patient, we can initiate discussions with other medical professionals and increase our credibility as eye care professionals. They will realize that we look beyond the cataract and see each patient as a whole, which helps us establish and maintain long-term relationships with them.

Dr. Stonecipher: To that end, electronic medical records enable us to communicate efficiently with our colleagues, whether they are retina specialists, internal medicine physicians, or rheumatologists.

Dr. Luchs: I completely agree. With electronic medical records, we can streamline patient care across different specialties.

THOROUGH EYELID EVALUATION

Dr. Beckman: The incidence of these conditions that can mimic DED underscores how important it is to assess the eyelids when we are working with the tear film. Everting the eyelids is critical during our examination.

The floppy eyelid diagnosis (Figure 2), in particular, is troubling because this condition is often associated with sleep apnea. When I see patients with that appearance, I ask about snoring, and I encourage them to see their primary care provider for a sleep evaluation.

Dr. Stonecipher: I see many patients with sleep apnea who are using continuous positive airway pressure (CPAP) machines. This treatment can cause or exacerbate dryness. Some patients have found relief with humidification goggles.

Dr. Beckman: A number of my patients have severe sleep apnea, and they say the continuous positive airway pressure machine dries their eyes. I recommend that they lubricate their eyes thoroughly at night and try a sleep mask. I have also suggested that they try a mouth device to help with the sleep apnea, which can work well and obviate the need for the mask.

Dr. Shamie: Exposure in general can cause the eyes to be dry. Patients who do not have a good Bell's phenomenon or who do not blink completely are at risk for severe ocular surface disease.

Dr. Stonecipher: People who play video games on their phones, computers, or TVs hardly blink at all.

Dr. Shamie: Epithelial basement membrane dystrophy can often be either exacerbated by DED or misdiagnosed as DED.

Dr. Beckman: Many people with thyroid disease have lid retraction, which affects their blink. They may be prone to superior limbic keratoconjunctivitis.

Dr. Shamie: I also find conjunctivochalasis is more common in patients I have seen with thyroid disease.

CONCLUSION

Dr. Beckman: I would like to thank all of you for participating in this discussion. As you all have pointed out, DED is an extremely common and often underdiagnosed disease with multiple mechanisms and serious potential ramifications. These potential consequences may be particularly relevant around the time of cataract or refractive surgery. Eye care professionals need to make the effort to look for the signs and symptoms and then aggressively treat this progressive disease. Fortunately, many new diagnostic instruments are available to us to aid in making the diagnosis. ■

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CME QUESTIONS

AMA PRA Category 1 Credit Expires July 2016

1. **In a study of refractive cases in Dr. Stonecipher's practice, which of the following was the most frequent influence for patients to receive enhancements?**
   a. poor fixation
   b. dry eye and dry eye-associated conditions
   c. neovascularization
   d. poor cooperation

2. **According to Dr. Stonecipher, what percentage of patients in the PHACO study showed conjunctival or corneal staining but did not complain of dry eyes?**
   a. 10% to 20%
   b. 30% to 40%
   c. 40% to 60%
   d. 60% to 80%

3. **Which of the following tear osmolarity readings is considered normal?**
   a. < 300 mOsm/L
   b. 300 to 320 mOsm/L
   c. 320 to 340 mOsm/L
   d. > 340 mOsm/L

4. **Which of the following tear osmolarity readings (right eye/left eye of same patient) suggests tear instability and dry eye, according to Dr. Beckman?**
   a. 290 mOsm/L and 300 mOsm/L
   b. 285 mOsm/L and 280 mOsm/L
   c. 290 mOsm/L and 297 mOsm/L
   d. 285 mOsm/L and 288 mOsm/L

5. **According to Dr. Shamie, which of the following can be used to temporize severe ocular surface damage while waiting for other treatments to take effect?**
   a. omega-3 fatty acid supplementation
   b. meibomian gland probing
   c. amniotic membrane grafts
   d. autologous serum drops

6. **Which of the following is more concerning to Dr. Stonecipher than visual fluctuations in surgery candidates with eyelid margin disease?**
   a. side effects of oral doxycycline
   b. allergy to lid scrubs
   c. Demodex
   d. endophthalmitis

7. **How many patients who used only artificial tears in Rao's 2010 study experienced disease progression by one ITF level?**
   a. more than one half
   b. about 60%
   c. about one-third
   d. about 20%

8. **Which of the following patient populations may not perceive that their eyes are dry because of decreased corneal sensation?**
   a. diabetics
   b. pseudophakes
   c. myopes
   d. the elderly

9. **Which of the following may masquerade as dry eye disease?**
   a. lid wiper epitheliopathy
   b. allergy
   c. epithelial basement membrane dystrophy
   d. all of the above

10. **Dr. Shamie may use a "nip-and-tuck" technique at the end of cataract surgery to address which of the following conditions?**
    a. floppy eyelid syndrome
    b. conjunctivochalasis
    c. tears draining off the eyelid
    d. incomplete eyelid closure

ACTIVITY EVALUATION

The content was delivered effectively.
❒ Strongly agree
❒ Agree
❒ Neutral
❒ Disagree
❒ Strongly disagree

The activity was objective, balanced, and free of commercial bias.
❒ Strongly agree
❒ Agree
❒ Neutral
❒ Disagree
❒ Strongly disagree

The learning methods or assessments of this activity were effective and appropriate.
❒ Strongly agree
❒ Agree
❒ Neutral
❒ Disagree
❒ Strongly disagree

The content presented in this activity was useful to my practice.
❒ Strongly agree
❒ Agree
❒ Neutral
❒ Disagree
❒ Strongly disagree

This activity has provided me with the tools/knowledge I need to make changes to my practice.
❒ Strongly agree
❒ Agree
❒ Neutral
❒ Disagree
❒ Strongly disagree

Please indicate which of the following learning objectives have been met.
"After completing this activity, I am better able to..." (select all that apply)
❒ Incorporate current glaucoma therapeutics into clinical practice
❒ Discuss the chemical structure and mechanism of action of topical glaucoma medications and evolving neuroprotective medications
❒ Effectively manage patients with compliance issues with glaucoma medications
❒ Explain effective combined treatment therapies, including sustained-release formulations
❒ Understand the differences between bioequivalent drugs and brand-name drugs

Please rate the following statements on the following scale: 1 (negligible) to 5 (outstanding)
How would you rate your competence* on this subject prior to attending this activity?
❒ 1
❒ 2
❒ 3
❒ 4
❒ 5

How would you rate your competence* on this subject after completing this activity?
❒ 1
❒ 2
❒ 3
❒ 4
❒ 5
* *Competence* is defined as the ability to apply knowledge, skills, and judgement in practice (knowing how to do something)

Please identify how you will change your practice as a result of completing this activity: (select all that apply)
❒ I will improve my methods for determining diagnosis.
❒ I will communicate more effectively with my patients.
❒ I will implement/change office protocols/policies/procedures to better meet requirements.
❒ I will integrate new pharmaceutical approaches into my patients' treatment.
❒ I will integrate new nonpharmaceutical approaches into my patients' treatment.
❒ I will reconsider treatment options I may have previously dismissed.
❒ I will change the way in which I monitor my patients' response to treatment.
❒ This activity validated my current practice; no changes will be made.
❒ I disagree with the suggested changes; no changes will be made (please specify).
❒ Other (please specify)

Please indicate any barriers you anticipate in implementing these changes: (select all that apply)
❒ Cost
❒ Lack of opportunity (patients)
❒ Lack of time to assess/counsel patients
❒ Lack of consensus or professional guidelines
❒ Lack of experience
❒ Lack of resources
❒ Reimbursement/insurance issues
❒ Patient compliance issues
❒ I do not agree with suggested changes
❒ I do not anticipate any barriers to change
❒ Other (please specify)

How long have you been in practice?
❒ Less than 5 years
❒ 5-10 years
❒ 11-15 years
❒ 16-20 years
❒ More than 20 years

What is your current type of practice?
❒ Private
❒ Hospital
❒ Academic
❒ Other (please specify)

(Continued on next page)

ACTIVITY EVALUATION (CONTINUED)

How many patients do you typically see per week?
❒ I do not see patients
❒ 1-10
❒ 11-20
❒ 21-30
❒ 31-40
❒ 41-50
❒ More than 50

Of these patients, to what percentage does this activity apply?
❒ 0
❒ 1%-20%
❒ 21%-40%
❒ 41%-60%
❒ 61%-80%
❒ 81%-100%

How did you hear about this activity? (Select all that apply)
❒ Publication ad
❒ Email
❒ Word of mouth
❒ Social media
❒ Flyer
❒ Dannemiller website
❒ Other (please specify)

Do you have any topic suggestions that would help to address other educational needs you and/or your colleagues may have?

_____

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Any other comments? Suggestions? Please let us know what you did or didn't like about this activity and how it can be improved!

_____

_____

_____

May we contact you to conduct a follow-up survey regarding this activity? The follow-up survey will take less than 5 minutes, and we will contact you via e-mail, unless otherwise indicated.
❒ Yes, please contact me
❒ No, thank you

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