

Novel Approaches to Treating Dry Eye Disease

The future of DED management will include more objective diagnostics.



By Christopher E. Starr, MD

In my practice, the dry eye disease (DED) workup typically begins with the technicians. Although I do not routinely use standardized questionnaires like the Ocular Surface

Disease Index outside of research, my technicians ask patients an abbreviated verbal version in order to identify likely dry eye sufferers. Once identified by this initial history, the technician then institutes our first-line diagnostic test, tear osmolarity (TearLab Corporation). This simple, quick, noninvasive test is performed at the very beginning of the examination before any drops are placed into the patient's eyes. It is preferable that the technician not administer any eye drops or perform tonometry before the patient is seen by me, because I like to examine the ocular surface before and immediately after the instillation of dye (fluorescein or lissamine green). A high osmolarity measurement (above 308 mOsm/L) alerts me that the patient has DED and gives me an indication of its severity. The patient's history and my clinical examination then tell me whether the etiology of DED is primarily aqueous deficient or evaporative. With point-of-care osmolarity testing, I find myself utilizing the more laborious Schirmer test less and less, and, as an added bonus, osmolarity is reimbursable, unlike Schirmer.

The correlation between signs and symptoms of DED is notoriously weak, thus making an accurate diagnosis of DED more difficult than many physicians care to accept.¹ The use of new, objective, and highly sensitive diagnostic tools such as TearLab have helped overcome some of these clinical dilemmas in many practices. In the near future, the state-of-the-art dry eye practice may routinely use other objective measures such as optical coherence tomography to quantify the tear meniscus' volume and height; confocal microscopy and point-of-care devices to assess ocular surface

inflammation; and lipid layer interferometry as well as new placido disk-based topographers to accurately measure tear breakup time. There has never been a more exciting time than now to be a dry eye specialist.

In terms of treatment, I initiate therapy in virtually every patient I see, but that term is used rather loosely. Counseling patients about simple environmental modifications (eg, avoiding air vents, humidifying the bedroom at night), trigger avoidance (eg, sunglasses on cold dry days, blinking more when using the computer), dietary supplementation (eg, increasing water and omega-3 fatty acid intake), and proper contact lens and eyelid hygiene are all forms of therapy that, like other interventions, aim to reduce patients' signs and symptoms of DED.

Many patients require more formal therapy, and my first-line treatments usually include one or more of the following: topical cyclosporine; short, tapered courses of topical steroids; off-label topical azithromycin for meibomian gland disease; punctal plugs (after inflammation reduction); and various adjunctive lubricants. As a general rule, I initiate treatment with a fairly aggressive multipronged approach and then scale back therapy over time. As with any chronic disease, the emphasis is on managing the condition rather than attempting a cure. My goal is always to get patients as comfortable as possible on as little therapy as possible and with minimal disruption to their daily activities and quality of life.

The need for long-term (often life-long) treatment and maintenance is explained in detail at the first visit, and I will ask the patient to commit to at least 6 months of strict compliance. Without upfront education and setting of realistic expectations, patients will often stop treatment prematurely, because the "drops burn and sting and thus must be harmful" or they "didn't feel better in the first week and thus the drops don't work." Treatment's efficacy over time is judged by a reduction in patients' symptoms; improved clinical signs such as stabilization of vision, longer tear breakup time, thicker tear meniscus, less ocular surface staining; and lower osmolarity scores and lesser patient-reported artificial tear usage. With proper education, realistic

expectations, and a 6-month commitment to strict compliance, most patients will exhibit a demonstrable clinical improvement in the signs and symptoms of DED and be more likely to continue appropriate treatment long term.

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1. Schein OD, Tielsch JM, Munoz B, et al. Relation between signs and symptoms of dry eye in the elderly. A population-based perspective. *Ophthalmology* 1997;104:1395-1401.

Patients' education and managing expectations are the keys to success.



By Elizabeth Yeu, MD

My approach to dry eye disease (DED) is to treat it fairly aggressively and to educate patients as comprehensively as possible. I have a low threshold for initiating treatment, because once the disease cycle starts, it can lead to debilitating microscopic damage (ie, goblet cell destruction) that will eventually have clinical consequences. There is also a neurotrophic component to DED, particularly in older patients, so patients may have disease that is worse than what they are able to perceive.

The lack of correlation between signs and symptoms of DED is well known, which makes it even more important to treat patients early and aggressively. Within the classification system for DED established by the International Dry Eye WorkShop,¹ the mild category is characterized by very little staining and is more reliant on clinical symptomatology. Once staining is involved, patients are considered to be in the moderate category with the associated implications of more serious disease. In my opinion, this implies that even mild disease is worthy of a more aggressive approach, because ocular surface changes have already begun. Once clinical signs appear, it becomes apparent that time is of the essence because of the chronicity—and oftentimes disease progression—that accompanies DED.

The lack of correlation between signs and symptoms also makes it important to consider the entire clinical

picture in evaluating patients. I start with a subjective questionnaire like the Ocular Surface Disease Index before patients enter the examination room. Other ancillary tools can be very helpful, including anterior segment optical coherence tomography to evaluate the tear film's quantity and conjunctival chalasis. Additionally, I will use corneal topography to examine the quality of the mires as an assessment of the regularity of the corneal surface, which is frequently affected by DED or other causes of epithelial irregularity. I spend a good amount of time gathering patients' histories, including their specific symptoms and duration, time of the day when they are most affected, and other relevant medical history (eg, medication use, diabetes, hypertension).

The emphasis in my clinic is on counseling and educating patients. This requires extra chair time, but it is important for success when managing patients' expectations. There are four basic messages I convey to patients. First, DED is not a single disease and there are multiple processes involved. Several parts of the eye are affected, and once DED starts in one area, the problems spill over into other parts of the eye. Second, the office visit is not a one-time thing; generally speaking, patients will need multiple visits to gain adequate control of their condition. Third, because DED is chronic and may worsen, therapy must be adhered to. Fourth, a certain therapy that may work for one patient may not for the next patient, and usually, a single therapy or treatment will not fix the problem: the goal is finding the right mix of modalities for that particular patient.

In the age of electronic medical records, it is fairly simple to create individualized literature for patients to review for specific disease states (ie, blepharitis treatment instructions). Because DED is a broad disease, I am also a proponent of general education for patients that includes information on the spectrum of artificial lubricants, proper lid hygiene, and computer ergonomics. For this, I rely on brochures that my colleagues and I have created—but I do not just hand patients a pamphlet and ask them to read it; I highlight and emphasize the important points for patients to note.

Not all patients are the same, and not all eyes are equally dry; it is therefore essential to tailor therapy as much as possible. Adding essential fatty acids and cyclosporine 0.05% (Restasis; Allergan, Inc.) can be very helpful, particularly in mild to moderate DED in perimenopausal women. Another example is surgical candidates, whom I treat even more aggressively so that I can properly plan the surgery. For patients seeking a premium IOL, if DED treatment does not result in a smooth precorneal tear film and minimal staining, I

will not implant a multifocal IOL. This emphasizes my underlying principle of taking the time to properly educate patients about their disease as well as to establish reasonable expectations regarding treatment.

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1. 2007 Report of the International Dry Eye Workshop (DEWS). *Ocul Surf.* 2007;5:65-204.

Empower patients to take responsibility for the management of their DED.

By Neda Shamie, MD



My evaluation of patients suspected to have dry eye disease (DED) or dysfunctional tear syndrome begins with the Ocular Surface Disease Index questionnaire, which I have patients complete at the time of initial presentation. Although obtaining a thorough history and inquiring about key symptoms are important in assessing risk factors and onset of disease, they cannot be the sum total of the evaluation. Many patients with ocular surface disease have atypical complaints or may simply be unaware of DED-related symptoms. Others may complain of symptoms but have minimal clinical signs, which may be overlooked during a compulsory evaluation. A thorough clinical examination of the lid anatomy/apposition, meibomian gland orifice and secretions, conjunctival and corneal surfaces, and corneal limbal structures may help delineate the processes involved and the sequelae of disease. Corneal epithelial staining, tear breakup time, and Schirmer testing may also help highlight the disease process. Newer diagnostic tools, such as the tear osmolarity test (TearLab Corporation) and the LipiView Ocular Surface Interferometer (TearScience), also help to identify an abnormal tear film on initial examination as well as on follow-up.

I have found that patients with early DED tend to have more symptoms and less obvious signs. It is patients with early-stage DED who benefit greatly from being evaluated by a highly attentive clinician who recognizes the first signs of what is often a progressive disease, starts engaging the patient in a discussion of DED, and, ideally, starts treatment to avoid worsening of the condition.

Patients who have already suffered years of ocular surface inflammation and resultant neurotrophic keratopathy often have fewer symptoms of ocular pain but significant signs and related deterioration of vision. These patients require more aggressive treatment, but they may be too far along the spectrum of disease to reap great benefit from treatment. In one common scenario, these patients present with decreased vision but also have visually significant cataracts. The physician may look past the ocular surface disease and treat the cataract, only to find himself or herself with a poor surgical outcome and an unsatisfied patient.

It is critical to recognize that DED is a chronic disease with an underlying pathophysiology suggestive of worsening if left untreated. Ocular surface inflammation is the hallmark of dysfunctional tear syndrome. Whether the condition occurs as a result of insufficient lacrimal tear production or rapid tear evaporation due to meibomian gland disease, an inflammatory cascade will ensue. This can lead to epitheliopathy, squamous metaplasia, goblet cell loss, and permanent corneal and conjunctival changes and scarring. Early recognition and aggressive treatment can halt this progression and even reverse damage. The onus is on the clinician to recognize the signs of disease and initiate effective treatment.

My approach to managing DED follows the recommendations of the International Dry Eye Workshop as well as the Meibomian Gland Disease Workshop in which early treatment is indicated even in mild cases. Education is also critical at the outset. A patient empowered with knowledge of his or her condition and the treatment plan is one who will more likely prove compliant. This applies especially to those patients who have clear signs of disease without symptoms. Theirs are often the most challenging cases, because the motivation to start treatment may be absent for the patient as well as the physician. If the physician makes it clear that a lack of intervention can lead to chronic and progressive ocular disease, however, the patient may agree to start therapy. As a corollary, when asymptomatic patients diagnosed with glaucoma or diabetes are strongly advised to start treatment, the key to success is that the physician convey the importance of treatment and the patient understand the course of disease. There is no reason why conscientious physicians should not place the same importance on compliance with the treatment of DED, as it, too, can threaten sight if left untreated.

For patients with evident ocular surface inflammation and/or epitheliopathy, I start with 3 to 6 months of topical cyclosporine 0.05% (Restasis; Allergan Inc.). Cyclosporine prevents death of the epithelial cells and

inhibits T-cell–mediated inflammation, both important sequelae of DED. This impact, though, can take at least 6 to 8 weeks to manifest, so the patient should understand that the treatment course needs to last at least 3 months for the clinician to assess response. To fast track the recovery and lessen the initial burn that patients with epitheliopathy tend to experience with any topical treatment, I also prescribe a 1-month course of a mild steroid. My preference is loteprednol suspension 0.5% (Lotemax; Bausch + Lomb) used four times a day for 2 weeks with a tapering down to twice a day for the next 2 weeks. I find that patients with evidence of meibomian gland disease benefit from the anti-inflammatory and lipid-modulating effects of topical azithromycin (AzaSite; Merck & Co, Inc.), usually used once nightly for at least 1 month.

To avoid starting too many treatments at the onset, I often target therapy at one aspect of the patient's DED and then follow up 6 weeks later to assess his or her response, both symptomatically through the Ocular Surface Disease Index questionnaire and in terms of signs. If the response to treatment is suboptimal or incomplete, I then modify or add to the treatment plan. In my experience, treatment for DED should start aggressively with a goal of tapering the patient off of medication for maintenance on minimal therapy. This can be done by adding oral omega-3 supplementation, a regimen of eyelid therapy, changing environmental triggers, and increasing hydration. Patients who take these steps may reap the benefit of having their therapeutic requirements reduced.

DED does not get as much attention as other conditions that have a more straightforward treatment schemata, perhaps because it does not specifically fall under the surgical realm of practice. Physicians' first challenge is to properly diagnose this often underdiagnosed condition. Their second challenge is to motivate patients to comply with a recommended treatment regimen. Ophthalmologists are only a small part of patients' success; once they leave the office, the work is in patients' hands. They must be empowered with knowledge about the pathophysiology of their disease and understand that it is a chronic condition that, if not addressed with effective treatment at the onset, will inevitably have an impact on their vision. ■

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