
CME ACTIVITY

Ocular Surface Disease: Understanding the Need for Early Diagnosis

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Ocular Surface Disease: Understanding the Need for Early Diagnosis

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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:

- Recognize the importance of early diagnosis and treatment of dry eye disease based on the presence of comorbid conditions and/or risk factors
- Assess the role of inflammatory markers/processes in dry eye disease
- Compare newer diagnostic tools and incorporate results into a dry eye disease management plan
- Formulate strategies to best treat dry eye disease based on the presence of comorbid conditions and/or risk factors

STATEMENT OF NEED

Almost 33% of patients in eye care clinics present with complaints about dry eye disease (DED).¹ Clinicians remain challenged with both the diagnosis and best treatment options for DED because, to date, no one single cause of the disorder has been identified.² The number of affected individuals is expected to rise in the next several decades as the population continues to age, having an ever increasing negative effect on the health care system. The overall treatment burden of DED to the US health care system has been estimated at more than \$3.8 billion; from a societal perspective the disease averages a cost of more than \$11,000 per person, or \$55.4 billion.³

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3. Yu J, Asche CV, Fairchild CJ. The economic burden of dry eye disease in the United States: a decision tree analysis. *Cornea*. 2011;30:379-387.

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Implementing DED Diagnostics

Modern diagnostics aid eye care providers in finding patients with dry eye disease.

By Karl G. Stonecipher, MD

Much of the recent research in dry eye disease (DED) has focused on mechanisms to better identify clinical signs of the disease so that providers can initiate intervention strategies earlier in the disease course and avoid progression to advanced disease. It should not be forgotten, however, that DED can have very serious symptoms that may have a dramatic effect on patient’s quality of life. One study highlighted that moderate DED may have an effect on patients that is comparable to that for moderate to severe angina (Table).¹ It is easy to imagine, then, that severe DED can have a meaningful impact on patients’ well-being, and that even mild symptoms can be disruptive.

Treatment strategies for DED often start with artificial tears, which, generally speaking, are hypotonic or isotonic buffered solutions containing electrolytes, surfactants, and various types of viscosity agents.² Such a broad definition, however, fails to acknowledge the plethora of formulations available both as prescription and over-the-counter (OTC) options. More importantly, patients often fail to realize the difference between eye drop formulations, and most patients self-medicate using OTC vasoconstrictors. The science and impact of such choices is well-established: (1) use of ocular vasoconstrictors may induce a rebound effect, resulting in a increased redness and irritations compared with pretreatment levels^{3,4}; (2) OTC formulations are often preserved with benzalkonium chloride, which intentionally debrides the ocular surface to effect drug penetration, but which is not recommended for use in lubricants for DED sufferers; and (3) FDA labeling recommends against use of these products for treating redness lasting longer than 72 hours, as prolonged self-treatment may delay proper diagnosis while damaging the ocular surface.

In short, the severity and life-disrupting nature of DED symptoms leaves patients desiring effective treatments. However, a lack of understanding about the DED entity, misinformation about appropriate treatment, and underappreciation of the side effects and complications of popularly used self-guided interventions serve as barriers to proper care. These obstacles can be overcome by modern diagnostics, which give patients a truer impression of the health of their ocular surface while also directing appropriate therapy choices. Yet, patients’ access to DED diagnostics will really only be feasible if eye care providers can implement screening and testing protocols that are not overly burdensome to regular clinical practice.

TABLE. SUMMARY OF SCORES FROM A STUDY IN WHICH PATIENTS WITH VARIOUS DISEASES WERE ASKED TO SCORE HOW MUCH SYMPTOMS IMPACTED QUALITY OF LIFE.	
Health State	Mean Score
Moderate dry eye disease*	0.78
Moderate angina*	0.75
Severe dry eye disease*	0.72
Class III/IV (severe) angina*	0.71
Disabling hip fracture	0.65
Monocular painful blindness*	0.64
*Comorbidity-adjusted	

STRATEGIES FOR IMPROVING EFFICIENCY IN DED TESTING

There are now a plethora of diagnostic modalities available to eye care providers with an interest in finding DED patients in their practice. In addition to the clinical and slit-lamp examination, classic testing with vital stains and measuring tear film breakup time are additive in narrowing the differential diagnosis. Such measures can typically be incorporated into the routine, comprehensive eye examination. Newer modalities, such as meibography, osmolarity testing, and advanced topography, offer greater insight into the relative health of the ocular surface. However, there is a necessary sacrifice of time in adopting additional testing.

Many providers utilize technicians to perform point-of-care testing. This makes rational sense, as matrix metalloproteinase 9 (MMP-9) testing and tear osmolarity scoring need to be performed prior to instilling dilating drops. Thus, technicians can be empowered to initiate simple testing based on the results of questionnaires patients fill out in the waiting room. They can even ask simple guided questions during the first encounter to gauge the necessity of evaluating the tear film—for instance, “Do you use artificial tears?” “Do your eyes ever feel irritated or dry?” “Are you bothered by your contact lenses?” “Are you having fluctuating vision?”

THE ROLE OF QUESTIONNAIRES

In the same way that technology has been a boon to the diagnostic testing realm, it may also prove a net positive in

screening patients for the need to assess the ocular surface. The Ocular Surface Disease Index (OSDI) questionnaire is now available as an app that is downloadable for use on smartphones and tablets. In my practice, I frequently find myself handing my phone to patients so they can use the OSDI app—it takes a very short time for patients to complete the 12-item questionnaire, and it provides me with valuable information to guide the encounter.

The Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire is a repeatable and validated instrument for measuring DED symptoms, and scores correlate significantly with ocular surface staining and clinical measures of meibomian gland function.⁵ It is useful both during the initial encounter and, if repeated over time, may also supply information about the response to treatment.

Clinicians at the University of North Carolina, Chapel Hill, recently introduced an even more simplified questionnaire. The UNC Dry Eye Management Scale has a happy face on one side and a frowning face on the other side of a 1 to 10 scale; patients are asked to circle the number that best describes how bad of an impact DED symptoms have on their lives over the previous week.⁶

Thus, the point may be that there is no single best method for determining if a patient should be considered for intervention; rather, the existence of numerous validated screening protocols means that care providers can select the one that is best suited for their practice and patient types.

ADVANCEMENTS IN DIAGNOSTIC SCREENING

In my practice, I have abandoned the use of Schirmer testing, as I feel it does not add much to the clinical impression, and it wastes valuable clinic time. I mention this test in this context, because it highlights that when better and more accurate testing modalities are available, it is prudent to consider how efficient older tests may be. If Schirmer were the only diagnostic available, the 5 minutes it takes and the discomfort it causes might seem more worthwhile.

With the availability of numerous, sophisticated DED diagnostics and point-of-care testing modalities, eye care providers may need to rethink their approach to evaluating DED.

Objective measures are useful not only for directing therapy; they also facilitate patients' education: if patients are able to see and appreciate the level of meibomian gland blockage, for example, they may be more willing to comply with therapy directions.

Objective testing also addresses the disconnect between DED symptoms and signs, which can be easily missed, overlooked, or confused for something else, especially among patients who do not report symptoms.^{7,8} Having quantifiable metrics, on the other hand, helps narrow the differential to ensure that therapy is targeted to the underlying cause.

Yet, starting down the path to evaluating ocular health need not be overly cumbersome to the eye care provider's practice. The use of three simple questions may suffice in identifying patients in need of additional workup: (1) Do your eyes ever feel dry or uncomfortable?; (2) Are you bothered by changes in your vision throughout the day?; and (3) Do you ever use or feel the need to use eye drops?

As well, DED evaluations can be a standard part of eye examinations in every patient, including contact lens assessment, so long as it is combined with an evaluation of the ocular surface.

Finally, when called for, treatment should be directed by findings in the workup with the goal of reducing signs and symptoms, preserving and/or improving vision, preventing or minimizing structural damage to ocular surface, improving patient comfort, and preparing the ocular surface for surgery.⁹ ■

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DED: Implications for Surgical Patients

Managing patients' DED preoperatively may improve visual results and surgical outcomes.

By Alice T. Epitropoulos, MD

The prevalence of dry eye disease (DED), which can have a substantial impact on patients' quality of life, continues to increase as the population ages. While significant on its own, DED deserves special consideration in patients who will be undergoing ocular surgery. DED has the potential to affect the accuracy of keratometry readings, affect or delay the healing process, and cause visual disturbances or a refractive surprise in the postoperative period. It is estimated that about 75% of the eye's refractive power occurs at the tear film interface, which highlights the importance of a healthy ocular surface prior to refractive cataract surgery. Furthermore, the conditions of surgery may cause stress to the ocular surface. There is inherent damage that occurs to the corneal nerves with laser refractive procedures and incisional surgeries, such as cataract surgery, and limbal relaxing incisions, setting the conditions for neurotrophic DED. Furthermore, topical drops used perioperatively may contain preservatives that exacerbate DED.

DED IN CATARACT SURGERY PATIENTS

DED among cataract surgery patients is a prevalent and underdiagnosed condition. In one prospective study, 87% of patients scheduled for cataract surgery were diagnosed with DED, and only a minority of these patients had a previous diagnosis of DED.¹ Blurred vision was more likely than typical

TABLE. SUMMARY OF OCULAR SURFACE FINDINGS FROM THE PREOPERATIVE EVALUATION.		
	OD Pretreatment	OS Pretreatment
Meibography	25-50% atrophy	50% atrophy
SPEED	24 (OU)	
MG Evaluation Score	4	1
TBUT	3	2
Tear Osmolarity	300	320
MMP-9	Positive	

symptoms of burning or foreign body sensation, but clinical signs were also very common: almost two-thirds of patients had an unstable tear film as evidenced by a reduced tear breakup time and 77% had corneal staining. Proceeding with cataract surgery in an eye with an unhealthy or unstable tear film can have several consequences, including selecting the incorrect IOL power, which, in turn, may expose the patient to refractive surprise and the need for an IOL exchange. This can be particularly significant in premium IOL patients. DED can compromise the assessment of the magnitude and axis of astigmatism, which could lead to incorrect lens selection or, if a toric lens is being implanted, positioning on the incorrect axis. Meibomian gland dysfunction (MGD), which may be the cause of DED in up to 80% of cases, is a progressive disease, and if it is not treated, can lead to glandular atrophy and loss of function (Figure 1).² By diagnosing DED preoperatively, I avoid unhappy patients by managing the disease before it becomes a problem, which will improve visual results and surgical outcomes. In particular, tear hyperosmolarity can cause significant variability in average keratometry, anterior corneal astigmatism, and IOL power calculations.³ In our study, a statistically significantly higher percentage of eyes in the hyperosmolar group (greater than 316 mOsm/L in at least one eye) were found to have an IOL power difference of more than 0.50 D when measured on separate clinical visits, whereas there was

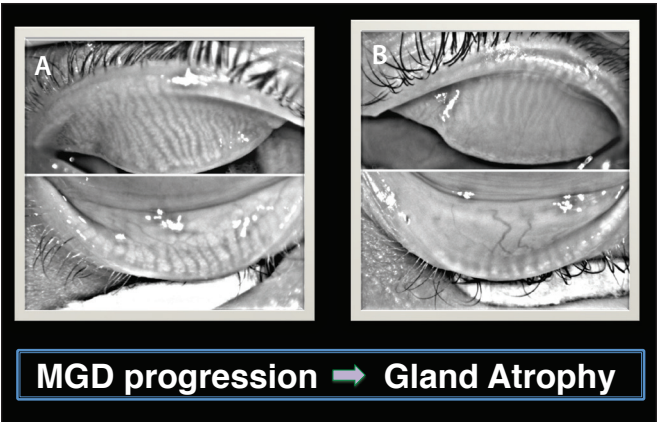


Figure 1. Clinical images of normal meibography (A) and advanced MGD (B) as seen on Dynamic Meibomian Imaging (LipiView II; TearScience).

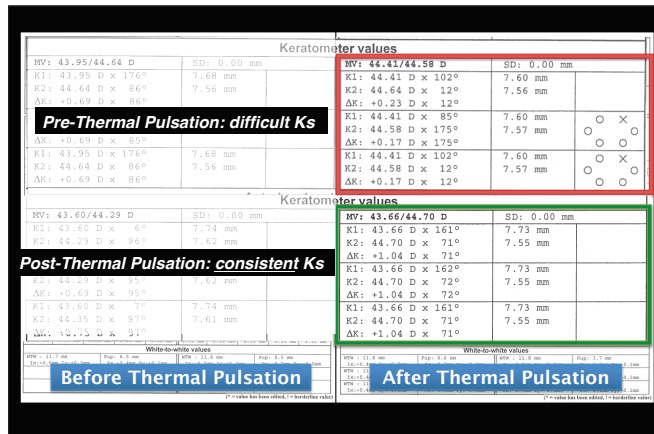


Figure 2. Treatment of MGD unmasked astigmatism and changed the IOL selection.

no significant difference noted in patients with normal osmolarity (<308 mOsm/L in both eyes).³ This study suggests a role for osmolarity testing to identify cataract surgery candidates who might experience unexpected refractive error as a result of an unstable tear film.

CASE EXAMPLE

A case in my clinical practice demonstrates the potential for an unstable tear film to affect IOL power calculations. A 75-year-old woman was referred for cataract surgery. The preoperative evaluation, however, suggested tear film instability with elevated tear osmolarity and a notable disparity in tear osmolarity scores between the two eyes (Table). A difference of 8 mOsm/L between the eyes is indicative of instability (data on file with TearLab Corporation); in this case, there was a difference of 20 between the eyes. Also concerning was a reduced tear breakup time and a positive matrix metalloproteinase 9 (MMP-9). Meibography demonstrated significant damage to her meibomian glands. Preoperative topography and keratometry readings were not reliable.

I delayed until I could treat the underlying MGD using the LipiFlow Treatment System (TearScience). Prior to treatment, I considered the possibility of placing a 23.00 D Crystalens

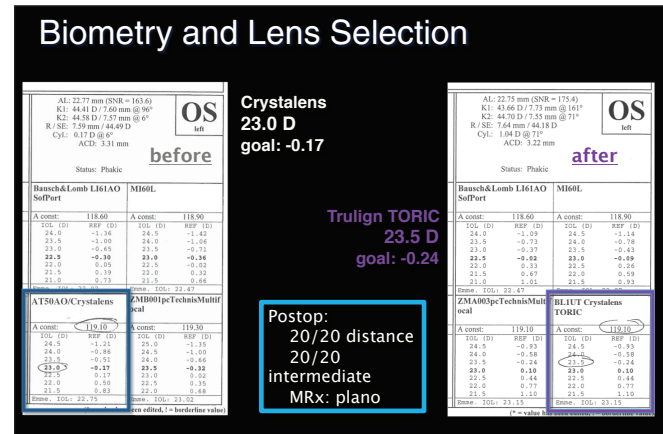


Figure 3. Treatment of underlying MGD resulted in the selection of a different power IOL for the patient; failure to treat the MGD would have yielded a significant refractive surprise.

(Bausch + Lomb); after treatment, we re-measured and placed a Trulign Toric (Bausch + Lomb) 23.50 D lens (Figures 2 and 3). The patient ended up very happy with 20/20 distance and intermediate visual acuity and a plano refraction. In this case, treating the ocular surface unmasked almost a full diopter of astigmatism, and the results of treatment significantly altered the surgical plan.

CONCLUSION

DED, and MGD in particular, can have a significant impact on the ability to achieve the refractive target after cataract surgery. DED is common but underdiagnosed and underappreciated, even though it can adversely affect surgical outcomes. It is important to maintain a high level of suspicion even in asymptomatic patients, and to never hesitate to delay surgery until the ocular surface is healthy enough to generate accurate measurements. ■

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Evolving Trends in Epidemiology, Etiology, and Pathophysiology of DED

The reasons for and causes of eye dryness are multifactorial and warrant thorough evaluation.

By Neda Shamie, MD

An evolving understanding of dry eye disease (DED) over the past decade-plus as an important cause of visual disturbances and ocular discomfort has led to a plethora of new research and market interest in new forms of diagnostics. One of the recent key findings relates to the role of inflammation in DED etiology, especially as it pertains to hyperosmolarity. Studies suggest that hyperosmolarity, which may be caused by abnormal water evaporation from the exposed ocular surface and/or low aqueous tear production, is a crucial instigator of ocular surface inflammation.¹

According to the consensus statement from the Dry Eye Workshop, "[DED] is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface."¹ The most common symptoms of DED include blurred or fluctuating vision, foreign body sensation, photophobia, stinging, itching, watery eyes, grittiness, burning, and irritation.²⁻⁴ However, none of these symptoms is necessarily pathognomonic, per se, and there is significant crossover with other ocular conditions that may be independent masquerading syndromes or comorbidities, such as allergic conjunctivitis, blepharitis, and bacterial conjunctivitis.^{5,6} Between 34% and 65% of DED cases involve a secondary comorbidity such as allergic conjunctivitis, blepharitis, or bacterial conjunctivitis.⁷

SHIFTING DISEASE BURDEN

DED is one of the most common ocular diseases in the United States,⁸ estimated to affect about 29 million adults.^{9,10} Nearly 40% of Americans experience symptoms on a regular basis¹¹ and 14.4% self-report a history of DED.¹² An estimated 7.8% of women aged 45 to 84 have been clinically diagnosed with DED.⁴

However, while women are nearly two times as likely to have DED compared with men,⁹ other risk factors are important as well. Women older than 50 years are at high risk for DED,⁸ especially if they are postmenopausal.¹³ Yet, patients with ocular comorbidities are also at increased risk, as are contact lens wearers.¹⁴ Individuals who use artificial tears three or more times per day are another high-risk category, and individuals with diabetes, thyroid conditions, rheuma-

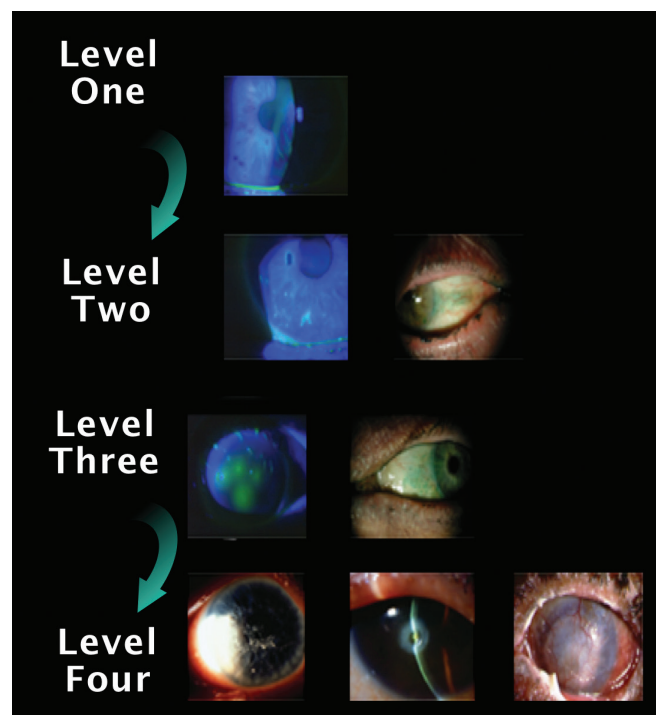


Figure. The International Task Force uses a 1 to 4 grading system for DED.

toid arthritis, and allergies are also more prone to developing DED.¹⁴

Adverse environmental conditions appear to be contributing to a precipitous rise in DED diagnoses. Influential factors, such as visual tasking, diet, alcohol, arid conditions, windy environment, pollutants, and systemic medications, are all known to contribute to DED.

DIAGNOSIS AND CONTRIBUTING FACTORS

DED is categorized into two types: evaporative or deficient aqueous tear production.⁷ Sjögren syndrome, an uncommon condition, is the primary cause of deficient aqueous tear production, although non-Sjögren inflammatory lacrimal deficiency is also a cause. Evaporative tear loss, meibomian gland dysfunction (MGD), blepharitis, environmental exposure, conjunctival chalasis, and contact lens use are all important

TABLE. INTERNATIONAL TASK FORCE GRADING SCALE¹⁸

At least one sign and one symptom of each category should be present to qualify for the corresponding level assignment

Level 1

- Symptoms mild conjunctival signs
- Mild to moderate symptoms and no signs
- Mild to moderate conjunctival signs

Level 2

- Symptoms and signs
- Moderate to severe symptoms
- Tear film signs
- Mild corneal punctate staining
- Conjunctival staining
- Visual signs

Level 3

- Symptoms, signs, and other findings (filaments)
- Severe symptoms
- Marked corneal punctate staining
- Central corneal staining
- Filamentary keratitis

Level 4

- Severe symptoms, signs, and systemic involvement
- Severe symptoms
- Severe corneal staining erosions
- Conjunctival scarring

causes. It is important to note that these categories of DED are not mutually exclusive, and that patients may have components of each: deficient aqueous tear production and evaporative tear loss.

Perhaps the most important component of DED pathophysiology is inflammation. In a healthy eye, relative levels of oils, lipids, proteins, and mucins that comprise the tear are regulated by the body's homeostatic mechanisms. When the normal homeostatic state is disrupted, such as due to lacrimal or MGD, compensatory mechanisms are induced. Thus, in the presence of hyperosmolarity, the body may release adhesion molecules, which promote the ingress of pathogenic immune cells¹⁵; and matrix metalloproteinases, enzymes that denigrate the extracellular matrix proteins on the ocular surface.

Eyelid inflammation, or blepharitis, is a frequent contributor to DED as well as being a cause of many of the same symptoms as DED. Blepharitis can be categorized as either anterior in nature (ie, seborrheic) or posterior (most commonly due to MGD).⁶ The latter of these is the far more common etiology, which, although common, has an extremely varied clinical

presentation. Some of the more common symptoms to note are early morning burning, scaling, redness, irritation, loss of lashes, crusting of the lashes, and unstable vision.⁶ MGD, which, as noted, can contribute to blepharitis, is a leading cause of DED.¹⁶ A frequently overlooked condition, MGD is present in about 40% of eyes.¹⁷

CONCLUSION

Recognizing signs and symptoms of DED is necessary for proper identification and imperative for knowing when and how to initiate treatment. Consensus guidelines from the International Task Force, for example, use a 1 to 4 grading system with treatment recommendations associated with each tier of severity (Table).¹⁸ ITF level 1 symptoms include mild conjunctival findings; when patients reach level 2, symptoms and signs are more moderate, with punctate staining of the cornea, and, as such, anti-inflammatory therapy is recommended. At level 3, higher levels and filamentary keratitis are present. Level 4, the most severe, is typically when scarring will occur (Figure).

The emerging evidence in DED epidemiology, etiology, and pathophysiology reveals that DED has a deceptively simple name. The reasons for and causes of eye dryness are multifactorial and warrant thorough evaluation. Furthermore, an evolving understanding of DED underscores that it is not just a disease of the elderly that is easily treatable with artificial tears. The complex nature of DED has been brought to light by advancements in diagnostic modalities, which, most prominently, have provided insight into the important role of inflammation in inducing symptoms. ■

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Shifting DED Burden and the Expansion of Diagnostic Testing

DED is now being seen in patient populations outside the traditional groups.

By Sheri Rowen, MD

Classic thinking in dry eye disease (DED) is that it is an entity affecting older individuals, primarily women, especially those who are peri- and postmenopausal. Recent epidemiologic studies, however, portray a vastly different picture than what eye care providers are used to: A significant number of younger patients are developing DED, men are increasingly affected, and changing visual demands and needs in our society are raising the prevalence of DED across all age ranges.¹

Although it is true that women, especially those going through menopause, are disproportionately affected by DED, there is growing evidence that unrecognized DED at an earlier age and among men may go underreported and untreated; around 12% of men and 13% of women age 21 to 34 years have signs and/or symptoms of DED.¹ That age group coincides with the subset of the US population most likely to utilize smartphones, tablets, and other display devices, which constitute a risk factor for developing visual sequelae. Furthermore, because DED is a chronic and progressive disease entity, such cases may advance beyond the point of being treatable. As a result, early recognition, diagnosis, and initiation of proper intervention (inclusive of education, preventive measures, and, when appropriate, treatment) may function to alleviate disease burden and forestall the development of advanced, irreversible disease.

CHANGING RISK FACTORS

A number of risk factors have been identified for the development of DED, including contact lens wear, use of digital devices, environment, female sex, medications, ocular surgery, diabetes, occupation, autoimmune diseases, age, and diet.¹⁻⁵ Several of these risk factors highlight the importance of mechanical failure in the blink response in inducing DED. For example, a pocket of fluid can sit under the contact lens, and, as a result, the blink response can be impeded, because the cornea is constantly bathed from this fluid, and the stimulus for a full blink is reduced. Likewise, when digital devices are used at eye level (instead of the more ergonomically correct position looking down), the user has an abnormal and incomplete blink; full apposition of the two lids together is fundamental for release of meibum into the tear film.

Another change in our society affecting DED is a major shift in dietary trends. Whereas a healthy diet would approach a 1:1 ratio of omega-3 fatty acids (anti-inflammatory) to omega-6 fatty acids (pro-inflammatory); the typical North American diet is about 1:25 or 1:50, with a heavy emphasis of potentially harmful omega-6 fatty acids.⁶ Because the American diet is heavily dependent on corn and corn products, Americans are quite literally feeding themselves pro-inflammatory mediators that function in

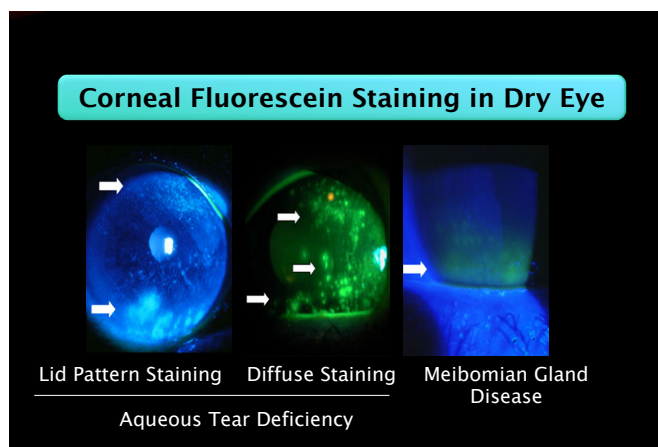


Figure 1. Staining is crucial for understanding the health of the ocular surface.

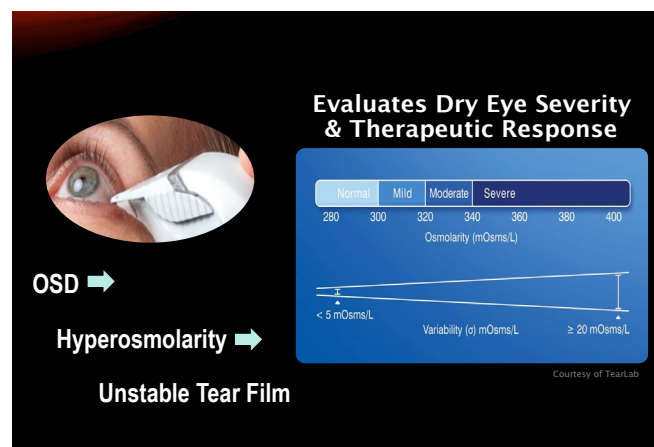


Figure 2. Osmolarity has been identified as an important biomarker of the health of the human tear.

LID WIPER EPITHELIOPATHY

By Sheri Rowen, MD

Recent evidence suggests that patients with dry eye disease (DED), particularly those with an aqueous deficient component, may have a mechanical failure of the lid wiper, the portion of the marginal conjunctiva of the upper lid that functions to clear the ocular surface during blinking. Its morphologic features suggest it is designed for close contact with the tear film and that it plays a crucial role in spreading the tear film over the ocular surface during blinking. An examination of patients with suspected DED signs and/or symptoms should include an evaluation of the backs of the lids to judge the relative health of this anatomic area. Of note, the lid wiper should be distinguished from the Line of Marx, the multilayered stratified squamous epithelium that serves as the transition from wet (palpebral conjunctiva) to dry tissue (keratinized lid margin).

If the tear film becomes thinned, such as due to insufficient meibum composition, drying of the lid wiper region may yield untoward friction as the lid travels across the ocular surface. This action may serve a sandpaper-like effect to debride the epithelium from the ocular surface, thereby exacerbating DED symptoms and causing the gritty effect patients sometimes report. Korb et al identified a strong correlation between presence of lid wiper epitheliopathy (LWE) and symptoms of DED.¹ In their study, 76% of eyes with DED symptoms had evidence of LWE compared with 12% of asymptomatic eyes.

In addition to physical examination, LWE is most readily identified using vital stains (Figure). LWE may be categorized by its severity on a 1 to 3 grading scale. Although sometimes associ-

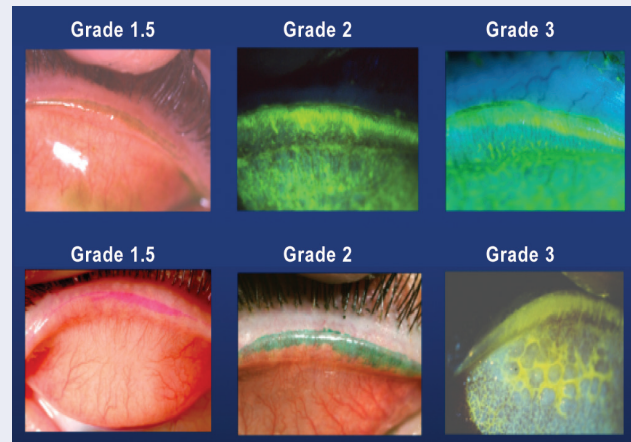


Figure. Lid wiper epitheliopathy may be categorized by its severity on a 1 to 3 grading scale.

ated with meibomian gland dysfunction, LWE can also result as a consequence of contact lens wearing. If the condition occurs in contact lens patients, it is suggested to change the type of material used for the lens; as well, relieving the meibomian glands may yield better equilibrium of water and oil components of the tear. Artificial tears may also play a role in restoring the health of the lid wiper region.

1. Korb DR, Herman JP, Greiner JV, Scaffidi RC, et al. Lid wiper epitheliopathy and dry eye symptoms. *Eye Contact Lens.* 2005;31(1):2-8.

the development of a number of conditions, one of which is DED.

All tolled, these risk factors suggest a massive swelling of the DED population. The use of digital devices is expanding, and contact lens wear is a popular option for patients who desire to be spectacle free. As well, ocular surgery is on the rise, and that, too, may increase the DED burden.

EXPANDING ROLE OF DIAGNOSTICS AND NEW MODALITIES

If there is an upside to the expanding proliferation of DED in modern society, it is the spawned interest in the development of objective diagnostic modalities that facilitate proper identification and classification. A thorough clinical and slit-lamp examination still form the basis for evaluating the health of the ocular surface. Several questionnaires (ie, the Standard Patient Evaluation of Eye Dryness [SPEED] and Ocular Surface Disease Index [OSDI]) have been validated as additive to the clinical impression and they may help steer the examination and subsequent testing. As well, staining

is crucial for understanding the health of the ocular surface (Figure 1; see also *Lid Wiper Epitheliopathy* sidebar). In addition, advancements in point-of-care testing supply quantitative and qualitative metrics for diagnosing DED and evaluating its severity.

Osmolarity has been identified as an important biomarker of the health of the human tear. In a study of 600 eyes of 300 patients, tear osmolarity testing was found to be 88% specific and 75% sensitive in mild to moderate disease; in cases of severe DED, an osmolarity score greater than 308 mOsm/L was found to have 95% sensitivity.⁷ Additional manufacturer-sponsored studies of the TearLab Osmolarity Testing System (TearLab) suggest its utility in categorizing the severity of DED; as well, that an inner-eye difference of 8 mOsm/L correlates with tear film instability, and is thus indicative of DED (Figure 2) (data on file with TearLab Corporation).

Another point-of-care diagnostic, the InflammDry test (RPS), identifies the presence and activity of matrix metalloproteinase 9 (MMP-9) on the ocular surface. In clinical study, MMP-9 activity was significantly higher in eyes with dysfunc-

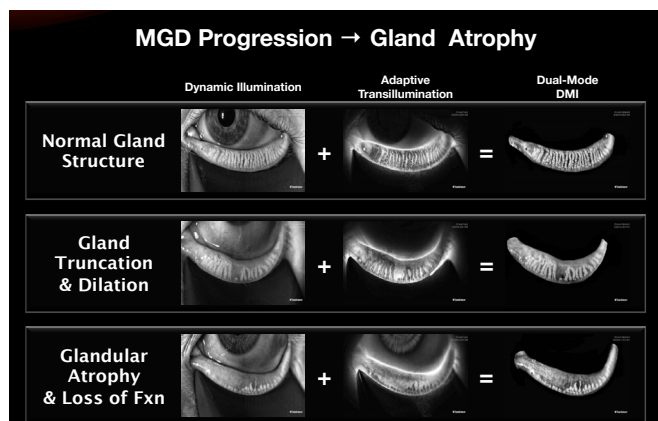


Figure 3. Dynamic illumination of the meibomian glands with LipiView II allows physicians to evaluate the health of the meibomian glands.

tional tear syndrome, irrespective of its severity, and it significantly correlated with symptom severity scores, decreased low-contrast visual acuity, fluorescein tear breakup time, corneal and conjunctival fluorescein staining, topographic surface regularity index, and percentage area of abnormal superficial corneal epithelia by confocal microscopy.⁸ The InflammDry test has been demonstrated to have 85% sensitivity and 94% specificity in the identification of DED.⁹

Thinning of the lipid layer has been correlated with an increase in DED symptoms in numerous studies.¹⁰⁻¹³ Thus, interferometry appears to play an important role in the differential diagnosis of DED, especially as it pertains to identifying aqueous deficiency. Additional modalities improve the ability to appreciate the relative health of the meibomian glands, such as dynamic illumination of meibomian glands (LipiView II; TearScience), which gives an impression of both structure and function (Figure 3); in turn, this information is useful for patients' education, tempering expectations, and for directing therapy. For example, glands that are atrophied (similar to what is depicted on the bottom row of Figure 3) are highly likely to have lost proper function, and therapy is likely to restore a modicum of function but unlikely to completely resolve the health of the glands.

CONCLUSION

Although the advent of diagnostic testing elevates the diagnostic acumen of eye care providers interested in identi-

fying DED, perhaps the most important new understanding in this realm during the past decade is the growing appreciation for the patients' role in managing his or her DED. Point-of-care testing provides a quantifiable metric to provide to patients to demonstrate a response to therapy, or, in cases of poor compliance, that the health of the ocular surface is in peril due to their inaction. Meibography provides stunning views of the structure and function of the meibomian glands with which the provider can demonstrate the importance of compliance with treatment protocols.

Overall, the modern management of DED requires a complete shift in thinking. Whereas traditional thinking with DED was to await the onset of symptoms to commence treatment, emerging evidence suggests a role for earlier identification and initiation of treatment to stop the progression of the underlying disease mechanisms—which is particularly true in cases involving meibomian gland dysfunction. As a result, classical approaches to DED management, including conservative and step-wise treatment decision trees, may need to be re-examined and replaced with comprehensive and holistic intervention strategies that aim to rehabilitate the ocular surface, address symptoms with adjunctive therapies, and forestall advancing disease with appropriate preventive mechanisms such as diet, medication, and nutritional supplementation when needed and ergonomic realignment when using digital display devices. ■

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CME QUESTIONS

OCULAR SURFACE DISEASE: UNDERSTANDING THE NEED FOR EARLY DIAGNOSIS

1 AMA PRA Category 1 Credit™

Expiration Date: March 1, 2017

1. Which of the following is most true about meibomian gland dysfunction (MGD)?

- a. It is the most common form of lid margin disease
- b. It is a chronic and progressive entity
- c. In more advanced stages, MGD may yield glandular atrophy and loss of function
- d. All of the above

2. Which of the following are true about hyperosmolarity with regard to dry eye disease?

- a. It is a feature of aqueous deficient but not evaporative dry eye
- b. It is a feature of evaporative but not aqueous deficient dry eye
- c. It is a feature of both aqueous deficient and evaporative dry eye
- d. It is not relevant for dry eye

3. Vasoconstrictors function to reduce redness and irritation soon after instillation; however, they are believed to result in the return of said symptoms to pre-treatment levels or above. This phenomenon is known as:

- a. Rebound effect
- b. Tachyphylaxis
- c. Progression of dry eye disease
- d. None of the above

4. Which of the following are validated dry eye questionnaires, which may be used to identify patients in need of further dry eye evaluation:

- a. SPEED and OSDI
- b. SPEED and The UNC Dry Eye Management Scale
- c. OSDI and The UNC Dry Eye Management Scale
- d. SPEED, OSDI, and The UNC Dry Eye Management Scale
- e. None of the above

5. Women are at a nearly two-times greater risk of developing dry eye disease compared with men.

- a. True
- b. False

6. What is the primary cause of aqueous deficient dry eye disease?

- a. Sjögren syndrome
- b. Lacrimal deficiency
- c. Meibomian gland dysfunction
- d. Conjunctival chalasis

7. Which of the following systemic condition is not associated with a risk of developing dry eye?

- a. Diabetes
- b. Thyroid conditions
- c. Heart disease
- d. Rheumatoid arthritis

8. What factors are contributing to the shifting epidemiology of dry eye disease?

- a. Increased use of computers, tablets, smartphones, and other viewing devices
- b. An increase in ocular surgery
- c. Contact lens wear
- d. All of the above

9. Lid wiper epitheliopathy:

- a. Is a mechanical failure of the lid wiper
- b. Is distinct from the Line of Marx
- c. Has been correlated with symptoms of dry eye disease
- d. All of the above

10. Which of the following is believed to be indicative of tear film instability:

- a. Tear osmolarity greater than 308 mOsm/L
- b. A difference in tear osmolarity of at least 8 mOsm/L between the two eyes
- c. Both A and B
- d. Tear osmolarity is not useful for determining tear film instability

ACTIVITY EVALUATION

OCULAR SURFACE DISEASE: UNDERSTANDING THE NEED FOR EARLY DIAGNOSIS

Did the program meet the following educational objectives?

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
Recognize the importance of early diagnosis and treatment of DED based on the presence of comorbid conditions and/or risk factors.	_____	_____	_____	_____	_____
Assess the role of inflammatory markers/processes in DED.	_____	_____	_____	_____	_____
Compare newer diagnostic tools and incorporate results into a DED management plan.	_____	_____	_____	_____	_____
Formulate strategies to best treat DED based on the presence of comorbid conditions and/or risk factors.	_____	_____	_____	_____	_____

Your responses to the questions below will help us evaluate this 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). Please complete the following course evaluation and return it via fax to (610) 771-4443.

Name and email _____

Do you feel the program was educationally sound and commercially balanced? ☐ Yes ☐ No

Comments regarding commercial bias:

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 _____

Would you recommend this program to a colleague? ☐ Yes ☐ No

Do you feel the information presented will change your patient care? ☐ Yes ☐ No

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