CME Monograph

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CONTEMPORARY CASE DISCUSSIONS

IMPROVING OUTCOMES OF DRY EYE DISEASE

Through Better Diagnosis and Management

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Proceedings from a CME symposium held on November 13, 2017, in New Orleans, Louisiana

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This continuing medical education (CME) activity captures content from a CME symposium held on November 13, 2017, in New Orleans, Louisiana.

ACTIVITY DESCRIPTION
The goal of this activity is to help ophthalmologists keep current with developments in dry eye disease (DED) pathophysiology, new methods for diagnosis, and new treatment. Through case illustrations, management of a variety of patients will be discussed.

TARGET AUDIENCE
This educational activity is intended for ophthalmologists caring for patients with DED.

LEARNING OBJECTIVES
Upon completion of this activity, participants will be better able to:
- Review the prevalence of DED in different patient populations
- Apply the appropriate diagnostic test for evaluating DED
- Articulate the implications of inflammation in DED on treatment
- Apply evidence-based treatment and guidelines for DED into practice

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INTRODUCTION

Dry eye disease (DED) is a common and often chronic disease affecting the ocular surface. Although awareness of DED among clinicians has increased, its occurrence is still underrecognized. Dry eye disease can have a profound effect on a patient's quality of life and outcomes of cataract/refractive surgery. Severe DED is noted to have a negative effect on quality of life similar to that of dialysis or severe angina.[1,2] Mild-to-moderate forms of DED can interfere with everyday tasks, such as work performance, nighttime driving, enjoyment of outdoor activities, success with contact lens wear, and satisfaction with ocular surgery.[3] Clinical observations, clinical trial results, and the concept of a pathophysiologic model of the disease suggest that DED can be progressive.[4-6] The following activity reviews the prevalence, diagnosis, and treatment of DED as well as offers ways to improve disease outcomes through case studies and clinical pearls for the practicing clinician.

PREVALENCE OF DRY EYE DISEASE: CURRENT AND FUTURE

EDWARD J. HOLLAND, MD

Dry eye disease affects approximately 344 million people globally and 20 million people in the United States.[7] Postmenopausal women currently constitute approximately 14 million people with DED in the United States, and this number is expected to surpass 15 million by 2021.[7] Approximately 3.7 million men aged > 65 years have DED, and this statistic is expected to reach more than 4.4 million by 2021. The prevalence of young adults (aged 21-49 years) with DED is approximately 14%.[8] In addition, given that 92% of eye care professionals suspecting that the use of modern digital devices contributes to dry eye symptoms,[9] the number of adults with DED can only be expected to increase. By 2030, 18% of the population will be aged > 65 years.[10] Aging baby boomers represent a large population at risk for dry eye and are a major consideration in determining the increase in dry eye prevalence over the next 20 years.[11]

Current and future prevalence data regarding several age populations demand that every eye care professional becomes a DED expert and warrants cooperation among all clinicians to provide a comprehensive and efficient approach to identify DED. The cases and related discussions described herein offer expert approaches to better manage DED.

CASE 1: DIAGNOSING DRY EYE DISEASE – A PATIENT WITH CLASSIC DRY EYE SYMPTOMS

FROM THE FILES OF ELIZABETH YEU, MD

A 50-year-old white female complains of tearing, more so in the right eye than in the left eye, as well as burning and mild itching. She has an ocular and medical history consistent with many years of soft contact lens wear. She has a history of ulcerative colitis that has been in remission for "a while." She takes minocycline 50 mg daily to treat facial rosacea, as prescribed by a dermatologist, in addition to oral valacyclovir, levothyroxine, and simvastatin. She has been treated previously by 2 other eye care clinicians for her ocular symptoms. Previous ophthalmic medications include erythromycin ointment; tobramycin/dexamethasone ointment; alcaftadine, 0.25%; cyclosporine, 5%; and loteprednol, 0.5%—none of which provided long-term relief.

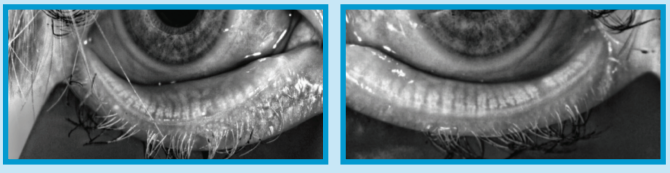
Discussion

No single diagnostic test is available to accurately diagnose DED, so employing several tests is more beneficial to the clinician. Three advanced diagnostic tests would be the most useful to employ for this patient. The point-of-care test to detect the presence of the inflammatory cytokine matrix metalloproteinase-9 (MMP-9) determines the presence of ocular surface inflammation.[12] Tear osmolarity testing analyzes the severity of dry eye and the stability of the tear film,[13] and meibomian gland imaging helps to examine the architecture of the meibomian glands.[14]

With meibomian gland dysfunction (MGD) being present in up to 86% of patients with DED,[15] one may think that truncation or missing glands upon meibography is common in these patients. In fact, many meibomian glands are quite healthy in architecture, especially in patients with less-advanced disease. The correlation between gland structure and function is weak.[16] Coupling the meibography with tests to evaluate the quality of gland expression and the meibum itself provides a clearer understanding of the patient's meibomian gland function.

Case Continued

*A meibography was performed, and the lids displayed minimal dropout and mild truncation and congestion **(Figure 1)**. Overall, the damage was mild, and gland architecture was good. Standard Patient Evaluation of Eye Dryness score was 15. Tear osmolarity was outside normal range at 296 mOsm/L OD and 305 mOsm/L OS. The MMP-9 test was positive, more strongly so in the right eye than in the left eye. Conjunctivochalasis was present in the cornea; devitalization and fluorescein staining were not observed. Lid telangiectasia was minimal. On the basis of these and other examination findings **(Table 1)**, the patient was diagnosed with epiphora, largely due to the aqueous form of DED, with a small component of MGD.*



A B

Figure 1. Meibomian gland architecture in left (A) and right (B) eyes
Images courtesy of Elizabeth Yeu, MD

Table 1. Examination Findings

Test	Results
SPEED	15
Autoimmune panel	Rheumatoid factor: elevated ANA, SS-A, SS-B, and CRP: negative Sjögren panel: negative
Tear osmolarity	296 mOsm/L OD 305 mOsm/L OS
MMP-9	Positive: OD >> OS
Lids	Tear film: ½ normal height Meibum: mild thickening Telangiectasia: minimal
Conjunctiva	1-2+ conjunctivochalasis
Cornea	No corneal staining

Abbreviations: ANA, antinuclear antibodies; CRP, C-reactive protein; MMP-9, matrix metalloproteinase-9; SPEED, Standard Patient Evaluation of Eye Dryness; SS-A, Sjögren-specific antibody A; SS-B, Sjögren-specific antibody B.

Discussion

Patients with conjunctivochalasis often have symptoms that mimic DED or that magnify existing DED. Even if there are only minimal folds at the lid margin, further examination by pulling the lower lid down is important to determine if there is greater redundancy at the base of the conjunctival fornix and/or if there is a problem with functional outflow due to a distorted tear film across the lower lid margin. Examination of the upper lid is also important because it can be critical in diagnosing floppy eyelid syndrome, allergic conjunctivitis, superior limbic keratoconjunctivitis, or the presence of a foreign body. Further, superior limbic keratoconjunctivitis is often present in patients with conjunctivochalasis.[17]

The tear osmolarity is outside the "normal" range, with normal being defined as having a score of < 300 mOsm/L or < 8 U intereye difference.[18,19] A tear osmolarity in the normal range does not, however, mean that there is no ocular surface disease (OSD) present. Osmolarity tends to be lower in patients with epiphora.[20] In this patient, the treatment goal is to address the epiphora and the inflammation, as indicated by the positive MMP-9 test.

Case Continued

The patient began an omega-3 fatty acid supplementation regimen. Also, a short, 3-week course of compounded, preservative-free dexamethasone, 0.025%, was administered with a 3-2-1 taper, and lifitegrast, 5%, was prescribed twice daily for both eyes because the positive MMP-9 test demonstrated the presence of inflammation. A preservative-free artificial tear drop was prescribed as needed. A follow-up visit occurred 6 weeks later, and the patient reported a 50% improvement in tearing, burning, redness, and itching. Tear osmolarity was 296 mOsm/L OD and 295 mOsm/L OS. Probe and irrigation of the punctae showed neither nasolacrimal duct obstruction nor stenosis in the lids. Continuation of daily omega-3 fatty acid supplementation and twice-daily lifitegrast, 5%, administration were prescribed. Future treatment considerations include thermal pulsation therapy to address the MGD and conjunctivochalasis repair and/or inferior punctoplasty of both eyelids if the epiphora persists.

Discussion

A meta-analysis of randomized controlled trials found that omega-3 fatty acid supplementation improved tear break-up time (TBUT) and Schirmer test scores in patients with DED.[21] Ocular Surface Disease Index (OSDI) score, TBUT, and MMP-9 levels have been shown to improve in patients with DED and MGD receiving thermal pulsation therapy.[22] The inflammation associated with DED can be controlled with several topical treatment options: corticosteroids, cyclosporine, and lifitegrast. Corticosteroids inhibit the expression of proinflammatory molecules and promote expression of anti-inflammatory molecules.[23] Long-term use of corticosteroids is not recommended because of side effects. Cyclosporine is indicated to increase tear production in patients whose tear production is presumed to be suppressed because of ocular inflammation associated with keratoconjunctivitis sicca.[24] Cyclosporine is available in a sterile, multidose, preservative-free solution that is administered twice daily. Lifitegrast is a lymphocyte function-associated antigen-1 antagonist that acts to prevent T-cell activation, cytokine release, and migration and extravasation of new T cells into inflamed ocular surface tissues by interfering with lymphocyte function-associated antigen-1 binding to intercellular adhesion molecule 1.[25] The 5% ophthalmic solution of lifitegrast was approved by the US Food and Drug Administration in June 2016 and by Health Canada in January 2018 for the treatment of the signs and symptoms of DED.[26,27]

Both cyclosporine and lifitegrast can effectively treat the inflammation associated with DED. In pivotal clinical trials, improvement, as evidenced by Schirmer test scores, was seen within 6 months of treatment with cyclosporine.[28,29] In 3 clinical trials evaluating lifitegrast, improvement was observed within 6 weeks after treatment initiation in all 3 trials and as early as 2 weeks in 2 of the trials.[30-32] Although the rapidity of treatment onset observed with lifitegrast may influence the prescribed treatment regimen for a patient with typical DED, it is important to note that the clinical trials for cyclosporine did not include assessments to determine if a similar rapid treatment response could be observed. Not all patients with DED will respond to lifitegrast. Some may already be on successful long-term therapy with cyclosporine and should therefore not be switched to another treatment.

A more severe form of DED that is due to multiple risk factors warrants a multimodal treatment approach that can include omega-3 fatty acid supplementation and a prescription anti-inflammatory agent.

CASE 2: THE UNHAPPY MULTIFOCAL PATIENT

FROM THE FILES OF PREEYA K. GUPTA, MD

*A 65-year-old female was referred for a second opinion for blurry vision after cataract surgery performed 3 months prior. The cataract surgery was performed without complications and involved femtosecond laser arcuate incisions and the placement of a multifocal intraocular lens (IOL) in each eye. An Nd:YAG (neodymium:yttrium-aluminum-garnet) capsulotomy was performed in both eyes 8 weeks after the cataract surgery. She was only administering artificial tears twice daily in both eyes. Her uncorrected visual acuity was 20/25 and J1 in both eyes **(Table 2)**. Some punctate corneal staining was present **(Figure 2)**, and she had a slightly reduced TBUT and a positive MMP-9 test. The multifocal IOL was well centered in each eye.*

Table 2. Examination Findings

Vision	UCDVA	20/25 OU
	UCNVA	J1 OU
	MR	Plano-0.25 x 180 OU
Anterior segment	Corneal PEE	Tr-1+ OU
	Multifocal intraocular lens	Well centered OU
	TBUT	6 s OD 7 s OS
	MMP-9	Positive
	Osmolarity	310 mOsm/L OD 320 mOsm/L OS
Posterior segment	Macular OCT	Normal

Abbreviations: MMP-9, matrix metalloproteinase-9; MR, manifest refraction; OCT, optical coherence tomography; PEE, punctate epithelial erosions; TBUT, tear break-up time; UCDVA, uncorrected distance visual acuity; UCNVA, uncorrected near visual acuity.

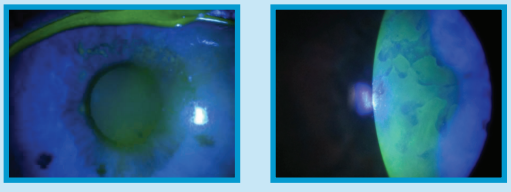


Figure 2. Punctate corneal staining of the cornea and break-up of fluorescein indicative of reduced tear break-up time

Images courtesy of Preeya K. Gupta, MD

Discussion

When a patient is unhappy with his/her vision after cataract surgery, multiple culprits can be considered during the differential diagnosis, including OSDs, cystoid macular edema, retinal diseases, residual refractive error, or complications with the IOL **(Table 3)**. In this patient, cystoid macular edema is not likely because her vision is very good, and her multifocal IOLs are centered. On the other hand, DED is highly suspected, and this disease is, in general, significantly underdiagnosed prior to cataract surgery. In a study by Gupta and colleagues, DED signs were present in up to 82% of patients presenting for cataract evaluation, yet DED was diagnosed in only 28% of patients prior to surgery (P.K.G., unpublished data, 2018). In the Prospective Health Assessment of Cataract Patients' Ocular Surface (PHACO) study, which was designed to determine the incidence and severity of dry eye in patients being screened for cataract surgery, 62.9% of patients had a TBUT ≤ 5 seconds and 77% of patients had significant corneal staining, 50% of which was centrally located.[33]

The importance of evaluating patients for DED prior to cataract surgery cannot be minimized. Anecdotal evidence suggests that DED

Table 3. Diagnostic "Checklist" for the Unhappy Multifocal Intraocular Lens Patient

Ocular surface disease • Dry eye disease • Anterior basement membrane dystrophy • Salzmann nodules
Residual refractive error
Retinal disease • Epiretinal membrane • Vitromacular traction • Cystoid macular edema
Intraocular lens complication • Decentration

is asymptomatic in many patients prior to surgery. After surgery, the disease only worsens. A retrospective study of 192 eyes of 96 patients with DED who had undergone phacoemulsification surgery revealed a worsening in fluorescein staining patterns and OSDI scores during the first 3 months after surgery.[34] After 3 months, however, the staining patterns and scores returned to their preoperative values, suggesting surgery may aggravate the signs and symptoms of DED, at least in the short term.

The surgical method may also affect DED signs and symptoms postoperatively. In a study comparing DED symptoms after femtosecond laser–assisted cataract surgery (FLACS) with those after conventional phacoemulsification, although both methods worsened DED, postoperative fluorescein staining at 1 day (P = .001), 1 week (P = .047), and 1 month (P = .025) and postoperative OSDI scores at 1 week (P = .014) were significantly higher among patients receiving FLACS.[35] In patients diagnosed with DED prior to surgery, staining was significantly worse 1 day (P = .016) and 1 month (P = .009) in those treated with FLACS surgery than in those undergoing conventional surgery.

Effective assessment of patients for DED prior to cataract surgery does not need to be complex or overly time consuming. Administering dry eye questionnaires and conducting point-of-care tests **(Table 4)** should be a part of the routine preoperative screening of patients seeking cataract surgery. Even asking questions about fluctuating vision and the use of artificial tears can indicate ocular surface issues that warrant more extensive testing for DED prior to surgery. Furthermore, the use of lissamine green staining may be preferred over fluorescein staining because the former is better at detecting early DED, which would not be revealed with the latter.[36] Fluorescein staining, however, provides the ability to measure TBUT and observe corneal staining.

Table 4. Identifying Dry Eye Disease in the Cataract Surgery Patient

Screening
• Questionnaires: OSDI, SPEED, SANDE, DEQ-5 • Tear film diagnostics: osmolarity testing, topography, MMP-9 testing • Query patient to identify fluctuation in vision as the primary complaint
Clinical Examination
• Meibomian glands: Assess oil quality and flow • Conjunctiva: Look for staining with lissamine green or fluorescein • Cornea: Look for punctate erosions, measure TBUT

Abbreviations: DEQ-5, Eye Questionnaire 5; MMP-9, matrix metalloproteinase-9; OSDI, Ocular Surface Disease Index; SANDE, Symptom Assessment in Dry Eye; SPEED, Standard Patient Evaluation of Eye Dryness; TBUT, tear break-up time.

Case Continued

The patient was diagnosed with DED and was prescribed lifitegrast, 5%, twice daily in both eyes because of the relatively quick treatment response observed with the drug and to address the inflammation on the ocular surface. She also received thermal pulsation therapy at that initial visit because she did have some dysfunctional meibomian glands. A follow-up visit was scheduled for 6 weeks later. At follow-up, her TBUT was 9 seconds OU and the MMP-9 test was negative. Osmolarity scores were 285 mOsm/L OD and 290 mOsm/L OS, and her uncorrected visual acuity was 20/20 OU. The patient reported that her vision was more stable and that she was less symptomatic.

Discussion

This case highlights the need to diagnose and treat DED prior to cataract surgery to avoid patient dissatisfaction with the surgical outcome and further exacerbation of preexisting DED. Although surgery may need to be delayed to treat the ocular surface, treatment options are available to do so quickly and effectively. Thermal pulsation therapy can be done preoperatively and is effective in treating MGD and improving the tear film, such that more accurate biometry and keratometry can be achieved. When necessary, topical steroids can be used to treat inflammation as well; these agents often have a rapid onset of action.

Loteprednol, 0.5%, is indicated to treat inflammation postoperatively,[37] but is also useful preoperatively, especially if the lids are inflamed, and its ointment form is the only commercially available preservative-free corticosteroid on the market. As with most corticosteroids, patients should be monitored for increased intraocular pressure and increased risk of developing glaucoma. The addition of lifitegrast into our treatment options has allowed patients to achieve symptom relief as soon as within 2 weeks, making it an excellent option in the presurgical population needing optimization of the ocular surface.

CASE 3: CATARACT SURGERY FOR THE PATIENT WITH MEIBOMIAN GLAND DYSFUNCTION

FROM THE FILES OF KENNETH A. BECKMAN, MD, FACS

A male patient was referred as a candidate for a toric IOL. He complained of blurred vision and difficulty reading that worsened by the end of the day, as well as dryness and irritation. He also experienced tearing and mattering of the lashes upon waking in both eyes. Slit-lamp examination revealed thickened meibomian secretions and plugging in both eyes. Debris was present in the tear film and on the lashes. Tear break-up time was rapid in both eyes. Topography revealed 3 diopters (D) of astigmatism at approximately 60° axis in the left eye ***(Figure 3A)****. Placido imaging of the left eye showed a divot in the mires* ***(Figure 3B)****.*

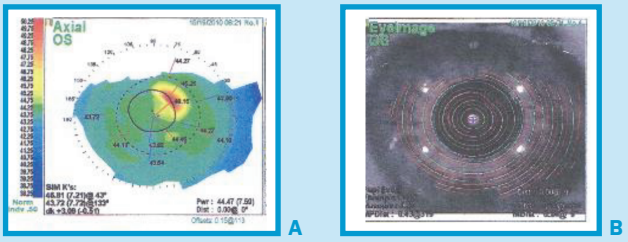


Figure 3. Topography of the left cornea reveals 3 diopters of irregular oblique astigmatism, with a "hotspot" at 60° (A). A corresponding divot can be seen in the mires in the Placido image of the left cornea (B).
Images courtesy of Kenneth A. Beckman, MD, FACS

Discussion

The irregularities seen in the topography warrant further examination, even more so if a toric or presbyopic IOL is being recommended. They could be due to various types of OSD, including epithelial basement membrane dystrophy, to Salzmann nodules, scarring, or DED.

Case Continued

The patient's cornea was normal. Manual expression of the meibomian glands revealed meibum that was thickened and cloudy. This suggests the problems presented were associated with lid margin disease. The patient was diagnosed with MGD and evaporative DED. Treatment included warm compresses and lid scrubs. The patient was instructed to use preservative-free artificial tears, and topical azithromycin ophthalmic solution, 1%, was prescribed twice daily for 2 days, and then at bedtime for 2 weeks. At the 2-week follow-up visit, improvements were seen in meibomian secretions, conjunctival and corneal staining, and TBUT. Topography revealed the disappearance of the hotspot, a decrease from 3 D to 0.5 D of astigmatism, and circular mires, with resolution of the divot ***(Figure 4)****. Surgery was scheduled to occur a few weeks later with an aspheric monofocal IOL.*

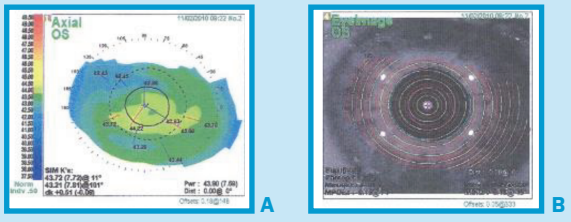


Figure 4. After 2 weeks of treatment for meibomian gland dysfunction and dry eye disease, the astigmatism is significantly reduced, the hotspot is no longer seen (A), and the Placido image shows no irregularities of the mires (B)

Images courtesy of Kenneth A. Beckman, MD, FACS

Discussion

In a small study of 21 patients diagnosed with blepharitis and randomized to receive either 2 weeks of warm compresses (5-10 minutes, bid; n = 11) or warm compresses plus topical azithromycin, 1% (1 drop bid for 2 days, then 1 drop qd for 12 days; n = 10), the group receiving the combination therapy demonstrated greater clinical benefit in meibomian gland plugging and secretions as well as eyelid redness compared with the group that applied only the compresses.[38] Such a combination regimen improved the findings in this case, so much so that implantation of a toric IOL was no longer an option. Once the OSD improved, it was evident that no significant corneal astigmatism was present and the findings on the initial topography were due to an abnormal tear film. In the absence of significant astigmatism, an aspheric monofocal IOL, rather than a toric IOL, was recommended. If improvement in both distance and near vision was a major goal, a multifocal IOL could also have been considered because the patient's symptoms improved rapidly. As a caveat with this option, the patient should be educated on the possibility of worsening DED symptoms after surgery if maintenance therapy is not continued. Nonadherence could lead to postoperative aberrations and visual disturbances that may be intolerable to the patient.

Regardless of the type of lens selected for cataract surgery, the risk of experiencing negative outcomes from performing surgery with a poor ocular surface is great. Not only is the risk of infections increased, the chances of having inaccurate IOL calulations[39] and postoperative abberations are increased.[40,41] Careful attention to a patient's complaints and history, detailed examination of the lid margin and tear film, review of multiple kerotometry (K) readings (eg, IOL master, topography, and manual K readings) for consistency, and ensuring that visual acuity is consistent with the cataract are all ways to determine if there is a problem with the ocular surface prior to surgery.

CASE 4: A PATIENT WITH DRY EYE DISEASE SYMPTOMS BUT NORMAL TEAR OSMOLARITY

FROM THE FILES OF CHRISTOPHER E. STARR, MD, FACS

A 48-year-old healthy male has a history of intermittent foreign body sensation, fluctuating vision, dryness, redness, and rare itching. He was previously diagnosed with DED by another physician. Artificial tears and warm compresses provided no noticeable relief. Clinical examination revealed 1+ conjunctival injection, mild inferior punctate epithelial erosions, and a normal TBUT of 12 seconds. Tear osmolarity level was also normal in both eyes: 295 mOsm/L OD and 293 mOsm/L OS. MMP-9 test was positive. He was diagnosed with allergic conjunctivitis and treated with a topical antihistamine drop.

Discussion

Despite having signs and symptoms associated with DED, a normal tear osmolarity level should raise suspicion of the accuracy of a DED diagnosis. A prospective study of 100 patients with a normal tear osmolarity level was conducted by Starr and colleagues to determine if a disorder other than DED would be diagnosed to explain the DED-like symptoms.[42] The majority of patients were diagnosed with either anterior blepharitis or allergic conjunctivitis **(Figure 5)**. Although some patients (11%) had a history of DED, they were treated with cyclosporine, which normalized their osmolarity before mitigating their DED symptoms.

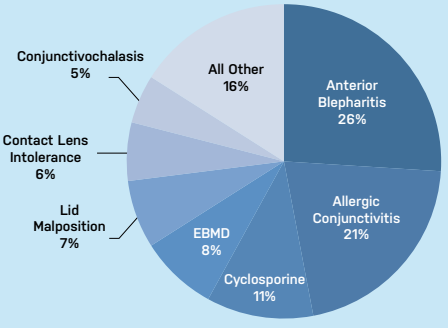


Figure 5. Alternative diagnoses among patients with dry eye disease–like symptoms but normal tear osmolarity

Abbreviation: EBMD, epithelial basement membrane dystrophy.

Adapted with permission from Brissette AR, Bohm KJ, Starr CE. The utility of a normal tear osmolarity test in symptomatic patients. Poster presented at: 8th International Conference of the Tear Film & Ocular Surface Society; September 7-10, 2016; Montpellier, France.

The symptoms of DED, conjunctivitis, and other OSDs largely overlap, and the presence of one condition does not preclude the coexistence of another.[43] Basing a diagnosis on symptoms alone is obviously difficult. Several point-of-care tests are available to accurately diagnose whether a patient has allergic conjuctivitis or DED. Tear immunoglobulin E testing detects the concentration of immunoglobulin E, a marker of allergic inflammation.[44] Such testing is useful to rule out DED and diagnose allergic conjunctivitis and its severity. Lactoferrin is a glycoprotein secreted by the lacrimal glands and is present in tears.[45] Low levels of lactoferrin is a diagnostic indicator of aqueous-deficient dry eye (ADDE) disease.[46] Lactoferrin testing can help distinguish between ADDE and evaporative DED.[47] Ocular allergy testing can also rule out or characterize allergic conjunctivitis from DED and other OSDs.[48]

CASE 5: A THIRD OPINION ON CHRONIC DRY EYE DISEASE DIAGNOSIS

FROM THE FILES OF CHRISTOPHER E. STARR, MD, FACS

A 52-year-old female sought a third opinion for symptoms of red, dry, and irritated eyes, present more in the left eye than in the right eye. Onset of symptoms reportedly began after the appearance of "cold sores" in the mouth, leading to an initial diagnosis of herpes keratitis. She was treated with valacyclovir, topical ganciclovir, artificial tears, corticosteroids, antibiotics, and tetrahydrozoline, all of which

resulted in no improvement. A second opinion was sought and she was diagnosed with severe, chronic DED. Treatment included topical corticosteroids, artificial tears, and warm compresses. Still, her symptoms did not improve. A third opinion was sought.

Clinical examination revealed 1+ conjunctival injection and fine papillae in both eyes. Mild inferior PEEs were also present in both eyes. Tear lake, TBUT, meibography, and meibum expression were all normal. Tear osmolarity was normal (289 mOsm/L OD and 291 mOsm/L OS), but she had a positive MMP-9 test, more so in the left eye than in the right. Lids displayed floppiness and laxity, which prompted further questioning.

The patient revealed a history of sleep apnea, for which she used a continuous positive airway pressure (CPAP) machine. Although she changes positions throughout the night, she sleeps primarily on the left side, and she complained that she could feel air blowing into her eyes from the CPAP machine. She was diagnosed with floppy eyelid syndrome and was instructed to stop the treatment regimen for DED and to sleep on her back. Lid taping or wearing a protective night mask/googles was recommended, and the CPAP machine was tightened to prevent air from escaping. She was also instructed to check for nocturnal lagophthalmos and to use an over-the-counter ointment at bedtime. She later reported that her symptoms quickly disappeared.

Discussion

New diagnostic and treatment protocols are now available to aid in the differential diagnosis of DED and other OSDs. In 2017, the Tear Film & Ocular Society published an updated Dry Eye WorkShop (DEWS) report. The DEWS II panel defined DED as a "multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[49] The diagnostic protocol in the DEWS II report recommends posing several questions to triage the suspicion of DED vs another OSD.[50] It then proceeds to give guidance on which diagnostic tests should be performed if DED is suspected and how to determine the primary DED subtype (ADDE or evaporative DED). Treatment and management recommendations take into account both disease etiology and severity.[51]

The Cornea, External Disease, and Refractive Society (CEDARS) also published its approach in 2017.[52] It bases treatment on diagnosis, separating DED into 4 categories according to the results of commonly used diagnostic assessments **(Figure 6)**. A fifth category addresses DED coconspirators/masqueraders, such as contact lens intolerance, floppy lid syndrome, and allergic conjunctivitis. Determining the type of DED leads to the selection of better tailored and more effective treatments.

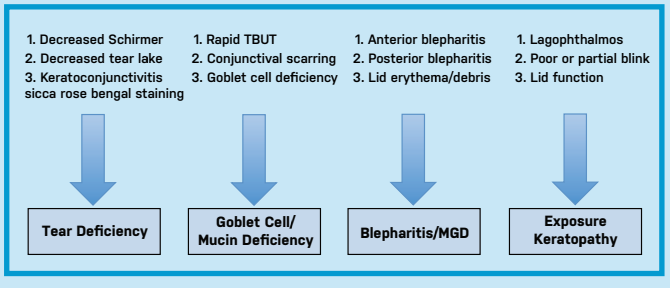


Figure 6. Categories of dry eye disease according to the diagnostic-based Cornea, External Disease, and Refractive Society approach[52]

Abbreviations: MGD, meibomian gland dysfunction; TBUT, tear break-up time.

A comprehensive algorithm soon to be published by the Cornea Clinical Committee of the American Society of Cataract and Refractive Surgery uses an evidence-based approach to diagnose OSDs, including DED (C.E.S., unpublished data, 2018). The algorithm incorporates all the diagnostic tests available at the present time and their possible results to determine diagnosis and treatment of OSDs preoperatively in patients seeking refractive and cataract surgery.

CONCLUSION

As the cases and discussions included in this program show, accurate diagnosis and effective treatment decisions are imperative in understanding DED. Clinicians should continue to gain a greater awareness of its prevalence, available diagnostic tools and treatments, and the existing guidelines **(Table 5)** and resources to achieve successful patient outcomes and satisfaction.

Table 5. Key Points to Remember About Dry Eye Disease

Understanding DED • DED is a very common disorder that is often ignored and underdiagnosed by clinicians • DED can be progressive, and consequences for the patient with DED are significant, with resultant chronic discomfort and loss of vision
Diagnosing and Treating Classic DED • DED is often multifactorial • Diagnostic and treatment guidelines and algorithms are available and serve as helpful resources to the clinician
Addressing DED Prior to Cataract Surgery • It is essential to diagnose DED preoperatively; do not rush into surgery, and use caution with premium intraocular lenses • Patient education is critical in managing expectation related to surgical outcomes and recovery
Differential Diagnosis of DED • Symptoms suggestive of DED are often symptoms of other diseases, NOT of DED • Diagnostic accuracy and treatment efficacy will increase through the use of an array of objective point-of-care tests and a directed examination

Abbreviation: DED, dry eye disease.

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