CME MONOGRAPH

MODERN PERSPECTIVES

IMPROVING THE IDENTIFICATION, DIAGNOSIS, AND TREATMENT OF DRY EYE

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FACULTY


Elizabeth Yeu, MD (Chair)


Brandon D. Ayres, MD


Marjan Farid, MD


Mark S. Milner, MD, FACS


Guillermo Rocha, MD, FRCSC

This continuing medical education activity is jointly provided by **New York Eye and Ear Infirmary of Mount Sinai** and MedEdicus LLC.

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MedEdicus LLC

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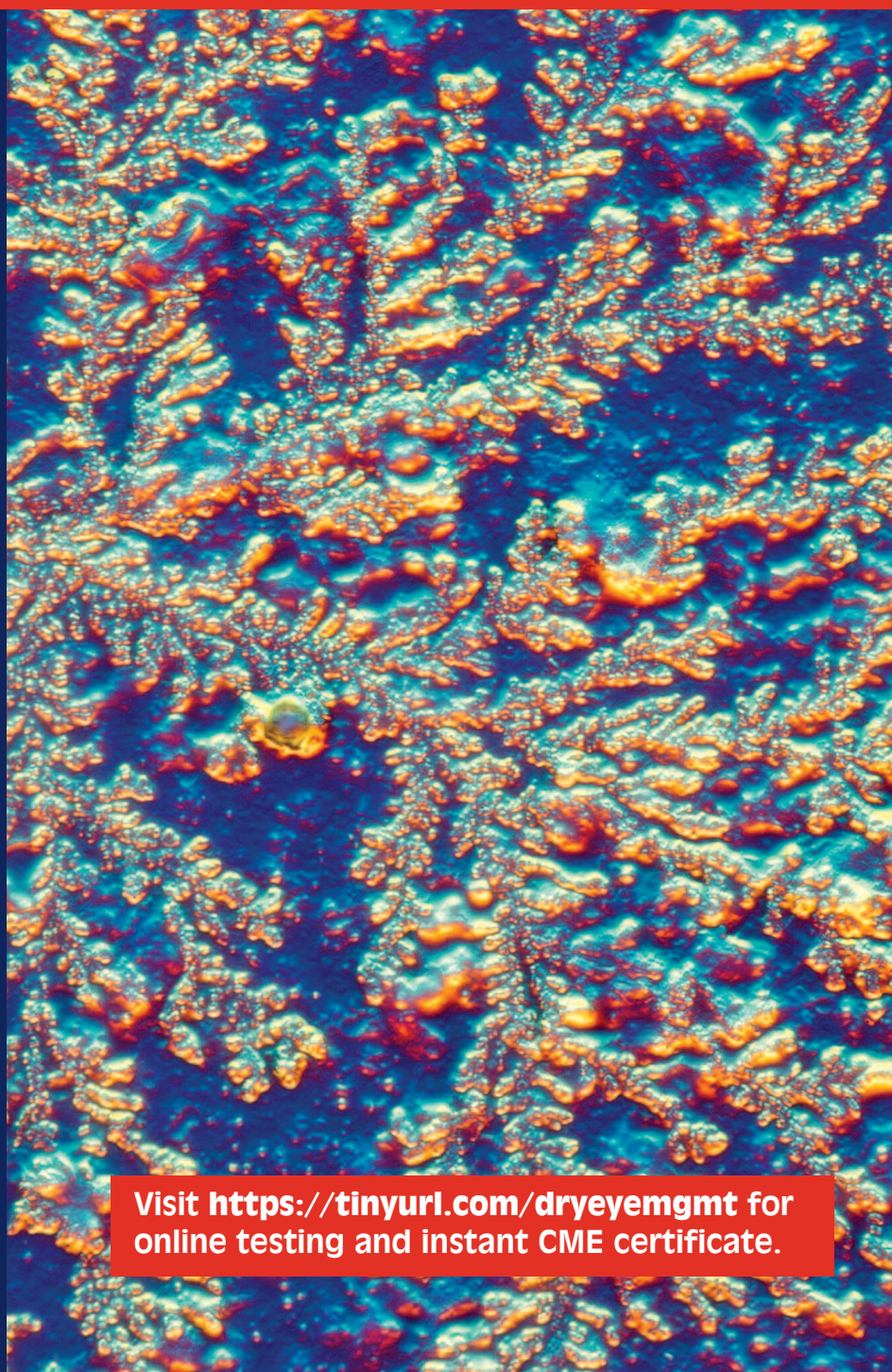

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PROGRAM CHAIR AND MODERATOR

Elizabeth Yeu, MD
Assistant Professor
of Ophthalmology
Eastern Virginia Medical School
Corneal, Cataract, and
Refractive Surgeon
Partner
Virginia Eye Consultants
Norfolk, Virginia

FACULTY

Brandon D. Ayres, MD
Instructor
Sidney Kimmel College
of Medicine
Thomas Jefferson University
Co-Director, Cornea Fellowship
Wills Eye Hospital
Philadelphia, Pennsylvania

Marjan Farid, MD
Associate Clinical Professor
of Ophthalmology
Director of Cornea, Cataract,
and Refractive Surgery
Vice-Chair of Ophthalmic Faculty
Gavin Herbert Eye Institute
University of California, Irvine
Irvine, California

Mark S. Milner, MD, FACS
Associate Clinical Professor
Department of Ophthalmology
Yale University
School of Medicine
New Haven, Connecticut
Partner
The Eye Center of
Southern Connecticut
Hamden, Connecticut

Guillermo Rocha, MD, FRCSC
Professor of Ophthalmology
University of Manitoba
Medical Director
Ocular Microsurgery &
Laser Centre
Brandon, Canada

CME REVIEWER FOR NEW YORK EYE AND EAR INFIRMARY OF MOUNT SINAI

Priti Batta, MD
Assistant Professor
of Ophthalmology
Icahn School of Medicine
at Mount Sinai
Director, Medical Student
Education
Assistant Director,
Comprehensive
Ophthalmology Service
New York Eye and Ear Infirmary
of Mount Sinai
New York, New York

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This educational activity consists of a supplement and ten (10) study questions. The participant should, in order, read the learning objectives contained at the beginning of this supplement, read the supplement, answer all questions in the post test, and complete the Activity Evaluation/Credit Request form. To receive credit for this activity, please follow the instructions provided on the post test and Activity Evaluation/Credit Request form. This educational activity should take a maximum of 1.5 hours to complete.

ACTIVITY DESCRIPTION

Dry eye disease (DED) is a common condition that is increasing in prevalence across all age groups. The purpose of this activity is to help ophthalmologists identify and manage DED. Expert faculty review the role of traditional and newer diagnostic techniques and modalities for management and illustrate their application in a series of case-based discussions.

TARGET AUDIENCE

This educational activity is intended for US and Canadian ophthalmologists.

LEARNING OBJECTIVES

Upon completion of this activity, participants will be better able to:

- Review the prevalence of DED in different patient populations
- Apply appropriate diagnostic testing for evaluating patients with suspected DED
- Consider the implications of the role of inflammation in DED when selecting treatment
- Apply evidence-based treatments for DED into clinical practice

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IMPROVING THE IDENTIFICATION, DIAGNOSIS, AND TREATMENT OF DRY EYE

INTRODUCTION

Identification and management of dry eye disease (DED) is evolving with the development of new diagnostic tools and therapeutic modalities. At the same time, ophthalmologists are becoming more aware of the importance of recognizing and treating this condition, which can negatively affect vision, quality of life, and outcomes of ophthalmic surgical procedures.

In this activity, expert faculty provide practical insights for optimizing DED diagnosis and patient care. They review the importance of a thorough history and anterior segment examination, along with the role of newer diagnostic technologies. Then, through a series of case-based discussions, the faculty highlight a directed approach to management that integrates newer treatment options and that is based on addressing DED features that are specific to the individual.

DRY EYE DISEASE PREVALENCE

DR YEU: The prevalence of DED increases with age, is higher in women than in men, and appears to be higher among Asians than among whites.[1] Recent data indicate that DED prevalence is increasing and that the condition is being seen more often in children and younger adults.[1-3] What are the reasons for these trends?

DR FARID: I think increased diagnosis by eye care providers is part of the explanation. I believe that because of growing awareness about DED, eye care providers have become more proactive about looking for it. I also think, however, that DED is truly becoming more common because more people are spending additional time using computers and other digital display screens.[3,4] Increased digital screen time also explains why we are seeing DED more often in younger individuals.[3]

DR MILNER: I agree that an increased rate of diagnosis is contributing to the rising rate of DED prevalence. With growth in the use of LASIK (laser in situ keratomileusis) and of premium intraocular lenses (IOLs), refractive and cataract surgeons are appreciating that a regular tear film and intact ocular surface are requisites for quality vision, so they are more careful about looking for DED when evaluating patients preoperatively in order to meet patient expectations for good vision outcomes.

In addition, industry-sponsored direct-to-consumer advertising and public education campaigns are raising public awareness about DED. This is causing more people to seek a diagnosis for their problems.

DR ROCHA: We also have newer tools that are enhancing our ability to identify inflammation, tear film abnormalities, and changes in the meibomian glands, thereby helping us make the diagnosis of DED.

DR AYRES: I think the expansion of treatment options for DED is also contributing to the rising rate of diagnosis by eye care providers. Clinicians are more willing to diagnose DED because they feel better equipped to treat it. At the same time, I think that many practitioners are unfamiliar with how to create a good treatment regimen for an individual patient. Therefore, although primary eye care providers may be diagnosing DED in more patients, many are still referring those patients to specialists for care.

DRY EYE DISEASE DIAGNOSIS

DR YEU: Patients with DED may not come in complaining specifically about eye dryness. What other symptoms should raise suspicion of DED?

DR ROCHA: Fluctuation in vision or even a general complaint of not seeing well are relevant clues.

DR YEU: Can DED be diagnosed on the basis of symptoms alone?

DR MILNER: Clinicians need to consider both signs and symptoms when they approach DED diagnosis because some patients have signs of DED, with minimal or no complaints, and others have a lot of symptoms but minimal or no signs.[5,6] This disconnect between signs and symptoms of DED can make the diagnosis seem more complex and may be a reason that some general ophthalmologists have been reluctant to undertake an evaluation for DED.

Newer Diagnostic Modalities

DR YEU: I think some of the newer diagnostic modalities have been very helpful for allowing us to identify DED and to understand the discordance between signs and symptoms that we sometimes see. For example, studies report that younger patients are more likely to have more DED symptoms than signs.[7,8] This is consistent with my clinical experience because, not uncommonly, I see younger patients who are very symptomatic and have little to no evidence of ocular surface damage. When I measure their tear film osmolarity, however, I find it can be very elevated. On the basis of the hyperosmolarity, I know these younger patients have DED. Their hyperreflexive, compensatory tearing protects them from developing significant epitheliopathy, and thus an accurate diagnosis of DED would have been missed by not considering symptoms and from performing vital dye testing alone.

Are you using the newer diagnostic tests routinely?

DR ROCHA: We established a dry eye center of excellence at our institution and are using the newer diagnostic modalities there for DED detection and patient education **(see Sidebar: Dry Eye Center of Excellence, p 4)**.

We measure tear film osmolarity, which we and other investigators have found to have a fairly good correlation with symptom severity.[9,10] In addition, we are using the metalloproteinase-9 (MMP-9) assay, which has been reported to have good sensitivity (85%) and specificity (94%) for diagnosing DED.[11]

A multifunctional imaging tool is also used in our comprehensive diagnostic evaluation. This tool features meibography; evaluates conjunctival redness, lipid layer thickness, tear meniscus height, tear dynamics, and tear break-up time (TBUT); and generates a summary report that can include results of other diagnostic tests **(Figure 1)**. We use the tear film and meibography images along with the summary report in our initial and follow-up counseling because they help patients understand their condition and motivate them to comply with recommended therapy.

DR FARID: I am using tear film osmolarity, meibography, and the MMP-9 assay, and I agree that these newer objective diagnostic tools provide benefits for patients. The meibography images probably make the greatest impression on patients. A picture speaks a thousand words, and

DRY EYE CENTER OF EXCELLENCE

A Comprehensive Approach to Optimize Outcomes for Patients With Dry Eye Disease

Guillermo Rocha, MD, FRCSC

Because of our commitment to provide better care to patients with dry eye disease (DED), we implemented a dry eye center of excellence at our practice facility. The center has a multidisciplinary staff, and its core aims are to provide diagnostic testing, education, and management that is evidence based, cost effective, and patient centered.

Our diagnostic evaluation integrates newer tools with conventional DED tests. We focus on patient education because we believe that the outcome for anyone with a chronic medical condition, whether it is hypertension, diabetes, or DED, will be better if the patient understands the disease and its management. Our education efforts are also directed at outside health care professionals who are involved in our patients' care, including family physicians, respiratory therapists, pharmacists, and optometrists.

Consistent with the recommendations of the Canadian consensus panel on dysfunctional tear syndrome management, we take a holistic approach to DED management that includes educating patients about lifestyle measures and other nonpharmacologic strategies for improving DED **(see Sidebar: The Canadian Consensus on the Management of Dysfunctional Tear Syndrome, p 8)**.[1] We are also incorporating newer treatment modalities for DED, including multidose, preservative-free artificial tears and cyclosporine, along with unique products containing trehalose or hyaluronic acid as well as treatments for pain management. Lifitegrast has recently been approved in Canada,[2] making it another treatment option. Patients with meibomian gland dysfunction are treated with thermal pulsation therapy, and we are performing the procedure in an approach designed to provide a spa-like experience that we think raises patient satisfaction with their care.

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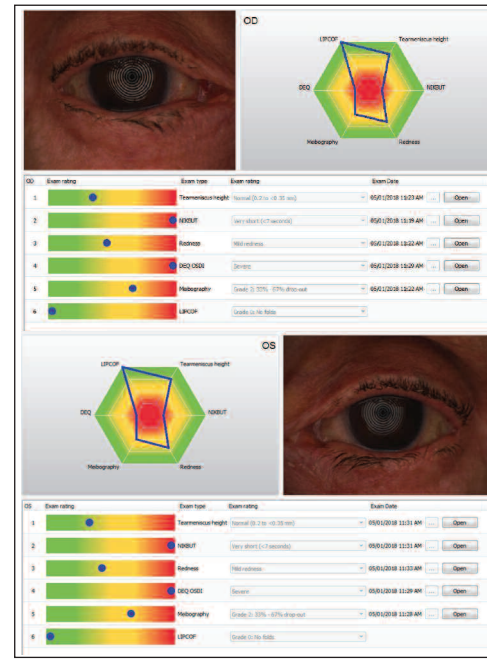

Figure 1. Multifunctional Summary Diagnostic Report showing moderate to severe findings (JENVIS, Keratograph, Oculus GmbH, Wetzlar, Germany)

Image courtesy of Guillermo Rocha, MD

meibography has been a powerful tool for educating and motivating patients. Abnormal osmolarity or MMP-9 results are also significant tools to help patients accept the importance of therapy.

These objective tests, along with topography and ocular surface staining, are also useful for educating cataract surgery patients who are found to have DED in the course of the preoperative evaluation. DED-related vision problems may be masked by the cataract, but manifest after surgery; if this happens, patients may blame the surgeon for their DED. The objective evidence demonstrates to patients that they have a preexisting condition and helps them accept that the DED needs to be treated before surgery to achieve a better outcome.

DR AYRES: We evaluate all patients with the MMP-9 assay, tear film osmolarity, and a multifunction instrument that provides lipid layer interferometry, blink measurements, and meibography. There is controversy among eye care professionals regarding the need for the newer tools to diagnose DED, but I think they provide information about the microenvironment that is very helpful for enhancing management decisions. For example, if I see a patient with elevated tear film osmolarity and a positive MMP-9 assay, I would start anti-inflammatory treatment. I would not insert punctal plugs until the inflammation is controlled because my experience indicates it is counterproductive to retain an "inflamed" tear film on the ocular surface.

DR MILNER: I think the newer diagnostic tests, such as MMP-9 to identify an inflammatory tear film, can also be very helpful for focusing the diagnosis on other ocular surface diseases that masquerade as DED. For example, if I see a patient with severe symptoms that seem out of proportion with DED signs—and the newer diagnostic tests show no evidence of DED—I consider that the patient has corneal neuralgia or central pain.

DR YEU: The updated definition of DED from the Dry Eye WorkShop II (DEWS II) recognized that dysfunction of the corneal nerves can be a pathogenic factor in the development of DED.[12] I also believe that patients can develop neuralgia when they have DED that is not adequately treated.

Value of Conventional Diagnostic Tests

DR YEU: As Dr Ayres noted, the role of the newer diagnostic tests for DED is controversial, and these tools are not available to all clinicians. Therefore, the clinical examination remains an integral part of the diagnostic evaluation.

What do you include in your standard clinical examination for DED?

DR FARID: I measure TBUT, which tells me about tear film regularity and stability, and I use lissamine green for staining because compared with fluorescein, lissamine green picks up epithelial breakdown and ocular surface stress earlier.[13,14] In addition, I do a thorough examination of the lid margins with expression to assess the quality and quantity of secreted meibum.

DR YEU: Recognizing the importance of meibomian gland dysfunction (MGD) as a cause for DED, I am looking very carefully for other findings associated with MGD, including telangiectasias and pitting at the lid margins and saponification of the tear film.

A thorough clinical examination should also include lid eversion to look for conjunctival changes, but it is my impression that many practitioners are omitting this step.

DR AYRES: Clinicians should make it a point to look for conjunctival changes. The way to do this is to retract the lower lid and direct patients to look up, then left, and then right. I also ask patients if they have any history of conjunctivitis or chemical injury.

As part of my lid evaluation, I look for *Demodex* infestation in suspicious patients by plucking a few lashes and examining them under the microscope for mites **(Figure 2)**. I believe that *Demodex* infestation is more likely in patients with severe rosacea or blepharitis, but it is more common in general than we think, and, if found, the infestation should be treated.

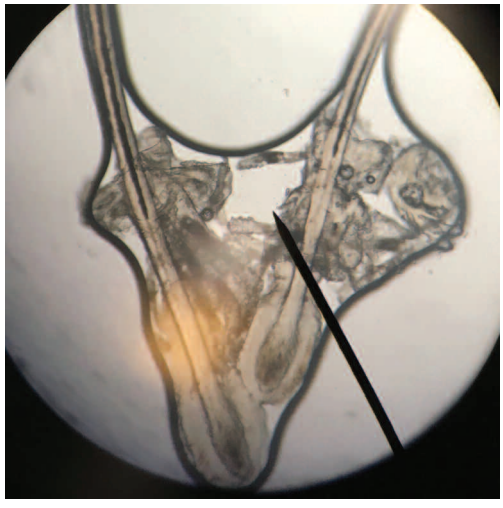

Figure 2. *Demodex* mites observed under microscopic examination of a lash sample

Image courtesy of Brandon D. Ayres, MD

DR MILNER: I do a Schirmer test without anesthesia because I think it is useful for diagnosing aqueous deficiency. I use lissamine green or rose Bengal for ocular surface staining, measure TBUT, do a lid examination with gland expression, and check the blink reflex and lid function. I believe images from slit-lamp photography are widely underused for helping asymptomatic patients with corneal evidence of DED understand their disease. The photographs allow them to see the damage and can be used to monitor change over time.

A thorough history is also critical in the evaluation for DED, and I include questions about atopic disease, smoking, and facial position while sleeping.

DR ROCHA: Clinicians also need to get a thorough medication history, and, as I like to say, "Do not turn off the lights too soon." Before beginning the ophthalmic examination, look at the skin for evidence of systemic diseases that may be contributing to DED.

It is my impression that one of the reasons clinicians have not been giving MGD and DED the attention these conditions deserve is that the conventional diagnostic evaluation and education about management with such basic strategies as lid hygiene and addressing lifestyle issues were seen as too time consuming. Now, some clinicians have adopted the new point-of-care tests and medications, with the idea that their use takes less time. Regrettably, when the new modalities are used as a substitute for conventional approaches instead of as an adjunctive measure, patients may not achieve the desired outcomes, and, consequently, the true value of the new tests and treatments is underestimated. Therefore, I am glad that we are emphasizing the importance of the basic elements of DED diagnosis and treatment.

DR YEU: If a clinician was to use only 1 instrument to help with DED diagnosis, I would recommend a topography unit because it gives useful information about surface irregularity and is necessary for surgical planning. Among the diagnostics that are more specific to DED, meibography has been a game changer for me because the information it gives about architecture connects to function, and that, in turn, helps me decide on therapy.

DR FARID: Anyone who is implanting toric IOLs needs to have a topography unit, but the idea of looking at the information it provides in terms of DED is a paradigm shift. Irregularity in the Placido mire rings or topography patterns should raise suspicion that tear film instability may be present.

MANAGEMENT OF DRY EYE DISEASE

DR YEU: Management for DED has evolved over the past decade with the introduction of many new treatment options that were developed because of growing understanding that DED is an inflammatory disorder and that MGD is a leading cause. Recent algorithms for DED management developed by DEWS II and by the Cornea, External Disease, and Refractive Society Dysfunctional Tear Syndrome (CEDARS DTS) Panel incorporate these newer treatment modalities.[15,16] Algorithms from these groups also highlight the importance of using findings from the history and diagnostic evaluation to subtype patients and to individualize therapy **(see Sidebar: Diagnostic and Treatment Algorithms [CEDARS DTS], p 6)**.

The following cases illustrate how findings from the diagnostic evaluation are used to guide management decisions for patients with DED.

CASE 1: A PATIENT WITH DRY EYE DISEASE AND SEASONAL ALLERGIES

From the Files of Marjan Farid, MD

A 57-year-old female presents with significant ocular surface burning, increased tearing OU, and irritation of the periocular skin that she complains is caused by her "stinging" tears. The patient works as an administrative assistant and says her symptoms prevent her from working on the computer for

DIAGNOSTIC AND TREATMENT ALGORITHMS (CEDARS DTS)

Recent Dry Eye Disease Recommendations: Dry Eye WorkShop II (DEWS II) and Cornea, External Disease, and Refractive Society (CEDARS) Dysfunctional Tear Syndrome (DTS) Panel

Mark S. Milner, MD

Guidelines for the diagnosis and treatment of dry eye disease (DED) from a Delphi consensus group in 2006 and from the Tear Film & Ocular Surface Society International Dry Eye WorkShop in 2007 are based on disease severity and recommend building on treatment in a stepwise manner.[1-3]

Published in 2017, the Dry Eye WorkShop II (DEWS II) presented a decision algorithm for classifying patients suspected of having DED **(Figure)**.[4] By using triaging questions and tests, patients are ultimately identified as having DED, preclinical DED or a predisposition to DED, neuropathic pain, or poor corneal sensitivity. Patients with DED are subtyped according to etiology as aqueous deficient, evaporative, or mixed, and although the DEWS II recommendations for management of DED are presented as a 4-step severity-based approach, the algorithm was developed to be used as an organizational tool for treatment decisions that take into account disease etiology and severity. Step 1 comprises conventional, low-risk treatments that are appropriate for mixed-etiology DED, and the treatments become more specific and advanced at successive levels.[5]

In contrast, the Cornea, External Disease, and Refractive Society Dysfunctional Tear Syndrome (CEDARS DTS) Panel developed diagnosis-based recommendations for treatment.[6] The CEDARS DTS Panel defined 4 disease subtypes—aqueous deficiency; blepharitis/meibomian gland dysfunction (evaporative and nonevaporative); goblet cell or mucin deficiency (evaporative); and exposure keratopathy—but also recognized that patients may fit into more than 1 of these categories. Dysfunctional tear syndrome co-conspirators, which are conditions that can masquerade as or contribute to DED, were also described, and they include superior limbic keratoconjunctivitis, medicamentosa, Thygeson superficial punctate keratitis, mucus fishing syndrome, contact lens–related toxicity, chemical toxicity, allergic/atopic conjunctivitis, conjunctivochalasis, floppy lid syndrome, and corneal hyperalgesia.

The CEDARS DTS diagnostic classification provides a foundation for providing targeted treatment **(Table)**.[6] Options that comprise the usual modalities and lesser-used or innovative treatments, including compounded medications, are listed. Clinicians are directed to use their judgment to develop a specific regimen for each patient, taking into account disease severity.

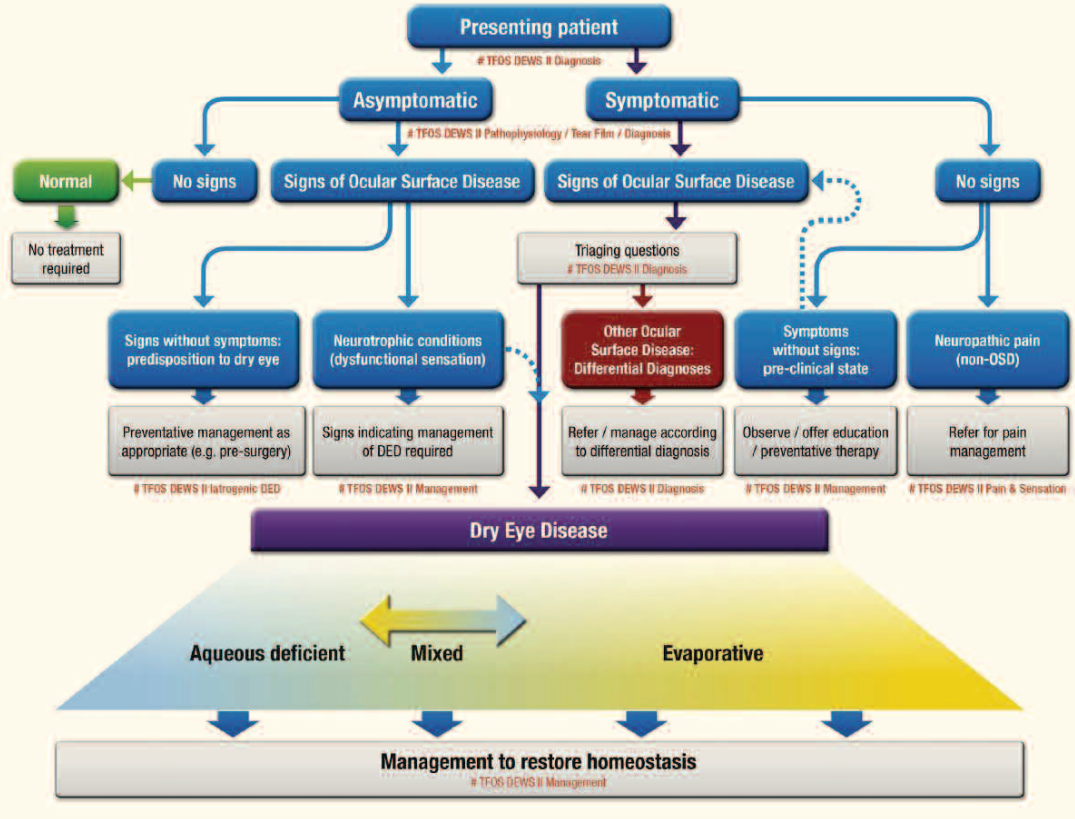

Figure. A decision algorithm for diagnosis and management of patients suspected of having DED[4]

Abbreviations: DED, dry eye disease; DEWS II, Dry Eye WorkShop II; OSD, ocular surface disease; TFOS, Tear Film & Ocular Surface Society.

Reprinted from *The Ocular Surface,* 15, Craig JP, Nichols KK, Akpek EK, et al, TFOS DEWS II definition and classification report, 276-283, Copyright 2017, with permission from Elsevier.

Table. CEDARS DTS Algorithm: Diagnostic-Based Approach[6]

Tear Deficiency		**Blepharitis/Meibomian Gland Dysfunction**	
1. Tear supplements 2. Cyclosporine A, lifitegrast 3. Topical steroids 4. Punctal plugs/ Cautery 5. Autologous serum 6. Secretagogues 7. Topical hormones a. Medroxyprogesterone b. Dehydroepiandrosterone – androgen (compounded) c. Testosterone/ Progesterone (50/50)	8. Hydroxypropyl cellulose ophthalmic inserts 9. Moisture chamber eyewear 10. Nutritional supplements – omega-3 fish oils 11. Albumin 12. Dapsone 13. Intranasal neurostimulation 14. Scleral lenses 15. Surgery – Self-retained amniotic membrane and amniotic cytokine extract drops, membrane transplant, salivary gland transplant	1. Lid hygiene 2. Cyclosporine A, lifitegrast 3. Topical azithromycin 4. Metronidazole ointment (compounded) 5. Oral doxycycline/ tetracycline 6. Lid scrubs/cleansers	7. Other compounded antibiotics a. Topical doxycycline drops b. Topical clindamycin ointment 8. Nutritional supplements a. Omega-3 fish oils b. Flax seed oil 9. Meibomian gland probing 10. Pulsed light therapy 11. Thermal pulsation, thermal hydration
Goblet Cell/Mucin Deficiency		**Exposure Keratopathy**	
1. Cyclosporine A, lifitegrast 2. Vitamin A ointment – retinoic acid (compounded) 3. Moisture chamber eyewear 4. Scleral lenses		1. Lubricating gels 2. Lid tape qhs 3. Lid surgery 4. Gold weight	5. Tarsorrhaphy 6. Moisture chamber eyewear

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long hours and from reading comfortably. During the spring and summer, she suffers from seasonal allergies, mainly rhinitis, for which she takes an oral antihistamine. The patient states she is mildly depressed and feels she cannot go on with her job because of her severe ocular discomfort.

Findings on examination are corrected distance visual acuity, 20/20 OU; 1+ lissamine green staining of the temporal, nasal, and palpebral conjunctiva; no fluorescein staining; TBUT, 7 to 8 seconds OU; 1+ MGD; tear osmolarity, 304/315 mOsm/L OD/OS; and positive MMP-9 assay OU.

Discussion

DR FARID: A diagnosis of DED is made on the basis of the patient's history and findings from the ophthalmic examination: DED-related symptoms, low aqueous tear production, and inflammation. The tear film osmolarity in the left eye also exceeds the diagnostic cutoff for DED, which is > 308 mOsm/L, and she has an inter-eye difference > 10 mOsm/L, which is considered suggestive of DED.[17]

The pathophysiologic pathway leading to and perpetuating DED through a vicious cycle can be initiated by a variety of triggers that act by causing ocular surface stress/irritation, inflammation, or tear deficiency/instability **(Figure 3)**. The patient in this case has features representing each of these mechanisms, and elimination or minimization of modifiable offending factors should be part of the strategy for managing her DED.

Considering that oral antihistamines can cause ocular dryness and because the patient's seasonal allergies manifested predominantly with rhinitis, she was switched to a nasal corticosteroid. She was not bothered by allergic conjunctivitis, but was told that she could be treated with a topical ophthalmic antihistamine/mast cell stabilizer if she developed significant ocular itching.

As an immunologically mediated inflammatory disease, allergy can also trigger or exacerbate dry eye. A study by Vehof and colleagues undertaken to identify predictors for the disconnect between signs and symptoms of DED found

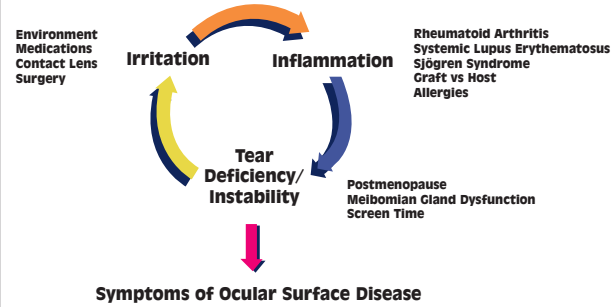

Figure 3. Dry eye disease can be triggered by multiple endogenous and exogenous factors that act through 3 basic mechanisms that interact with one another in a vicious cycle that perpetuates the condition

Image courtesy of Mark S. Milner, MD

THE CANADIAN CONSENSUS ON THE MANAGEMENT OF DYSFUNCTIONAL TEAR SYNDROME

Guillermo Rocha, MD, FRCSC

In 2009, a Canadian consensus panel developed a dysfunctional tear syndrome (DTS) diagnostic and treatment algorithm intended for use by comprehensive ophthalmologists **(Figure)**.[1] Because patient symptoms are a consideration for dry eye disease (DED) diagnosis and when evaluating response to treatment, the panel also developed the Canadian Dry Eye Assessment tool to provide clinicians with a simple questionnaire for identifying and following DED-related symptoms.[1]

According to the algorithm, the initial diagnostic evaluation incorporates the questionnaire, additional history taking about medications and medical problems, and an anterior segment examination for DED signs.[1] Patients diagnosed with DTS on the basis of the findings from the screening steps are categorized by severity into 3 groups, but the algorithm also includes a separate diagnostic category for lid disease/rosacea. The recommendations for treatment of DTS are severity based and represent a stepwise approach that begins with conservative measures and adds on when necessary.

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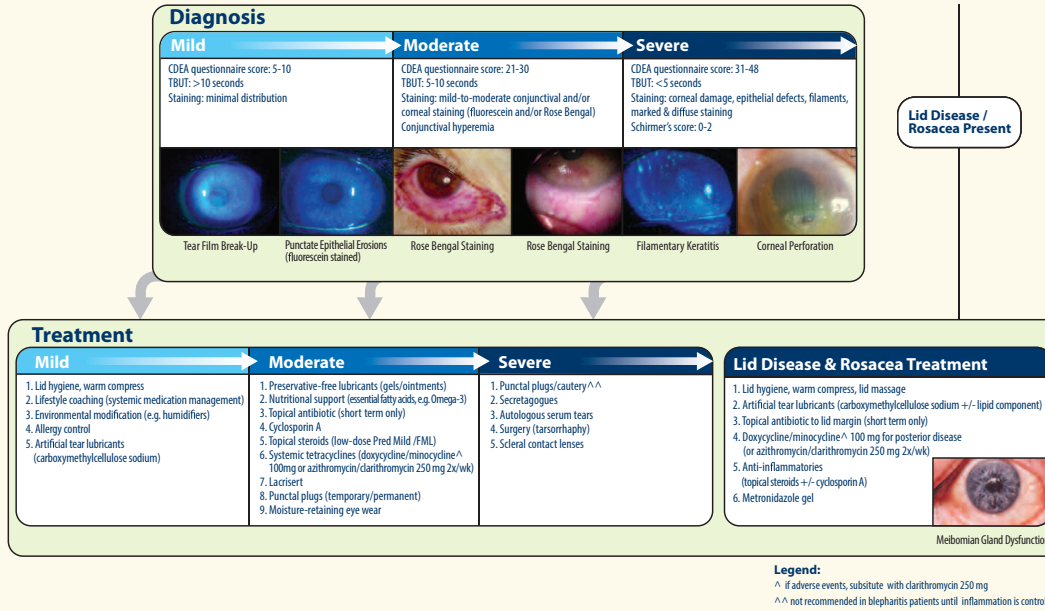

Figure. The Canadian Consensus Panel diagnostic and treatment algorithm

Abbreviations: CDEA, Canadian Dry Eye Assessment; TBUT, tear break-up time.

Reprinted from *Canadian Journal of Ophthalmology*, 44, Jackson WB, Management of dysfunctional tear syndrome: a Canadian consensus, 385-394, Copyright 2009, with permission from Elsevier.

that allergy and use of antihistamines were significantly associated with having greater symptoms than signs.[8] According to that evidence, it seems logical that this patient may also find relief from her severe DED symptoms using local therapy rather than a systemic antihistamine to control her allergy. As reported by Vehof and colleagues, other significant predictors of having greater symptoms than signs were chronic pain syndrome, depression, atopic disease, antidepressant use, and lower self-perceived health. Older age, Sjögren syndrome, and graft-versus-host disease were significant predictors of signs being worse than symptoms.

The patient was also instructed to use nonpreserved artificial tears and was started on a topical anti-inflammatory medication. Because she was so symptomatic, I chose lifitegrast, which has been shown in clinical trials to be associated with significantly greater improvement in symptoms compared with placebo as early as day 14.[18,19] A short course of a topical corticosteroid can also be considered for rapid control of DED-related inflammation and symptoms.[20] The patient was educated about using warm compresses to treat her MGD.

DR YEU: Dr Ayres, is there anything else you would do to control seasonal allergies in a patient with DED who is using an oral antihistamine?

DR AYRES: It is important to control allergy-related inflammation because it can exacerbate DED. If a patient has allergic conjunctivitis, I like to use a topical dual-acting antihistamine/mast cell stabilizer or cromolyn sodium, which is a mast cell stabilizer.

DR MILNER: It is important to distinguish seasonal allergies, which are a type I immunoglobulin E–mediated disease, from atopic conditions that are type I and type IV immunoglobulin E– and T cell–mediated disorders. Therefore, I always ask patients if they have a personal or family history of asthma or eczema. If a patient has atopic disease, starting a T-cell immunomodulator such as lifitegrast or cyclosporine will help with the atopic condition, in addition

to treating the signs and symptoms of DED. A large observational study found benefit of topical cyclosporine for treatment of type IV ocular allergies.[21] Although there are no reports on the use of lifitegrast in atopic disease, the presumption is it would work well because it suppresses T-cell activation. Anecdotally, both cyclosporine and lifitegrast have been a benefit for my atopic patients.

DR YEU: We should also keep in mind that nasal corticosteroids can lead to intraocular pressure elevation.[22] Therefore, a nasal antihistamine may be a better choice for controlling rhinitis. Oral montelukast, which is a leukotriene receptor antagonist, is another option that is particularly helpful for controlling atopic disease or allergic rhinitis, without causing ocular dryness.[23-25]

DR ROCHA: Minimizing allergen exposure is also important, and using artificial tears is helpful for diluting allergens on the ocular surface as well as for the dry eye. I recommend products that are nonpreserved or that contain a low concentration of a preservative. Keeping the drops in the refrigerator seems to be particularly helpful for providing symptomatic relief.

Case Conclusion

At a 2-month follow-up visit, the patient's symptoms were improved, she had less tearing, and the MMP-9 assay was negative OU. The patient said she was taking more frequent breaks while at work, but she still had some "rough days".

To optimize control, she was prescribed loteprednol as a rescue medication to use for controlling symptoms on "rough days". To optimize her lipid layer and tear film, she had thermal pulsation treatment and started omega-3 fatty acid supplementation.

DR AYRES: Ophthalmologists are reluctant to use corticosteroids for long-term management of DED, but I think they are a reasonable and valuable option when used intermittently in short bursts as needed to control breakthrough symptoms.

CASE 2: A PATIENT WITH DRY EYE DISEASE AND GLAUCOMA

From the Files of Guillermo Rocha, MD, FRCSC

An 85-year-old female presents with a 3- to 4-year history of blurry vision and itchy eyes that she says feel "thick". The woman states that her glasses do not work, her vision fluctuates, and she has a gritty feeling and light sensitivity. She has been applying hot cloths to her eyes but has not been cleansing the lids. She has been to other physicians in the past and used various fixed-combination steroid/antibiotic medications, without success.

The patient has open-angle glaucoma OU. She is compliant with her medical treatment (fixed-combination timolol/travoprost qam) and is using an artificial tear with preservatives tid.

On examination, her lashes are thickened and she has significant periocular hyperemia and dermatitis. She has inferior superficial punctate keratopathy 1+ and marked MGD; osmolarity is 296/297 mOsm/L OD/OS; and MMP-9 is negative OU. The tear meniscus is borderline abnormal. Noninvasive TBUT is < 5 seconds OU ***(Figure 4)****. Meibography shows gland dropout, truncation, and dilation, which is worse in the left eye* ***(Figure 5)****.*

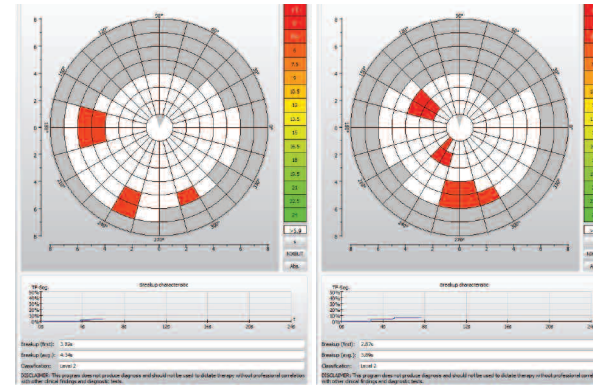

Figure 4. Noninvasive tear break-up time is lower than normal
Abbreviation: NIKBUT, noninvasive keratograph break-up time.

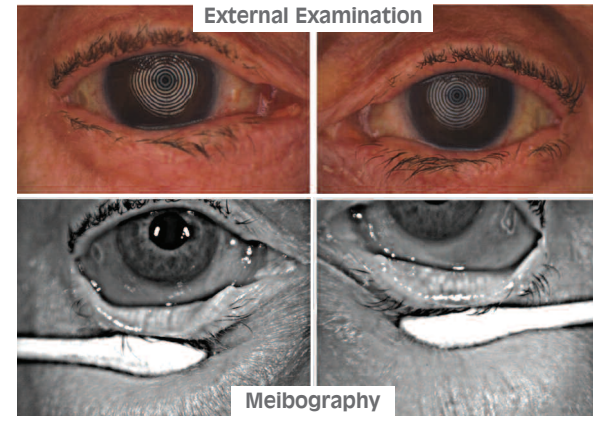

Figure 5. In vivo assessment of meibomian glands shows dilation

Discussion and Case Conclusion

DR ROCHA: The main issues in this patient were MGD and toxicity from her topical medications. Because her glaucoma was controlled with the fixed-combination product she was using, I decided to focus initially on her lid disease, which I felt had not been adequately addressed. I started her on lid hygiene, topical tea tree oil facewash, preservative-free artificial tears, an oral omega-3 fatty acid supplement, and an in-office lid treatment that delivers heat and massage. We perform in-office lid treatment as a series of 3 procedures over 1 month and assess patients for benefit after approximately 3 months.

The patient is scheduled to return for evaluation in a few months, and, depending on the findings, I will decide if I should switch her intraocular pressure–lowering medication to a preservative-free agent.

DR YEU: It was interesting that this patient had a normal osmolarity and negative MMP-9 assay. How was this information helpful to you?

DR ROCHA: Although I believe there was still an inflammatory component to her condition despite the negative MMP-9 assay, the information guided my decision to focus initial intervention on the lid disease. The patient was responding well to her current treatment for glaucoma, and I wanted to avoid making too many changes at one time.

DR MILNER: On the basis of the patient's other signs and symptoms, including the dermatitis around her eyes, I would also suspect inflammation was present. We have to remember that our diagnostic tests can have false-negative results, and when we decide on treatment, we should take into account how the patient looks and feels.

DR FARID: Switching to preservative-free glaucoma medications is essential in these patients who suffer worsened ocular surface problems related to toxicity. Additionally, with the progress and success of MIGS (minimally invasive glaucoma surgery) procedures for IOP control, an earlier surgical approach to managing IOP may be of value in such cases.

DR AYRES: I believe this case is a good illustration of how ocular surface irritation and inflammation can be caused by topical medication use and of how these problems might be treated by addressing the underlying cause, that is, modifying the medication regimen, rather than by adding medication to treat the signs and symptoms. More is not necessarily better.

CASE 3: A PATIENT WITH DRY EYE DISEASE AND ANTERIOR BASEMENT MEMBRANE DYSTROPHY

From the Files of Brandon D. Ayres, MD

A 74-year-old female who recently underwent cataract surgery with toric IOL implantation in the left eye presents complaining of difficulty seeing, chronic irritation, and foreign body sensation. On examination of the left eye, uncorrected visual acuity (UCVA) is 20/100 and manifest refraction is -1.00 + 1.00 x 25, but it is difficult to get an accurate refraction because the measurement is highly variable. Corrected distance visual acuity is 20/40. The patient states that she wants the IOL exchanged so she can have better vision.

*Slit-lamp examination shows a rapid tear break-up time, significant central and paracentral anterior basement membrane dystrophy (ABMD), and mild inferior SPK (superficial punctate keratitis **(Figure 6)**. The toric IOL is aligned at 165°, the inferior optic is out of the bag, and there is mild capsular phimosis. The posterior segment examination is normal. MMP-9 assay is positive OU, and topography shows irregular astigmatism OU **(Figure 6)**, although the patient is not complaining about vision in her right eye.*

Discussion

DR YEU: How vital is topography to the cataract surgeon for diagnosing DED?

DR AYRES: It is critical, and the Placido rings are particularly informative. They should be round and complete, not wavy and broken as they are in this patient's image **(Figure 6)**. I think the Placido image also provides another good tangible tool for educating patients about their condition. I explain that the rings should be round, and it is clearly evident to patients when they are not.

DR ROCHA: Cataract surgeons often trust and rely only on the keratometry data generated by the optical biometer, but I get a topography on every patient. Our technicians are trained to identify a very irregular topography and repeat the imaging in that situation after instilling artificial tears. If the irregularity is improved, we are prompted to look for and treat DED.

DR YEU: Considering that the ABMD is bilateral in this case, it seems likely that the condition was present in the left eye before the cataract surgery. The diagnosis of ABMD can be overlooked because it can be subtle enough to be missed on slit-lamp examination alone, or it may be subclinical, but

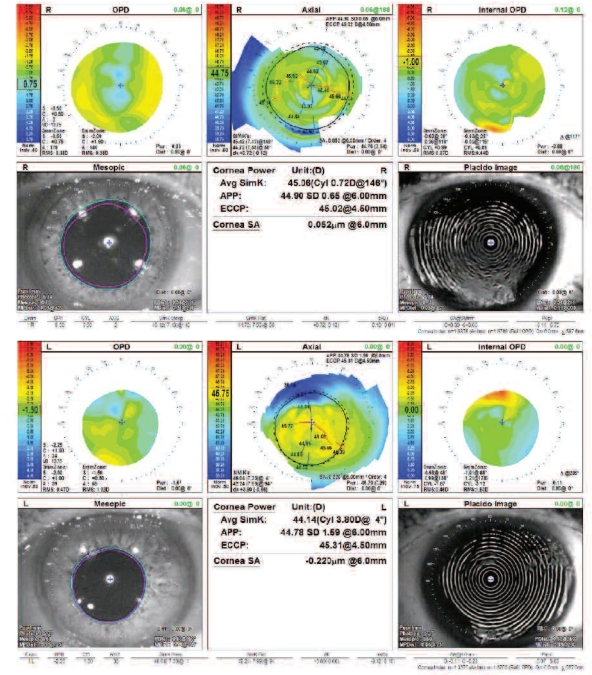

Figure 6. Pretreatment topography of the right and left eyes. Significant irregular astigmatism can be seen on the axial scans as well as the Placido disc images. No clear axis astigmatism can be determined because of the irregular nature of the corneal surface and anterior basement membrane changes.

Abbreviations: APP, average pupil power; ECCP, effective central corneal power; OPD, optical path difference; SA, spherical aberration.

ABMD can worsen after cataract surgery with provocation by intraoperative abrasion or drop toxicity.

DR MILNER: I teach residents that from a corneal standpoint, ABMD is 1 of the 2 most common diagnoses that explain decreased vision of unknown etiology; the other is tear film dysfunction. Clinicians often miss ABMD, and the way to identify it is by looking for negative staining with fluorescein and a cobalt blue light and by looking at the topography for irregular astigmatism. The diagnosis of ABMD can then be confirmed if vision improves with placement of a rigid contact lens

DR YEU: Dr Ayres, how did you manage this patient?

DR AYRES: I planned to treat the ABMD by performing a superficial keratectomy. Once the topography had stabilized after the procedure, I would be able to determine if the patient needed to have the toric IOL exchanged. Before doing the superficial keratectomy, however, I had to treat the DED to improve the condition of the ocular surface. The patient needed treatment for inflammation. I think either cyclosporine or lifitegrast would have been effective, but I chose lifitegrast in combination with a topical corticosteroid to quickly rehabilitate the ocular surface. I also told the patient to use preservative-free artificial tears in both eyes.

Case Conclusion

*Six weeks after starting treatment with lifitegrast, the ocular surface was improved, UCVA improved to 20/70, and ABMD changes were still present **(Figure 7)**. Superficial keratectomy was performed to remove the central folds in the corneal epithelium. After 2 months, the ocular surface was further improved and MMP-9 was negative. The topography was normalized and showed very little cylinder **(Figure 7)**.*

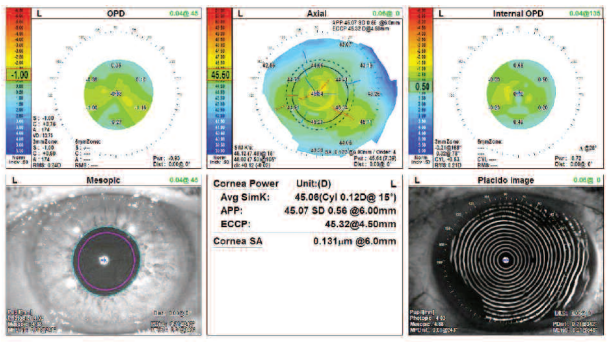

Figure 7. Topographic image of the left eye after optimization of the ocular surface and 4 weeks after superficial keratectomy to removal anterior basement membrane changes to the cornea. Most notable is the reduction in astigmatism on the axial scans and significant improvement in the quality of the Placido disc images.

Abbreviations: APP, average pupil power; ECCP, effective central corneal power; OPD, optical path difference; SA, spherical aberration.

The patient subsequently underwent surgery that included removal of some of the capsular phimosis and exchange of the toric IOL for a spherical implant, as guided by the preoperative topography and intraoperative aberrometry. She was left with -0.25 D sphere, 20/25 UCVA, and 20/20 best corrected visual acuity. Although the patient still complained of some mild tearing, she was very happy.

TAKE-HOME POINTS

Dry eye disease occurs in patients of all ages, and its prevalence is increasing.

It is critical to identify and treat DED because it affects quality of life, vision, and outcomes of cataract and refractive surgery.

Dry eye disease is a multifactorial disease, and each patient is unique. Isolate the risk factors and target treatment to the individual.

Do not overlook systemic diseases or medications that may be causing or exacerbating DED.

Newer diagnostic tests can be a useful adjunct in the comprehensive evaluation of patients suspected to have DED.

Although there are multiple inciting factors for DED, they all lead to inflammation, and it is important to treat inflammation early because it drives the pathogenic vicious cycle, leading to disease progression.

Patient education about DED is important for improving compliance with treatment recommendations and optimizing outcomes.

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1. Which of the following statements about the prevalence of DED is FALSE?
   A. It is increasing in children and teens
   B. It is higher in women than in men
   C. It increases with age
   D. It is higher in blacks than in Asians and whites

2. A positive result from the MMP-9 assay is diagnostic of:
   A. Central neuropathy
   B. Anterior basement membrane dystrophy
   C. Inflammation
   D. Stem cell dysfunction

3. Diagnosis-based recommendations for management of DED have been developed by the:
   A. National Eye Institute/National Institutes of Health Industry Workshop
   B. CEDARS Dysfunctional Tear Syndrome Panel
   C. Delphi Consensus Group
   D. DEWS 2007

4. The DEWS II DED management algorithm lists treatments by:
   A. DED type (aqueous deficient, evaporative, mixed)
   B. DED severity
   C. DED type and severity
   D. Therapeutic class/Mechanism of action

5. A diagnosis of DED should be considered when the tear film osmolarity test is:
   A. > 288 mOsm/L
   B. > 298 mOsm/L
   C. > 308 mOsm/L
   D. < 5 mOsm/L difference between eyes

6. Signs of conjunctival damage associated with DED will be detected earliest using:
   A. Fluorescein
   B. Indocyanine green
   C. Lissamine green
   D. Phenol red

7. A patient presents for cataract surgery in the right eye. Tear film osmolarity is 316 mOsm/L, MMP-9 is positive, Schirmer score is 11 mm, there is diffuse 1 to 2+ stain within the central and inferior cornea, and the patient has 1+ MGD. What would you use to rapidly rehabilitate the ocular surface so the patient is ready for surgery?
   A. Artificial tears and topical loteprednol
   B. Autologous serum tears
   C. Punctal plugs and cyclosporine
   D. Topical loteprednol and topical bromfenac

8. In a study of patients with DED, Vehof and colleagues reported _____ was predictive of having greater symptoms than signs.
   A. *Demodex* infestation
   B. History of allergy
   C. Older age
   D. Sjögren syndrome

9. Which agent has NOT been implicated as a causative or exacerbating factor for DED?
   A. Oral antihistamines
   B. Preservative-containing artificial tears
   C. Tea tree oil lid cleansers
   D. Topical glaucoma medications

10. In clinical trials, patients treated with lifitegrast achieved significantly greater symptom improvement than placebo-treated controls by treatment day ___.
    A. 7
    B. 14
    C. 21
    D. 28