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THE ART AND SCIENCE

OF TREATING OCULAR SURFACE DISEASE

Minimizing Patients' Discomfort and Maximizing Outcomes

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THE ART AND SCIENCE OF TREATING OCULAR SURFACE DISEASE

Minimizing Patients' Discomfort and Maximizing Outcomes

We convened this panel to discuss the impact of dry eye disease on our cataract and refractive surgical patients. No matter what climate we work in or the differences in our patient populations, all ocular surgeons can benefit from learning more about how to identify, recognize, and effectively treat ocular surface disease (OSD) in both symptomatic and asymptomatic patients. Dry eye disease causes the most problems for patients after surgery. We have all seen patients with suboptimal outcomes because we failed to recognize the signs and symptoms of OSD preoperatively. Therefore, we will share cases within this discussion that we hope will educate our peers about the importance of proactively identifying and treating OSD in surgical candidates. *—P. Dee G. Stephenson, MD, moderator*

P. Dee G. Stephenson, MD, is the founder and director of Stephenson Eye Associates in Venice, Florida. Dr. Stephenson is also associate professor of ophthalmology at the University of South Florida in Tampa and president of the American College of Eye Surgeons. She serves as a consultant to Allergan and Bausch + Lomb. Dr. Stephenson may be reached at (941) 485-1121; eyedrdee@aol.com.

Sheri Rowen, MD, FACS, Physician CEO, is the founder of Rowen Vision and Cosmetic Center, and has served as a clinical instructor at Johns Hopkins Hospital as well as a clinical assistant professor at the University of Maryland. She is now with NVision Centers in Newport Beach, California, and is an in-house consultant for Alphaeon and Strathspey Crown. She serves as a consultant to Allergan, Bausch + Lomb, NovaBay, PRN, and Shire. Dr. Rowen may be reached at (410) 402-0122; srowen10@gmail.com.

Alice T. Epitropoulos, MD, is cofounder and owner of The Eye Center of Columbus and partner at Ophthalmic Surgeons & Consultants of Ohio. Dr. Epitropoulos is also clinical assistant professor at The Ohio State University Department of Ophthalmology. She serves as a consultant to Allergan, Bausch + Lomb, NovaBay, PRN, Shire, TearLab and TearScience. Dr. Epitropoulos may be reached at (614) 221-7464; aepitrop@columbus.rr.com.

Neda Shamie, MD, is associate professor of ophthalmology at the University of Southern California (USC) Eye Institute, Keck School of Medicine at USC; medical director at the USC Eye Center-Beverly Hills; and medical director at Tissue Banks International. She is a consultant to Alcon, Allergan, Bausch + Lomb, Nicox, Shire, and Tissue Banks International. Dr. Shamie may be reached at neda.shamie@med.usc.edu.

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THE BASICS: WHERE TO START

Patient History and Diagnostics

Sheri Rowen, MD: According to recent literature, the prevalence of dry eye disease (DED) is estimated to be between 7% and 8% of the US population, which is equal to 22 to 25 million at the time of this writing.[1-4]

Alice T. Epitropoulos, MD: Yes, DED is very prevalent, and becoming more so because of the increased use of technology in our modern lifestyle.

Neda Shamie, MD: Younger patients are presenting with symptoms and signs that we used to see in much older patients. Environmental factors such as more time on tablet devices and other electronics likely has a lot to do with this increased incidence.

P. Dee G. Stephenson, MD: How should ophthalmic clinicians begin to approach the diagnosis of DED?

Dr. Rowen: A general eye care practitioner can implement certain diagnostic regimens in his or her practice that will identify DED in patients we normally may have missed. That said, the diagnosis begins with taking the proper patient history. The key understanding is that patients do not always know they have DED. If they cannot feel it or know what the signs and symptoms of dry eye are, they most likely do not know they have it. Therefore, the first step is to give every patient a questionnaire about ocular signs and symptoms when they arrive in the office (Figure 1). This questionnaire should be front and center in the patient's chart when the surgeon walks in to meet the patient. If the answers to that questionnaire add up to a positive number, we know that the patient is exhibiting some classic symptoms of DED.

Dr. Epitropoulos: Having this questionnaire helps guide our technicians as to when to perform point-of-care tests. If the technician sees that the patient's score is at a certain level, he or she is trained to automatically test the patient's tear osmolarity, matrix metalloproteinase 9 (MMP-9), and/or meibography. These parameters also ease patient flow and ensure no patient is overlooked.

Dr. Stephenson: One of the most important questions to ask patients is, "Are you experiencing blurry vision?" The No. 1 cause of blurry vision is refractive error. The second one is DED.

Dr. Rowen: If a practice does not have all of the diagnostic tools we are discussing, then I find that using fluorescein and lissamine green staining dipped in plain balanced salt solution with no anesthetic works well to identify ocular surface staining and gauge the tear breakup time (TBUT). This is a basic diagnostic method that every preoperative workup should include if an office lacks advanced diagnostic tests. If this protocol is not part of the routine workup, however, it is a missed opportunity, because once a patient is dilated and anesthetized, they cannot blink normally, and we can no longer tell what that ocular surface truly looks like. It is best for the technician to check vision, take out the strip, and alert the doctor if he or she sees anything abnormal. Any staining is abnormal, so do not forget to look for the line of green lissamine stain on the dry lid margin.

DRY EYE QUESTIONNAIRE (DEQ-5) (A)

1. Eye discomfort
2. Intensity
3. Eye dryness (how often)
4. Eye dryness (how intense)
5. Watery Eyes (how often)

Graded on frequency scale from 1 to 5.
Below 7 does not meet criteria for test.

DED SYMPTOM CHECKLIST (B)

	OD	OS
Fluctuation in vision	❑	❑
Contact lens discomfort	❑	❑
Light sensitivity	❑	❑
Watery eyes	❑	❑
Tired Eyes	❑	❑
Redness	❑	❑
Burning	❑	❑
Itching	❑	❑
Feeling of sand or grit	❑	❑
Dry	❑	❑

TEAR OSMOLARITY DATA CHEAT SHEET (C)

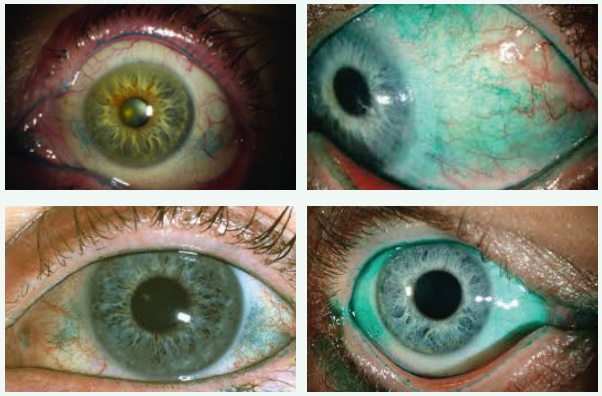
280-299 NORMAL	320-339 MODERATE
300-319 MILD	340-400 SEVERE

Figure 1. Dry eye questionnaire (A), DED symptom checklist (B), and TearLab cheat sheet (C) may be used by technicians to screen for DED.

Dr. Stephenson: Absolutely. I find lissamine green (Figure 2) extremely helpful, sometimes more so than fluorescein. TBUT is also a very useful tool.

Dr. Epitropoulos: I agree. I evaluate the lid margin, the quality of the tear film, and check for corneal staining in all my patients. This should be a part of every ophthalmic examination, and is a tried-and-true method for identifying DED and meibomian gland disease (MGD) in the absence of point-of-care testing. We will not miss many patients that way.

Dr. Shamie: Undoubtedly, having access to advanced diagnostic tests that help us validate our clinical acumen and findings supports our discussion points with our patients. In turn, this validation can help impact our patients' compliance with the treatment regimens we prescribe. Nonetheless, an observant clinician can best ascertain the staining pattern on the conjunctiva produced with lissamine green, the TBUT highlighted with fluorescein in the tear film, and the general quality of the tear film. The tear film's ecosystem has great complexity, and treating it successfully necessitates all the tools available to us, starting with the proper diagnostic questionnaire, our



(Courtesy of P. Dee G. Stephenson, MD)

Figure 2. Lissamine green is used to identify DED and MGD.

own clinical acumen and diagnostic skills, and the support of advanced technology such as point-of-care testing.

Dr. Rowen: An important next step is evaluating the tear film and not missing the meibomian glands. The gland architecture and contents will reveal the significant cause in a vast majority of cases.

Dr. Stephenson: I still look at the TBUT and the lid margins—these tell me a lot of information. My technician has already collected the patient's questionnaire, and if the score is 7 or higher, then he or she administers the TearLab osmolarity test (TearLab). This arms me with information before I enter the room.

Dr. Epitropoulos: I use the SPEED questionnaire, which is a validated dry eye questionnaire and does not slow down patient flow.

Dr. Rowen: I find that sometimes the questions alert the patient to recognize symptoms that they did not know were a problem.

Dr. Shamie: I look closely at the meibomian glands, the consistency of the expressed meibum, the appearance and the position of the meibomian gland orifice, and the presence of any telangiectasia at the lid margin to determine to what degree MGD is a contributing factor to DED. Often, MGD is present in dry eyes, but we must seek out the symptoms related to the unstable tear film associated with MGD and the inflammation on the ocular surface. Patients with MGD tend to complain of ocular burning and discomfort upon waking, as well as unstable and fluctuating vision. These symptoms are especially important in our surgical patients, as MGD can impact our surgical planning and, ultimately, the outcome. The Prospective Health Assessment of Cataract Patients Ocular Surface (PHACO) study by Trattler et al[5] sought to evaluate the prevalence of dry eyes in 136 patients (272 eyes) scheduled for cataract surgery. Of these eyes, 63% had a TBUT of less than 5 seconds, which suggests a very unstable tear film, and 77% had corneal staining, whereas 50% had central corneal staining (Figure 3).

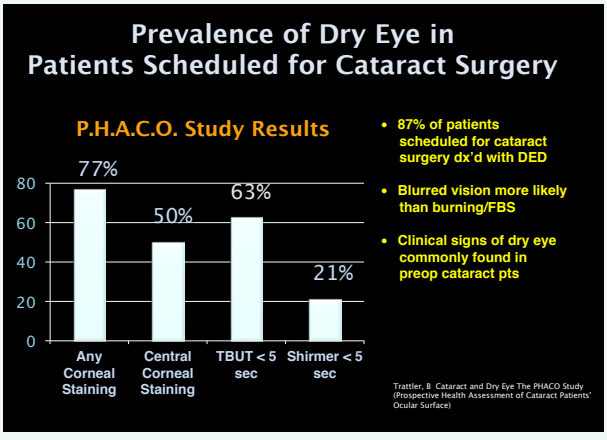
Dr. Epitropoulos: I think it is important for surgeons to remember that the prevalence study[1-4] concluded that 43% of all patients who have DED are asymptomatic. Therefore, taking a complete patient history and ophthalmic evaluation is important, including systemic medications, computer usage, an eyelid assessment, and examining the meibomian gland structure using a pipe light if the clinic does not have meibography, such as with the LipiView II (TearScience). Also, assessing for Sjögren syndrome has become easier with the Sjö test (Bausch + Lomb), which has 78% specificity and 89% sensitivity.[6]

Dr. Rowen: Ideally, surgeons who want to enhance their ability to diagnose DED should purchase a device that tests tear osmolarity, and they can order the disposable tests for assessing MMP-9 (InflammaDry [RPS]) (Figure 4). Likewise, a LipiView interferometer helps to see the form and structure of the meibomian glands. When patients can view images of their own glands with the LipiView, they realize what a problem they have and are willing to comply with their treatment. All of these tests are markers, and we have to combine their data to make a proper diagnosis. With the MMP-9 test, for example, not everybody who has inflammation will test positive. We must use these test results with our common sense as practitioners.

When Signs and Symptoms Do Not Match, and Looking for Pathologic Conditions

Dr. Stephenson: I agree that observation is key. For example, patients with rosacea and *Demodex* and debris collerettes on their lashes (Figure 5) are not always older; many are fairly young, with loss of lashes and symptoms of itching and erythema.

Dr. Shamie: Determining the presence of pathologic conjunctival chalasis (Figure 6) is also critical, as significant conjunctival redundancy can collapse the inferior forniceal space and hinder the tear reservoir. Additionally, the redundant conjunctiva can rub against the cornea with each blink and lead to localized epitheliopathy and discomfort. The inferior staining of a cornea in the absence of lagophthalmous is highly suspicious for



(Courtesy of Alice T. Epitropoulos, MD)

Figure 3. The PHACO study[5] evaluated the prevalence of DED in patients scheduled for cataract surgery.

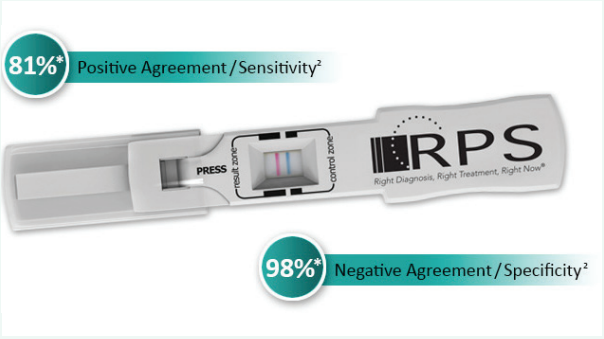


Figure 4. Surgeons who want to enhance their ability to diagnose DED may purchase a device such as InflammaDry.

conjunctival chalasis. Optimizing the tear film conservatively can help, but the definitive treatment may be a surgical resection of the redundancy and reinforcement of the conjunctival laxity to the sclera with the use of amniotic membrane grafting.

Dr. Stephenson: Conjuntival chalasis is something I think many of us miss when we are first examining a patient for DED. We all have patients that do their treatment, have improved tear osmolarity, improved meibomian gland function, etc, yet they still complain of foreign body sensation or burning. We should re-evaluate the conjunctiva and the inferior corneal staining to rule out conjuntival chalasis. A small amount of cautery to shrink this will improve these patients and may put off an amniotic graft surgery and, more importantly, relieve the patient's symptoms.

Dr. Rowen: Patient flow is standardized in our practice for dry eye evaluations. First, we administer the tear osmolarity test and follow that with InflammaDry and then LipiView imaging.

Dr. Stephenson: As valuable as these point-of-care tests are, looking and listening are still the art of our medicine. I believe that performing a basic proactive assessment of ocular surface disease (OSD) is what will lead to better outcomes.

(Courtesy of Neda Shamie, MD)

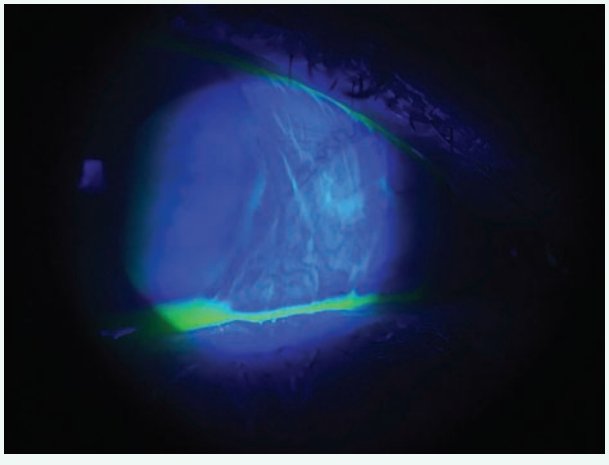
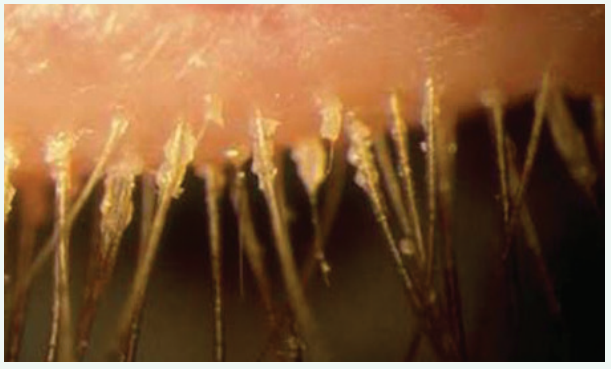


Figure 6. Determining the presence of pathologic conjunctival chalasis is critical.



(Courtesy of P. Dee G. Stephenson, MD)

Figure 5. Crusty lids and lashes are a symptom of blepharitis.

Dr. Rowen: I agree. Also, one of the reasons that signs and symptoms do not match DED is because it becomes a neuropathy, wherein patients lose the sensation of the symptoms.[7] In addition, any refractive surgery that has caused damage to the nerves will contribute to the progression of DED, if not managed responsibly.

Dr. Stephenson: It is a very important part of the intake to ask all patients if they have undergone previous ocular procedures or had previous inflammation. This information can affect the treatment plan.

PREFERRED TREATMENT OPTIONS FOR OSD

Dr. Rowen: Today's ophthalmologists are busier than ever with surgeries, and ODs are taking over a lot of the primary care evaluations in some of the busier practices. Surgeons who treat referred cataract patients might go right to the cataract and bypass an examination of the lids, cornea, etc. We have to be looking for epithelial basement membrane dystrophy and Fuch dystrophy, in addition to basic DED, MGD, and blepharitis.

Dr. Shamie: We simply cannot look past the tear film and the cornea when planning for cataract surgery. Our reliance on accurate IOL measurements, especially when considering implanting premium IOLs, is founded on the assumption that the corneal measurements are accurate. When I have confirmed the presence of an abnormal tear film via topography and the diagnostic tools mentioned previously, I first educate the patient about the need to delay surgery, then aggressively treat the eye with steroids, topical cyclosporine (Restasis; Allergan), and sometimes a self-retained amniotic membrane graft (to speed up the recovery). Thereafter I have the patient return at a specified date for remeasurements. I have seen a shift of up to 2.00 D in an eye's required IOL power, and a significant shift in the toric calculation by optimizing the ocular surface in this manner.

Dr. Stephenson: It is very important to describe the tear quality: Is the tear film foamy? Does it have debris, mucoid strands, or have an increase in evaporation?

Dr. Epitropoulos: It is also important to evaluate the quality of the tear film via TBUT and look for debris in the tear film

along with the health of the meibomian glands. MGD is a progressive disease that may lead to atrophy and loss of function if not treated. Meibography is an excellent tool to identify these patients with evaporative DED and educate them, because we can show them what their glands look like, versus what they should look like. If we can get to these patients before they have severe damage, they are likely to respond better than if we wait until the glands are atrophied and nonfunctional.

Dr. Rowen: I agree. The biggest game changer in my patients' acceptance for treatment is the ability to see the state of their meibomian glands. A 2012 study[8] showed that 86% of DED patients have meibomian gland involvement, whether from obstruction or tear composition/dysfunction, and we corroborate that in practice as a highly significant percentage of patients have MGD.

Dr. Epitropoulos: Treatment of the ocular surface depends on the severity and type of DED (evaporative vs volume deficient). A typical regimen for my patients with OSD prior to cataract surgery includes the use of re-esterified omega-3 essential fatty acids (EFAs), topical cyclosporine, and Avenova (NovaBay) in conjunction with LipiFlow thermal pulsation treatment (TearScience) to treat MGD. Lipiflow remains the only FDA-cleared treatment for evaporative DED, and this combination has become the most effective therapy in my experience for this condition. I use Avenova in patients with MGD and blepharitis and before cataract surgery.

I also like the Bruder microwavable hot mask (Bruder Healthcare). It stays hot longer than warming a washcloth. To improve the quality of tear film and subsequently preoperative keratometry, I recommend patients take re-esterified omega-3 fish oil supplementation. A recent study[9] on the effect of oral re-esterified omega-3 supplementation on DED, the results of which were presented at the 2015 American Society of Cataract and Refractive Surgery meeting, showed that re-esterified omega-3 EFAs significantly benefitted patients with DED. We showed a significant improvement in ocular surface disease index (OSDI) symptoms scores, tear osmolarity, MMP-9, the omega-3 index, and TBUT in patients taking Physician Recommended Nutriceuticals (PRN) re-esterified omega-3 supplementation.[9] Based on the results of this study, I believe that a re-esterified fish oil supplement should be used as a primary treatment in patients with MGD and DED.

Dr. Rowen: There are only two re-esterified products available in the United States: those from PRN and Nordic Naturals. The PRN formula is the only omega-3 EFA product that has been studied in a multicentered clinical trial, where it was shown to statistically improve TBUT, OSDI scores, MMP-9, and patients' omega-3 blood index.[9]

Dr. Epitropoulos: Reducing inflammation is one of the primary goals in treating OSD. Restasis has been proven

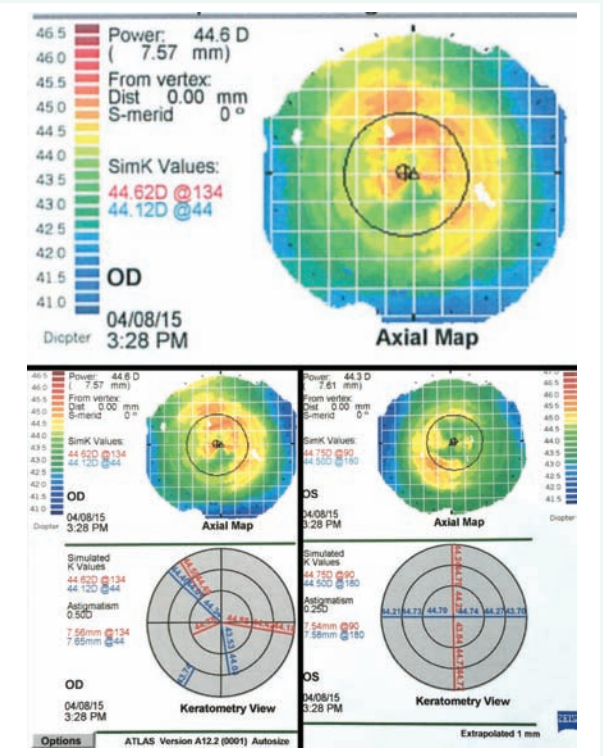


Figure 7. The patient's preoperative biometry was unreliable due to an unstable tear film, which produced poor-quality K readings and topography.

(Courtesy of Alice T. Epitropoulos, MD)

in clinical studies to increase patients' natural tear production and reduce the progression of DED.[10] To help improve patients' compliance with Restasis, many physicians pair it with a corticosteroid that is friendly to the ocular surface. The corticosteroid rapidly reduces ocular surface inflammation and works synergistically with the cyclosporine.

Dr. Stephenson: I also think it is important to tell patients that Restasis (to improve production of one's own natural tears) and PRN (to improve OSDI and symptoms) does not work overnight. It can take up to several months. The patient needs to understand the degree to which this treatment is effective.

Dr. Rowen: Optimizing the ocular surface is critical for patients who want multifocal implants. And this surface treatment needs to be done, even if surgery is delayed. If the surface does not have an excellent resolution of dry eye, consider changing the lens option to an accommodating lens instead of a multifocal implant.

Avenova is a new treatment utilizing pure hypochlorous acid for bacteria control on the lid margins and combined with BlephEx (BlephEx) treatment offers another way to counteract blepharitis. LipiFlow offers the full necessary treatment of heating and expression, and other devices such as intense pulsed light and MiBo Thermoflow (MiBo Medical Group) offer warmth with manual expression done by ophthalmic personnel.

Dr. Epitropoulos: I agree. We have to continuously educate our patients that DED is the root of what causes many of them to be unhappy or dissatisfied with their results after cataract surgery. If patients understand this, they will be more motivated to cooperate with a DED protocol and will understand the benefits of delaying surgery.

HOW DOES DED IMPACT SURGICAL OUTCOMES?

Dr. Epitropoulos: The consequences of not treating DED are myriad. A compromised ocular surface can affect topography and keratometric readings. It can delay healing. Lid margin disease and bacterial overgrowth can increase the risk of endophthalmitis. We have already mentioned how DED can cause our patients to be unhappy with their surgical outcomes. I took part in a recent study[11] that showed that patients with hyperosmolarity (based on TearLab testing) had greater variability in their K readings and IOL calculations compared to those who had normal osmolarity. The increased risk of refractive error postoperatively in hyperosmolar patients is one of the more important reasons why cataract surgeons should be looking for DED.

Dr. Stephenson: I also believe that surgeons should be performing topography preoperatively, and repeating it more than once. There is such a learning curve with topography in the presence of DED.

Dr. Epitropoulos: All of these tests—the SPEED questionnaire, corneal staining, TBUT, keratometry, topography, etc—need to be repeated after the patient has been following a therapeutic regimen for the prescribed amount of time, and before he or she is scheduled for surgery. The ocular surface should show a marked improvement in the tear film, and preoperative measurements demonstrate stability before proceeding with cataract surgery. The one test that does not need to be repeated is meibography. Furthermore, many of us will use the ORA System (Alcon) on our previous refractive or premium IOL surgical patients. Here again, a healthy ocular surface provides the best ORA measurements.

Dr. Stephenson: I usually add a viscoelastic to the cornea to keep it as moist as possible before taking the ORA measurements. However, the ophthalmic viscosurgical device must be removed completely from the cornea and out of the cul-de-sac before you take a measurement.

OSD CASE STUDIES

Case No. 1: Presented by Alice T. Epitropoulos, MD

A 67-year-old woman was referred to me for cataract evaluation. She presented with cataracts, OSD, symptoms of discomfort, and complaints of reduced vision. She expressed a desire to reduce her dependence on corrective lenses.

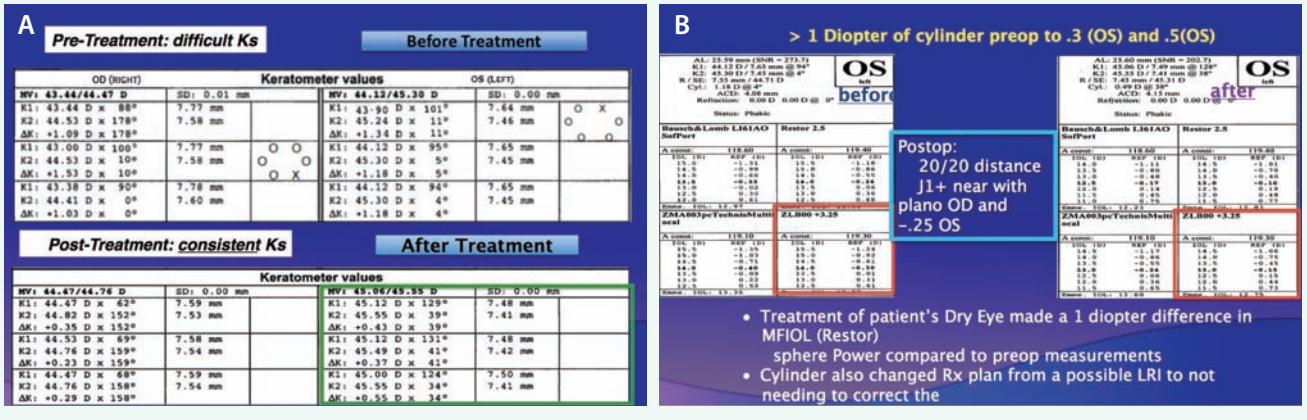
The patient's preoperative biometry was unreliable due to an unstable tear film, which produced poor-quality K readings and topography (Figure 7).

I decided to delay this patient's cataract surgery until we could improve the health of her ocular surface. I prescribed oral supplementation of re-esterified omega-3 fatty acids, a single 12-minute thermal pulsation treatment, topical cyclosporine preceeded by a topical corticosteroid, and the use of Avenova lid cleanser twice a day. I asked the patient to return for evaluation in 6 weeks.

There was significant improvement in the patient's tear quality and biometry after 6 weeks of treatment (Table). Treatment of patient's DED made a 1.00 D difference in

TABLE. PATIENT'S TEAR FILM PRE- AND POSTTREATMENT

	OD Pretreatment	OS Pretreatment	OD at 6 weeks	OS at 6 weeks
SPEED test	19	19	9	9
TBUT	2 mins	1 min	8 mins	7 mins
Tear osmolarity	295	324	285	288



(Courtesy of Alice T. Epitropoulos, MD)

Figure 8. The patient's K readings changed significantly after her ocular surface was treated, changing our plan for a possible limbal relaxing incision to not needing to correct the cylinder after treatment (A). Treating the patient's DED made a 1.00 D difference in her final outcome (B).

(Courtesy of Sheri Rowen, MD)

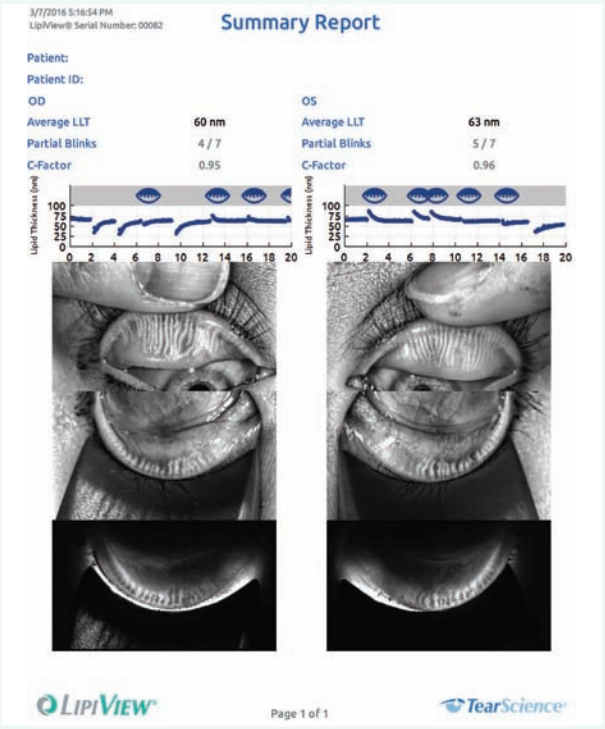


Figure 9. A 35-year-old woman's LipiView images indicating MGD.

Figure 10. A 46-year-old man's LipiView images indicating MGD.

multifocal IOL's (ReSTOR; Alcon) spherical power compared to preoperative measurements. Cylinder also changed the surgical plan from a possible limbal relaxing incision to not needing to correct the cylinder after treatment. Her visual acuity was 20/20 distance and J1+ at near uncorrected with plano OD and -0.25 D OS (Figure 8).

Case No. 2: Presented by Sheri Rowen, MD

Figures 9 and 10 show the eyes of a 35-year-old woman and a 46-year-old man, respectively. Both patients had become intolerant of contact lenses, having worn them for many years (the woman for more than 20 years, and the man for more than 30 years), and were scheduled for LASIK. When my staff and I performed a full dry eye workup, both patients were noted to have elevated tear osmolarity, punctate erosions in the cornea, and poor expression from their meibomian glands. With LipiView imaging, we noticed significant drop-out and truncation of the glands, despite their young ages.

Because of their symptoms and findings, my team and I postponed their LASIK surgeries until we could stabilize the tear film. If we had taken these patients to surgery without treating their tear films, I believe they would have experienced postoperative DED that they likely would blame on the LASIK surgery. Our protocol helped them to understand that their DED preceded LASIK and was related to their long-term use of contact lenses.

CONCLUSION

Dr. Stephenson: Patients will be satisfied if they understand that treating DED is not instantaneous, and that we may not be able to cure everything that is wrong with their eye. DED is a lifelong disease, and patients will have to learn to do their part to manage it. We can, however, get our patients to the point of ocular stability that does not put them at risk for poor surgical results. For patients scheduled for surgery, it is critical to inform them that their corneal symptoms may get worse after cataract surgery. Informed patients are much happier than uninformed ones.

Dr. Epitropoulos: Evaluating for OSD in our presurgical patients should be incorporated into our routine ophthalmic examination. DED can significantly reduce surgical predictability and can adversely affect our outcomes.

Dr. Rowen: We should work with patients to improve and maintain their visual health and comfort. We should be thinking of instituting standard procedures in our practices to recognize and treat DED at a much earlier stage for our future. ■

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