# **REVIEW/UPDATE**

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# An algorithm for the preoperative diagnosis and treatment of ocular surface disorders

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Any ocular surface disease (OSD), but most commonly, dry-eye disease (DED), can reduce visual quality and quantity and adversely affect refractive measurements before keratorefractive and phacorefractive surgeries. In addition, ocular surgery can exacerbate or induce OSD, leading to worsened vision, increased symptoms, and overall dissatisfaction postoperatively. Although most respondents of the recent annual American Society of Cataract and Refractive Surgery (ASCRS) Clinical Survey recognized the importance of DED on surgical outcomes, many were unaware of the current guidelines and most were

ry-eye disease (DED) is a common cause of patients seeking medical advice and a frequent source of blurry or fluctuating vision.<sup>1</sup> We know that patients who have DED and are considering keratorefractive surgery, in particular, laser in situ keratomileusis (LASIK), should be cautioned that these surgeries might worsen their DED or other ocular surface conditions.<sup>2</sup> DED should be treated effectively before the patient has keratorefractive or phacorefractive surgery.<sup>3</sup> DED can cause a reduced visual function and might compromise the overall results of corneal, cataract, and refractive surgery.<sup>4,5</sup> The incidence of DED and ocular surface disease (OSD) in cataract surgery candidates who are asymptomatic is higher than previously thought. In one study,<sup>6</sup> upwards not using modern diagnostic tests and advanced treatments. To address these educational gaps, the ASCRS Cornea Clinical Committee developed a new consensus-based practical diagnostic OSD algorithm to aid surgeons in efficiently diagnosing and treating visually significant OSD before any form of refractive surgery is performed. By treating OSD preoperatively, postoperative visual outcomes and patient satisfaction can be significantly improved.

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of 60% of routine cataract patients were asymptomatic, yet 50% had central corneal staining. In another study,<sup>7</sup> the incidence of OSD in patients presenting for cataract surgery was over 80%, and in those who were asymptomatic, over 50% had an abnormal tear osmolarity or matrix metalloproteinase-9 (MMP-9) level. The impact of DED and OSD on topography, biometry, keratometry, and higher-order aberrations is one of the major causes of disappointing postoperative outcomes.<sup>8,9</sup>

The annual American Society of Cataract and Refractive Surgery (ASCRS) Clinical Survey of its membership identified DED and OSD as recurring general sources of confusion. In the past few years, more than 75% of respondents were unfamiliar with the TFOS DEWS II (Tear Film &

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Ocular Surface Society Dry Eye WorkShop II)<sup>10</sup> and the Delphi Panel International Task Force recommendations.<sup>11</sup> Although only 9% were using osmolarity and 5% were using MMP-9 testing, 91% felt that mild-to-moderate DED impacts patient satisfaction in cataract and refractive surgery. In 2017, 83% of respondents indicated they would find an algorithm for ocular surface diagnostics valuable, especially in relation to refractive surgical patients. These perceived gaps in clinical practice, lack of awareness of the most current OSD tools and guidelines, and the additional complexities of managing OSD in surgical populations motivated the ASCRS Cornea Clinical Committee to undertake this novel educational effort.

There has been a rapid rise in commercially available point-of-care diagnostic tests; however, their adoption, especially with presurgical patients, has been slow. The following ASCRS Cornea Clinical Committee recommendations were created with the intent to reduce surgeon chair time via greater reliance on physician extenders, technicians, and these novel point-of-care objective tests while increasing the preoperative diagnosis of potentially visually significant OSD (VS-OSD). Although some of our recommendations might suggest nonreimbursed tests (eg, osmolarity in an asymptomatic patient), our thought is that the small cost of performing these potentially nonreimbursable point-of-care tests can be bundled into a premium intraocular lens (IOL) and/or keratorefractive surgery package.

DED advancement has historically been limited by a lack of uniformity in its definition and the inability of any single diagnostic test or set of diagnostic tests to confirm or rule out the condition. Publications such as the Cornea, External Disease and Refractive Society's dysfunctional tear syndrome (DTS),12 TFOS DEWS II,10 and the Delphi Panel DTS<sup>11</sup> brought together multiple experts to create consensus documents on recommended practices to help advance and unify the field of DED. The recommendations of our committee are in no way a difference of opinion, or competitive in nature; in fact, many of our recommendations are synthesized and adapted from the knowledge gained from these seminal publications. Unlike previous protocols and algorithms, ours is intended specifically for the perioperative refractive surgery patient. Our algorithm is based on the ASCRS Cornea Clinical Committee members' collective consensus on preferred practices. We are not suggesting that these recommendations are the new standard of care or should be rigidly adhered to in every practice. Although easily adoptable by most, our novel algorithm and questionnaire can also be easily modified and personalized to suit any practice workflow.

As a uniquely challenging yet highly critical patient encounter in the modern era, the preoperative office visit is demanding of patients, physicians, and office staff alike. As busy cataract and refractive surgeons, the ASCRS Cornea Clinical Committee members understand the increasing daily demands of a surgical ophthalmic practice and the time and energy involved for each preoperative patient visit (eg, obtaining consent, counseling, scheduling, billing, paperwork, diagnostic testing, multiple IOL and refractive options, out-of-pocket costs, etc.). Although addressing OSD proactively might add time and complexity to an already lengthy preoperative workup, its importance cannot be underestimated. Failure to do so could potentially result in a trio of adverse outcomes: (1) unsatisfactory vision (eg, refractive misses, fluctuating vision, induced higher-order abberrations); (2) new or worsened OSD symptoms (eg, foreign-body sensation, redness, pain); and (3) postoperative infection such as endophthalmitis. Our new management algorithm aims to sensibly guide the preoperative patient encounter to avoid these postoperative complications.

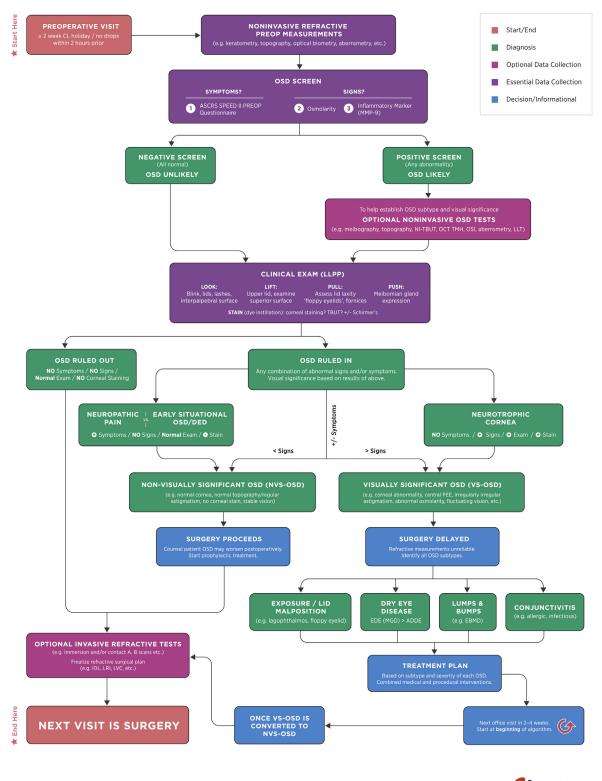
The preoperative OSD algorithm and preoperative OSD questionnaire developed by the ASCRS Cornea Clinical Committee are included as Figure 1 and Figure 2 of this article, and also were included in the polybag with this issue of the JCRS.

# CME ITEMSOVERVIEW OF THE PREOPERATIVE OSD ALGORITHM

Although any corneal or lens-based surgery today could reasonably be considered *refractive* because most patients will expect improved vision afterward, we designed our algorithm primarily for lens-based and corneal-based refractive surgeries, cataract and LASIK being the most common. These surgeries typically involve the highest visual expectations of spectacle independence, require highly precise preoperative refractive measurements, and typically also involve significant patient costs for noncovered services. Nonetheless, the general principles and methodology of the algorithm could reasonably apply to any patient encounter in which DED or OSD is suspected. Moreover, although our algorithm (Figure 1) is designed for integration into the preoperative visit (ie, the last office visit before surgery is performed), we recommend clinicians attempt to identify and treat significant OSD as early as possible, ideally at previous visits, using the same diagnostic methodology. Because preoperative refractive surgery visits already involve significant, often technician-driven, refractive and biometric testing, we created the algorithm with an emphasis and reliance on technician-performed objective noninvasive point-of-care testing, which saves the physician time, is educational for patients, and is not disruptive to the ocular surface, cornea, or tear film.

Several published algorithms exist for symptomatic DED and/or DTS in routine patients; however, to our knowledge, ours is the first presurgical-specific algorithm for diagnosing all OSDs before refractive surgery. We acknowledge that DED, in particular evaporative DED (E-DED), is the most common subtype of OSD, but many other non-DED subtypes of OSD can also have a negative impact on vision and postoperative visual outcomes. Thus, our algorithm was designed to identify any form of OSD before surgery, regardless of the presence of suggestive symptoms. Many non-DED subtypes of OSD can masquerade as DED with overlapping symptomatology; however, if the symptoms are misdiagnosed or mistreated as DED, they will likely worsen with time and from surgery, and lead to unsatisfactory postoperative vision.

# ASCRS PREOPERATIVE OSD ALGORITHM



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Figure 1. The ASCRS preoperative OSD algorithm (ADDE = aqueous-deficient dry eye; CL = contact lens; DED = dry-eye disease; EBMD = epithelial basement membrane dystrophy; EDE = evaporative dry eye; IOL = intraocular lens; LLPP = Look, Lift, Pull, Push; LLT = lipid layer thickness; LRI = limbal relaxing incisions; LVC = laser vision correction; MGD = meibomian gland dysfunction; MMP-9 = matrix metalloproteinase-9; NI-TBUT = noninvasive tear breakup time; NVS-OSD = nonvisually significant ocular surface disease; OCT = optical coherence tomography; OSD = ocular surface disease; OSI = ocular scatter index; SPEED = Standard Patient Evaluation of Eye Dryness; TBUT = tear breakup time; TMH = tear meniscus height; VS-OSD = visually significant ocular surface disease).

Symptom assessment will always be an integral part of any OSD diagnostic protocol. Unlike others, however, our algorithm proceeds even in the absence of OSD symptoms. Many patients, especially older patients with significant cataracts, either do not have OSD symptoms or do not feel compelled to report them, leading to normal results of traditional validated DED questionnaires, such as the Ocular Surface Disease Index (OSDI) or Standard Patient Evaluation of Eye Dryness (SPEED). The signs and symptoms of DED have long been known to be poorly correlated, and studies<sup>6,7</sup> have shown this disparity can be even more significant in older preoperative cataract surgical patients who are often asymptomatic despite having advanced signs of OSD. Although we believe it is important to identify and address all subtypes of OSD in each preoperative patient, not every subtype of OSD requires delaying refractive measurements and surgery. Postponing a planned surgery date can be highly disruptive and costly to patients and surgeons alike; thus, we strive to limit this course of action to only those cases of OSD that are likely to lead to adverse postoperative outcomes. Toward this goal, our algorithm introduces new terminology for classifying any OSD into two important presurgical categories: nonvisually significant OSD (NVS-OSD) and VS-OSD. Examples of NVS-OSD could include diagnoses such as early, preclinical, or situational DED; mild conjunctivochalasis with a normal tear film; nonobvious meibomian gland disease; pinguecula; and neuropathic corneal pain syndrome, among many others. Although final refractive measurements and surgery can proceed as planned, patients with NVS-OSD should be educated about their conditions and counseled about the potential for worsening after surgery. Prophylactic treatment should be initiated preoperatively and continued postoperatively to minimize the risk for OSD exacerbations.

VS-OSD, via multiple potential mechanisms, leads to reduced visual quality and potential errors in preoperative (topography, measurements keratometry, refraction, aberrometry). Any OSD that results in corneal staining or hyperosmolarity (eg, DED, meibomian gland disease [MGD], neurotrophic or exposure keratitis, etc.) and/or irregular astigmatism (eg, epithelial basement membrane dystrophy [EBMD], pterygium, Salzmann nodules, etc.) and/or increases the risk for surgical infection (eg, infectious conjunctivitis, staphylococcal blepharitis, etc.) would be deemed as VS-OSD. When VS-OSD is identified by the preoperative algorithm via the combination of symptoms, objective tests, and a physical examination, we recommend postponing surgery and delaying the final refractive measurements until it is fully treated and resolved. At each follow-up, the algorithm should be repeated from the beginning until the VS-OSD is converted to NVS-OSD, at which time the final measurements can be performed and surgery can proceed.

# CME ITEMSALGORITHM PART 1: OSD SCREEN (SIGNS AND SYMPTOMS)

## Symptoms: A Novel Preoperative OSD Questionnaire

Similar to other diagnostic protocols, ours starts with a standardized symptom questionnaire. Assessing patient

symptomatology in a systematic manner is important before any surgery. OSD is often multifactorial and the severity of symptoms is variable, depending on the environment, activity stressors, and disease severity. To our knowledge, none of the published validated DED questionnaires were created specifically with the preoperative patient in mind. Well-established questionnaires, such as the OSDI<sup>13,14</sup> and 5-Item Dry Eye Questionnaire,<sup>15</sup> which are recommended in the TFOS DEWS II DED algorithm,<sup>16</sup> as well as the SANDE (Symptom Assessment iN Dry Eye)<sup>17</sup> and SPEED questionnaires,<sup>18,19</sup> although useful for DED in a general population, do not address the specific concerns of a preoperative population. With permission from Johnson & Johnson Vision, Inc., we amended their validated SPEED questionnaire to include extra questions relevant to identifying OSD in preoperative patients. The SPEED questionnaire was shown to have a good correlation between ocular surface staining and clinical measures of meibomian gland function.<sup>19</sup> It comprises questions related to frequency and severity of eye irritation (dryness, soreness, burning, fatigue), and it assesses impairment of daily activities. The validated numerical scoring system of SPEED is useful for identifying and grading the severity of DED-related symptoms, and it was validated against the OSDI (mean scores of  $\leq 2 =$  asymptomatic, 5 = mild, 6.6 = moderate, 9.9 = severe DED.<sup>20</sup> The total score (X/28) should be tallied by a technician or other office staff and recorded at the bottom of the page for quick reference. This validated numerical scoring system has been retained in our ASCRS-modified Preoperative OSD SPEED II questionnaire, the first designed specifically for preoperative refractive surgery patients (Figure 2). In addition, we have included extra questions to help screen for other subtypes of OSD (blepharitis, allergic conjunctivitis, contact lens-related); visual significance (fluctuating vision, improvement with blinking or lubricants); and potential infection risk (styes, crusting of lashes, eyelid irritation, blepharitis). Last, because patient expectations, desire for spectacle independence, willingness to pay out-of-pocket fees for noncovered services, and self-ascribed personality type (easygoing to perfectionist) can all guide preoperative treatment decisions, we have adapted these items with permission from Dr. Steven Dell's Cataract & Refractive Lens Exchange Questionnaire.<sup>A</sup> Although our additional questions to SPEED do not have a validated scoring rubric, the number of checked red boxes can be tallied by a technician and recorded at the bottom of the page for easy reference (X/18). The higher total number of red boxes (ie, red flags) and higher total SPEED scores should raise the suspicion for VS-OSD and the likely need for a custom, multifaceted, aggressive preoperative treatment regimen.

## Signs: Objective Noninvasive Tear Testing

After the questionnaire is completed and independent of its findings, the technician can proceed with noninvasive objective testing, first for refractive and IOL measurements (eg, noncontact optical biometry, keratometry, tomography, topography, aberrometry) and second for objective



# SPEED II<sup>®</sup> PREOP OSD QUESTIONNAIRE

Dry Eye Disease is a common reason that patients visit eye doctors, and it can have an impact on surgical outcomes. Please take a moment to thoughtfully complete the questionnaire.

Patient Name:			

Date: \_\_\_\_

1. Report the **FREQUENCY** of your symptoms using the rating list below:

SYMPTOMS	0	1	2	3	0 = Never 1 = Sometime
Dryness, Grittiness or Scratchiness					<b>2</b> = Often
Soreness or Irritation					<b>3</b> = Constant
Burning or Watering					
Eye Fatigue					

2. Report the **SEVERITY** of your symptoms using the rating list below:

SYMPTOMS	0	1	2	3	4
Dryness, Grittiness or Scratchiness					
Soreness or Irritation					
Burning or Watering					
Eye Fatigue					

Within past 3 months

**0** = No problems

Sometimes

- 1 = Tolerable not perfect but not uncomfortable
- 2 = Uncomfortable irritating but doesn't interfere with my day
- **3** = Bothersome irritating and interferes with my day
- 4 = Intolerable unable to perform my daily tasks

3. Please check if you have experienced above symptoms:

WIthin last 3 days

Today

Dryness).

Do you use eye drops for lubrication?	Yes	No If yes,	how often?	
Do you have fluctuating vision?	□ Never	Sometimes	Frequently	Always
If yes, does the fluctuating vision improve with blin	nking and/or	lubricating drops?	□ Yes □ No	
Have you been told you have <b>blepharitis</b> ?	Yes	□ No		
Have you been treated for a <b>stye</b> ?	Yes	🗖 No		
Have you had any of these symptoms recently?	🗖 Eyelid r	edness 🛛 🗖 Crust	ing around lashes	Lid irritation
Do you wear contact lenses?	Yes	🗆 No		
If yes, when was the last time you wore them?				
If yes, do your eyes feel worse when they're on?	Yes	🗖 No		
Do your eyes itch?	Never	Sometimes	Frequently	Always
If yes, do you have known environmental allergies	or allergic co	onjunctivitis?	🗆 Yes 🛛 🗆 No	
Are your ocular symptoms symmetric between bo	th eyes?	🗆 Yes 🗖 N	D	
If no, which eye is the most symptomatic?	🗖 Right	🗖 Left		
Do you mind wearing glasses and/or contact lense	es for improvi	ing your vision?	□ Yes □ No	
If yes, would you be willing to pay out-of-pocket c	osts to reduc	e or elimminate you	r dependence on the	em? 🗖 Yes 🗖 No
Please place an "X" on the following scale to desci	ibe your pers	sonality as best you	can:	
ŀ		-		
<ul> <li>Easy Going</li> </ul>				Perfectionist 🕨
For office use only: Total Speed Score (Frequ	oncy + Sovority	) = /28 Num	her of Ped hoves checke	d = / 18

signs of OSD. Despite a wide variety of currently available point-of-care OSD diagnostic tests, the ASCRS Cornea Clinical Committee recommends the initial essential screening battery to include assessments of both tear osmolarity and tear inflammation (MMP-9). These two point-ofcare tests are widely available, relatively inexpensive, rapidly and easily performed by trained technicians, and have favorable sensitivity and specificity in the diagnosis of DED. It is important that patients not apply eyedrops within 2 hours before testing of either tear osmolarity or MMP-9 because this might alter the accuracy.

## Essential Screening Tests: Osmolarity and MMP-9

Tear hyperosmolarity is central to the modern definition of DED.<sup>21</sup> In the United States, the TearLab Osmolarity System (TearLab Corp.) is a U.S. Food and Drug Administration (FDA)-approved device that can perform the Clinical Laboratory Improvement Amendments (CLIA)-waived in-office test of tear osmolarity and can be easily integrated into a routine workflow. A microchip test card is placed in the lower lateral tear meniscus to collect a 50 nL tear sample. This tool has been shown to be a valid and reliable way to assess tear osmolarity.<sup>22,23</sup> An osmolarity value greater than 307 mOsm/L has been identified as the most sensitive threshold to differentiate between normal and mild-tomoderate DED patients.<sup>22</sup> Osmolarity is also considered abnormal if there is an intereye difference greater than 7 mOsm/L. In general, mild-to-moderate DED is typically diagnosed at a mean osmolarity of 315 mOsm/L, and severe DED has a mean value of 336 mOsm/L. Intereye variability and day-to-day variability have also been shown to correlate with increasing DED severity.<sup>24</sup>

MMP-9 is an enzyme that is released during an inflammatory response, and it plays a role in ocular surface breakdown. It was found to be elevated in patients with different types of OSD, including Sjögren syndrome and MGD.<sup>25</sup> Inoffice testing of MMP-9 is currently possible with Inflammadry (Quidel Corp.); this CLIA-waived test has an 85% sensitivity and 94% specificity.<sup>26,27</sup> The testing applicator is applied against the palpebral conjunctiva to collect the tear sample, and within 10 minutes, the test is positive if 40 ng/mL or more of MMP-9 is detected. MMP-9 testing can help guide OSD treatment. Identification of elevated MMP-9 suggests a patient would likely benefit from antiinflammatory therapy, such as topical corticosteroids and/or topical lifitegrast or cyclosporine.<sup>28</sup> As a general rule, the ASCRS Cornea Clinical Committee recommends refraining from punctal occlusion for DED until ocular surface inflammation (MMP-9) is normalized because this could worsen patient symptoms.

The combination of osmolarity and MMP-9 screening tests has been shown to be valuable in identifying OSD in asymptomatic preoperative cataract surgery patients.<sup>7</sup> In addition, the various combinations of screening symptoms, osmolarity, and MMP-9 can be used together to infer potential diagnoses of OSD. In a study of symptomatic patients with normal tear osmolarity,<sup>B</sup> the most common non-DED diagnoses included anterior blepharitis (26%),

allergic conjunctivitis (21%), corneal EBMD (8%), contact lens intolerance (6%), conjunctivochalasis (5%), keratoneuralgia (4%), and computer vision syndrome (4%). If a patient is symptomatic and has abnormal osmolarity and elevated MMP-9, then inflamed-DED is highly likely and should be treated appropriately. Because MMP-9 is a nonspecific inflammatory marker, when elevated, especially when osmolarity is normal, other non-DED OSD subtypes that can lead to inflammation (eg, pterygium, allergic conjunctivitis, EBMD, recurrent corneal erosion syndrome, ocular rosacea, anterior blepharitis, conjunctivochalasis, and autoimmune diseases such as Sjögren syndrome and thyroid disease) should be ruled out.<sup>29–34</sup> MMP-9 positivity has also been shown to increase with increasing severity of meibomian gland obstruction as well as with the degree of corneal staining.<sup>32,35,36</sup> Therefore, if the MMP-9 screening test is positive, the clinician should carefully rule out potentially visually significant corneal staining preoperatively. In patients with symptoms but no signs on the screening tests, a diagnosis of neuropathic corneal pain should be considered, especially when the slitlamp evaluation is normal. Conversely, in patients with no symptoms but significant signs of OSD, neurotrophic keratitis should be considered and treated preoperatively.

If any one of the three components of the initial screening battery are abnormal, then the presurgical patient is at risk for OSD, and further diagnostic tests can be done to identify OSD subtypes. These extra diagnostic tools can be divided into noninvasive and invasive tests. The ASCRS Cornea Clinical Committee consensus is that noninvasive tests are preferable, if available, because the ocular surface, cornea, and tear film are not disrupted. Although not essential to the fundamental algorithm, objective tests for lipid layer thickness (LLT), meibography, noninvasive tear breakup time (NI-TBUT), quantification of tear meniscus height (TMH), tear lactoferrin levels, topography/tomography, aberrometry and ocular scatter index (OSI) can be useful adjuncts in determining OSD and DED subtypes as well as in assessing their visual significance.

#### **Optional Noninvasive Objective OSD Tests**

Meibomian Gland Imaging, LLT, and NI-TBUT The stability of the precorneal tear film is dependent on the health of the meibomian glands. A reduced TBUT can alter visual function and lead to symptoms of OSD. As MGD progresses and becomes chronic, the meibomian glands begin to dilate, become tortuous, and eventually atrophy. Meibomian gland imaging can be used clinically to identify gland atrophy and stage disease severity; this information can help the clinician to anticipate response to treatment. The multipurpose corneal topographer (Keratograph 5M, Oculus, Inc.) uses infrared light to obtain surface images of the meibomian glands. By contrast, two meibography interferometers (LipiView II and LipiScan, Johnson & Johnson Vision, Inc.) use dynamic surface illumination and adaptive transillumination to provide high-definition images of the meibomian glands. In addition to quantifying blink rates and blink quality, the LipiView can also measure the LLT of the precorneal tear film. LLT has been correlated with the number of expressible glands present. An LLT lower than 60 nm has been shown to have 90.2% specificity for the presence of MGD.<sup>37</sup> The multipurpose corneal topographer can also measure NI-TBUT without the need for vital dyes, unlike the traditional invasive methods (TBUT). The device obtains thousands of datapoints from Placido rings projected onto the tear film. The change in the ring image identifies areas within the tear film that are breaking up, and the time in which this occurs is reported. This test can be used to diagnose an unstable tear film and can be followed over time. An autorefractor keratometer device (RT-7000, Tomey Corp.) can also perform NI-TBUT using its tear stability analysis system.

Corneal Topography and Ocular Scatter Most Placido ring-based corneal topographers can be used as screening tools to identify possible VS-OSD in addition to assessing corneal astigmatism and surface regularity. Data might be absent or mires irregular when the ocular surface is dry or in the setting of anterior basement membrane dystrophy or pterygium. An "irregularly irregular" topographic pattern, especially when highly variable between tests, is highly suggestive of DED in the absence of causative corneal lesions. In addition, many topographers provide quantifiable irregularity indices, which when elevated, can potentially signify a VS-OSD. An optical quality analysis device (HD Analyzer, Visiometrics SL) employs a doublepass technique as light passes through the ocular interfaces to measure forward scatter resulting from localized deviations of light. The measurements are objective and noninvasive and do not require any subjective component from the patient or examiner. The OSI can be used to objectively assess the visual significance of cataracts and the ocular surface and tear film separately, and it can provide useful measures of visual quality and performance rather than simple Snellen acuity.<sup>38</sup> Measuring changes in the OSI between blinks can objectively quantify the effect of the tear film on visual quality as well as measure NI-TBUT. An increase in OSI between blinks suggests VS-OSD, and it should be addressed preoperatively.

The multipurpose corneal topographer also has the ability to objectively measure the TMH, as do many highresolution optical coherence tomography devices, which are readily available in many offices. Objective and noninvasive quantification of the TMH and volume can be useful in differentiating between primarily aqueous-deficient DED (AD-DED) and E-DED subtypes, a distinction that neither osmolarity nor MMP-9 testing can make. These noninvasive no-touch measures of tear production are preferable to more invasive tools (eg, Schirmer testing) in preoperative refractive patients.

**Sjögren Disease Antibody Testing** Traditional laboratory testing for Sjögren disease includes Sjögren-specific antibody A and Sjögren-specific antibody B, in addition to antinuclear antibody and rheumatoid factor testing. Early detection of Sjögren disease is important because it can be associated with systemic diseases such as lymphoma, lupus, sclerosis, and other autoimmune conditions.<sup>39,40</sup> Antibody testing should be considered in any patient with signs of significant AD-DED and symptoms of dry eyes, skin or mouth, joint aches, fatigue, and/or dental problems. Sjögren syndrome is more common in females, but it occurs in males as well. In younger preoperative keratorefractive surgery patients with suggestive symptoms and abnormalities in osmolarity and/or MMP-9, Sjögren disease should be ruled out. Similarly, in older preoperative cataract patients, since the diagnosis is often delayed by many years, Sjögren disease should be ruled out in those with suspicious systemic symptoms and an abnormal preoperative OSD screen. Although a point-of-care CLIA class II test for the quantification of tear lactoferrin levels exists (Tearscan System, Advanced Tear Diagnostics, LLC), no member of the ASCRS Cornea Clinical Committee has used it in clinical practice. However, if the device is available, abnormally low levels of tear lactoferrin can be associated with AD-DED and Sjögren syndrome.<sup>41</sup> A diagnostic laboratory panel (Sjö, Bausch & Lomb, Inc.) can be used to test for traditional and novel proprietary biomarkers for the early detection of Sjögren syndrome. The three proprietary markers are: (1) salivary protein-1 (SP-1, immunoglobulin A [IgA], immunoglobulin G [IgG], immunoglobulin M [IgM]); (2) carbonic anhydrase-6 (CA-6, IgA, IgG, IgM); and (3) parotid secretory protein (PSP, IgA, IgG, IgM). These markers increase sensitivity and specificity for early detection.<sup>42,43</sup> This in-office test is easy to adopt in an ophthalmic practice; blood can be drawn by finger stick and applied to a card or drawn in a vial and can then be sent for analysis.

# CME ITEMSALGORITHM PART 2: CLINICAL EXAMINATION

# Look, Lift, Pull, and Push Examination

Despite the use of the aforementioned noninvasive objective screening tests, no preoperative clinical assessment is complete without a physical examination. Although this portion of the algorithm is performed regardless of whether the screening battery was positive (OSD likely) or negative (OSD unlikely), 70% of the ASCRS Cornea Clinical Committee members feel comfortable allowing a trained physician extender (eg, technician or physician assistant) to perform this step. We recommend a quick focused ocular surface examination, dubbed Look, Lift, Pull, Push, to confirm the subtype, severity, and visual significance of any present OSD.

**Look**: Look at the blink quality and quantity; examine the eyelids for malposition, lagophthalmos, proptosis and exposure, entropion or ectropion, and trichiasis; and then visually assess the TMH. Look for signs of anterior and posterior blepharitis (scurf, collarettes, foamy tears, cylindrical dandruff, Demodex mites, bacterial overgrowth, biofilm, keratinization, telangiectasias, meibomian gland capping, chalazia, lid margin pitting, etc.). Look at the interpalpebral ocular surface for signs of conjunctival injection, follicles and papillae, discharge and mucus, concretions, conjunctivochalasis, pingueculae, pterygia, and conjunctival scarring and symblepharon. Look at the interpalpebral

cornea for any surface abnormality; loss of clarity; lumps and bumps including pterygia, subepithelial scarring, Salzmann nodules, and filaments; and anterior dystrophies including subtle EBMD. In some cases, punctate epithelial erosions and superficial punctate keratitis can be seen under direct illumination without dyes and stains.

Lift and Pull: Lifting up and then pulling out of the upper eyelid is an often overlooked portion of the ocular surface examination. Although superior limbic keratitis and superior corneal scars can be detected, the main reasons for lifting then pulling the upper lid are to rule out superior EBMD and to identify eyelid laxity and floppy eyelid syndrome. Both superior EBMD and floppy eyelid syndrome are very common, often missed, and can be visually significant preoperatively and postoperatively.

**Push:** By pushing on the lower lid margin, the meibomian glands are expressed and the quality, quantity, and flow of the meibum are assessed.<sup>44</sup> This can easily be accomplished using a finger, a cotton-tipped applicator, or a more formal device such as a meibomian gland evaluator (Korb, Johnson & Johnson Vision, Inc.), which applies about 1 g/mm<sup>2</sup> to the area in contact with the device to simulate the pressure generated with a normal blink. Gland expression can be particularly helpful in identifying patients with nonobvious MGD, a form of obstructive MGD in which classic inflammatory signs are absent.<sup>45</sup>

At this stage in the algorithm, symptoms have been assessed, baseline refractive measurements and noninvasive OSD tests have been completed, and the ocular surface has been examined for evidence of OSD. If no further refractive or preoperative measurements are required for surgical planning, the final phase of the algorithm can be initiated. This involves invasive testing, most importantly, corneal staining and TBUT, which can help distinguish between NVS-OSD and VS-OSD, but after which precise and reliable refractive measurements cannot be performed.

#### Vital Dye Staining

Sodium fluorescein is a nontoxic dye commonly used to assess tear-film stability and can also stain any epithelial defects. It can be applied in a solution or in an impregnated strip form. Generally, the strips apply a more controlled amount of dye, allowing better visualization of the corneal surface. The dye mixes with the precorneal tear film, and a cobalt blue light is used to illuminate the stained surface. The time of initial breakdown of the tear film or first appearance of any hypofluorescent area is the TBUT. In general, less than 10 seconds of TBUT is considered abnormal. The TBUT can be used to monitor DED status and response to therapy; it has been used for many years because of ease of integration into clinical practice. Rose bengal dye is a derivate of fluorescein that stains devitalized cells.<sup>46</sup> It can also be used in a solution or impregnated strip form, but some ocular discomfort after instillation can occur. Rose bengal and other dyes such as lissamine green can be used to detect DED earlier in the disease course because conjunctival staining might be present earlier than corneal staining.<sup>47,48</sup> After the instillation of vital dye, with or without anesthetic, aqueous tear production can be optionally assessed with a traditional Schirmer test or phenol red thread test. However, most ASCRS Corneal Clinical Committee members have largely abandoned these tests. Of note, when moderate-to-severe corneal staining is detected, especially if minimal symptoms are present, the clinician should consider a diagnosis of neurotrophic keratitis. Corneal sensation testing can be an adjunctive test to establish altered sensation.

# Visually Significant Versus Nonvisually Significant Ocular Surface Disease

At this point in the algorithm, the clinical investigation and data collection are complete. The final determination of the magnitude of the visual significance of OSD is ultimately at the discretion of the surgeon and is arrived upon by a careful synthesis of the results of the questionnaire, objective tests, and clinical examination with subsequent dye staining. Visual significance implies a potential direct adverse effect on visual quality and Snellen acuity, not only preoperatively, but postoperatively as well. In addition, visual significance also pertains to the likelihood that the identified subtypes and severity of the OSD will lead to imprecision of presurgical measurements resulting in refractive misses and residual ametropia. Any combination of fluctuating vision improved with blinking or lubrication, highly elevated osmolarity and MMP-9, irregularly irregular fluctuating topography and/or aberrometry, interblink increases of OSI, irregular astigmatism from corneal epithelial abnormalities, and significant corneal staining would all be considered visually significant. Last, visual significance also refers to the potential of the identified OSD leading to a postoperative infection, endophthalmitis being the most significant. Bacterial-associated subtypes of OSD-such as staphylococcal blepharitis, bacterial biofilms, and infectious conjunctivitisshould be identified and treated fully preoperatively. In any case of VS-OSD, the preoperative refractive measurements and surgery itself should be postponed until the VS-OSD is sufficiently treated and converted to NVS-OSD. In cases where OSD is identified but deemed nonvisually significant, surgery can proceed as planned, but the patient should be educated about his or her condition and prophylactically treated to prevent postoperative worsening.

By consensus of the ASCRS Cornea Clinical Committee, the treatment of OSD, especially VS-OSD, in the preoperative patient population generally requires a more aggressive, often multifaceted approach with a targeted combination of prescription medications and procedural interventions to rapidly reverse OSD and to minimize surgical delays.

# CME ITEMSALGORITHM PART 3: TREATMENT BASED ON SUBTYPES AND SEVERITY OF OSD

Although the recommended guidelines by the TFOS DEWS II report in 2017<sup>49</sup> are a great tool to aid clinicians in treatment considerations for DED, the treatment approach in the presurgical patient has some unique considerations. Specifically, in the preoperative cataract or corneal

refractive evaluation, if VS-OSD is diagnosed, treatment should be initiated at a higher, more advanced level. This is attributable in part to the need for rapid restoration of tear-film homeostasis to optimize preoperative measurements as well as to maximize postoperative outcomes and patient satisfaction. As such, a monotherapy approach and a waiting period to monitor for the addition of further therapy are often not sufficient to create a rapid turnaround of the tear-film homeostasis in this setting. Tear-film inflammation, lid margin disease, and ocular surface staining should be addressed simultaneously to achieve a rapid improvement in preparation for surgery.

With the goals of minimizing surgical delays, maximizing preoperative measurement confidence, and reducing postoperative complications, treatment options in the preoperative setting should minimally start at Step 2 of the TFOS DEWS II treatment guidelines. Step 1 treatments such as artificial tears and lubricants, warm compresses, lid hygiene, and nutritional supplements are reasonable adjuncts but often insufficient to rapidly reverse VS-OSD. A combination of medical and procedural interventions based on disease subtype and severity will dictate the best approach in the preoperative patient. Because DED is becoming more widely recognized as a multifactorial disease involving tear composition, ocular surface inflammation, and lid margin disease, there are increasingly more treatment approaches available.

#### **Antiinflammatory Treatments**

Given that both AD-DED and E-DED lead to a loss of tear homeostasis and ultimately inflammation, antiinflammatory treatments are often beneficial.<sup>50,51</sup> Rapid and potent antiinflammatory effects can be achieved with a pulse of topical steroids. Although topical steroids have immediate effectiveness in decreasing tear-film inflammatory cytokines, their long-term use is limited because of known side effects. In the preoperative setting, where rapid rescue and improvement of the ocular surface is required, steroids could play an important role. Clinicians can therefore have a lower threshold for initiation of steroids in cataract and refractive surgery candidates with OSD than they would for other patients with DED. Studies<sup>52,53</sup> have shown that the use of loteprednol etabonate 0.5% and fluorometholone demonstrate significant effects in improving signs and symptoms of DED. These studies found no significant steroid-related complications over a short 4-week course. As a rescue treatment and in pulsed dosing perioperatively, steroids can have a positive and rapid effect on the ocular surface. In addition, a 4- to 6-week course of a topical steroid, such as loteprednol, might help improve tolerability of other treatments with adverse effects such as burning and increased ocular surface sensitivity.<sup>54</sup>

Prescription topical antiinflammatory drugs, such as cyclosporin A (CsA) and lifitegrast, have been shown to be effective in the long-term management of DED.<sup>55–57</sup> CsA, which is a fungal-derived peptide, has been known to affect DED by its specific immunosuppressive and antiinflammatory effects. The decreased release of inflammatory cytokines, such as interleukin-2 and interferon gamma, through inhibition of T-cell activities are among its main sources of action.<sup>58</sup> Multiple studies comparing various dosing concentrations<sup>55,59</sup> concluded that in the 0.05% and 0.1% formulations, there was consistent improvement in subjective patient symptoms as well as an objective decrease of vital dye staining of the ocular surface and an increase in Schirmer scores. Significant increases in goblet cell density of the ocular surface has also been observed with CsA use.<sup>60</sup> CsA 0.05% used twice daily with an adjunctive topical corticosteroid was effective in managing dry eye in the cataract setting, with symptomatic and clinical amelioration in as few as 2 weeks.<sup>61</sup> Lifitegrast, which was approved by the FDA in 2016 for the treatment of DED signs and symptoms, might have an advantage in the preoperative setting because of its more rapid onset of action. Topical lifitegrast is the first choice immunomodulator in the preoperative setting of 70% of the ASCRS Cornea Clinical Committee members. Although we recommend instituting topical immunomodulator therapy as far in advance of surgery as possible, a minimum of 2 to 4 weeks prior should have a beneficial impact on the ocular surface. In two phase 3 studies with more than 700 patients each,<sup>56,57</sup> lifitegrast showed a significant improvement in eye dryness compared with vehicle as early as 2 weeks after starting treatment. In addition, a significant decrease in inferior corneal staining was observed at week 12.57,62 Lifitegrast works by blocking the interaction between intracellular adhesion molecule-1, which is upregulated on the ocular surface of DED patients, and lymphocyte functionassociated antigen-1 on the T-cell. Lifitegrast thereby inhibits the migration and binding of T-cells to the ocular surface and their activation and release of cytokines. It is postulated that its more rapid onset of action is because of its multitarget action on the inflammatory cycle and its ability to turn off already active T-cells.<sup>63</sup>

When there is significant ocular rosacea and lid margin inflammation, oral tetracyclines can be used. Doxycycline is particularly useful, not only for control of deleterious free fatty acids and bacterial overgrowth, but also for its inhibition of tear-film cytokines including MMP-9.64 This class of drugs works by a dual mechanism of action. Primarily, tetracycline derivatives work by decreasing the bioactivity of many cytokines in the inflammatory pathway including interleukin-1, tumor necrosis factor- $\alpha$  and MMP-1, MMP-3, and MMP-9.65,66 By decreasing MMP-9 in the corneal epithelium, these drugs improve the integrity of the tight junctions between cells, thus improving the barrier function of the epithelium and decreasing cell apoptosis.<sup>67</sup> The antimicrobial effects of the tetracycline analogs are also thought to play a role in alleviating bacterial lid margin disease. The secondary antibiotic effect can decrease bacterial lid flora with a resultant decrease in lipolytic enzymes and meibomian lipid breakdown products.<sup>67,68</sup> This might have an additional benefit of minimizing the risk for lid margin and blepharitis-related postoperative infection and endophthalmitis. Several studies using oral tetracycline derivatives<sup>67-70</sup> have

described significant improvement in signs and symptoms of chronic lid margin and DED. These oral tetracyclines are often prescribed for a 1- to 2-month course and can be repeated as a pulse therapy 2 to 4 times per year. In the preoperative setting, even a 1-month course might help with reducing inflammation and bacterial load before surgery.

#### Lid Margin Disease Treatments

The treatment of MGD and anterior blepharitis is particularly important before intraocular surgery. Relieving the chronic stasis and obstruction in the meibomian glands is essential to the successful treatment of MGD and improvement in DED symptoms.<sup>71,72</sup> Blepharitis is a common cause of cataract surgery cancellation and is a major risk factor for postoperative endophthalmitis.<sup>73</sup> MGD treatment can be initiated with regular warm compresses and lid hygiene at home. However, compliance can be low and expression of glands at home is often difficult to perform adequately, especially in the elderly. Bacterial blepharitis should be treated with the use of regular lid cleansing products. Antiinfective therapies, such as antibiotic ointments and lid scrubs, should be initiated more aggressively in the preoperative setting to manage lid margin bacterial overgrowth. Hypochlorous acid solutions to clean the lid margin have also been shown to significantly decrease biofilm of the lid margin and can be of benefit for preoperative lid margin disinfecting.<sup>74</sup> In confirmed or suspected cases of Demodex mite infection, lid scrubs with a tea tree oil component should be initiated.<sup>75</sup> Mechanical blepharoexfoliation (BlephEx, LLC) of the lid margin in cases of significant anterior blepharitis with biofilm, scurf, collarettes, and/or debris is a quick procedural adjunct in the preoperative setting for rapidly reducing infectious loads, reducing bacterial and biofilm resistance, and likely decreasing the risk for postoperative infections.<sup>76</sup>

Because warm compresses used at home often do not reach adequate temperatures for sustained periods, the use of in-office thermal pulsation treatments can be offered to preoperative patients for more rapid efficacy. A thermal pulsation device (LipiFlow, Johnson & Johnson Vision, Inc.)-a 12-minute automated procedure for heating, massaging, and expressing of the meibomian glands-can be used in-office and is the favored preoperative MGD procedural treatment of over 80% the of ASCRS Cornea Clinical Committee members.<sup>77</sup> Thermal pulsation applies constant heat and a sequence of pressure pulsations that help evacuate the meibomian glands of static oils and improves glandular flow. The heat is directed immediately over the meibomian glands and avoids going through the anterior skin of the eyelid, thereby reducing the skin irritation and vascular inflammation experienced by some patients with at-home hot compresses. In this way, the temperature is also maintained, and heat is not lost before reaching the glands. In a trial comparing a single thermal pulsation device treatment (n = 69) to daily warm compress therapy (n = 70),<sup>77</sup> the thermal pulsation device group had significant improvement in their TBUT and symptoms at 2 weeks and 4 weeks compared with the warm compress group. With a single treatment, the improvement in gland scores and patient-reported improvement in symptoms (OSDI and SPEED questionnaire) were maintained up to 9 months.<sup>78</sup> The rapid improvement of the lipid layer to this treatment makes it an ideal preoperative tool to optimize tear-film homeostasis.<sup>79</sup> In patients with signs of significant anterior blepharitis and MGD, a combination in-office procedure with blepharoexfoliation of all 4 eyelids immediately followed by a thermal pulsation procedure can quickly treat both conditions, and it is recommended by ASCRS Cornea Clinical Committee members in the preoperative setting. Other commercially available in-office procedures for lid margin disease include the iLux (Tear Film Innovations, Inc.) and the MiBo ThermoFlo (MIBO Medical Group).

Intense pulse light, originally developed for patients with acne or rosacea, is being used off label for the treatment of chronic MGD with evidence of improvement in some patients.<sup>80</sup> This technology uses bursts of light at particular wavelengths (between 500 to 1200 nm) that cause changes in the blood vessels, thereby eliminating telangiectasias and erythema of the skin. Meibomian gland probing for severe MGD has also shown benefit in restoring glandular function and improvement in symptoms in small studies.<sup>81,82</sup> In the preoperative setting, these procedural treatments might be of value in certain cases for which advanced lid margin disease is the source of VS-OSD.

Increasing dietary intake of omega-3 fatty acids can also improve lid health by reducing inflammation and improving the quality of oil secretions from the meibomian glands.<sup>83</sup> Omega-3 fatty acids have been shown in a number of clinical studies to improve DED symptoms.<sup>83–85</sup> Specifically, eicosapentaenoic acid and docosahexaenoic acid are long-chain polyunsaturated omega 3-fatty acids that play a role in multiorgan health. These essential fatty acids inhibit inflammatory mediators and block production of inflammatory cytokines such as interleukin-1 and tumor necrosis factor-α.<sup>86</sup> The large multicenter Dry Eye Assessment and Management study, which compared the effects of 3000 mg fish-derived n-3 eicosapentaenoic and docosahexaenoic acids (active supplement group) with olive oil (placebo group),<sup>87</sup> found no significant benefit on the ocular surface between the treatment and control groups. Despite its many strengths and compelling conclusions, limitations of the study include the lack of a true placebo group and the inclusion of patients with non-MGDrelated DED. In light of this mixed evidence, 80% of the ASCRS Corneal Clinical Committee members continue to recommend dietary omega-3 supplements as adjunctive therapy for MGD and blepharitis. Its use in the preoperative setting should be left to the discretion of the clinician and the extent of lid margin disease.

#### Treatments to Improve Ocular Surface Staining

The consensus of the ASCRS Cornea Clinical Committee is that corneal staining is the single most critical sign of OSD that should be normalized before refractive surgery followed by topography, TBUT, osmolarity, and MMP-9; each of which have a high likelihood of causing VS-OSD when abnormal. Aggressive lubrication with preservativefree artificial tears should be initiated when there is significant punctate staining in the preoperative setting. Preserved artificial tears, especially if used more than 4 times daily, can promote further surface irritation and corneal damage.<sup>88</sup> In many cases, however, artificial tears might not be sufficient to result in rapid resolution of punctate staining and more aggressive action will be required. The novel use of neurostimulation (TrueTear, Allergan, Inc.) to promote aqueous, mucin, and meibum secretion has been shown to effectively improve punctate staining and positively impact DED symptoms.<sup>89</sup> Its use in the preoperative patient with VS-OSD might be of value in addition to other treatments.

The use of autologous serum drops gained initial popularity in the treatment of nonhealing ocular surface erosions.<sup>90,91</sup> Its effects at improving erosions led to the concept of using this biological treatment for chronic DED.<sup>92</sup> The growth factors, vitamins, and antibodies present in tears are also present in blood serum drops, thus offering advantages over commercial artificial tears. In 2004, Noble et al.93 compared 50% autologous serum eyedrops with standard artificial tear solutions in a prospective, randomized, controlled crossover study. Significant improvements in ocular surface cytology and vital dye staining scores were observed in the autologous serum group, whereas these effects were reversed when the treatment was reverted back to artificial tears alone. Improvements in vital dye staining, tear stability, and pain scores have also been seen in other studies comparing autologous serum to nonpreserved artificial tears.94 The nonpreserved nature of this product does raise the concern for bacterial contamination in the preoperative setting. There is no evidence to support a higher risk for endophthalmitis with the use of autologous serum in the preoperative setting and thus its use perioperatively is left to the discretion of the clinician; 60% of the Corneal Clinical Committee members support the use of autologous serum drops in the perioperative period.

A self-retaining amniotic membrane or therapeutic bandage contact lens to address severe punctate keratitis and to restore a smooth ocular surface can be used preoperatively. Human amniotic membrane transplantation has become a popular alternative technique for several ocular surface disorders. Comprised of a single epithelium layer, a thick basement membrane, and an avascular stromal matrix, the innate properties of the amniotic membrane create an environment for wound healing and tissue regeneration when placed on the eye. Amniotic membrane transplantation has been used successfully for many severe OSDs, including ocular surface burns and Stevens-Johnson syndrome.<sup>95,96</sup> The ability to place a self-retaining cryopreserved amniotic membrane (Prokera, Bio-Tissue, Inc.) has expanded its use in the clinical setting, especially in severe VS-OSD patients, such as those with neurotrophic ulcers, filamentary keratitis, DED, infectious keratitis, and recurrent corneal erosion.<sup>97,98</sup> More recently, the placement of a self-retaining cryopreserved amniotic membrane for 5 days showed an improvement in corneal nerve density as well as signs and symptoms of dry eye.<sup>99</sup> The Dry Eye Amniotic Membrane study<sup>100</sup> assessed the potential benefits of Prokera to treat DED. In the study, in 97 eyes of 84 patients who had the amniotic membrane transplant in place for an average of 5.4 days, 88% showed a significant improvement in the corneal staining score. A physician implants the amniotic membrane in a manner similar to the placement of a large-diameter contact lens. The use of antibiotic drops in conjunction with the device should be considered to prevent any secondary infection. Amniotic membrane extract in the form of a topical drop has also been used with success for improving the ocular surface.<sup>101</sup> In preoperative patients with refractory VS-OSD, in particular those with significant corneal staining and erosions, the use of amniotic membrane therapy might facilitate more rapid resolution. The ASCRS Cornea Clinical Committee recommends continuing topical antibiotics and waiting at least 7 days between discontinuing amnionbased therapies and proceeding with intraocular surgery.

The therapeutic use of contact lenses for severe OSD cases—including corneal ulcers, persistent epithelial defects, corneal perforation, and chemical burns—has been described.<sup>102,103</sup> The clinical uses for bandage contact lenses might include patients with significant corneal pain because of DED.<sup>104</sup> A soft contact lens might be used in the preoperative setting to allow epithelial healing of punctate keratitis and smoothing of the surface before preoperative biometry measurements. If the contact lenses are left in place more than 24 hours, antibiotic drops should be used to prevent any secondary infection.

Punctal occlusion has been well demonstrated in clinical practice to improve DED by increasing ocular surface moisture. This can be achieved by punctal plug placement or by punctal closure via cautery or suture placement. In the setting of inflammatory DED, however, patients with a significant increase in tear inflammatory cytokines (MMP-9) might have a negative response to plugs and experience a worsening of symptoms. These patients might benefit from managing the tear-film inflammation before punctal occlusion.<sup>105</sup>

Eyelid abnormalities, including lagophthalmos, ectropion, entropion, and lid laxity, are common causes of VS-OSD. For patients with mild lagophthalmos, the combination of a nighttime gel or ointment along with a moisture goggle can be considered. Environmental modifications can have a significant impact on OSD, and education preoperatively to reduce risk factors can be valuable. The increase of environmental moisture can have a dramatic effect on symptomatology. Patients who live in dry climates are encouraged to use humidifiers. An increase in periocular humidity has been shown to increase the tear-film lipid layer, increase interblink intervals, and increase the duration of blink.<sup>106</sup> The wearing of moisture goggles or spectacles increases the periocular humidity, which can alleviate symptoms of DED.<sup>107</sup> Increased computer screen time can also dramatically impact DED symptoms.<sup>108</sup> Modifications to screen position as well as encouragement of regular and frequent breaks for DED patients whose occupations require many hours of computer work can improve DED symptoms.<sup>109</sup>

Finally, many systemic medications, such as antihistamines, might also contribute to worsening of DED. A modification of systemic medications might help to optimize the ocular surface preoperatively. If possible, systemic antihistamines should be discontinued and local antiallergy treatments initiated. Although the exact relationship of hormonal balance and DED is vague, hormonal replacement medications can be adjusted in conjunction with the patient's internist or gynecologist to ameliorate DED symptoms.<sup>110</sup> In the elderly male population, a decline in androgens can trigger significant DED symptoms. Although it is not FDA-approved for DED and it requires specialty compounding, there is limited evidence that topical hormone treatment can improve DED symptoms.<sup>111</sup>

In cases where there are superficial abnormalities of the corneal surface with topographic irregular astigmatism, such as from Salzmann nodular degeneration, pterygia, or EBMD, the surgeon might consider superficial keratectomy or pterygium excision to smooth the corneal surface before finalizing refractive measurements. After such procedural interventions, it is important to wait for refractive, astigmatic, and topographic stability as well as proper healing of the ocular surface before surgical planning is completed. Contact lens wear can also lead to corneal warpage, irregular astigmatism, and an unstable ocular surface before surgery. Most ASCRS Cornea Clinical Committee members recommend a soft contact lens holiday of at least 2 weeks before the preoperative visit, and for hard or rigid gaspermeable (RGP) lenses, at least a 1-month holiday, then waiting for topographic and keratometric stability over 2 successive visits. For long-term RGP wearers, the general rule of a 1-week holiday per decade of RGP wear is followed by the majority of ASCRS Cornea Clinical Committee members.

After initiating a multifaceted treatment regimen based on severity and subtypes of OSD, the patient can be reassessed in approximately 2 to 4 weeks. A patient who is educated preoperatively about OSD, including its impact on visual outcomes and the need to treat it aggressively, is more likely to adhere to the recommended treatment regimen. At the follow-up visit, the preoperative OSD algorithm methodology should be repeated from the beginning. If improvement in symptoms, normalization of the ocular surface, and reliable preoperative testing has been achieved, then surgical planning can be finalized at this visit. The patient should be counseled that ongoing treatment for DED must be maintained postoperatively to optimize and retain long-term visual outcomes.

# CME ITEMSINTRAOPERATIVE AND POSTOPERA-TIVE CONSIDERATIONS

There are numerous perioperative, intraoperative, and postoperative considerations in patients with preexisting OSD who are undergoing ocular surgery. On the day of surgery, patients are usually given a series of multiple dilating, anesthetic, antiinflammatory, and antibiotic drops. These drops often contain preservatives, such as benzalkonium chloride, which have been shown to cause or exacerbate epithelial toxicity.<sup>112,113</sup> Alternatively, drops with other preservatives, such as chlorobutanol, might be less toxic than benzalkonium chloride.<sup>112,114,115</sup> In the operating room, the eye is prepped and draped with povidone-iodine, which can disturb the ocular surface. During the procedure, the eye is kept open with a speculum and subject to prolonged exposure. Frequent rewetting with a balanced salt solution is required. Some surgeons prefer to apply an ophthalmic viscosurgical device to the ocular surface to help keep it lubricated without the need for repetitive balanced salt solution applications. Limiting the time between the application of the speculum and the initiation of the surgery can minimize desiccation from exposure. Any surgical techniques that increase operative efficiency and decrease the length of the procedure will also limit exposure time.

Cataract surgery in general, and the creation of corneal incisions in particular, have the potential to aggravate DED.<sup>116,117</sup> Surgical procedures that cause denervation of the cornea result in impaired epithelial wound healing, increased epithelial permeability, and decreased epithelial metabolic activity.<sup>112,116</sup> Neuroregulation is essential to maintain the integrity of the corneal epithelium.<sup>112,117</sup> Corneal sensitivity and tear production have been shown to decrease after cataract surgery.<sup>118</sup> Oh et al.<sup>119</sup> demonstrated a decrease in central and incisional site sensitivity for up to 1 month after cataract surgery. Longer corneal relaxing incisions used for astigmatic correction increase the risk for further denervation. One study<sup>C</sup> demonstrated that 39% of patients with paired limbal relaxing incisions developed decreased corneal sensation for up to 3 months. Opting for a lens-based rather than an incision-based treatment of the astigmatism might limit the risk for postoperative DED. Another study<sup>120</sup> found femtosecond laser-assisted cataract surgery to be associated with a higher risk for corneal staining and DED symptoms when compared with conventional phacoemulsification surgery.

As part of the overall surgical plan, the postoperative eyedrop regimen should be carefully considered in patients with OSD. Postoperative drops, in particular, those with preservatives, might lead to toxicity and exacerbations of OSD. Intraocular or subconjunctival injections of antibiotics and/or steroids at the conclusion of surgery might limit or even eliminate the need for these topical medications postoperatively. In addition, there are numerous newer formulations of drops that require a lower daily dosage to achieve equal efficacy. The use of once- or twice-daily preserved drops is preferable to drops administered 4 times daily. Topical nonsteroidal antiinflammatory drug drops have been shown to slow corneal epithelial healing and lead to corneal melting; their use postoperatively in patients with severe OSD should be considered carefully.<sup>121,122</sup>

Finally, the surgeon should continue to monitor the ocular surface closely during the postoperative course, especially in those patients who received presbyopiacorrecting IOLs (eg, multifocal or accommodating). If the postoperative visual result is suboptimal, or the patient is dissatisfied, the OSD algorithm should be reinstituted postoperatively and the treatment regimen should be adjusted and/or increased based on the findings. For any unhappy postoperative patient, OSD should be identified and fully treated before considering other surgical options, such as Nd:YAG capsulotomy or an IOL exchange. Patients with presbyopia-correcting IOLs might be more susceptible to visual disturbances from a poor tear film or other forms of OSD and often require close surveillance and long-term treatment postoperatively.

# **CME ITEMSCONCLUSION**

The ASCRS Cornea Clinical Committee's suggested protocol for identifying and managing OSD in the cataract and refractive surgery patient commenced because of educational gaps found in recent annual ASCRS clinical surveys. Although over 90% of respondents felt even mild-to-moderate dry eyes affected patient satisfaction after cataract and refractive surgery, less than 10% were using currently available point-of-care diagnostic testing in their routine preoperative assessments. Our diagnostic algorithm and treatment recommendations have been specifically tailored to the preoperative refractive surgery patient who requires an accurate and efficient diagnosis of VS-OSD as well as an aggressive multifaceted treatment regimen for its rapid reversal. Incorporating the novel ASCRS Preoperative OSD Questionnaire and Diagnostic Algorithm into the preoperative visit workflow will aid refractive surgeons in optimizing preoperative measurements, improving refractive outcomes, reducing postoperative infection risk, and increasing overall patient satisfaction.

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