



Eric Donnenfeld, MD

Advanced OSD diagnostics and treatments play key role in surgical results

Patients older than 70 years have an almost 100% chance of having meibomian gland disease, and many also have aqueous deficiency dry eye. If dry eye remains undiagnosed or is not treated properly before

Preoperative strategies help clinicians achieve optimal postoperative outcomes

by Eric Donnenfeld, MD

surgery, refractive cataract surgeons are less likely to achieve the surgical outcomes patients seek.

Diagnostic advances

Dry eye is often misdiagnosed, and if patients are treated for the incorrect disease, they will not respond to therapy.

To improve treatment, ophthalmologists need to make the correct diagnosis the first time, but we need to do it simply and efficiently.

Point-of-care tests have changed the way we diagnose dry eye. Ophthalmologists should empower technicians to order and perform this testing based on patients' symptoms. Combining these results with our other findings from the examination,

“Refractive cataract surgeons cannot perform premium surgery without a premium ocular surface.”

—Eric Donnenfeld, MD

we are more likely to diagnose the condition accurately.

In addition to point-of-care tests, I use lissamine green staining. We perform dynamic meibomian gland imaging on almost every surgical candidate and patient with dry eye symptoms. It

allows us to examine patients' lids and meibomian glands. Furthermore, we can show our findings to patients so they understand their disease, especially if they have no symptoms.

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Educational Objectives

Ophthalmologists who participate in this activity will:

- Improve practice protocols for the screening, diagnosis, and classification of ocular surface disease

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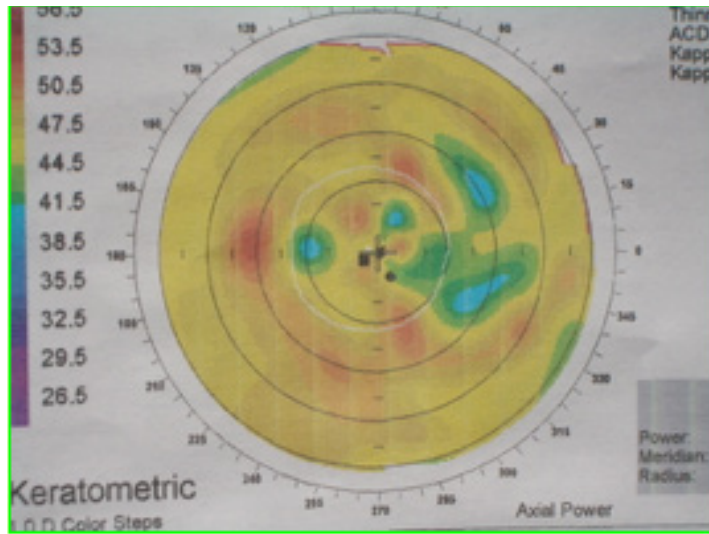
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Supported by unrestricted educational grants from Allergan, Shire Pharmaceuticals, TearLab, and TearScience

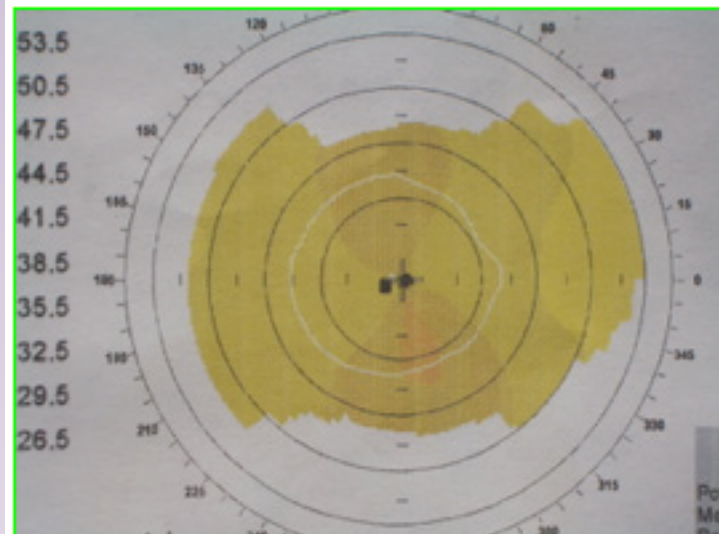
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Irregular cornea

IOLMaster Ks: 44.80 @ 90°/43.62 @ 180°
CYL: 1.18 D Mean K 44.20

Figure 1. Dry eye disease affecting preoperative topography measurements



Bow tie astigmatism

IOLMaster Ks: 45.66 @ 104°/43.31 @ 180°
CYL: 2.35 D Mean K 44.49

Figure 2. Corneal topography after treatment of dry eye

Corneal topography is an important diagnostic before surgery. When correlated with the examination, an irregular surface may confirm a diagnosis of dry eye.

Dry eye treatment

The 2016 ASCRS Clinical Survey revealed that 93% of members think mild to moderate dry eye impacts satisfaction after cataract or refractive surgery. However, 74% of members use artificial tears and lubricants to treat dry eye. Only 10% use cyclosporine or thermal expression, and 28% use omega-3 supplements.

Tears can be useful in treating symptoms, but dry eye is a progressive disease. I prefer definitive therapies to treat the cause of the disease early rather than palliative treatments.

Patients with severe dry eye do not respond as well to treatment, so we need to begin

treatment before it reaches this stage.

Dry eye is multifactorial. Depending on the type of dry eye and severity, we can choose from topical steroids, punctal occlusion, omega-3 supplements, cyclosporine, and lifitegrast. For patients with primary meibomian gland disease, I usually prefer thermal expression, which rapidly returns gland function. Patients often do not use hot compresses when they are recommended. I also recommend and prescribe an eyelid cleanser with hypochlorous acid and oral re-esterified omega-3 supplements.

Case report

A 67-year-old woman had cataracts in both eyes, and her vision was a bit hazy. She was contact lens intolerant, a key indicator of ocular surface disease, although allergies or other conditions may

cause this problem. Her vision also fluctuated.

Osmolarity was 322 and 311 mOsm/L. Her MMP-9 results were positive, and she had significant staining and dropout of meibomian glands.

The patient's mean keratometry measurement was 44.2, and she had 1.18 D of cylinder (Figure 1).

I began by treating her with artificial tears, loteprednol 0.5% four times a day, and a T-cell modulator twice a day. We treated her meibomian gland disease with thermal pulsation and omega-3 supplements (2 g/day).

Two weeks later, her eyes were more comfortable. There was also a significant difference in corneal topography (Figure 2). The axis changed, she had 2.35 D of cylinder, and her mean keratometry was 44.49. After implantation of a toric intraocular lens, she was

pleased with her vision. Grittiness and a foreign body sensation developed after surgery, and she continues maintenance therapy for long-term dry eye.

Conclusion

Refractive cataract surgeons cannot perform premium surgery without a premium ocular surface. To deliver the surgical outcomes patients anticipate, refractive cataract surgeons need to take the steps necessary to identify and effectively treat dry eye before performing preoperative measurements.

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Kenneth Beckman, MD

Diagnosis of widespread condition critical to surgical outcomes

Ocular surface disease (OSD) often is present in patients with cataracts, but it may remain undetected if patients

Why catching OSD in advance matters to surgical patients

by Kenneth Beckman, MD

do not have symptoms. If it is not diagnosed and treated before surgery, it can adversely impact patients' postoperative outcomes.

Early detection

In 272 eyes of 136 patients, Trattler et al. found that most had dry eye, and the majority did not have symptoms or had minimal symptoms.¹ Seventy-seven percent had abnormal corneal staining, and half had central corneal staining.

If OSD is not identified and treated before cataract surgery, it can alter preoperative K readings,

A-scans, and corneal topography, which will ultimately affect surgical results.

Epitropoulos et al. reported that patients with a hyperosmolar tear film showed significant variability in their average K readings and corneal astigmatism between measurements, resulting in significant differences in IOL power calculations.²

Seventeen percent of hyperosmolar eyes showed a greater than 1-D difference in cylinder between readings. Ten percent of patients in this study had an IOL power change greater than 0.5 D.

Figures 1 and 2 demonstrate the impact of OSD on preoperative measurements.

Tear film optical power

We also need to diagnose and treat OSD preoperatively to prevent postoperative aberrations.

The greatest change in refractive index occurs between the air and tear film. The tear film is the greatest ocular power surface on the eye.

The cornea and tear film account for two-thirds of the eye's

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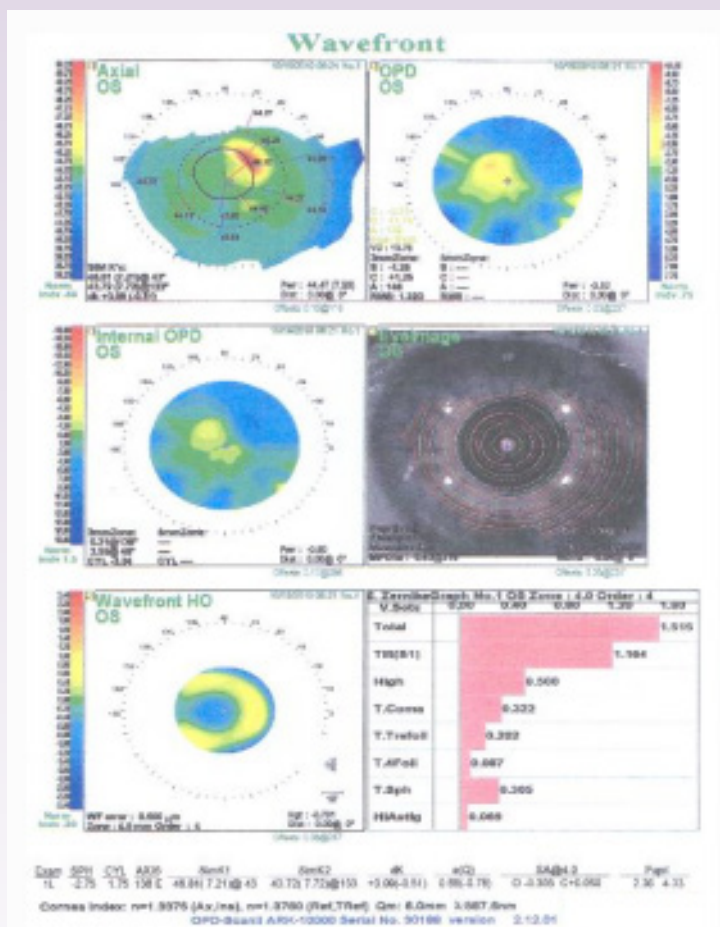


Figure 1. A patient was referred for a toric IOL but was found to have blepharitis and mixed dry eye. The patient had 3 D of irregular astigmatism preoperatively, with irregular mires.

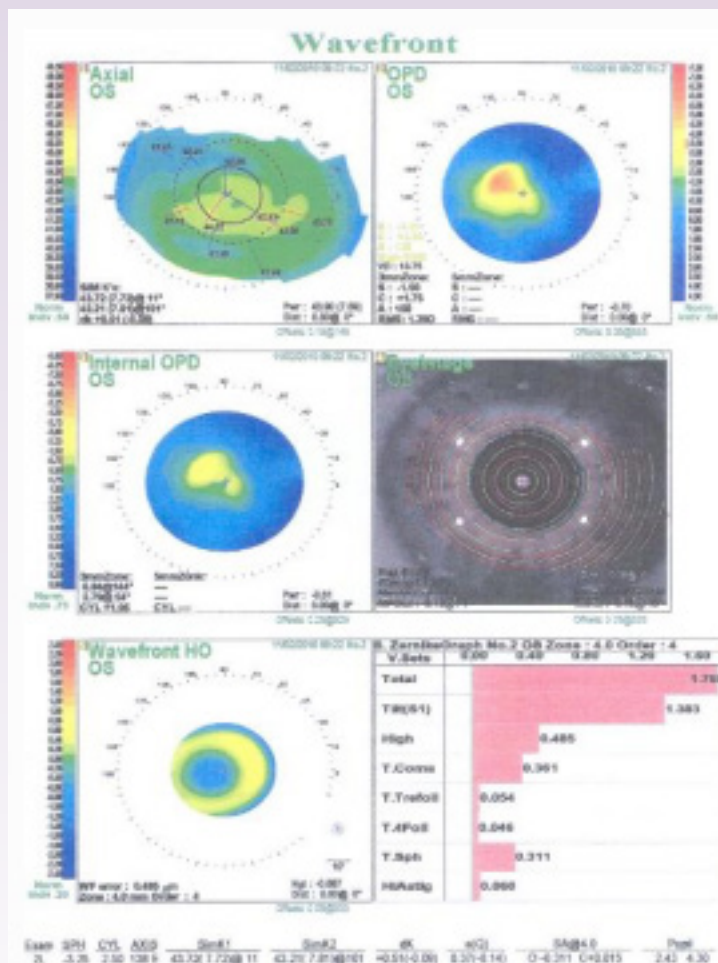


Figure 2. The patient in Figure 1 used warm compresses, lid scrubs, preservative-free artificial tears, and azithromycin ophthalmic solution (b.i.d. x 2, then q.h.s. x 2 weeks). After treatment, astigmatism decreased to 0.5 D and was much more regular, and the patient was found not to be a toric IOL candidate.



Christopher Starr, MD

**New tests help
clinicians diagnose
OSD accurately
and efficiently**

It has been an unprecedented decade in ocular surface disease (OSD) diagnosis.

Multiple seminal publications have been published, and new diagnostic tests and treatments have emerged, with expansion of research and development and a strong pipeline.

However, news of these advances may overwhelm or perplex clinicians seeking the most accurate diagnostics.

Diagnostic challenges

Dry eye is a complex condition that is often multifactorial. Furthermore, accurate diagnosis may be difficult with traditional means, such as Schirmer's, symptoms, and signs. The cause of conjunctivitis or common OSD is misdiagnosed in as many as 75% of cases.¹⁻³

Symptoms, such as itchiness, grittiness, redness, and dryness, overlap in almost all OSD.

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focusing power. If the tear film is irregular, much larger variations in optical power occur. Variable refractive powers on the ocular surface can lead to higher order aberrations.

Image quality is best immediately post-blink, but it degrades with rapid disappearance of the tear film.

Research has shown that an unstable tear film can increase dry eye symptoms as well as higher order aberrations.

**Efficiently and accurately diagnosing
OSD with advanced tests**

by Christopher Starr, MD

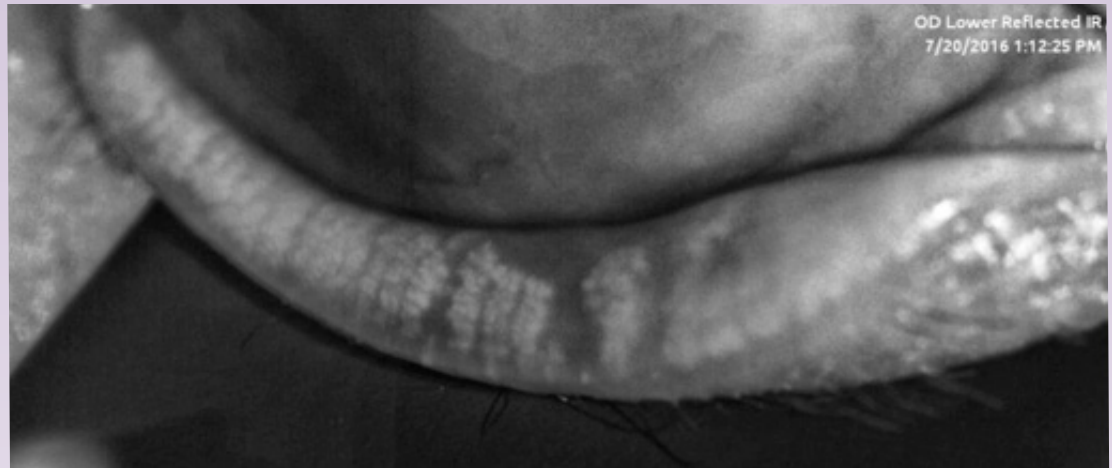


Figure 1. Meibomian gland dropout and attenuation in a patient with symptomatic MGD

Diagnostic challenges make it difficult to choose effective treatments and monitor the patient's response. In addition, patients without symptoms may not accept treatment.

Therefore, clinicians need objective sensitive and specific OSD diagnostic tools with a high positive predictive value.

Latest OSD diagnostics

Ophthalmologists have an array of available objective tests for OSD. The tear osmolarity point-of-care test is noninvasive and objective and correlates strongly with all dry eye levels. It is also useful in monitoring treatment efficacy. Technicians can perform

it rapidly, and it is reimbursable. If the reading in either eye is 308 mOsm/L or greater or if the inter-eye difference is 8 mOsm/L or greater (even if the value for either eye is less than 308), this indicates tear instability and dry eye (308–320 mOsm/L, mild; 320–340 mOsm/L, moderate; greater than 340 mOsm/L, severe dry eye).

The rapid point-of-care MMP-9 test measures ocular surface inflammation levels with high sensitivity and specificity for dry eye disease (DED). Normal osmolarity with elevated MMP-9 may suggest a non-dry eye cause of OSD.

Once DED is diagnosed, treatment should be based on the underlying DED subtype. Assorted objective tests help differentiate between evaporative and aqueous deficient dry eye.

Lipid layer interferometry measures lipid layer thickness, which has been well correlated to dry eye severity and symptoms. It also measures partial blink rate, an often overlooked diagnosis.

Meibography helps clinicians identify and grade the severity of meibomian gland disease (Figure 1). It also visually demonstrates the disease to patients, greatly helping patient understanding and acceptance of interventions.

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Mucin deficiency can lead to a rapid tear breakup time, affecting ocular health and vision. Tear film fluctuation may play a major role in determining wavefront aberrations and visual acuity. In addition, cataract surgery causes microscopic ocular surface damage contributing to dry eye.

Conclusion

OSD decreases the predictability of surgery and postoperative outcomes. The tear film has the

greatest optical power of any surface, and a poor tear film leads to poor image quality. Therefore, preoperative diagnosis and treatment of OSD are crucial in every patient to ensure accurate measurements and increase vision quality.

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Elizabeth Yeu, MD

New therapies help clinicians take aim at specific causes of dry eye

With the range of therapies now available for ocular surface disease (OSD), clinicians can customize treatment, developing targeted strategies based on its severity, cause, and signs and symptoms.

Current options

Approximately 80% of patients with dry eye have meibomian gland dysfunction (MGD); less than 10% of patients have purely aqueous deficient dry eye.

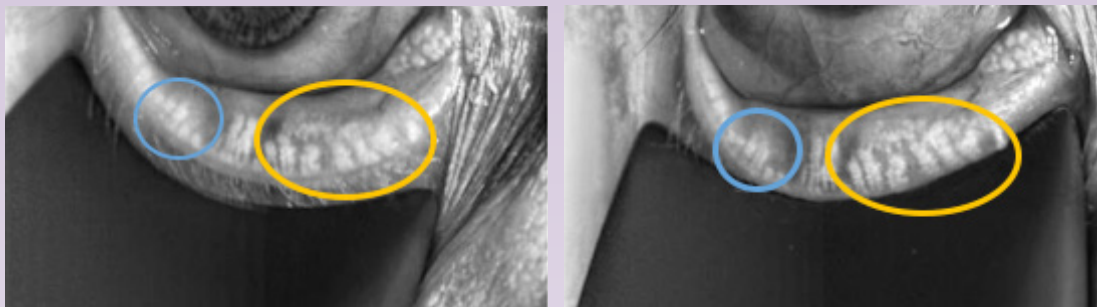
Healthy meibomian gland function is foundational to ocular surface health. Optical coherence tomography with meibography allows us to examine the gland architecture and determine function. If meibum is good with some meibomian gland dropout, early aggressive treatment is important because the clinician can reverse the disease process more readily than in a severe case.

More customized lubricants are available, such as emulsions and emollient-friendly solutions to treat evaporative disease, and methylcellulose-based preparations can be used for aqueous deficient disease.

In addition, we will soon have omega-3 based artificial tears. From a nutritional standpoint, omega-3s, particularly triglyceride-based supplements, will be very important (Figures 1A and B). Vitamin A ointment, which is not available in the

New and emerging therapeutics in dry eye disease

by Elizabeth Yeu, MD



Figures 1A and B. Infrared meibography of the left lower lid taken 6 months apart in a 69-year-old woman who had MGD treatment with thermal pulsation and omega-3 fatty acid supplements. Notice the lid appears to have repopulation of the meibomian glands inferiorly where there was great disorganization of architecture originally.

U.S., is helpful for keratinized lid margins and keratinized palpebral conjunctiva.

Although warm compresses and lid massage are often recommended to manage lid margin disease, they can be detrimental and compliance may be a problem. Lid scrubs with hypochlorous acid, commercial soap scrubs, and tea tree oil are also available, and many more effectively treat blepharitis.

We can perform in-office lid margin cleansing, manual meibomian gland expression or thermal pulsation therapy, or microblepharoexfoliation.

Cyclosporine 0.05% and lifitegrast are available as anti-inflammatory treatments, as well as macrolides and tetracyclines, which can reduce MMP-9 levels, and topical corticosteroids, which usually are not used for chronic treatment.

Many of my patients like the multi-dose cyclosporine 0.05% bottles, but single-dose vials are still available.

Lifitegrast 5% is the first anti-inflammatory for dry eye approved by the U.S. Food and Drug Administration (FDA) to treat both signs and symptoms of dry eye. Onset of action occurs as early as 2 weeks, with greater reduction in dryness by week 6 and in inferior corneal staining at week 12.¹

Looking ahead

A nasal neurostimulation device approved recently by the FDA can increase tear production and decrease dry eye symptoms.²

In addition, new artificial tear formulations will be available, as well as a cyclosporine 0.09% ophthalmic solution in a different type of vehicle compared with cyclosporine 0.05%. It has been shown to improve Schirmer's score in 12 weeks.

Newer formulations of amniotic membrane (AM) are on the horizon. What we do know is that AM improves corneal sensation and tear stability.³ AM inhibits inflammation, and the presence of proteinase inhibitors may facilitate wound healing.⁴ Several companies are working on AM drop formulations. I've been very pleased with my early experience with their amniotic cytokine extract for my patients with dry eye.

Different corticosteroid formulations such as an intracanalicular depot plug of dexamethasone has shown promise in treating OSD, in addition to loteprednol etabonate in a nanoparticle technology that penetrates tissues more readily. Cis-urocanic acid may serve as another anti-inflammatory.

Tavilemide, a naturally found protein that is being investigated, supports the corneal epithelium and nerves and

helps induce mucin production. Researchers are also investigating SkQ1, an antioxidant reactive scavenger, and RGN-259, a thymosin beta-4 antagonist.

Conclusion

A range of treatment options are available to treat OSD, and more will be at our disposal within the next few years. They will help clinicians customize treatment, which should simplify the management of dry eye disease.

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Francis Mah, MD

New algorithm will guide ocular surface disease management

To help clinicians navigate the complex maze of diagnostics and treatments for ocular surface disease (OSD), the ASCRS Cornea Clinical Committee will soon provide a logical algorithm for guidance.

This will be a revolutionary year, with the release of many different protocols.

Dry eye management

The following case illustrates how the algorithm will be used.

A 55-year-old woman was referred to our practice who had small incision cataract surgery with a multifocal intraocular lens and astigmatism correction with limbal relaxing incisions. Although she had 20/20 vision, a month after surgery she was unhappy. She had blurring, vision fluctuation, and discomfort, as well as punctate epithelial keratitis. Several treatments were tried, including artificial tears, cyclosporine 0.05%, and lifitegrast, but she still had symptoms.

Dry eye can impact contrast sensitivity because the tear film is the most important refractive surface. Many studies have shown the prevalence of postoperative dry eye in cataract and refractive surgery. However, because dry eye is common in cataract patients, it is essential that we diagnose and treat it before surgery, which optimizes the ocular surface and

Establishing a system for approaching ocular surface disease therapy

by Francis Mah, MD

surgical outcomes. We also need to educate our patients so they are aware that they have dry eye before surgery and continue treatment after surgery.

Diagnostic process

When a patient arrives in our practice, the first thing we need to do is to identify dry eye. Many cataract patients have no symptoms. Therefore, we begin with the SPEED questionnaire after the technician speaks with them about their vision and symptoms.

If a patient has blurred vision, we need to know if it is constant or fluctuates, which is almost pathognomonic for OSD. With fluctuating vision, we can skip the questionnaire and begin osmolarity testing and then inflammation testing.

If osmolarity and inflammation are positive, this indicates dry eye disease. Treatment may include lubrication, omega-3 fatty acids, steroids, and cyclosporine 0.05% and/or lifitegrast. This testing does not detect meibomian gland dysfunction (MGD), so it will be necessary to treat that if present. Serum tears may be considered, as well as amniotic membrane or extract.

If osmolarity is positive and MMP-9 testing is negative, this might be considered dry eye without significant inflammation. Treatment may include cyclosporine 0.05% and/or lifitegrast, lubrication, and omega-3 fatty acids, as well as MGD treatment if necessary.

If osmolarity is negative and MMP-9 testing is positive, the patient may not necessarily have dry eye but may have allergic conjunctivitis, conjunctival chalasis, anterior basement membrane disease, or another condition that would cause inflammation of the ocular surface.



Figure 1. Meibomian inspissation

After the testing, the clinician performs the examination, taking a careful history that will help determine whether the patient has MGD, blepharitis, or aqueous deficiency.

Next, we perform a dry eye examination, with tear film break-up time, corneal and conjunctival staining with the aid of vital dyes such as fluorescein and/or lissamine green, and meibomian gland assessment by expression (Figure 1). Serum Sjögren's testing may be necessary if the patient has dry mouth or eyes.

In addition to the aqueous component, we need to address the possible evaporative component based on the examination, history, and meibum.

Case: Diagnosis

The patient explained that ocular burning in the morning was very bothersome. On examination, she had very thick meibomian secretions, which is why cyclosporine and lifitegrast did not achieve

their full benefit. The entire ocular surface was not managed. Therefore, we needed to continue cyclosporine and/or lifitegrast and address MGD.

Additional treatments may include warm compresses and lid hygiene, omega-3 fatty acids, an emulsion-type lubricant, antibiotic ointment, systemic tetracycline derivative, thermal pulsation, and steroids, as well as cyclosporine and lifitegrast. Punctal plugs may be considered when the eyes are quiet.

Conclusion

Optimizing the ocular surface can improve the patient experience and surgical outcomes. The ASCRS algorithm will guide the use of an increasing number of point-of-care ocular surface tests.

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Francis Mah, MD

ASCRS to release new OSD management tool in upcoming months

Responses from the ASCRS Clinical Survey indicate that clinicians may be puzzled by the number of diagnostic technologies available to detect ocular surface disease (OSD), as well as how to use them to their greatest advantage in OSD management.

When asked about an algorithm for OSD diagnostics, 35% of members responded that such a tool would be valuable (Figure 1).

After years of work, **Christopher Starr, MD**, and the ASCRS Cornea Clinical Committee will soon release and publish an algorithm that will guide practitioners in OSD management. The two-part tool covers OSD dry eye and other conditions that cause or

Potential impact of new algorithm on OSD management

by Francis Mah, MD

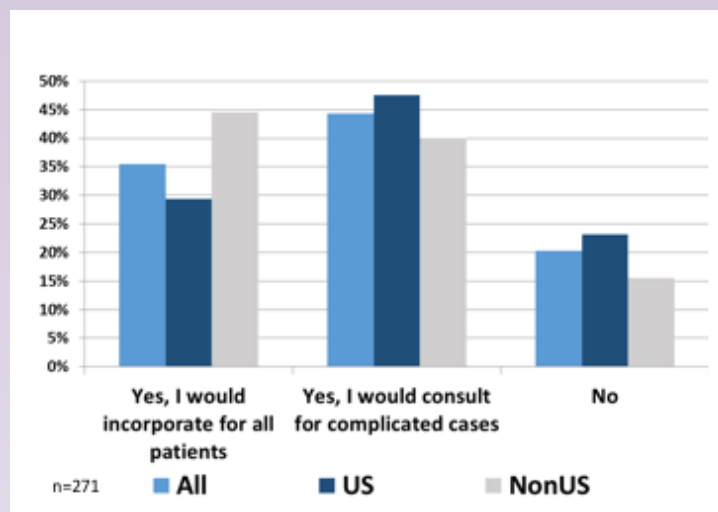


Figure 1. The 2016 ASCRS Clinical Survey asked, "Would an algorithm for ocular surface diagnostics be valuable to you?" 35% responded, "Yes, I would incorporate for all patients."

mimic OSD, such as bacterial or viral conjunctivitis.

Many papers have been published on dry eye, but this will be a user-friendly guide that clinicians can refer to in the ophthalmology or optometric eyecare lane for every patient.

When developing this tool, the committee considered all commercially available diagnostic

technologies, and it will recommend how to implement these devices when diagnosing and managing dry eye. However, clinicians using the algorithm will not need to purchase all of these tests. The algorithm will help them determine how to use the tests they currently have to diagnose and manage dry eye.

It also will help ophthalmologists assess new technologies as they consider which OSD testing devices to add to their armamentarium.

The algorithm will guide clinicians in using tests logically and efficiently. For example, based on test results, the ophthalmologist will not waste resources by prescribing an antibiotic when the diagnosis is dry eye. He or she will reach an accurate diagnosis much faster and develop an appropriate treatment strategy.

The algorithm will help clinicians interpret test results. For example, they will know what constitutes a negative or positive result or a false-positive or false-negative result. In addition, it will help them understand the diagnostic value of conflicting results.

As new technologies and treatments emerge, we look to this algorithm to help clinicians streamline the process of diagnosing and managing OSD.

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Traditional fluorescein tear breakup time is highly variable and poorly reproducible, but tear breakup time is rapid, objective, and noninvasive, requiring no drops.

Optical coherence tomography is noninvasive and does not disrupt the tear film or ocular surface. It is objective and quick, allowing clinicians to measure the tear meniscus height, area, and volume.

Case report

A 48-year-old man had a history of intermittent foreign body sensation, fluctuating vision, dryness, redness, and mild itchiness.

Another physician diagnosed dry eye. Artificial tears did not reduce his symptoms.

He had 1+ conjunctival injection, mild inferior punctate epithelial erosions, and a normal tear breakup time. Osmolarity was 295 and 293 mOsm/L, indicating it most likely was not dry eye.

The patient had positive MMP-9 results, indicating inflammation, and allergic conjunctivitis was diagnosed. Tear IgE and allergen skin testing also would be useful, as well as adenovirus testing if infection was suspected.

Conclusion

These objective diagnostics are easy to incorporate into our practice and will help us diagnose most cases of complex OSD accurately and efficiently.

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The third refractive surface: Improving surgical outcomes with advanced diagnostics and therapeutics

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CME questions (circle the correct answer)

1. A 55-year-old woman with a history of dry eye tried artificial tears, cyclosporine, and lifitegrast but still had symptoms of foreign body sensation and her eyes were red. Tear osmolarity was elevated (375 mOsm/L), MMP-9 was positive, the tear film was foamy, and meibum was thickened. What would be the best course of management?
 - a. Represcribe cyclosporine and/or lifitegrast and stress compliance
 - b. Consider topical antihistamine therapy for allergic conjunctivitis
 - c. Recommend warm compresses and lid scrubs and possibly consider automated thermal pulsation
 - d. Increase preservative-free artificial tears to every hour and prescribe ointment for nighttime

2. A 48-year-old man with intermittent foreign body sensation, fluctuating vision, dryness, mild itching, and redness was diagnosed with dry eye, but artificial tears provided no relief. He had mild inferior punctate epithelial erosions, osmolarity was normal, and MMP-9 testing had positive results. Which of the following would be most likely to yield useful information at this point?
 - a. Fluorescein tear breakup time
 - b. Schirmer's
 - c. Tear IgE testing
 - d. All of the above

3. If a positive tear osmolarity and negative MMP-9 testing confirm the presence of dry eye, the clinician next needs to:
 - a. Ask the patient to complete a SPEED questionnaire
 - b. Perform thermal pulsation
 - c. Prescribe preservative-free artificial tears and a T-cell modulator
 - d. Determine whether meibomian gland disease is present

4. _____ was the first FDA-approved prescription anti-inflammatory drug to treat the signs and symptoms of dry eye.
 - a. Azelastine hydrochloride
 - b. Lifitegrast
 - c. Cyclosporine 0.05%
 - d. Topical azithromycin

5. A 67-year-old patient with cataracts was contact lens intolerant and her vision was slightly hazy. Tear osmolarity was 322 and 311 mOsm/L, and MMP-9 was positive in both eyes. She had significant staining and significant meibomian gland dropout. Her mean keratometry measurement was 44.2, and she had 1.18 D of cylinder. She was treated with artificial tears, a short course of steroids, oral omega-3 fatty acids, and thermal pulsation. Which additional treatment would likely be prescribed?
 - a. T-cell modulator
 - b. Alcaftadine ophthalmic solution 0.25%
 - c. Oral doxycycline
 - d. Gatifloxacin ophthalmic solution

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