There is a lack of consensus on treatment protocols at all stages of dry eye

Despite advances in diagnostics, many ophthalmologists continue to rely on traditional diagnostic methods and treatment protocols for the management of ocular surface dysfunction (OSD). This may stem from beliefs regarding the incidence and impact of OSD. In the 2014 ASCRS Clinical Survey of clinical opinions and practice patterns (1,501 unique respondents), the majority of respondents said that only about 20% of their cataract patients present with Level 2 OSD requiring treatment beyond artificial tears according to Dry Eye Workshop (DEWS) guidelines. Forty-one percent strongly agreed that mild or moderate OSD affects refractive/cataract surgery.

Educational Objectives
Ophthalmologists who participate in this activity will:
• Recognize symptoms and relate common ocular surface problems and their consequences for optical image quality to reduced outcomes in refractive/cataract surgery, particularly with the advanced technology refractive cataract patient.
• Inflammation and aqueous deficiency
• Poor meibomian gland function and evaporative dry eye
• Exposure and blink rate-related dryness
• Identify strategies and processes to integrate new tools for evaluating ocular surface health into routine preoperative protocols, with the goal of making faster and more accurate diagnoses to guide treatment decisions.
• Assess potential benefits for advanced diagnostics at initial point of care for various patients.
• Develop protocols and construct treatment plans that not only provide symptomatic relief but also improve the health of the ocular surface and tear film sufficiently to result in accurate preoperative testing and optimize visual outcomes of surgery.

Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint providorship of the American Society of Cataract & Refractive Surgery (ASCRS) and EyeWorld. ASCRS is accredited by the ACCME to provide continuing medical education for physicians.

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Financial Interest Disclosures
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Figure 1. The 2014 ASCRS Clinical Survey assessed respondents’ beliefs regarding dry eye diagnostic tests.
Impact of OSD on surgical outcomes

by Alice T. Epitropoulos, MD, FACS

Cataract and refractive surgery advancements have improved postoperative visual quality dramatically, but these advances may be lost if a patient’s ocular surface is not optimized.

Studies have shown that the majority of patients (77%) presenting for cataract surgery have some corneal staining and that about half have central corneal staining.1 Almost six in 10 (59%) have blepharitis.2

If surgery is performed in patients with an unhealthy preoperative tear film, keratometry and IOL power calculations may not be accurate, potentially leading to delayed healing and suboptimal visual outcomes. An unhealthy ocular surface may also increase the need for enhancements or secondary procedures and increase the chance of having unhappy patients postoperatively.

Surgery itself is likely to exacerbate any pre-existing dry eye condition because postoperative corneal nerve damage can lead to neurotrophic dry eye and toxicity from preservatives in eye drops can adversely affect the tear film as well.

Predicting and avoiding problems

I recently participated in a multicenter clinical trial to evaluate the relationship between tear osmolarity, keratometry, and IOL power calculations in patients scheduled for cataract surgery.4 Hyperosmolarity, as measured by the TearLab Osmolarity System, is a key indicator and hallmark of dry eye disease, so we wanted to prospectively document the effect of hyperosmolarity on preoperative measurements.

Fifty patients with hyperosmolarity and 25 patients with normal osmolarity were enrolled. The hyperosmolar eyes had a statistically significantly greater variability in K readings, and 10% of these hyperosmolar eyes had a greater than 0.5-D difference in intraocular lens power, compared to none of the normal osmolar eyes (Table 1). Vector analysis of the keratometric cylinder demonstrated that 17% of hyperosmolar eyes had more than 1.0 D of cylinder difference between 2 preoperative visits.

Case report

A 75-year-old woman referred for cataract evaluation presented with intermittent blurred vision, tearing, dryness, and eye fatigue and irritation. Her SPEED score was 24. Evaluation revealed 25%–50% damage to her meibomian glands (Figure 1), an unstable tear film, abnormal osmolarity, and positive MMP-9 results.

Preoperative measurements were unreliable, so we delayed surgery until the ocular surface was optimized. One month after bilateral LipiFlow thermal pulsation treatment (TearScience), her SPEED score had improved to 2, the meibomian glands were functioning again, and the tear film was much more stable. Osmolarity and MMP-9 results were normal.

Most importantly, our treatment plan changed from a spherical 23.0-D Crystalens (Bausch + Lomb) to a 23.5-D Trulign toric lens (Bausch + Lomb). The patient was very happy postop, with 20/20 distance and intermediate vision with a plano refraction.

This is an excellent example of the value in delaying surgery until the ocular surface is healthy enough to generate accurate measurements and power calculations.

References


Dr. Epitropoulos is clinical assistant professor at The Ohio State University Medical Center in Columbus, Ohio. She practices with Ophthalmic Surgeons and Consultants of Ohio at The Eye Center of Columbus.

Table 1. Hyperosmolar eyes had significantly more variation in keratometry and IOL power than normal eyes.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Hyperosmolar</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Average K &gt; 0.5 D</td>
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<td>8/100 (8%)</td>
<td>0.049</td>
</tr>
<tr>
<td>&gt;0.5 D difference in IOL power (Holladay 1)</td>
<td>0</td>
<td>10/98 (10%)</td>
<td>0.02</td>
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</tbody>
</table>

Figure 1: MGD is a progressive disease and if not treated can lead to glandular atrophy and loss of function.
Technologies advance dry eye assessment

by Victor L. Perez, MD

Ocular surface evaluation prior to surgery is critical; a comprehensive evaluation should be similar to a glaucoma workup

Because the ocular surface is such a complex environment, we must adopt systematic workups similar to those used for glaucoma and advance our technology to develop a comprehensive picture of the ocular surface prior to any surgical treatment.

Traditional dry eye assessment techniques provide a good starting point, including a questionnaire and a comprehensive slit lamp examination with careful lid evaluation, meibomography, staining, and Schirmer’s testing.

It is important to standardize tests for data consistency. For example, staining or tear breakup time tests should be performed in the correct order, using a consistent amount of stain, with results recorded after a set time.

Expanded testing

Advanced diagnostic testing can greatly contribute to understanding of any ocular surface problems and highlight the appropriate path to treatment more quickly.

Osmolarity testing, for example, provides insight into the dynamic status of the ocular surface if an underlying condition is causing ocular surface inflammation. Results are expressed as numbers on a severity scale, from 280 to 400 mOsms/L. MMP-9 testing identifies the presence of an inflammatory marker, matrix metalloproteinase, indicating whether to treat with anti-inflammatory medications. The TearScan MicroAssay (Advanced Tear Diagnostics) evaluates lacrimal gland secretory function by testing for lactoferrin and IgE.

Clinicians are still learning how best to interpret ocular surface images. At Bascom Palmer, for example, we perform interferometry and meibomian gland imaging using the LipiView II system (TearScience). Collected data are teaching us a great deal about the ocular surface and blink rate. With this system it is possible to score meibomian gland disease and share results with patients. When data are collected in a standardized manner, patients are better able to see whether their ocular surface dysfunction is improving or progressing. Identifying the presence of Demodex mites in patients with meibomian gland dysfunction is also very important in planning a treatment strategy.

Additionally, high-resolution optical coherence tomography enables us to analyze microscopic ocular surface changes that can be early indicators of dry eye disease. Real-time, noninvasive, in vivo ocular surface imaging is truly the new frontier in ocular surface diagnosis and treatment guidance.

As in evaluating glaucoma, ophthalmologists should take a standardized and validated approach to assessing the ocular surface. Although some older tests are valuable, advanced diagnostics and imaging add value, enabling physicians to customize treatment to each patient, better facilitating preoperative and preventative therapies.

Dr. Perez is director of the Ocular Surface Center, Walter G. Ross Chair in Ophthalmic Research, and associate professor of ophthalmology, microbiology and immunology at the University of Miami Miller School of Medicine and the Bascom Palmer Eye Institute in Miami.
Current and emerging treatments for dry eye and meibomian gland dysfunction

by Marjan Farid, MD

What physicians know, and what’s coming down the pike to better treat patients with ocular surface disease

Treating the ocular surface preoperatively is imperative if we want to give patients excellent post-cataract surgery outcomes. With newer point-of-care diagnostics, we can now more easily identify the root cause of the particular type of dry eye disease that we need to treat for each patient. Although most patients with dry eye disease have mixed-mechanism pathology, I try to categorize them into mostly aqueous versus mostly evaporative dry eye. An inflammatory ocular surface and tear film is a final result of both types of dry eye disease. As such, I start with anti-inflammatory drops as my first line of treatment.

Restasis (cyclosporine 0.05%, Allergan) is currently the only approved topical therapy for dry eye. Studies have shown that it increases tear production and goblet cells and decreases corneal staining and artificial tear use (Figure 1). As the effects of Restasis can take several weeks to initiate, I typically prescribe corticosteroids for a short 4-week course when initiating cyclosporine therapy. This allows for a quick onset of the anti-inflammatory effects on the ocular surface and helps to ease any stinging sensation early in the course of treatment. I prefer the better side effect profile of newer corticosteroids, such as Lotemax (lotepronol etabonate, Bausch + Lomb), FML (fluorometholone, Allergan), and Durezol (difluprednate, Alcon). As rescue therapy, corticosteroids can be used BID for 2 weeks during times of symptom exacerbation.

Autologous serum drops have been shown to improve symptoms, surface staining and cytology. Using serum drops does require collaboration with a phlebotomy lab that can communicate well with a compounding pharmacy to produce a consistent and sterile product. I start patients on a 100% solution, as it is easier for the lab not to have to dilute the serum and I can be sure there is a high concentration of nerve growth factors interacting with the ocular surface.

While punctal occlusion is still a viable treatment, it has fallen lower on my list of ocular surface treatments. I prefer to “cool off” any ocular surface inflammation first before inserting plugs. Placement of plugs early in the treatment course can often exacerbate symptoms as it maintains the inflammatory tear cytokines longer on the ocular surface.

Meibomian gland disease

Meibomian gland disease (MGD) is being much more widely recognized as a key player in dry eye disease that needs to be addressed earlier in the treatment course. Some studies are beginning to show thermal pulsation is more beneficial than manual techniques.

Effective heat immediately over the glands is needed to restore normal lipid flow into the tear film, and it is difficult to achieve adequate temperatures at home with external methods. Ideally, thermal pulsation should be performed before there is inspissation of the glands, with warm compresses continued afterward as maintenance therapy.

Topical treatments, including azithromycin, may be able to clear the bacterial burden on the lids. Oral doxycycline and minocycline can decrease the bioactivity of the cytokines, and they are overall well tolerated as their sub-antibiotic level has minimal effect on the normal gut bacterial flora.

Intense pulsed light (IPL) treatment is used off-label for MGD; thus far, evidence of its efficacy is limited.

Nutritional support is the low-hanging fruit of ocular surface treatment. There is no reason to avoid putting patients on omega-3 fatty acids to improve the lipid content of the tear film. Studies have shown dramatic improvement in symptom scores and tear breakup time after 6 months of use (Figure 2).

Patients with chronic MGD may be affected by Demodex mites. Some commercially available lid scrubs now incorporate tea tree

continued on page 6
Treatment protocols and surgical planning

by Sheri Rowen, MD

The more info that anterior segment surgeons have about the health of the ocular surface, the easier it is to plan a surgical strategy

Superior post-cataract surgery vision that takes advantage of the best technology surgeons have is only possible if the patient’s ocular surface is optimized and healthy. Ocular surface disease is a pervasive, chronic problem that begins at an earlier age than many think—and it culminates when patients are in our offices expecting to receive great postop vision.

In our practice, all cataract consults complete an ocular surface symptom questionnaire, and technicians routinely perform fluorescein and lissamine green staining and draw a picture of the surface staining pattern. Symptomatic patients also undergo osmolarity and MMP-9 screening by the technician before I see them.

My initial exam includes a quick review of the technician’s report and patient questionnaire. I perform a quick ocular surface exam, then I perform a meibomian gland evaluation on every patient, regardless of symptoms. I express glands to assess the quality and consistency of the meibum, and document the findings. Only by expressing the glands can you determine if they are healthy and fully functioning because glands that at first appear healthy may not actually be secreting liquid.

Preop treatment need not be complex

I have a fairly simple decision tree so that I can quickly treat preoperative patients to get them ready for surgery. I begin with thermal pulsation or intense pulsed light therapy and a course of cyclosporine just to quell concomitant inflammation. I add a re-esterified or triglyceride form of omega-3 as early as possible in all cases where the surface is unhealthy. If the glands are healthy but the tear film is not, I start with cyclosporine 0.05% and add in topical steroids. If both inflammation and MGD are present, all of the above treatments should be used. I also insist on lid and lash hygiene with a new compound, Avenova (NovaBay), that uses hypochlorous acid to inactivate the bacterial lipase of the bacteria that are blocking the meibomian glands.

The reality is that patients with a healthy ocular surface have better surgical outcomes. We’ve now begun educating our younger patients about the benefits of lid hygiene and complete blinks.

It is time to take a dental hygiene approach to ocular surface management. That is, we should be informing patients in their 20s, 30s, and 40s about gland hygiene and the tear film, encouraging routine preventive care, and educating patients about the role of diet and computer use in ocular comfort and clear vision. That way, when it is time for refractive cataract surgery we can offer them the best technologies we have available instead of having to limit their options.

Dr. Rowen has a simple decision tree for treating ocular surface problems in preoperative cataract patients.

The decision tree quick synopsis:

- **Tear film OK**
  - Glands bad
    - Thermal pulsation or IPL
    - Omega-3 TG form

- **Glands OK**
  - Tear film bad
    - Cyclosporine for 1 month
    - Topical steroids for 1 month
    - Omega-3 TG form

- **Inflammation and MGD**
  - All of the above

Dr. Rowen is clinical assistant professor at the University of Maryland and is now performing surgery at NVision Centers in Newport Beach, Calif.
many ophthalmologists, and especially surgeons, are reluctant to get too involved in dry eye care, reasoning that it has low margins, distracts from their surgical focus, and slows down the schedule. However, we have found that expanding dry eye product lines, diagnostic testing, and therapeutic services not only improves patient care, but leads to strong practice growth as well.

The now 15 providers in our practice together order more than 50,000 point-of-care (POC) tests annually, which typically includes tear osmolarity and MMP-9 testing and may also include allergy panels, corneal topography, lipid interferometry or meibomography. These tests lead to focused services, including punctal occlusion, thermal pulsation therapy, and amniotic membrane procedures, which generate a significant amount of revenue, while providing our patients with necessary care that precludes many symptoms and problems.

Analysis finds that practice and the healthcare system overall benefit from establishing a dry eye center of excellence

In a typical intermediate patient visit covered by insurance, adding our routine POC testing represents a 237% increase in revenue for the visit. However, it costs the practice only 5 extra minutes of technician time and a modest amount of interpretation time for the doctor. In fact, the doctor’s time opportunity cost is probably reduced because the test results make it easier to determine the most appropriate treatment, thereby

Dry eye care: good for patients, good for business

by John D. Sheppard, MD, MMSc

Pipeline therapy

Exciting upcoming treatments include Shire’s lifitegrast ophthalmic solution 5%, which has just been given priority review for FDA approval. Lifitegrast is an integrin inhibitor that works on multiple points in the inflammatory pathway to not only prevent T cell activation but to also shut down activated T cells. As such, it may have a rapid onset of action and potent effects on symptomatology.

A number of dry eye treatments, including Mimetogen’s TrkA agonist, Eleven Biotherapeutics’ interleukin-1 receptor antagonist, and EyeGate Pharma’s dexamethasone delivery system, are in phase 3 clinical trials. A host of others are in phase 2 or earlier stage testing. However, it is has been challenging for new drugs to show efficacy compared to vehicle on both signs and symptoms of dry eye.

No one therapy is going to “fix” everything for every patient. We need to use a combination of all the tools in our armamentarium to individualize ocular surface care. By doing so, and especially by catching ocular surface disease earlier, we can ensure better post-cataract outcomes for our patients.

In a typical intermediate patient visit covered by insurance, adding our routine POC testing represents a 237% increase in revenue for the visit. However, it costs the practice only 5 extra minutes of technician time and a modest amount of interpretation time for the doctor. In fact, the doctor’s time opportunity cost is probably reduced because the test results make it easier to determine the most appropriate treatment, thereby

References

Dr. Farid is associate professor of ophthalmology; director of cornea, cataract and refractive surgery; and vice chair of ophthalmic faculty at the Gavin Herbert Eye Institute at UC Irvine.

Cataract patient with irregular topography

History: A 68-year-old female presented for cataract surgery complaining of dry, gritty eyes. She used frequent artificial tears and had a history of glaucoma, managed with Xalatan (latanoprost, Pfizer).

Exam: Topography was irregular, with a 10.0-D difference within the visual axis. Osmolarity was elevated at 288 OD and 320 OS, with a positive MMP-9 test and moderate corneal staining. The meibomian glands were normal.

Diagnosis: This patient has aqueous deficient dry eye with significant inflammation. Accurate IOL power calculation is not possible with highly irregular topography. Twice-daily Lotemax and Restasis were prescribed, along with non-preserved tears QID and omega-3 nutritional supplements. Two weeks later, the topography was notably more regular, and the patient was deemed ready for surgery.
avoiding shotgun therapy and costly mistakes.

Taken together, the testing, products, and services identified in the accompanying graphic represent revenue for the practice that is equivalent to 3 new providers, yet was obtained entirely through patient education, internal marketing and existing (but optimized) providers.

These implied costs or debits to the healthcare system are more than balanced by the assumed savings or credits created by better diagnosis and getting the treatment right the first time around. Assuming that our initial debit calculations encompass unique patients, and that improved diagnosis and targeted therapy can result thereafter in 1 fewer office visit, 1 less over-the-counter (OTC) oral medication, 1 less OTC topical drop and 1 less prescription drop per year per patient tested, the overall savings to the healthcare system and our patients is estimated to be $1,517,272 annually for the hypothetical practice of our size. Truly, appropriately utilized diagnostic technology and advanced yet focused treatment options have great potential to improve the quality of healthcare for our ocular surface disease and dry eye patients.

The most important asset in our practice is the providers’ time, and we need to use it efficiently. Our most important product is patient satisfaction: Correct, timely diagnosis, focused treatment, minimal doctor visits and cost savings all contribute. When we deliver appropriate care, patients, payers, providers, and practices win.

Dr. Sheppard is president of Virginia Eye Consultants in Norfolk, Va. He is also professor of ophthalmology, microbiology and molecular biology; clinical director of the Thomas R. Lee Lab for Ocular Pharmacology; and ophthalmology residency research director at Eastern Virginia Medical School.

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### Healthcare system overall profit and loss statement for the hypothetical dry eye center of excellence

<table>
<thead>
<tr>
<th>Debits</th>
<th>Credits</th>
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<tbody>
<tr>
<td>Punctal occlusion collections</td>
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<tr>
<td>Collagen and silicone plugs</td>
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<td>Punctal cautery</td>
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<td>Thermal pulsation</td>
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<td>Total additional cost</td>
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<td>Unnecessary patient transportation costs (1 visit/patient tested/year x 20 mile round trip x $0.55/mile)</td>
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<td>Unnecessary OTC oral medications (1 med/patient tested/year @ $20/med x 25,152 patients)</td>
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<tr>
<td>Unnecessary OTC topical medications (1 med/patient tested/year @ $20/med x 25,152 patients)</td>
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<td>Unnecessary prescription topical medications (1 med/patient tested/year @ $45 copay/med x 25,152 patients)</td>
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<tr>
<td>Total cost savings (not including opportunity loss to patient and family) (not including prescription payment loss to insurance company)</td>
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<tr>
<td>NET ESTIMATED SAVINGS TO MEDICAL SYSTEM AND SOCIETY</td>
<td>$1,517,272</td>
</tr>
</tbody>
</table>
1. What percentage of patients presenting for cataract surgery have at least some corneal staining?
   a. 22%
   b. 33%
   c. 66%
   d. 77%

2. According to the study cited by Dr. Epitropoulos, hyperosmolar eyes have:
   a. Stable K readings
   b. More variable K readings
   c. Greater white-to-white
   d. More inspissated glands

3. According to Dr. Farid, punctal occlusion should be considered:
   a. As primary therapy in most cases
   b. In combination with loteprednol etabonate
   c. In combination with cyclosporine
   d. After resolving inflammation

4. If the tear film is healthy, but the glands are not, Dr. Rowen recommends which of the following as primary therapy?
   a. Punctal occlusion
   b. Thermal pulsation or IPL
   c. Lid hygiene
   d. Cyclosporine and topical steroid

5. According to Dr. Sheppard’s calculations, what is the financial impact of a dry eye center of excellence?
   a. Retail collections decline with additional dry eye services
   b. Point of care testing is not profitable
   c. There is a net estimated savings to the medical system due to reduced visits, treatments, and medications
   d. There is a net estimated cost to the medical system due to increased visits, treatments, and medications

To claim credit, please fax the test and fully completed form by December 31, 2015 to 703-547-8842, email to GPearson@ascrs.org, or mail to: EyeWorld, 4000 Legato Road, Suite 700, Fairfax, VA 22033, Attn: June 2015 CME Supplement