Dry Eye – Diagnosis & Treatment

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Dry eye is a complex and potentially debilitating disorder that drives patients to seek eye care. Overall prevalence estimates range between approximately 5.5 and 33.7% of the population.\(^1\) It is a primary reason for patients to discontinue contact lens wear and may impede the daily activities of otherwise healthy patients. Many of these patients are frustrated and desperate for relief. Therefore, practitioners need a strategy to manage these patients and to keep up-to-date with new treatment options to help these challenging, yet potentially rewarding patients.

In the past two decades, our knowledge of dry eye has increased and the definition of dry eye has evolved. An updated definition proposed by the International Dry Eye Workshop (DEWS) in their 2007 report reflects the current understanding of dry eye: “Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.”\(^2\) This updated definition acknowledges the roles of tear osmolarity and inflammation contributing to compromised visual function.

Risk Factors

Age and female gender are two of the major risk factors that have been consistently reported for dry eye. Over 3.2 million women aged 50 years and older in the United States are affected by dry eye.\(^3\) Conversely, approximately 1.68 million men aged 50 years and older are affected by dry eye.\(^4\) There is a significant increase in the prevalence with age for both males and females. It is speculated that the hormonal changes following menopause...
are involved in the pathogenesis of dry eye in women. Other risk factors include androgen deficiency, postmenopausal estrogen therapy, systemic medications (antihistamines, antidepressants), systemic conditions (diabetes mellitus, Sjögren syndrome), contact lens wear and refractive surgeries that sever corneal nerves (LASIK). Environmental risk factors include ceiling fans, air conditioners, heaters, low humidity environments, air travel, reading and computer use. A careful case history that reveals dry eye risk factors is important for managing these patients. Relieving dry eye symptoms may entail a spectrum of treatment options, including consultation with the patient’s primary care physician in altering medications, recommending a humidifier in the office, or changing a patient’s contact lens solution.

Symptoms

Dry eye is a symptom-based disorder and patients with dry eye report a wide-range of symptoms. Some commonly reported patient symptoms include, but are not limited to, blurry vision, burning or stinging sensation, tearing, crusting, dryness, foreign body sensation, photophobia, or soreness (pain). Patients with dry eye also report being adversely affected in daily activities such as reading and computer use. Incorporating a dry-eye questionnaire in clinical practice can be useful in determining the effectiveness of treatment and severity of the dry eye.

Practically, the questionnaire should be quick to administer in office and readily available. One widely used dry eye questionnaire is the Ocular Surface Disease Index (OSDI) questionnaire, popular because of its established reliability and validity. The OSDI is a 12-item questionnaire that is designed to quickly indicate the degree of dry eye severity. The questionnaire is divided into three subscales relating to ocular symptoms, vision-related function, and environmental triggers. Patients report the frequency in which various symptoms occur and the scoring is weighted. An interactive version of the OSDI can be found on-line at http://www.focusondryeye.com/_resources/quiz.htm.

A dry eye questionnaire can be filled out prior to the initial examination and at each follow-up so that it can provide the practitioner a “snap-shot” of the patient’s current dry eye complaints. It can also provide monitoring of symptoms during treatment.

Classifying Dry Eye

It has been generally accepted within the dry eye community that there are two major classification schemes for dry eye based on etiology: 1) aqueous tear-deficient dry eye (ADDE), and 2) evaporative dry eye (EDE). This classification scheme was first proposed by the National Eye Institute (NEI)/Industry workshop and later refined in the 2007 DEWS report. Patients with ADDE have a reduced tear secretion, either from the main or accessory lacrimal glands. The ADDE major classification group is further divided into Sjögren’s and non-Sjögren’s dry eye. Patients with EDE have normal lacrimal gland function, but there is an excessive loss of water from the ocular surface. The EDE major classification group is further divided into intrinsic causes (meibomian gland disease, incomplete blink, low blink rate, etc.) and extrinsic causes (medications, contact lens wear, etc.). The International Workshop on Meibomian Gland Dysfunction recently released an extensive summary report on this condition, and it is believed that meibomian gland dysfunction is the most common cause of EDE.

Even though there are distinct classification groups, it is possible for patients to exhibit characteristics of both ADDE and EDE in a mixed form. Classifying subtypes can be helpful
in tailoring dry eye treatments, however the challenge to practitioners is with the “mixed forms” where delineation between subtypes is not always clear.

**Diagnostic Tests**

On the day of testing, advise patients to refrain from using artificial tears, topical medication, or applying make-up as these can alter the tear film and contaminate the results of the testing. For patients who are contact lens wearers, advise them to discontinue lens wear for at least two days, as lens wear may interfere with the mucin layer. Table 1 suggests a battery of tests that can be utilized in practice, using instrumentation that is readily available for practitioners. This list represents a simple dry eye evaluation, and certainly not an exhaustive list of dry eye tests. Sequencing of dry eye tests should be performed from noninvasive to invasive to prevent one test from contaminating the results of another. The final goal of the dry eye evaluation is to determine the classification and severity of dry eye.

**TABLE 1:** Dry Eye Evaluation Sequence

<table>
<thead>
<tr>
<th>Test</th>
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<tbody>
<tr>
<td>Case History</td>
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<tr>
<td>Symptom Survey</td>
</tr>
<tr>
<td>Biomicroscopy</td>
</tr>
<tr>
<td>TBUT with Wratten Filter</td>
</tr>
<tr>
<td>Corneal Staining with Wratten Filter</td>
</tr>
<tr>
<td>Conjunctival Staining</td>
</tr>
<tr>
<td>Meibomian Gland Evaluation</td>
</tr>
<tr>
<td>Schirmer’s Testing</td>
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</tbody>
</table>

During the case history, a complete ocular and medical history should be taken. A gross observation of the patient’s facial features in normal room illumination should be noted. Facial redness, telangiectasia, dermal pustules, and rhinophyma can indicate the presence of rosacea and significant orbital and lid erythema can signal inflammatory lid disease. A symptom survey should be utilized as noted previously. This survey can be conducted and scored while the patient is in the waiting room under the supervision of a trained staff member to save time in a busy practice.

Biomicroscopy in a dry eye evaluation is no different than one you would perform during a routine examination, however, particular attention is made to the lid margin and lashes. Lid margin irregularity and notching, poor lid apposition, thickened or calloused lid margin, telangiectasia, orifice squamous metaplasia, plugging of the meibomian orifices are clinical signs of the presence of meibomian gland dysfunction. Figure 1. Madarosis, crusting, matted lashes, and oily residue on lashes are indicators of blepharitis. Meibomian gland dysfunction and blepharitis can be present simultaneously.
FIGURE 1. Telangiectasia along lid margins can be a sign of meibomian gland dysfunction.

Tear breakup time (TBUT) is a key test in evaluating the stability of the tear film, simple to administer, but several sources can cause variation in results. Most practitioners do not have access to a tearscope to evaluate the tear film non-invasively, and so fluorescein to measure TBUT is more commonplace. A wide slit lamp beam, illumination set at high, and the use of a Wratten 12 yellow filter can enhance the visibility of the dark spots in the areas where the tear film is thin or absent. Care must be taken not to instill a large volume of fluorescein and not to trigger reflex tearing as both give a false reading by artificially lengthening the TBUT time. It is difficult to control the volume into the conjunctival sac with a standard fluorescein strip. The Dry Eye Test (DET; Nomax, Inc., St. Louis, MO) fluorescein strip can be purchased which instills 1 microliter of fluorescein. Samples of the DET can be obtained on-line at: http://www.fluoresceinstrips.com/index.asp. A stopwatch can be used to time the interval from the last regular blink to the appearance of the first dark spot. Table 2 presents the cut-off ranges for TBUT based on the DEWS dry eye grading scheme.10

TABLE 2: TBUT Cut-Off Ranges

<table>
<thead>
<tr>
<th>Level</th>
<th>Cut-Off Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 Mild</td>
<td>Variable</td>
</tr>
<tr>
<td>Level 2 Moderate</td>
<td>≤ 10 seconds</td>
</tr>
<tr>
<td>Level 3 Severe</td>
<td>≤ 5 seconds</td>
</tr>
<tr>
<td>Level 4 Severe and/or Disabling</td>
<td>Immediate</td>
</tr>
</tbody>
</table>

Though there is no single, universally accepted approach to quantify corneal and conjunctival staining, a systematic approach can help facilitate uniform grading at each visit. The NEI Industry Workshop recommends grading staining by sectors, as shown by figure 2 below.

FIGURE 2. Corneal staining can be graded by sectors.
If corneal staining is performed shortly after TBUT test, then additional fluorescein does not need to be instilled. A Wratten 12 yellow filter can help highlight subtle corneal staining. Rose bengal staining can be enhanced using a red-free light source. The disadvantage of using rose bengal is the discomfort and stinging, particularly in patients with heavy staining. Lissamine green is much better tolerated by patients and stains similarly to rose bengal. Figure 3. A red-free light source is not needed with lissamine green.

**FIGURE 3.** Lissamine green can help highlight conjunctival staining.

Meibomian gland evaluation consists of examining the integrity of the gland and the ease of meibum expressibility, as well as its quality. A sterile cotton tipped applicator is pressed firmly against the globe at the lid margin to express meibum from the temporal aspect to the nasal aspect. Figure 4.

**FIGURE 4.** A sterile cotton tip applicator can be used to express and evaluate the quality of meibum.

Mathers et al\textsuperscript{12} has proposed a useful grading scheme to evaluate both the volume and viscosity of the meibum using a 1-4 scale which is presented in Table 3 below.

**TABLE 3.** Grading scheme to evaluate expressed meibum.

<table>
<thead>
<tr>
<th>Volume Scale</th>
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<tbody>
<tr>
<td>Level 1</td>
<td>normal volume, just covers orifice</td>
</tr>
<tr>
<td>Level 2</td>
<td>increased 2-3x normal volume</td>
</tr>
<tr>
<td>Level 3</td>
<td>increased more than 3x normal</td>
</tr>
<tr>
<td>Volume</td>
<td>Level 4 increase to 10x normal volume</td>
</tr>
<tr>
<td>--------------</td>
<td>---------------------------------------</td>
</tr>
</tbody>
</table>

**Viscosity Scale**

<table>
<thead>
<tr>
<th>Level 1</th>
<th>normal, clear, may have a few particles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 2</td>
<td>opaque with normal viscosity</td>
</tr>
<tr>
<td>Level 3</td>
<td>opaque with increased viscosity</td>
</tr>
<tr>
<td>Level 4</td>
<td>severe thickening (toothpaste)</td>
</tr>
</tbody>
</table>

The ease of expressibility should be noted, particularly if no meibum is secreted on repeated attempts, suggesting complete obstruction of the glands. Extent of the meibomian gland atrophy can be observed using a technique called meiboscopy where a transilluminator is used to evert the lower lids of the patient while they are seated behind the slit-lamp. Figure 5. The transilluminator light, not the slit lamp illumination, is used to highlight the areas of missing glands.

**FIGURE 5.** A transilluminator can be used to observe meibomian gland atrophy (meiboscopy).

In meiboscopy, the dark areas along the lid represent the meibomian glands. In normal subjects there are approximately 24 meibomian glands in the lower lid. Meibography, is another technique that captures the extent of atrophy by utilizing a near infrared sensitive camera to photodocument the meibomian glands. Photodocumentation allows for more accurate monitoring over time, but meibography does require specialized equipment.

The Schirmer I test is a key test to differentiate between ADDE and EDE. The Schirmer strip is placed gently over the lower lid margin and the amount of wetting over a 5-minute period is measured. This test can be performed with anesthetic as the Schirmer strips can cause irritation and induce reflex tearing. However, the NEI Industry Workshop recommends the test be performed without anesthetic as it provides a better measure of the capacity of the lacrimal glands to produce tears. Patients who are unable to wet the strip without anesthetic, probably suffer from a truly diminished aqueous tear production. As suggested by the DEWS report, a reasonable cutoff for the Schirmer I test without anesthetic is <5.0 mm in 5 minutes.

**Specialized Equipment**

Tear osmolarity has been considered the single best test to diagnose dry eye disease. Until recently, measuring tear osmolarity has been limited to research laboratories,
however, the TearLab Osmolarity System (TearLab Corporation, San Diego, CA) is an osmometer intended for clinical use. It is compact and can quickly obtain osmolarity readings from the inferior tear meniscus.

Treatment

Managing patients with dry eye can be challenging because most treatments available are targeted at relieving symptoms, and do not provide a cure. The treatment approach recommended by the DEWS Therapeutic subcommittee is based on disease severity. This is a systematic approach and can be easily adopted by practitioners.

Mild Dry Eye

Artificial tears and ointments with lid hygiene are the main form of therapy for patients who have a mild presentation of dry eye (few symptoms and objective signs). Artificial tears can provide temporary relief for patients, particularly during tasks such as computer use or extended reading. There are many artificial tears available on the market and practitioners should help patients navigate through the choices. Lipid-based artificial tears such as Systane Balance (Alcon, Fort Worth, TX) and Soothe XP (Bausch + Lomb, Rochester, NY) are targeted for patients with MGD. Unit-dose preservative-free artificial tears are important for patients with ADDE who need to dose more frequently and are susceptible to epithelial toxicity from preservatives. Gels and ointments can create visual blur, and are used at night with nocturnal lagophthalmos or for patients with Bell’s palsy as the retention times are longer.

Routine lid hygiene should be prescribed for patients with MGD. Compliance with lid hygiene (warm compresses in conjunction with digital lid massage) can be increased with a written instruction sheet which should be distributed to patients along with regular follow-up visits to monitor improvement in symptoms. Lid hygiene hand-outs can be found at: http://www.ossopt.com/reasearch.html.

Moderate Dry Eye

Oral antibiotics, topical anti-inflammatory medication, punctal plugs, and omega-3 fatty acid supplementation are additional treatment options for patients who have a moderate presentation of dry eye (limiting visual symptoms, variable corneal and conjunctival staining, variable lid disease, moderate tear secretion).

Tetracycline antibiotics also have anti-inflammatory properties which make them particularly useful for patients with ocular rosacea and lid disease. Doxycycline and minocycline can be prescribed in 50 mg per day dose for the initial two weeks and then 100 mg per day for three to six months. Doxycycline is available in 20, 50, and 100 mg at generic pricing. Patients should be monitored after four weeks to determine if there is an improvement in symptoms. Advise patients of the potential side effects of tetracyclines, such as photosensitivity, diarrhea, and vaginal candidosis. Topical corticosteroids such as Lotemax (Bausch + Lomb, Rochester, NY) four times a day can help quell the inflammatory component rapidly. Consider topical steroids for patients who have moderate levels of corneal staining or cannot find relief with artificial tears. However, long-term use of corticosteroids should be avoided due to the well-known ocular side effects. Patients should be regularly monitored for rising IOP levels and cataracts.

Restasis (Allergan, Irvine, CA), a topical cyclosporine, has been FDA-approved for patients with dry eye.
Cyclosporine is an immunosuppressant and has widespread application in prevention of organ transplant rejection and to treat autoimmune disease. In the eye, it is thought to stimulate tear production by suppressing inflammation and inhibiting apoptosis of the cells in the lacrimal gland. Therefore, cyclosporine should be considered for patients with ADDE. Patients who find relief with topical steroids can be transitioned to Restasis for long-term treatment.

Punctal plugs are helpful in preserving natural tears and come in both temporary and permanent forms. Punctal plugs are indicated for patients who have ADDE. It is important that ocular surface inflammation is controlled prior to insertion of punctal plugs, otherwise the ocular tissue has a prolonged contact time with poor quality tears.

**Omega-3 Fatty Acid Supplements**

Essential fatty acids (EFA) are crucial for maintaining normal bodily function, but cannot be synthesized by humans, so EFA intake occurs through diet. Of the two EFA families, omega-3 and omega-6, the former produces eicosanoid molecules with anti-inflammatory properties, which may be beneficial in modifying the inflammatory component contributing to dry eyes. If the ratio of omega-3 to omega-6 in the diet is 1:4, it creates more of an anti-inflammatory effect, but when the ratio is skewed towards omega-6 there is an increase in pro-inflammatory levels, which has been associated with a greater prevalence of dry eye in women. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are found in cold-water fish such as salmon, mackerel, halibut, sardines, tuna, and herring. Alpha linoleic acid (ALA) is plant-derived and found in flaxseeds, flaxseed oil, walnuts, canola oil, and olive oil. The body cannot convert ALA to EPA and DHA efficiently, so flaxseed oil should not be prescribed.

Nutritional supplements sold over-the-counter (OTC) are not governed by any agencies, such as the FDA, so the ingredients in OTC omega-3 may vary substantially. The amount of fish oil is not critical, rather the total dosage of EPA and DHA. Be cautious of recommending patients to take a number of capsules per day as the amount of EPA and DHA can vary markedly between brands. Instead, educate patients to read the nutritional labels for the exact dosing of EPA and DHA in supplements. Currently, there are no formal recommendations for the amount of EPA and DHA intake for the treatment of dry eye. The FDA recommends patients not exceed more than a total of 3 grams per day of EPA and DHA omega-3 fatty acids, and 2 grams per day of dietary supplements.  

**Severe Dry Eye**

For patients who have a severe presentation of dry eye (constant visual symptoms, marked corneal and conjunctival staining, frequent lid disease, little tear secretion), permanent punctal occlusion and scleral contact lenses are additional treatment options. Scleral lenses are beneficial when other conventional treatments have not been effective. Scleral lenses vault the cornea and rest on the sclera, providing a tear reservoir to lubricate the cornea. Non-preserved artificial tears or saline can also be placed in the bowl of the scleral lens prior to insertion to enhance lubrication. Scleral lenses have been indicated for patients with Stevens-Johnson syndrome, ocular cicatrical pemphigoid, exposure keratitis, toxic epidermal necrolysis, postherpetic keratitis, superior limbal keratoconjunctivitis, Sjögren syndrome, congenital deficiency of meibomian glands and corneal degeneration. Consider scleral lenses as an option for those patients that have severe dry eye and corneal irregularity due to scarring as it can optimize vision and provide improved comfort during waking hours.
TABLE 4: Summary of dry eye treatment based on level of severity (not an exhaustive list)

<table>
<thead>
<tr>
<th>Level</th>
<th>Treatments</th>
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| Mild        | Artificial tears and ointments  
              | Lid hygiene  
              | Environmental modifications  
              | Eliminate offending agent |
| Moderate    | All the above including:  
              | Oral antibiotics  
              | Topical anti-inflammatory medication (steroids and cyclosporine)  
              | Punctal plugs  
              | Omega 3-FA supplements |
| Severe      | All the above including:  
              | Scleral lenses  
              | Permanent punctal plugs |
| Severe +    | May require a referral for systemic anti-inflammatory agents or lid surgery. |
| Disabling   |                                                                            |

Treatments On The Horizon

Perhaps the exciting part of the dry eye field is the ever-changing availability of treatment options. Two surgical treatments that have garnered some press are Intense Pulse Light (IPL) therapy and intraductal meibomian gland probing. IPL therapy has been used primarily by dermatologists to treat vascular skin lesions, such as rosacea. The laser light is preferentially absorbed by hemoglobin, which generates thermal energy, and diffuses into the vascular region damaging the vessel wall. The effectiveness of IPL on MGD has been primarily anecdotal, but reports state an improvement in dry eye symptoms possibly by stimulating the meibomian glands or decreasing the lid telangiectasia.20

Intraductal meibomian gland probing involves using 2 or 4mm probes to mechanically dilate and remove the obstructed meibum. One case study on this experimental procedure involved 25 patients and all reported short-term symptomatic relief within 4 weeks of the procedure. 21 Long-term side-effects of meibomian gland scarring with intraductal probing is unknown. Certainly further studies need to be performed to confirm the effectiveness of these treatments, but these initial reports do offer some promise to dry eye patients. New formulations of medicated and OTC topical therapy will continue to be released as companies conclude their clinical trials.

Patient Education

Dry eye is a commonly encountered condition in practice. Practitioners need to perform a careful assessment and diagnosis in order to properly manage these patients. Invested time and care with dry eye patients, many of whom are desperately seeking relief, can not only build your practice, but become a rewarding aspect of your career!

Supplemental Materials

Websites that provide useful information and supplemental materials regarding dry eye:

- [http://www.tearfilm.org/](http://www.tearfilm.org/)


Self Assessment Test

1. According to the updated definition of dry eye proposed by the International Dry Eye Workshop (DEWS), increased tear film osmolarity and ocular surface inflammation contribute to compromised visual function.
   A. True
   B. False

2. The two major risk factors for dry eye are female gender and ____________.
   A. age
   B. contact lens wear
   C. refractive surgery
   D. Sjögren syndrome

3. The most common cause of evaporative dry eye is:
   A. computer use
   B. contact lens wear
   C. incomplete blink
   D. meibomian gland dysfunction

4. Based on the DEWS report, moderate dry eye has a TBUT of:
   A. 1 second
   B. \( \leq 5 \) seconds
   C. \( \leq 10 \) seconds
   D. \( \leq 15 \) seconds

5. A test to differentiate between aqueous deficient dry eye and evaporative dry eye is:
   A. corneal staining
   B. presence of lid erythema
   C. Schirmer’s score
   D. TBUT

6. The following are known side effects of oral tetracyclines except for:
   A. diarrhea
   B. eyelash lengthening
   C. photosensitivity
   D. vaginal irritation

7. Based on the DEWS report, a reasonable cutoff for the Schirmer I test without anesthetic is \(<5.0\) mm in:
   A. 1 minute
   B. 3 minutes
   C. 5 minutes
   D. 7 minutes

8. Ocular surface inflammation should be controlled prior to insertion of punctal plugs.
   A. True
   B. False

9. The body converts alpha linoleic acid (ALA) found in flaxseed more efficiently than eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in cold-water fish.
   A. True
   B. False

10. All the following are uses of cyclosporine except for:
    A. lowering high blood pressure
    B. prevention of organ transplant rejection
    C. stimulation of tear production in aqueous deficient dry eye
    D. treatment of autoimmune disease
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