Diagnosing dry eye: It’s now a fine art

Research has led to better, more diverse ways to reach a diagnosis, let alone more knowledge about DED itself.

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This article briefly examines how decades of research have advanced the accuracy and precision of tools used to diagnose dry eye. Arming the patient with knowledge about his condition, such as it is a chronic disease and not a random phenomenon, will greatly improve compliance to therapy and life style changes needed to adequately manage this trying disease.

Patient history

Proper diagnosis starts with the doctor-patient relationship. A careful examination and history will lead to a focused diagnosis of dry eye and a treatment plan that encourages patient compliance. Patients may not be aware of dry eye but may complain of symptoms. Patients may notice changes in symptoms at different times of day, or with different visual tasks and environmental conditions. Dry eye can develop in association with systemic diseases such as diabetes, systemic lupus and rheumatoid arthritis, or with medications such as oral antihistamines and antidepressants.

Schirmer’s test

Schirmer’s test without anesthetic is the gold standard for evaluating tear production. A clinician can conduct a more patient-friendly tear volume estimation by looking at the tear meniscus height during a slit lamp exam. Fluorophotometry measures tear production less invasively by capturing the rate of fluorescein dye dilution from the tear film. Heckley and colleagues showed that an improved fluorophotometry technique (with decreased drop volume and concentration, and blink synchronization) was superior to the Schirmer’s test for measuring aqueous secretion.

Ocular surface staining

Ocular surface staining is a common, though sometimes problematic, diagnostic test. Fluorescein staining visualizes the effects of desiccation on the corneal surface. But large amounts of fluorescein can make it difficult to distinguish staining due to oversaturating the epithelium. Assessments should be made approximately 3 to 5 minutes after drop instillation. Patients with severe dry eye may demonstrate high levels of staining yet experience minimal symptoms due to decreased corneal sensitivity. Lissamine green and rose bengal are also valuable dyes. Krenzer and colleagues observed a greater change in ocular surface staining with lissamine green than with rose bengal.

The Ora Calibra Corneal and Conjunctival Staining scale is a validated scale for use in clinical trials. Investigators grade staining with scores ranging from 0 to 4; these scales divide each eye into five areas: the inferior, superior and central regions relative to the cornea, and the temporal and nasal regions relative to the conjunctiva. Each area is graded separately; the sum of the three corneal regions generates a corneal sum score, and addition of the nasal and temporal conjunctival scores generates a combined total score. The inferior corneal surface usually displays the most staining, as it is exposed to the elements more than other regions due to decreased and incomplete blinks. Staining assessments have since been improved with the addition of automated image analysis via a continuous numerical scale. This system provides a consistent output of data across sites in multicentered studies.

Tear film breakup time (TFBUT)
TFBUT, or time between the last complete blink and the first appearance of tear film breakup, is a widely used test.\textsuperscript{11} Historically, TFBUT was measured with ~50 µL of sodium fluorescein, which greatly exceeds average tear volume (~6-7 µL).\textsuperscript{12} From this, a dry eye diagnosis was determined as a TFBUT < 10 seconds. This methodology has been improved by using lower quantities of sodium fluorescein (1–5 µL).\textsuperscript{12} This recalibrated technique affords more reproducible and physiologically relevant diagnostic reference values whereby TFBUT is ≥5 seconds in healthy patients (mean = 7.1 ± 1.17 seconds) and <5 seconds in dry eye patients (mean = 2.2 ± 0.82).\textsuperscript{12,13}

**Symptomatic tear-film breakup time (SBUT)**

Approximately 70% of patients with dry eye report ocular awareness and discomfort after TFBUT. The Symptomatic Tear Film Breakup Time (SBUT), or time to patient-reported ocular discomfort, is a diagnostic tool that can be performed anywhere. Patients are asked to blink twice, then to stare without blinking for as long as possible until they become aware of discomfort. Dry eye patients with low corneal sensitivity have a longer SBUT, thus these patients may be at greater risk of ocular surface exposure.\textsuperscript{14} This is a particularly useful home test for patients to determine the status of their tear film.

**Blink rate, patterns and visual function**

In 1977, Abelson and Holly linked partial or incomplete blinks to the development of punctate keratopathy.\textsuperscript{8} Subsequent video evidence showed that complete blinking was noted in 80% of normals and in 7.5% of those with punctate keratitis. This was the first time blinking was proposed to have an etiological basis in ocular surface disease.

Blink is a contributing factor to dry eye and one of the few objective endpoints available that incorporates both signs and symptoms.\textsuperscript{15} Average blink rate is 8.0 blinks/minute and the interblink interval (IBI), is about 7.5 seconds.\textsuperscript{15} To ensure that the ocular surface remains protected, ensure that the TFBUT matches or exceeds the IBI. The larger the interval between tear film breakup and the following blink, the greater potential for damage to the ocular surface.

The Ocular Protection Index (OPI) was developed with the division of TFBUT by IBI. A protective OPI score <1.0 indicates breakup and exposure before blinking, whereas an OPI score ≥1.0 indicates a protected surface, with breakup occurring after blink time.\textsuperscript{15} The OPI 2.0 system was developed to assess TFBUT and IBI simultaneously, implementing fully automated software algorithms that provide real-time measurements of corneal exposure, known as breakup area.\textsuperscript{16}

Blink patterns are particularly useful in the clinical diagnosis of dry eye. Dry eye patients have extended blink closure times — more than six times longer than those of normal subjects. This is similar to those who describe microsleeps as fatigue states, and may be due to subconscious compensatory mechanisms.\textsuperscript{17} Dry eye subjects also blink more, blink longer and spend a great deal of time with their eyes closed — all likely to affect visual function.

Blurred vision and keratitis are known to affect visual function.\textsuperscript{18} Dry eye patients are known to maintain their best corrected visual acuity for shorter periods of time than patients without dry eye.\textsuperscript{19,20} The interblink interval visual acuity decay (IVAD) test measures visual acuity decay during the interblink interval. By studying visual function also through a battery of reading tests, it was shown that subjects with dry eye had significantly lower reading rates and poorer quality of vision.\textsuperscript{21,22}

Some recent research on dry eye:


www.ncbi.nlm.nih.gov/pubmed/26989953

*The authors found SS-OCT a valuable tool in quantifying early-phase fluid dynamics.*


Data show, the authors say, that optical ophthalmic corticosteroid loteprednol etabonate has a “favorable IOP-safety profile,” both long- and short-term.


A summary of the pathophysiology of neuropathic corneal pain, a systematic approach to diagnosing these patients, and current treatments.

Redness pattern

Redness is used as a diagnostic indicator, however little attention has been given to patterns which can vary greatly according to location, hue or depth of color, and intensity. Redness is characterized by the presence of fine horizontal conjunctival vessels in the exposed ocular surface. We have incorporated a grading system into clinical studies of dry eye. Recently, an automated computer system has been developed that records the same characteristics measured in the clinical scale and grades images collected in multi-centered clinical trials to minimize variability and provide a statistically powerful dataset.

Miscellaneous tests

Other diagnostic techniques include confocal microscopy, impression cytology, tear film biomarker analysis and meibomian gland status.

The inevitable lifestyle changes

It is important that the clinician spends time with patients and informs them about the necessary lifestyle changes to maintain a healthy ocular surface. Patients should treat their eyes like an African Violet; the time to water is before it dries up, not afterward. Symptoms such as burning represent early onset damage, so it’s important that patients understand that they need to regularly use lubricants and other agents. Teaching patients about situational awareness is also critical. They should be told about exacerbating factors like the level of humidity, strong winds, dust and toxins in the air, avoiding prolonged visual tasks and extended contact lens wear. Patients should be aware of the time of day when dry eye symptoms are worse. Patients should also exhibit common sense: a fireplace in winter, fumes of any kind, or direct airflow should be avoided. Similarly, it is very important to remain well hydrated and reduce the use of ocular drying medications such as antihistamines, if possible. These lifestyle changes are important because once symptoms of dry eye emerge, it can take up to two weeks to normalize the epithelial surface.

Summary

The diagnosis of dry eye begins with a careful examination and thoughtful questioning. A battery of objective dry eye tests should be performed to accurately diagnose patient subtypes. Refinement of diagnostic tools may help clinicians develop a more comprehensive clinical picture and a well-tailored treatment plan that will encourage patient compliance. New medications are being developed that target different mechanisms of action underlying dry eye disease. These face difficult regulatory hurdles, therefore, testing requires sensitive assessments that can detect changes in clinical endpoints. OM

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