

# Identifying Subgroups of Dry Eye Patients

Constructing an extensive database of patients will give your practice a well-defined dry eye population for potential clinical investigation.

**BY GEORGE W. OUSLER III**

**D**ry eye syndrome may be one of the most common diseases that eye care providers encounter in daily practice. Patients who present with symptoms are diagnosed with dry eye after they undergo diagnostic testing. Yet, the diagnostic tools available to clinicians to clearly define dry eye have been limited or underutilized. Although an objective measurement is the only way to definitively diagnose dry eye, virtually no diagnostic tools, with the exception of tear osmolarity, are reimbursable.

Nevertheless, to help build your practice and expedite future clinical trials, a battery of standard, objective dry eye tests should be employed to accurately diagnose and categorize your patients. Knowing what each dry eye patient needs and then tailoring treatment to specifically address those needs will help you construct an extensive database of patients. This will give your practice a well-defined dry eye population for upcoming dry eye studies.

My colleagues at Ora, Inc. (Andover, MA), have been pioneering clinical research in dry eye in collaboration with a number of pharmaceutical companies for more than 15 years. It is our experience that the careful examination and the proper questioning of patients leads to a better diagnosis of dry eye and facilitates the creation of treatment plans that are more rewarding for you and your patients. Eventually, your carefully defined patient databases can lead to the successful enrollment of your patients in clinical trials. Various investigational therapies are currently under evaluation, such as anti-inflammatory agents, secretagogues, and hormonal therapies. This article describes a number of ways to strengthen your practice's efforts to identify patient populations and facilitate potential dry eye clinical trials in the future.

## DIAGNOSTIC TESTS

When patients complain of dry eye, it may be instinctive to diagnose them based on their subjective

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symptoms; however, precise diagnostic tests will improve your assessment of dry eye and create measurable criteria. For example, is the dryness the result of aqueous deficiency or meibomian gland dysfunction (MGD)? These standards can later be used to evaluate the severity of disease and, in many cases, serve as a screening tool for the potential enrollment of patients in clinical trials. Generally accepted symptoms of dry eye include ocular dryness, burning, stinging, foreign-body sensation, grittiness, sensitivity to light, and blur- riness.<sup>1</sup> A number of clinical tests, such as corneal and conjunctival staining, tear film breakup time (TFBUT), Schirmer, and visual function, can help you diagnose dry eye and determine its underlying etiologies.<sup>2</sup> You may also use additional research endpoints such as flu- orophotometry and osmolarity, but these are not found as frequently in the clinical setting.

Ocular staining serves as an indicator of the health of the ocular surface. Fluorescein staining penetrates areas of the corneal epithelium and conjunctival epithelium where intercellular junctions are disrupted.<sup>2</sup> The volume of fluorescein and the timing of observation and evaluation are critical for proper assessments. Large, uncontrolled amounts of fluorescein can make it difficult to distinguish staining from an oversaturation of the epithelium.<sup>3</sup> Although every patient is different, the ideal time to measure the presence of staining is approximately 3 to 5 minutes after you instill the drops. Typically, eyes with more severe dryness show higher

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levels of fluorescein staining. It is also common, however, for some patients to exhibit high levels of fluorescein staining with minimal symptoms, which may be due to an associated decrease in corneal sensitivity.<sup>4,5</sup> Rose bengal staining and lissamine green staining, which color desiccated and dying cells on the ocular surface, have also been used as diagnostic tests. Historically, lissamine green has been better accepted by patients, as it lacks the slight burning or stinging sensation typically found with rose bengal upon instillation.

An unstable tear film can leave the cornea exposed and ultimately result in damage to the ocular surface and symptoms of dry eye. The TFBUT test measures the interval between the individual's last complete blink and the breakup of his or her tear film, appearing as a black streak, spot, or blob on the otherwise continuously stained tear film.<sup>3</sup> Like ocular staining, TFBUT measurements are most accurate with well-controlled microquantities (1-5  $\mu$ L) of fluorescein.<sup>3,6-8</sup> As such, more reliable and reproducible reference values have been established where TFBUT was determined to be greater than 5 seconds in normal eyes (mean = 7.1  $\pm$  1.17 seconds) and less than 5 seconds in dry eyes (mean = 2.2  $\pm$  0.82).<sup>3</sup>

Tear volume and production are also components of tear film stability and can be affected by dry eye. One common method for determining tear volume is the Schirmer test, which involves placing paper strips on each eye for approximately 5 minutes to assess aqueous production. Although the strips can cause reflex tearing and may require the use of anesthetic agents, they provide a clinical indication of dry eye. Additionally, fluorophotometry is an effective and reproducible method for measuring tear production. Although this research tool is not often found in clinics, it determines tear turnover rate, volume, and flow by measuring the decay of fluorescein in the tear film.

## POSITIONING YOUR PRACTICE

When screening for dry eye, keep in mind that it is possible for some patients to have mild-to-moderate symptoms but no clinical signs. This caveat can make it a difficult disease to diagnose, and it may cause some practitioners to underestimate the condition's severity or misdiagnose it altogether. Because you and your staff cannot rely solely on clinical signs or your patients' ability to convey their symptoms, it is important to ask the right questions and to use the proper diagnostic techniques as described previously.

Maintaining a broad spectrum of diagnostic criteria will make it easy to build a database of patients to

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enroll in clinical studies. Some tests may be as simple as administering questionnaires about patients' symptoms, which take only a few minutes. More extensive diagnostic modalities are important for gathering baseline information on your dry eye patients. For example, a sample set of inclusion criteria may contain the presence of ocular surface staining, compromised tear volume as measured by the Schirmer test (< 10 mm), and patient-reported symptomatology.

With the exception of tear osmolarity, which now has a dedicated CPT code (83861), diagnostic tests for dry eye syndrome are typically not reimbursable. They are, however, easy ways to make your patients happy and more accurately build a database to facilitate a study, if performed prior to enrollment. Additionally, expanding your practice to include patients with dry eye specifically may help draw in those who have been discouraged by the lack of effective resources. Keeping dry eye-specific brochures, informational sheets, and videos in your waiting area will demonstrate to your patients your commitment to managing this disease, which is a primary ocular complaint. Begin your outreach to this population with your own patients. In time, through word of mouth, your population will gradually extend beyond this threshold. ■

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