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MAJOR REVIEW

Evaluation of Dry Eye

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Abstract. Dry eye is a common yet complex condition. Intrinsic and extrinsic factors can cause dysfunction of the lids, lacrimal glands, meibomian glands, ocular surface cells, or neural network. These problems would ultimately be expressed at the tear film–ocular surface interface. The manifestations of these problems are experienced as symptoms such as grittiness, discomfort, burning sensation, hyperemia, and secondary epiphora in some cases. Accurate investigation of dry eye is crucial to correct management of the condition. Techniques can be classed according to their investigation of tear production, tear stability, and surface damage (including histological tests). The application, validity, reliability, compatibility, protocols, and indications for these are important. The use of a diagnostic algorithm may lead to more accurate diagnosis and management. The lack of correlation between signs and symptoms seems to favor tear film osmolarity, an objective biomarker, as the best current clue to correct diagnosis. (**Surv Ophthalmol** 57:293–316, 2012.

Key words. dry eye • tear quality • ocular surface • tear secretion • tear break up • osmolarity • evaporation • lipid layer • staining

I. Introduction

Dry eye is a common, complex condition that can reduce ocular comfort and visual performance. The impact on quality-of-life has been rated as similar to the effect of moderate angina[226] and, in more severe cases, dialysis and severe angina.[33] In 2006 a panel of dry eye experts used the Delphi approach to establish diagnosis and treatment guidelines for dry eye. This consensus method had been used successfully to standardize diagnosis and treatment in cardiovascular disease.[193] Four levels of disease severity were outlined as well as recommendations for patients with lid margin disease and abnormal tear distribution. These guidelines primarily focused on patient signs and symptoms and were accompanied by the suggestion that the terminology *dysfunctional tear syndrome* could replace the term "dry eye disease."[17] The Dry Eye Workshop (DEWS) added to the criteria and made additional treatment recommendations. They did not adopt the term dysfunctional tear syndrome, but redefined dry eye as "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, accompanied by increased osmolarity of the tear film and inflammation of the ocular surface."[154] The key additions to their 1995 definition were the inclusion of symptoms of visual disturbance, osmolarity, and inflammation.[149,154]

The importance of inflammation in the pathogenesis of dry eye had been established and confirmed by the presence of immune-based inflammation in Sjögren and non-Sjögren dry eye[250] and marked improvement in signs and symptoms following use of anti-inflammatory therapies such as cyclosporine, corticosteroids, tetracyclines, and autologous serum.[206] In 2009 a Canadian consensus panel decided there was little difference between grades 1 and 2 of the severity scale and combined

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them to produce a simplified system to grade dry eye as mild, moderate, or severe.[110] A similar conclusion was drawn in a prospective, multi-site clinical study, where a combination of clinical measures were converted to a 'score' for dry eye severity. Seven clinical indicators were measured and the resulting data showed "insufficient resolution to separate mild and moderate patients into two groups," leading to a simplified classification system of normal, mild/moderate, and severe.[253]

The categorization of dry eye is complicated by considerable variation in the disease's symptoms and signs and the often multiple causes. The condition can involve the tear film, lids, main and accessory lacrimal glands, meibomian glands, and a wide spectrum of ocular surface cells including epithelial, goblet, inflammatory, and immune cells.[112,146] The two main classes of dry eye identified by the DEWS report were *aqueous deficient dry eye* and *evaporative dry eye*. In aqueous deficient dry eye, there are insufficient tears secreted by the lacrimal glands, and this encompasses Sjögren syndrome (an autoimmune disease) and non-Sjögren. The term keratoconjunctivitis sicca has been used historically instead of non-Sjögren syndrome, although it is now recognized as a more general term for any form of dry eye.[154] The common feature of these conditions is lacrimal gland dysfunction. In evaporative dry eye there are intrinsic and extrinsic causes. Intrinsic causes are structural (e.g., abnormalities of the lids) or functional (e.g., meibomian gland dysfunction). Extrinsic causes include ocular surface irregularities, allergies, and contact lens wear.[154] Smoking causes deterioration in the lipid layer of the precorneal tear film leading to dry eye symptoms such as grittiness and burning sensations.[7] The rate of evaporation also increases with a larger palpebral aperture (such as in up gaze), a longer blink interval, increased air flow, increased temperature, or reduced humidity.[290]

Tear hyperosmolarity, tear film instability, and inflammation are all mechanisms for dry eye. Tear hyperosmolarity may occur as a result of increased evaporation or reduced aqueous secretion. The increase in concentration of proteins and electrolytes causes a reduction in tear volume that initially irritates the ocular surface, but goes on to cause inflammation and subsequent damage in evaporative dry eye, as thinning of the lipid layer allows increased evaporation.[28,74] Tear film instability detected by reduced tear film break-up time has also been linked with the increased rate of local evaporation from the tear film surface.[127,129] Inflammation as a result of auto-immune disease or even ageing can act as an inciting event for dry eye.[206]

Epidemiological studies of dry eye in the United Kingdom indicated a prevalence of 10% in people under the age of 60, not including those who wear contact lenses. The number of symptomatic patients consulting an optometrist over this age is considerably higher, with a larger proportion of women being affected, especially post menopause.[6] In the United States prevalence of dry eye has been reported as being between 0.6% and 57% depending on the classification.[257] The Beaver Dam Study found an incidence of 21.6% in a population ranging from 43–86 years in age, increasing with female sex and with age in both sexes.[177] Johnson and Murphy[112] give a more generalized estimation of 10–20% prevalence in the adult population, based on a number of large studies.

In summary, aqueous deficient dry eye and evaporative dry eye may co-exist and have features in common, including increased tear film osmolarity and reduced stability. Various assessment techniques need to be carried out in order to be able to manage the patient appropriately. We summarize the main features of clinical and research techniques used to assess dry eye and the indications for their use.

II. Subjective Evaluation

A. HISTORY AND SYMPTOMS

Examination of a patient with dry eyes invariably starts with history and symptoms; there is often a lack of correlation between the severity of the symptoms and ocular signs of dry eye, however.[16,99,116,190,280] Symptoms of dry eye have been found to be quite severe, even with relatively mild surface changes, yet paradoxically when the severity of dry eye reaches a certain level, symptoms decrease as a result of loss of corneal sensitivity.[3,16,23,116,240,293] Reduced ocular surface sensitivity has been documented as a normal age-related change[222] and as a consequence of contact lens wear.[207] Symptoms assessed by investigators have included dryness, grittiness, soreness, redness, photophobia, and ocular fatigue, although this is not an exhaustive list of patient's complaints with this condition. The variability of reported symptoms can be simplified by a defined list of questions to make comparisons between visits and between patients more straightforward.

B. VALIDATED QUESTIONNAIRES

Validated questionnaires are available to ensure consistency in recording symptomatic information. They consist of a series of questions with numerical values attributed to the answers, allowing the symptoms to be scored. This also means that patients can be monitored by comparing subsequent