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The Definition & Classification of Dry Eye Disease

Guidelines from the 2007 International Dry Eye Workshop

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The diagnosis of dry eye and its treatment has long been approached somewhat subjectively. Even more so, it's an ocular ailment that hasn't always been treated with enough gravity given the impact this disease can have on the people who live with it. We believe this will start to change with the publication of the DEWS Report. The 2007 International Dry Eye Workshop, sponsored by the Tear Film and Ocular Surface Society [TFOS] was created to provide an evidence-based critical review and summary of the classification, epidemiology, diagnosis, techniques of basic and clinical research, and management of dry eye disease.

This report, recently published in *The Ocular Surface*,[1] provides an encyclopaedic, evidence-based review of dry eye disease. The report was a product of a team of international experts who spent three years appraising the present state of knowledge for dry eye disease and the methods used to evaluate, diagnose and manage the disorder.

This article summarizes the section of the report addressing the definition and classification of dry eye disease. Members of the DEWS Definition and Classification Subcommittee developed a contemporary definition of dry eye disease and a three-part classification system based on etiology, causative mechanisms and disease severity. The guidelines described are not intended to override the clinical assessment and judgement of an expert clinician in individual cases, but they should prove helpful in the conduct of clinical practice and research.

Definition of Dry Eye Disease

The committee began by reviewing the following definition of dry eye disease that was adopted by the 1995 National Eye Institute (NEI)/Industry Dry Eye Workshop: *Dry eye is a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.*

The group decided to update this definition to take account of new knowledge about the roles of tear hyperosmolarity and ocular surface inflammation in dry eye, and the effects of dry eye on visual function. The following updated definition was produced:

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.

Classification

Although the 1995 NEI/Industry Dry Eye Workshop classification has served as a useful and durable scheme for over a decade, it does not reflect newer knowledge on pathophysiological mechanisms, effects on vision, and the clinical value of an assessment of disease severity. To address this, DEWS based the revised classification scheme on the updated Triple Classification published in 2005 and the report of the Delphi Panel published in 2006. A three-part classification system was developed. The first part is etiopathogenic and illustrates the multiple causes of dry eye. The second is mechanistic and shows how each cause of dry eye may act through a common pathway, and that any form of dry eye can interact with and exacerbate other forms of dry eye as part of a vicious circle. The third is a scheme based on the severity of dry eye disease, which is expected to provide a rational basis for therapy.

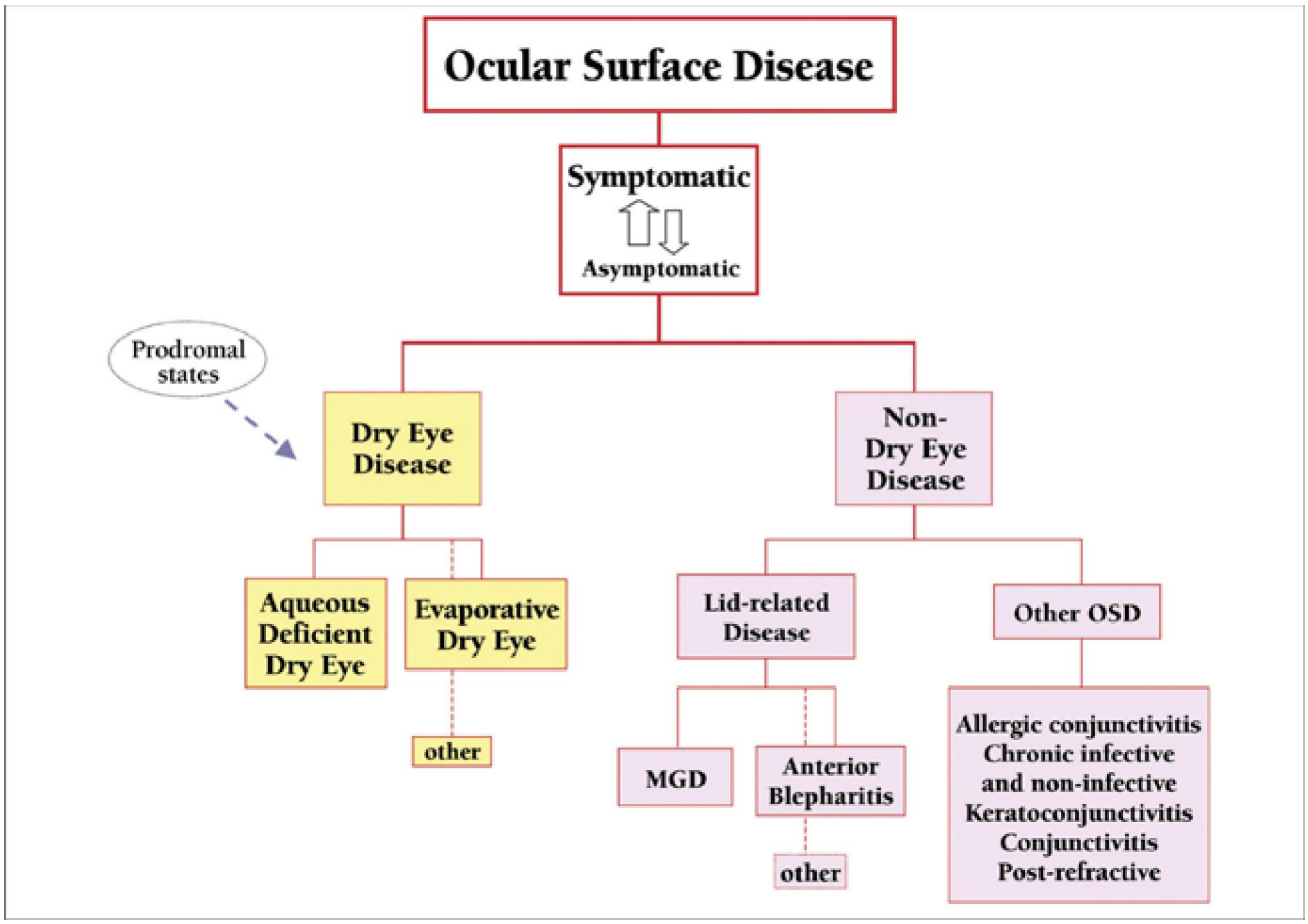

Figure 1. Major etiological causes of dry eye disease[1]

Etiopathogenic Classification of Dry Eye Disease

The etiopathogenic classification developed is shown in **Figure 1.** As in the 1995 NEI/Industry Dry Eye Workshop report, DEWS regarded the term "dry eye" as synonymous with the term "keratoconjunctivitis sicca" (KCS). The left hand box in

Figure 1 shows the influence of environmental factors on an individual's risk of developing dry eye. The term ‘environment’ is used broadly to include physiological conditions particular to an individual (the *milieu interieur*), as well as the external conditions that they encounter (the *milieu exterieur*).

The recommended scheme retains the two major classes of dry eye used in the 1995 NEI/Industry Dry Eye Workshop classification — aqueous tear-deficient dry eye (ADDE) and evaporative dry eye (EDE).

ADDE, as its name implies, is primarily due to a failure of lacrimal tear secretion, although a failure of water secretion by the conjunctiva can also be a contributing cause. ADDE has two major subclasses, Sjögren Syndrome Dry Eye (SSDE) and non-SSDE. SSDE is an exocrinopathy in which the lacrimal and salivary glands, as well as other organs, are targeted by an autoimmune disease. Primary Sjögren Syndrome consists of this systemic autoimmune disease in the absence of another discrete autoimmune disease. Secondary Sjögren Syndrome consists of primary Sjögren Syndrome features together with an overt autoimmune connective disease, most commonly rheumatoid arthritis. Non-SSDE is a form of ADDE due to lacrimal dysfunction, where systemic autoimmune features of SSDE have been excluded. It most commonly presents as age-related dry eye (ARDE), a form that is caused by lacrimal deficiency and to which the term KCS has sometimes been applied in the past. Non-SSDE may also result from obstruction of the lacrimal glands due to cicatrizing conjunctivitis, reflex hyposecretion due to sensory or motor block, and the use of systemic drugs including antihistamines, beta-blockers, antispasmodics and diuretics.

EDE is due to excessive water loss from the exposed ocular surface in the presence of normal lacrimal secretory function. Its causes have been described as intrinsic and extrinsic, although the boundary between these two categories is inevitably blurred. Intrinsic EDE is where the regulation of evaporative loss from the tear film is directly affected, for example, by meibomian lipid deficiency, poor lid congruity and lid dynamics, low blink rate, and the effects of drugs such as systemic retinoids. Extrinsic EDE includes those etiologies that increase evaporation by their pathological effects on the ocular surface. Causes include Vitamin A deficiency, the action of toxic topical agents such as preservatives, contact lens wear and a range of ocular surface diseases, including allergic eye disease.

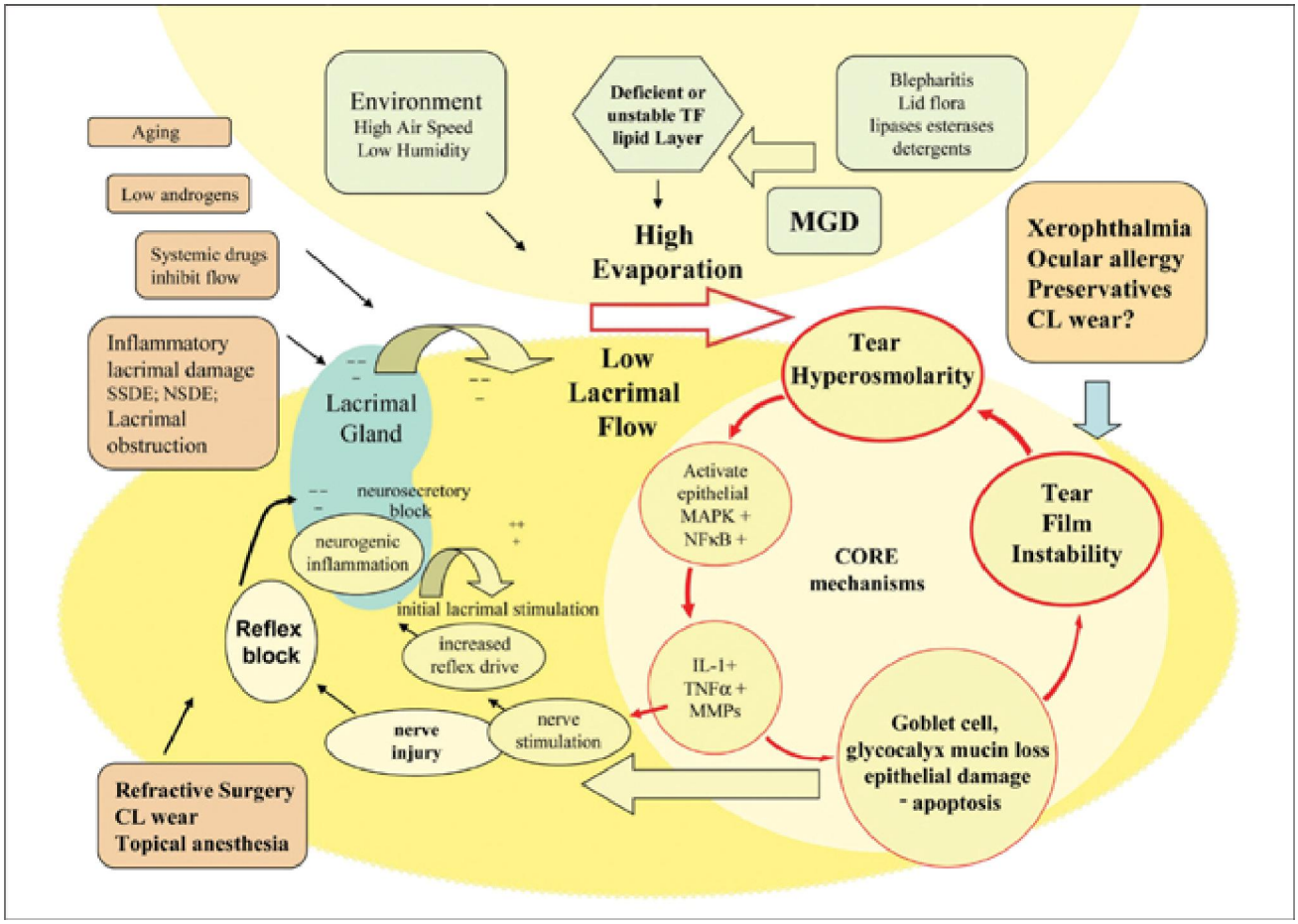

Figure 2. Mechanisms of dry eye[1]

The Causative Mechanisms of Dry Eye

In general terms, dry eye is caused by a disturbance of the lacrimal function unit (LFU), an integrated system comprising the lacrimal glands, ocular surface and lids, and the sensory and motor nerves that connect them. This functional unit controls the major components of the tear film in a regulated fashion and responds to environmental, endocrinological and cortical influences. Its overall function is to preserve the integrity of the tear film, the transparency of the cornea, and the quality of the image projected onto the retina. While disease or damage to any component of the LFU can result in dry eye, the core mechanisms of dry eye are driven by tear hyperosmolarity and tear film instability. In this section the report shows how the several etiopathogenic subclasses of dry eye activate these core mechanisms, and that disease initiated in one major subgroup may coexist with or even lead to events that cause dry eye by another major mechanism. Based upon a schema proposed by Christophe Baudoin, M.D. and reformatted by Anthony Bron, FRCP, this depiction of core mechanisms operative in dry eye disease facilitates understanding the complexity of the disease.

Tear hyperosmolarity is regarded as a central mechanism causing ocular surface inflammation, damage, and symptoms, as well as the initiation of compensatory events in dry eye. Tear hyperosmolarity arises as a result of water evaporation from the exposed ocular surface, in situations of a low aqueous tear flow and/or as a result

of excessive evaporation (**Figure 2**). Hyperosmolarity causes damage to the surface epithelium by activating a cascade of inflammatory events and the release of inflammatory mediators into the tears. Epithelial damage involves cell death by apoptosis, a loss of goblet cells, and a reduction in mucus secretion, and leads to tear film instability. This instability exacerbates ocular surface hyperosmolarity, thereby creating a vicious circle. Tear film instability can also be initiated without the prior occurrence of tear hyperosmolarity by several etiologies, including xerophthalmia, ocular allergy, topical preservative use and contact lens wear.

Table 1. Dry eye severity grading scheme[2]

Dry Eye Severity Level	1	2	3	4*
Discomfort, severity & frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity-limiting episodic	Annoying, chronic and/or constant, limiting activity	Constant and/or possibly disabling
Conjunctival injection	None to mild	None to mild	+/-	+/++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked central	Severe punctate erosions
Corneal/tear signs	None to mild	Mild debris, ▽ meniscus	Filamentary keratitis, mucus clumping, △ tear debris	Filamentary keratitis, mucus clumping, △ tear debris, ulceration
Lid/meibomian	MGD variably present	MGD variably present	Frequent	Trichasis, keratinization, symblepharon
TFBUT (sec)	Variable	≤ 10	≤ 5	Immediate
Schirmer score (mm/5 min)	Variable	≤ 10	≤ 5	≤ 2

* Must have signs *and* symptoms. TBUT: fluorescein tear break-up time. MGD: meibomian gland disease

The epithelial injury caused by dry eye stimulates corneal nerve endings, leading to symptoms of discomfort, increased blinking and, potentially, compensatory reflex lacrimal tear secretion.

Alteration of normal tear and ocular surface mucins by elevated tear osmolarity contributes to symptoms by increasing frictional resistance between the lids and the globe.

In the initial stages of dry eye, it is considered that ocular irritation results in reflex stimulation of the lacrimal gland. However, with time, inflammation accompanying chronic secretory dysfunction and a decrease in corneal sensation eventually compromises the reflex response and results in even greater tear film instability.

Classification of Dry Eye Basis of Severity

Regardless of which individual risk factor or group of factors initiates the disease process, the final common expression involves tear hyperosmolarity and tear

instability leading to ocular surface damage. Since both aqueous tear deficiency and increased evaporative tear loss occur in most cases of dry eye disease and are linked by common pathogenetic mechanisms, expert clinicians are increasingly basing treatment decisions on an assessment of severity rather than discrete deficiencies.

The group believed that a classification of disease based on severity would be of considerable value in clinical practice, particularly in terms of guiding therapeutic decisions. This third component of our classification system was based on the severity grading scheme included in the Delphi Panel report (**Table 1**).

By establishing these definitions and classification of dry eye disease, we believe clinicians will be better able to determine the level of DED, as well as the best treatment course for their patients. **OM**

Reference

1. 2007 Report of the International Dry Eye Workshop (DEWS). *The Ocular Surface. 2007*;5:65-204. For a full copy of the DEWS report, please visit the TFOS website: www.tfos.org.
2. Behrens, A, Doyle, J, Stern, L, et al. Dysfunctional Tear Syndrome: A Delphi Approach to Treatment Recommendations. *Cornea*. 25:900-907, Sept. 2006.

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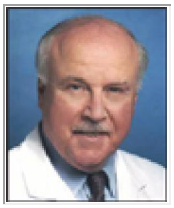

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Neither author has any financial arrangement with any of the products or techniques mentioned in this article.