New Perspectives on Dry Eye Definition and Diagnosis: A Consensus Report by the Asia Dry Eye Society

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ABSTRACT For the last 20 years, a great amount of evidence has accumulated through epidemiological studies that most of the dry eye disease encountered in daily life, especially in video display terminal (VDT) workers, involves short tear film breakup time (TFBUT) type dry eye, a category characterized by severe symptoms but minimal clinical signs other than short TFBUT. An unstable tear film also affects the visual function, possibly due to the increase of higher order aberrations. Based on the change in the understanding of the types, symptoms, and signs of dry eye disease, the Asia Dry Eye Society agreed to the following definition of dry eye: "Dry eye is a multifactorial disease characterized by unstable tear film causing a variety of symptoms and/or visual impairment, potentially accompanied by ocular surface damage." The definition stresses instability of the tear film as well as the importance of visual impairment, highlighting an essential role for TFBUT assessment. This paper discusses the concept of Tear Film Oriented Therapy (TFOT), which evolved from the definition of dry eye, emphasizing the importance of a stable tear film.

KEY WORDS consensus, definition of dry eye, diagnosis of dry eye, dry eye, tear film breakup time, tear film oriented therapy

I. INTRODUCTION

The concept of tear deficiency was first proposed in 1903 by Schirmer, who developed the famous Schirmer test, a modified version of which is still in clinical use.[1] Keratoconjunctivitis sicca in Sjögren syndrome was proposed by Sjögren in 1933.[2] For many years afterward, dry eye was considered to be equivalent to keratoconjunctivitis sicca, the aqueous tear deficiency.

OUTLINE

II. PREVIOUSLY PUBLISHED DEFINITIONS OF DRY EYE DISEASE

Historically, dry eye disease (**DED**) was considered to be due to either insufficient production or impaired stability of tears. There is now evidence that any abnormality of the ocular surface can trigger disequilibrium in all the other components of tear dynamics. In 1995, the National Eye Institute/Industry Workshop headed by Lemp concluded that "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."[3] This was a very solid beginning for establishing a consensus among dry eye researchers. Tear deficiency was still the central concept in dry eye. In 1995, the Japanese Dry Eye Society proposed their first definition and diagnostic criteria.[4] At that time, the Japanese definition did not include the symptoms of DED because the ocular surface in end-stage Stevens-Johnson syndrome patients may be totally keratinized, resulting in absence of symptoms. However, such patients may still suffer from visual disturbances, which are now considered to be among the important symptoms of severe dry eyes. A new definition and diagnostic criteria was proposed in 2006 as follows[5]:

> "Dry eye is a chronic disease of tear fluid and keratoconjunctival epithelium that results from various factors, and accompanies ophthalmic discomfort and abnormal visual function. The diagnostic criteria are: 1) assessment of symptoms, 2) qualitative or quantitative disturbance of the tear film (quantity: Schirmer I test less than 5 mm/5 min; quality: BUT less than 5 sec), 3) keratoconjunctival epithelial damage (staining score greater than 3 points). The presence of all criteria renders a diagnosis of definite dry eye and the presence of two out of the three criteria renders a diagnosis of probable dry eye (Figure 1)."[5]

In 2007, a consensus on definition and diagnosis was achieved at the first International Dry Eye WorkShop (DEWS) sponsored by the Tear Film and Ocular Surface Society (**TFOS**), as follows[6]:

> "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."[6]

The definition of DED in the DEWS report was similar to the Japanese definition, but inflammation and osmolarity were highlighted as potential risk factors for DED. The definitions clearly suggested that symptoms of dry eye should be present for the diagnosis. The report proposed that if there were no symptoms (including visual disturbances), the condition could not be diagnosed as dry eye. However, the report emphasized requirements of the presence of a decreased tear volume and ocular surface damage by vital staining for the definite diagnosis of dry eye. The report also described the ocular surface and tear parameters to consider when diagnosing dry eye severity, and these were the basis for a proposed stepladder approach to treatment (Table 1). On the other hand, short tear film breakup time (**TFBUT**) with severe symptoms seems to comprise the major type of dry eyes, so a new definition and diagnostic criteria were needed.

In 2006, the Delphi panel proposed a new term, the *dysfunctional tear syndrome* (**DTS**), and concluded that treatment strategies should rely on symptoms and signs rather than tests.[7] The panel defined the clinical signs to be considered in assessing the severity of DTS upon which a severity-based treatment algorithm was suggested (Figure 2).

The multinational ODISSEY European Consensus Group aimed to establish a clear and practical algorithm for evaluation and diagnosis of severe DED.[8] The ODISSEY group, comprised of 10 ophthalmologists who all contend with ocular surface disease issues on a daily basis, was formed in 2012. The purpose of their meeting was to review clinical and scientific challenges in diagnosis and management of severe DED, and to achieve consensus agreement on a simplified approach to evaluation of severe DED (Figure 3). A total of 14 criteria for DED severity, based on corneal fluorescein staining (**CFS**), tear hyperosmolarity, Schirmer test, impression cytology, filamentary keratitis, conjunctival staining, impaired visual function, meibomian gland disease or eyelid inflammation, blepharospasm, TFBUT, aberrometry, in vivo corneal confocal microscopy, inflammatory biomarkers (i.e., human leukocyte antigen-DR [**HLA-DR**], matrix metalloproteinase 9 [**MMP9**], cytokines, tear proteomics) and DED refractory to standard disease treatments were discussed. The specificity and sensitivity of these tools for diagnosing severe DED were addressed.

The modern definitions of DED combine objective findings, subjective symptoms, and mechanistic considerations, among which hyperosmolarity and inflammation play a key role. A second International Dry Eye Workshop commenced in May 2015 and will generate a report by 2017, which will revise the definition and diagnostic guidelines for DED.