

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



Asia Dry Eye Society

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## 1 Proposal of a new definition of dry eye

New definition of dry eye in Asia Dry Eye Society (ADES) Consensus 2017<sup>1)</sup>.

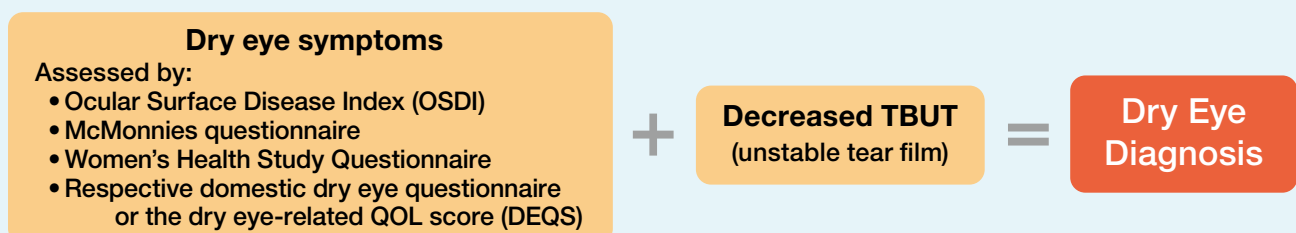
**“Dry eye is a multifactorial disease characterized by unstable tear film causing a variety of symptoms and/or visual impairment, potentially accompanied by ocular surface damage.”**

### Reference

Definition of dry eye in International Dry Eye WorkShop (DEWS) Consensus 2007<sup>2)</sup>

“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.”

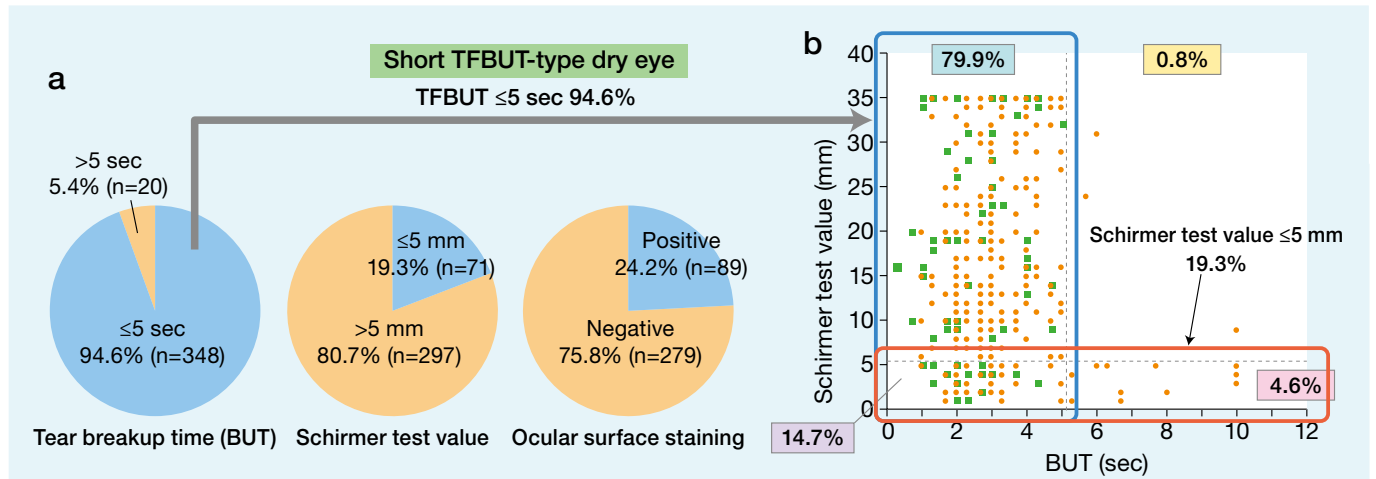
For the last 20 years, a great amount of evidence has accumulated through epidemiological studies that most of the dry eye disease (DED) encountered in daily life, **especially in video display terminal (VDT) workers, involves short tear film breakup time (TFBUT)-type dry eye**, a category characterized 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 DED, 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.**



**Figure 1** Dry eye disease is diagnosed by the combination of symptoms and unstable tear film.

## 2 Concepts of the new definition of dry eye

Recent findings in the field of epidemiology revealed that the short TFBUT-type dry eye (unstable tear film) was more prevalent than other types of dry eye<sup>3</sup>. In the Osaka study, Uchino et al conducted a dry eye survey among VDT workers in Osaka, Japan, and reported that the major type of dry eye was the short TFBUT-type dry eye (Figure 2, revised from Table in Uchino et al., 2013<sup>3</sup>). Tong et al also reported that Meibomian gland dysfunction (MGD) resulted in tear instability and DED<sup>4</sup>. The percentage of dry eye patients with a TFBUT  $\leq 5$  seconds was 94.6%, whereas 19.3% had a Schirmer test value  $\leq 5$  mm in the Osaka study (Figure 2a). Figure 2b shows the distribution pattern of TFBUT and Schirmer test values in the Osaka study<sup>5</sup>, and these were similar to those in Tong's report<sup>6</sup>.



**Figure 2** Distribution of TFBUT, Schirmer test value, and ocular surface staining in dry eye patients in the Osaka study<sup>3,5</sup>.

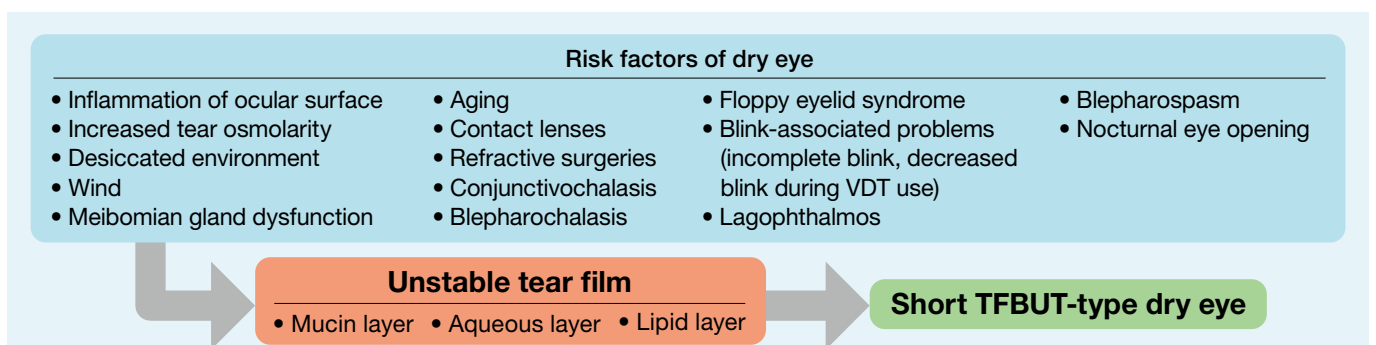
Relative to the previous definition, the new definition retains the concept that dry eye is a multifactorial disease. The most important agreement was that the unstable tear film is the pivotal mechanism of dry eye causing symptoms and/or visual impairment. This concept is consistent with the visual impairment in dry eye patients; aberrations due to the unstable tear film comprise an integral feature of the deterioration of vision. This concept also fits well with the corneal neuralgia hypothesis. The most sensitive part of the ocular surface is the corneal epithelium, and continuous stimulation by blink itself can cause chronic pain in a neuralgia patient<sup>7</sup>.

Previously, vital staining of either the cornea or the conjunctiva was considered to be critical; however, in this new definition, ocular surface damage is not required for the definite diagnosis of dry eye. In other words, just the combination of symptoms and an unstable tear film (short TFBUT) is considered to be sufficient to make a definite diagnosis of dry eye. This definition is simplistic and suggests that since many individuals suffering from dry eye have the short TFBUT-type dry eye, they should be treated not as dry eye suspects but as patients with DED.

## 3 Features of dry eye according to the new definition

### 3-1. Unstable tear film is the central feature of dry eye

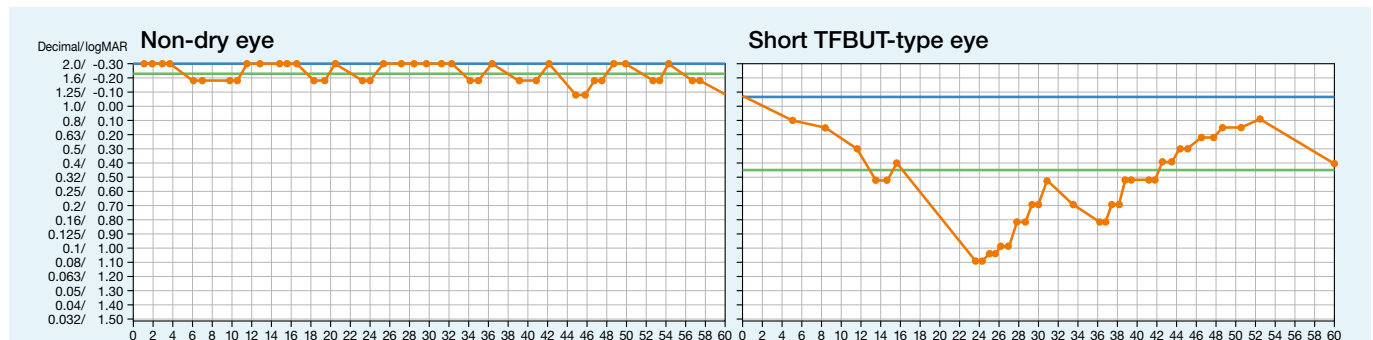
- Although there are various risk factors of dry eye, unstable tear film is the central feature (Figure 3).



**Figure 3** Various risk factors of unstable tear film.

### 3-2. Visual disturbances in dry eye

- The last 20 years of research have revealed that dry eye with unstable tear film affects the quality of vision (Figure 4).
- In daily life, patients keep their eyes open for a certain period of time, during which the tear film layer becomes irregular and the visual acuity may not be maintained.
- Treating visual deterioration by targeting the unstable tear film is one of the important goals of treatment of dry eye, in addition to improvement of discomfort.



**Figure 4** Comparison of functional visual acuity for non-dry eye and short TFBU-type dry eye.

### 3-3. Role of inflammation in dry eye

- Ocular surface inflammation and increased osmolarity of the tear film have not been emphasized in the definition of dry eye at this time.

#### Ocular surface inflammation

The reasons are:

- Although ocular inflammation may be one of the risk factors, not the central core mechanism related to the definition.
- Inflammation may affect all three tear film layers, but in VDT users, dry eye is not due to inflammation but develops due to the suppressed blink and increased evaporation, resulting in a short TFBU. In this type dry eye, the inflammation will also present in some patients if their tear film has not recovered quickly.

#### Increased osmolarity of the tear film

The reasons are:

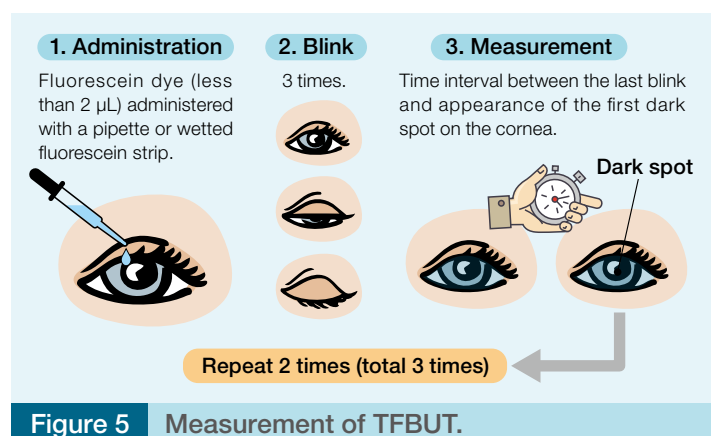
- Although hyperosmolarity of the tear fluid is a suitable marker to assess DED, and an increase in tear evaporation and a decrease in tear production induces an increase in tear osmolarity, but due to the variations of the measurement, controversial reports exist suggesting that this methodology is difficult for practical clinical application.
- Further studies are necessary to investigate the relationship of osmolarity to dry eye conditions.

## 4 Diagnosis of dry eye according to the new definition

- Since the unstable tear film is pivotal in the new definition of dry eye, the measurement of TFBU is essential (Figure 5).
- A cutoff value of TFBU is less than and equal to 5 sec for the diagnosis of dry eye.

The following tests are unessential, but important:

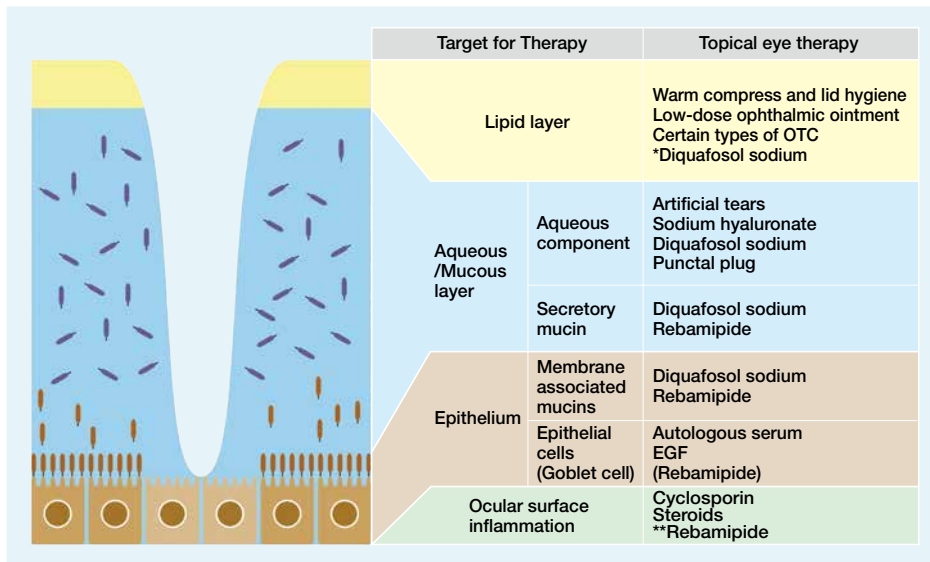
- Direct or validated questionnaires for additional information
- Check of ocular surface for evaluation of the ocular damage
- Schirmer I test for diagnosis of aqueous deficiency type dry eye



**Figure 5** Measurement of TFBU.

## 5 Treatment of dry eye according to the new definition

- Since the unstable tear film is pivotal in the new definition of dry eye, a new strategy called “TFOT” was developed.
- The concept of TFOT is easy to understand “If there is an abnormal layer, the layer should be targeted for treatment.”
- For example, if a patient has mucin deficiency, the mucin secretion should be recovered first, and prescribing a mucin secretagogue such as diquafosol sodium or rebamipide eye drops would be appropriate (Figure 6).



**Figure 6**

**The concept of TFOT (Tear Film Oriented Therapy).**

Figure provided by Dry Eye Society Japan.  
\*Diquafosol sodium may increase the function of the tear film lipid layer by promoting spreading of the lipid layer through lipid and tear fluid secretion.  
\*\*Rebamipide may suppress the inflammation of the ocular surface in dry eye by its anti-inflammatory action.

## 6 Future directions

- A global consensus about dry eye in addition to the new definition of the Asia Dry Eye Society is necessary in the near future.
- There are several subjects of further investigations for dry eye definition, diagnosis and therapy (Figure 7).

### New definition of dry eye in Asia Dry Eye Society (ADES) Consensus 2017<sup>1)</sup>

Subjects of further investigations are:

- Is tear deficiency type of dry eye in an independent category?
- Is evaporative DED categorized as oil deficient (meibomian gland dysfunction) variant?
- Is the short TFBUT-type dry eye the major type of mucin deficiency dry eye?
- Why is there an association between more symptoms and fewer signs (ocular surface damage) in short TFBUT-type dry eye?

### Global consensus about dry eye in the near future

**Figure 7** Future investigations and directions.

1) Tsubota K, et al. Ocul Surf 2017;15:65-76.  
2) No authors listed. Dry Eye Workshop. Ocul Surf 2007;5:75-92.  
3) Uchino M, et al. Am J Ophthalmol 2013;156:759-766.  
4) Tong L, et al. Invest Ophthalmol Vis Sci 2010;51:3449-3454.  
5) Yokoi N, et al. Am J Ophthalmol 2015;159:748-754.  
6) Tong L, et al. Eye 2010;24:1486-1491.  
7) Rosenthal P, et al. Ocul Surf 2012;10:2-14.

## Asia Dry Eye Society

The Asia Dry Eye Society (ADES) was founded in 2012 by doctors from Japan, China and Korea. The number of dry eye patients has increased in line with rapid global changes, and dry eye has become an increasingly important academic field in ophthalmology. The goal of ADES is to contribute to the advancement of healthcare for dry eye patients through closer, more active research ties and clinical implementation throughout the wider Asian region. In the short term, we aim to develop a guideline-based, standardized medical system to diagnose and treat dry eye based on consensus. In the long-term, we hope to promote advocacy and education on the best possible methods of detecting and treating dry eye in each country. Our society is currently composed of 85 dry eye specialists from all over Asia who meet annually to interact and discuss advancements in dry eye research. Our society is open to all doctors in Asia who are keen to learn about dry eye. We look forward to interacting and discussing about advanced dry eye therapies. With everyone's efforts, let us place dry eye on the forefront of medical science!

Asia Dry Eye Society

Sincerely,  
President of Asia Dry Eye Society

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