

DRY EYE DISEASE REDEFINED

The TFOS DEWS II report could affect the way DED is diagnosed and examined.

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The long-awaited Tear Film & Ocular Surface Society (TFOS) Dry Eye Workshop II (DEWS II) report was published on July 21, updating the definition of dry eye disease (DED) and potentially affecting the way it is diagnosed and examined.

The workshop involved 150 clinical and basic research experts from 23 countries who used an evidence-based approach and open communication, dialogue, and transparency to achieve a global consensus concerning multiple aspects of DED. The TFOS DEWS II report is the sequel to the landmark TFOS DEWS publication in 2007.¹

“The original DEWS stimulated a huge amount of new research throughout the world—both basic and clinical,” David A. Sullivan, PhD, a senior scientist at the Schepens Eye Research Institute/Massachusetts Eye and Ear and an associate professor at Harvard Medical School in Boston, said in an interview with *CRST Europe*. “Over the past 10 years, there has been a dramatic increase in our understanding of [DED]. And to effectively update our understanding of the classification, diagnosis, epidemiology, pathophysiology, and management therapy of the disease, we launched the TFOS II workshop.”

According to the consensus of the workshop, which was published in *Ocular Surface*,² dry eye is “a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.”

Inclusion of the phrase “loss of homeostasis” is novel, Dr. Sullivan said. This definition clarified, based on recent peer-reviewed evidence, that tear film hyperosmolarity and ocular surface inflammation have causal etiologic roles, along with the addition of neurosensory abnormalities (contributing to the common mismatch between signs and symptoms), according to the report.

The report also updates the classification and diagnosis of dry eye; critically evaluates the epidemiology, etiology, mechanism, and impact of the disorder; addresses its management and therapy; and proposes recommendations for the design of clinical trials to assess new pharmaceutical interventions for the treatment of DED. Key findings of the TFOS DEWS II report are summarized in the accompanying sidebar.

“[The DEWS II report] has redefined dry eye disease; it has reclassified dry eye disease,” Dr. Sullivan said. “It has made recommendations concerning diagnostics as well as an algorithm to associate that with management and therapy.” ■

SEX, GENDER, AND HORMONES



- DED occurs **more frequently in women than men**, suggesting that sex-related differences underlie its etiology.
- Higher rates of DED in women compared with men only become significant with **increasing age**.
- Further research is needed to clarify the precise nature, extent, and mechanisms of these sex, gender, and endocrine effects on the eye in health and disease.

EPIDEMIOLOGY

- The epidemiology of DED continues to be a challenge due to the **lack of a standardized worldwide definition**.
- The prevalence of DED, with and without symptoms, ranges from **5% to 50%**.
- Prevalence of DED based only on signs reaches **up to 75%** in some populations. (Challenge: the criteria for positive signs, which may reflect secondary outcomes or be attributed to aging changes, have varied between studies.)
- Studies in **younger patients** suggest a lower prevalence of DED in this population.
- **Asian ethnicity** appears to be a risk factor for DED.
- The most severe economic impact of DED likely results from indirect costs related to **decreased work productivity**.



TEAR FILM

- DED implies **major changes** to the tear film structure and function.
- It may be that the whole tear film (lipids, mucins, proteins, and salts) prevents tear film evaporation and collapse, but additional studies are needed.
- **Tear proteins** change in DED, but no definitive set of proteins or changes in protein levels has been validated to aid in diagnosis.
- There is need to further characterize the biochemistry of the tear film to **identify new markers** that can be used to diagnose, predict, and treat DED.
- There is need for ways to dynamically **measure** tear film osmolarity and markers of inflammation over the whole ocular surface.



IN A NUTSHELL: KEY FINDINGS FROM TFOS DEWS II

PAIN & SENSATION

- Studies to date suggest potential merit in exploring treatment strategies involving **cold thermoreceptors** to manage DED symptoms.



PATHOPHYSIOLOGY

- Meibomian gland dysfunction, Sjögren lacrimal disease, and non-Sjögren lacrimal disease are the **leading causes of DED**.
- The **vicious circle** is an accepted central mechanism in DED that explains how ocular surface damage is initiated and perpetuated.
- **Tear hyperosmolarity** can damage epithelial cells directly or initiate inflammatory events that damage epithelial cells, surface microvilli, barrier function, the glycocalyx, and goblet cells.
- Epithelial cell damage, lipid layer and blinking abnormalities, defective glycocalyx, loss of gel mucin, and reduction in tear volume could result in **loss of lubrication** between the globe and eyelids and in increased friction and DED symptoms.
- **Inflammation** of the ocular surface can inhibit lacrimal secretion and cause a loss of epithelial barrier function at the ocular surface.
- **Tear film breakup**, leading to localized hyperosmolarity, can result in ocular surface damage directly or through the cascade of inflammation that it initiates.



IATROGENIC DRY EYE

- Topical and systemic medications, **contact lenses** and associated care solutions, ophthalmic surgeries, and nonsurgical procedures can cause DED.
- Preservatives such as benzalkonium chloride in ophthalmic formulations can **exacerbate DED**.
- **Systemic medications** can result in decreased tear production, altered sensory input, and reflex tear secretion.
- Refractive and corneal surgeries can cause or **aggravate DED** due to the transection of corneal nerves and the use of postoperative topical medications.
- Cosmetic and functional eyelid surgeries, botulinum toxin injections, cataract surgery, and postoperative topical medications can lead to DED.



DIAGNOSTIC METHODOLOGY

- The **sensitivity and specificity** of tests for DED diagnosis are highly dependent on the inclusion criteria for DED studies, the severity of the disease group, and the population studied.
- The best clinical approach involves use of **triaging questions** and risk factor analysis as part of a traditional patient history, detailed anterior eye examination, and differential diagnosis based on the answers.
- If DED is suspected, a positive result on a **screening questionnaire** such as the Dry Eye Questionnaire (DEQ-5) or the Ocular Surface Disease Index (OSDI) should trigger further evaluation, including tear breakup time (noninvasive methods preferred); tear film osmolarity; and ocular surface staining of the cornea, conjunctiva, and lid margin with fluorescein and lissamine green.
- **Identification** of a disruption in tear film homeostasis allows a diagnosis of dry eye to be made. This standardized approach will facilitate improved epidemiologic DED research and therapeutic regulatory approvals in the future.
- Other tests include meibography, lipid layer interferometry, evaporation, and tear volume measurements. These can help clarify where the individual with DED falls on the evaporative and aqueous-deficient DED subtype classification spectrum and promote the selection of **appropriate therapeutic interventions**.



MANAGEMENT AND THERAPY

- Restoration of tear film homeostasis is **the ultimate goal** in the management of DED, and this involves breaking the vicious circle of the disease.
- Determining whether the **major causes of an individual's DED** pertain predominantly to aqueous tear deficiency, to evaporative causes, or to both can help to establish the most appropriate management strategy.
- Failure in resolving symptoms and signs of DED may relate more to a **lack of success in determining and targeting the underlying nature or cause of DED** than a failure of the treatment itself.
- The heterogeneity of the DED patient population mandates that patients be managed and treated based on **individual profiles**, characteristics, and responses.



1. 2007 Report of the International Dry Eye WorkShop. *Ocul Surf.* 2007;5(2):65-206.

2. Nelson J, Craig J, Akpek E, et al. TFOS DEWS II introduction. *Ocul Surf.* 2017; 15(3):269-275.