TFOS DEWS III: **Management & Therapy Summary**

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The TFOS DEWS II Management and Therapy report described approaches to treating and managing dry eye disease (DED) based on the available evidence at the time.[1] Since its publication in 2017, a significant number of new treatments have emerged and existing treatments have been investigated more robustly, leading to updated recommendations presented in TFOS DEWS III Management and Therapy report.[2] This updated report categorizes the management strategies based on underlying mechanisms and contributing factors to DED and divides the treatment options into 10 categories, including tear supplementation and conservation, anti-inflammatory and antimicrobial interventions, biologics and regenerative therapies, nutritional therapy, and surgery.

The report begins by addressing lifestyle challenges that impact the ocular surface, as extensively detailed in recent TFOS reports.[3] Recommendations for patients focus on eliminating or reducing controllable risk factors, such as screen-related reduced blink rate and completeness, poor sleep, the use of cosmetics, and exposure to various environmental factors. The proposed changes, including taking breaks from digital devices, increasing indoor humidity and optimizing blink quality, can help reduce symptom severity and complement other prescribed therapies.

The management of tear insufficiency offers a broad variety of options, with opportunities to replenish, conserve, and restore tears. Tear replenishment is the cornerstone therapy, employing a wide array of topical supplements and stabilizers, including viscosity-enhancing polymers (e.g., hyaluronic acid, carboxymethylcellulose), lipid-containing emulsions, osmoprotectants (e.g., trehalose, ectoine), and novel agents like perfluorohexyloctane, to mimic natural tears, stabilize the tear film, and break the vicious cycle of inflammation and ocular surface damage. Tear conservation encourages preservation of natural tears by blocking their drainage through punctal plugging and reducing evaporation with moisture-retaining spectacles and contact lenses, such as protective bandage lenses or scleral lenses, thus improving ocular comfort. Lastly, tear restoration or stimulation techniques attempt to activate production of various components of the tear film. These include at-home treatments such as warm compresses, in-office device-driven therapies (e.g., intense pulsed light (IPL) or thermal devices), tear production through neuromodulation (e.g., intranasal sprays like varenicline or topical agents such as Acoltremon that stimulate trigeminal nerve reflexes), and topical secretagogues (e.g., diquafosol) that pharmacologically stimulate the secretion of tears.

Eyelid abnormalities are considered frequent drivers of evaporative DED and seven broad treatments are described; management of blink and lid closure anomalies such as lagophthalmos, incomplete blinking and thyroid eye disease; methods to reduce microbial load on the eyelids (including treatments for Demodex blepharitis such as topical lotilaner and tea tree oil and mechanical methods such as blepharoexfoliation); at-

home eyelid hygiene products including wipes, gels, foams, solutions, suspensions and sprays; emerging therapies such as low-level blue light therapy, okra-based cleansers and Manuka honey and topical antibiotics such as azithromycin.

Anti-inflammatory pharmacological therapies can assist in managing DED because of their ability to break the inflammatory cycle caused by ocular surface damage. While providing rapid, albeit short-term, relief for acute inflammatory flares, corticosteroids need to be monitored due to their potential side effects. For long-term control, the therapy of choice remains immunomodulators, including various formulations of cyclosporine A, and lifitegrast, which suppress the activation of T-cells and the release of cytokines. Tacrolimus ointment is an option for refractory cases of blepharitis or Sjögren-related DED.

Oral antibiotics in the form of doxycycline and azithromycin are sometimes used to treat DED caused by MGD. Their benefits primarily come from their anti-inflammatory effects and ability to improve oil quality.

In advanced disease, when standard therapies fail, ocular surface promoters and regenerative therapies provide options for restoring epithelial health. Blood-based eye drops, made from a patient's own blood (autologous serum) or donor blood (allogeneic serum), contain natural growth factors that aid in healing the ocular surface in cases of severe dry eye. Other regenerative options include amniotic membrane grafts and onlays, and nerve growth factor drops.

Treatments for anatomical surface abnormalities focus on addressing physical irregularities that disrupt the tear film and exacerbate DED. Conjunctivochalasis is typically managed with lubricants, anti-inflammatory medications, or surgical techniques, such as excision or laser treatment, to improve tear distribution and drainage. Lid parallel conjunctival folds are primarily treated with regular lubrication. The presence of a pterygium or pinguecula can also disrupt tear spreading; surgical excision often improves both signs and symptoms of DED by restoring typical ocular surface topography. These structural issues are not uncommon drivers of DED, and addressing them is crucial for effective management.

Nutritional and alternative therapies can support DED management. Omega-3 fatty acids from fish oil or flaxseed may help reduce ocular inflammation, although the evidence of their benefit is mixed. Vitamin supplementation (A, B12, D) can be beneficial if a deficiency is present, with some studies showing improvements in tear film stability and symptoms. Some natural approaches show promise in providing relief for dry eyes. Early research suggests that antioxidant-rich herbs and spices, such as curcumin (derived from turmeric) and goji berry extracts, may help reduce inflammation. Lactoferrin supplements may reduce inflammation and oxidative stress, while acupuncture may provide symptomatic relief for some patients. While these approaches can be beneficial, especially as adjuncts, they are generally not standalone treatments and should be combined with conventional DED therapy.

Ocular surgeries such as cataract extraction or refractive surgery may induce or worsen dry eye. To reduce this risk, optimizing the ocular surface preoperatively by treating MGD or any other obvious cause of DED is highly beneficial. After surgery, it may be necessary to continue management if dry eye persists. This proactive approach improves surgical outcomes and reduces symptoms.

Finally, surgical options, including permanent punctal occlusion, lid surgery and tarsorrhaphy, are reserved for severe, refractory cases. Specialized procedures include salivary gland transplantation to facilitate lubrication of the ocular surface in severe alacrimia and lacrimal gland reinnervation for neurogenic dry eye. These complex surgeries carry significant risks and are options of last resort.

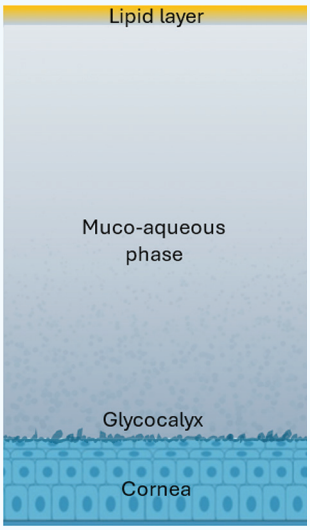
In addition to the evidence-based synthesis of the available methods to manage DED detailed above, the reports include three detailed prescribing algorithms that connect the etiological driver findings to the best-evidence treatments, classified as tear film deficiencies ***(Figure 1),*** eyelid anomalies ***(Figure 2),*** and ocular surface abnormalities ***(Figure 3),*** as determined in the TFOS DEWS III Diagnostic Methodology report.[4]

These algorithms assist practitioners in identifying the specific underlying disease causes, which are often multiple in nature, and match them to appropriate treatments. The report highlights the frequent need for a combination of therapies to manage multiple underlying causes and emphasizes the importance of patient education, compliance, and lifestyle adjustments in achieving optimal outcomes for all subtypes of dry eye.

An example of such an approach is where a patient exhibits a tear film lipid deficiency, as determined by assessment of lipid layer thickness/interferometry and/or meibomian gland expressibility/quality. There is research evidence that this patient can be managed via the use of tear supplementation/stabilisation, tear conservation devices such as moisture retaining spectacles, various pharmacological approaches, device tear stimulation, blink therapies and topical lid hygiene. A more detailed breakdown of the current high quality evidence supporting management choices according to proven effectiveness for specific DED etiological subtypes can be found in the tables that accompany these figures.

TEAR FILM DEFICIENCIES

ETIOLOGIC DRIVER TESTS
Lipid
Tear film lipid layer thickness / interferometry
Meibomian gland expressibility
Meibum quality
Aqueous
Tear meniscus height
Meniscometry / Schirmer⁺ / phenol red thread test⁺
Mucin / glycocalyx
Lissamine green / rose bengal staining
Conjunctival impression cytology



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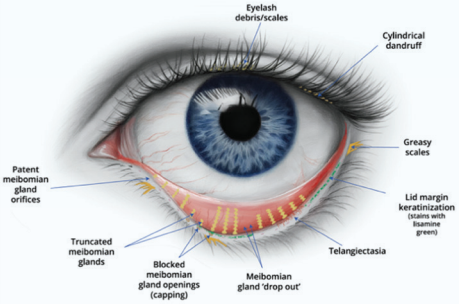
EVIDENCE-BASED INTERVENTIONS
Lipid
Tear supplementation / stabilization (lipomimetics)
Tear conservation devices (moisture-retaining spectacles)
Pharmacological tear stimulation / restoration
Device tear stimulation / restoration
Blink therapies
Topical lid hygiene
Aqueous
Oral nutrition (Omega 3)
Tear supplementation / stabilization
Tear conservation devices
Pharmacological / device tear stimulation / restoration
Topical anti-inflammatories
Ocular surface regenerators
Surgical options
Mucin / glycocalyx
Tear supplementation / stabilization (HP guar)
Topical anti-inflammatories
Pharmacological tear stimulation
Device tear stimulation (neurostimulation)

Figure 1. Diagnostic tests and evidence-based treatments to manage the underlying causes of tear film deficiency-related dry eye subtypes.

EYELID ANOMOLIES

ETIOLOGIC DRIVER TESTS
Blinking / lid closure
Incomplete blinking
Anterior blepharitis
Eyelid biomicroscopy - greasy (seborrheic) or flaky (staphylococcal)
Eyelash base - cylindrical dandruff - *Demodex*
Meibomian gland dysfunction
Pouting, missing, displaced gland orifices
Meibomian gland expressibility
Meibography – truncated, dilated glands, 'drop out'
Telangiectasia
Lid margin keratinization



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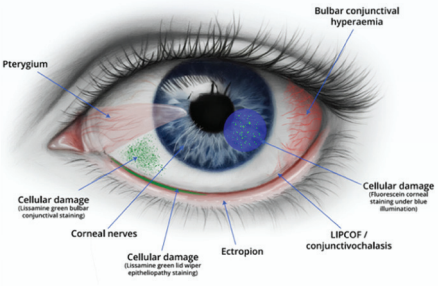
EVIDENCE-BASED INTERVENTIONS
Blinking / lid closure
Blink exercises
Anterior blepharitis
Topical lid hygiene
Oral antibiotics
Meibomian gland dysfunction
Oral nutrition (vitamin D3)
Tear supplementation / stabilization (lipid-based, androgen)
Pharmacological tear stimulation / restoration (topical azithromycin, selenium sulfide)
Device tear stimulation / restoration (internal and external lid heating; IPL; LLLT; QMR; radio-frequency
Lid margin debridement for significant keratinization
Oral antibiotics

Figure 2. *Diagnostic tests and evidence-based treatments to manage the underlying causes of eyelid-related dry eye subtypes.*

OCULAR SURFACE ABNORMALITIES

ETIOLOGIC DRIVER TESTS
Anatomical misalignment
Biomicroscopy e.g. pterygium, LIPCOF / conjunctivochalasis, ectropion / entropion, lagophthalmos
Neural dysfunction
Corneal sensation
In vivo confocal microscopy
Cellular damage / disruption
Cornea (fluorescein)
Bulbar Conjunctiva (lissamine green)
Lid wiper epitheliopathy (lissamine green)
Inflammation / oxidative stress
Bulbar conjunctival hyperemia
Inflammatory markers



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EVIDENCE-BASED INTERVENTIONS
Anatomical misalignment
Surgical options
Neural dysfunction
Tear supplementation / stabilization
Surgical options (punctal occlusion)
Cellular damage / disruption
Oral nutrition (vitamin D3)
Tear supplementation / stabilization
Pharmacological tear stimulation / restoration
Device tear stimulation / restoration
Topical lid hygiene
Topical anti-inflammatories
Ocular surface regenerators
Surgical options (punctal occlusion)
Inflammation / oxidative stress
Oral nutrition (omega 3 / vitamin D3)
Tear supplementation / stabilization
Pharmacological tear stimulation / restoration
Device tear stimulation / restoration (IPL)
Topical lid margin hygiene / debridement
Topical anti-inflammatories
Ocular surface regenerators (amniotic membrane)
Surgical options (punctal occlusion)

Figure 3. *Diagnostic tests and evidence-based treatments to manage the underlying causes of ocular surface-related dry eye subtypes.*

Key References

1. Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. *Ocul Surf.* Jul 2017;15(3):575-628. doi:10.1016/j.jtos.2017.05.006
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