

ADVANCES IN DRY EYE MANAGEMENT

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Course description: Dry eye syndrome is more than just an ocular nuisance. Newly recognized theories suggest that dry eye is a unique autoimmune disorder with inflammatory components and a propensity toward significant ocular morbidity, through a variety of mechanisms. This course presents an overview of dry eye disease, focusing on current management strategies in clinical practice. The discussion includes the use of various tear replacement therapies, anti-inflammatory agents, oral supplements and punctal occlusion.

DEWS – “Dry Eye Workshop”

- A team of international experts assembled to conduct an evidence-based review of the present state of knowledge for dry eye disease, as well as the methods used to evaluate, diagnose, and manage the disorder.
 - Delineated the multitude of factors that may contribute to or induce a dry eye state
 - Developed a classification scheme for dry eye disease, based upon etiopathogenesis; also
 - Discussed dry eye within the framework of specifically targeted glands and tissues
 - Incorporated the Delphi Panel’s classification scheme based upon disease severity
 - Reviewed the epidemiology of dry eye disease
 - Reviewed the clinical methodologies to diagnose and monitor dry eye disease
 - Reviewed the various treatment modalities for dry eye disease, and made treatment recommendations based on the ITF Delphi Panel conclusions
 - Reviewed the research methodologies relevant to dry eye disease

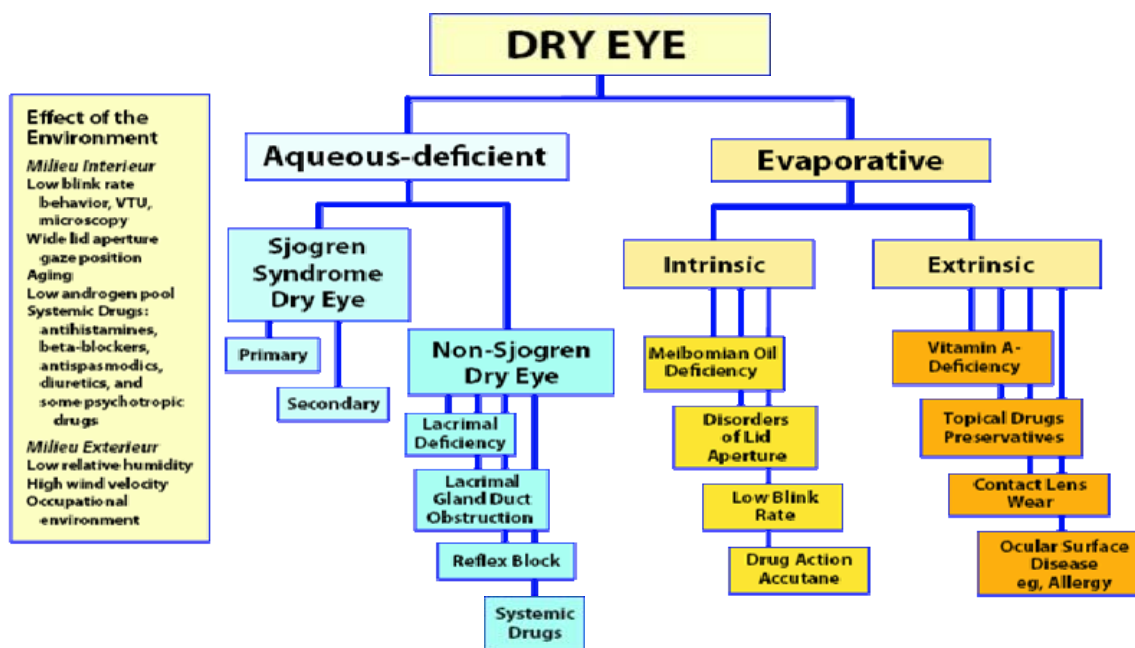


Dry Eye Defined: 2007

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.

The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr;5(2):75-92.

The DEWS Classification of Dry Eye Disease



- DEWS also utilized recommendations from the International Task Force (ITF) “Delphi Panel” – a group of renowned dry eye experts in ophthalmology and optometry – in adopting a severity-based classification scheme for dry eye.

Table 5. Dry eye severity grading scheme

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 glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TFBUT (sec)	Variable	≤ 10	≤ 5	Immediate
Schirmer score (mm/5 min)	Variable	≤ 10	≤ 5	≤ 2

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

Reprinted with permission from Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome. A Delphi approach to treatment recommendations. *Cornea* 2006;25:90-7

- Dry Eye Management – the ITF Panel’s guidelines have been widely adopted and recommended by members of DEWS.
 - Behrens A, Doyle JJ, Stern L, et al; Dysfunctional tear syndrome study group. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006;25(8):900-7.

SEVERITY	SIGNS AND SYMPTOMS	RECOMMENDED TREATMENT
1	Mild to moderate symptoms; no signs Mild to moderate conjunctival signs	Patient counseling, preserved tears, environmental management, use of hypoallergenic products, water intake.
2	Moderate to severe symptoms Tear film signs Mild corneal punctate staining Corneal staining Visual signs	Unpreserved tears, gels, ointments, cyclosporine A, secretagogues, topical steroids, nutritional support (flax-seed oil).
3	Severe Symptoms Marked corneal punctate staining Central corneal staining Filamentary keratitis	Tetracyclines, Punctal plugs
4	Severe symptoms Severe corneal staining, erosions Conjunctival scarring	Systemic anti-inflammatory therapy, oral cyclosporine, moisture goggles, acetylcysteine, punctal cautery, surgery

Therapeutic Considerations for Dry Eye

- What are the objectives in caring for patients with dry eye disease?
 - to improve the patient’s ocular comfort and, in turn, quality of life
 - to stabilize and restore normal integrity to the tear film
 - to promote ocular surface health, and return it to its normal homeostatic state
- Level 1 Therapies:
 - **Tear Replacement** (i.e. “artificial tears”)
 - Rationale for tear replacement therapy:
 - Replenish surface moisture & dilute ocular surface debris
 - Diminish pathologic surface changes (e.g. keratinization) secondary to dessication
 - “Downside” of tear replacement therapy:
 - Multitude of products
 - ◆ Approved under the US FDA monograph on OTC products (21 CFR 349), and not based on clinical efficacy
 - ◆ Vary by polymeric base, viscosity, preservatives, electrolyte composition, osmolarity, and delivery system
 - Limited palliative/therapeutic effect (~ 5 minutes in some studies)
 - Summation of preservatives may have toxic effect on ocular surface

It is difficult to demonstrate that topical lubricants improve the ocular surface and the tear film abnormalities associated with dry eye. To date, there have been no large-scale, masked, comparative clinical trials to evaluate the wide variety of ocular lubricants.

- Level 2 Therapies:
 - **Restasis** (cyclosporine A 0.05% ophthalmic emulsion)
 - Currently the only FDA-approved prescription pharmaceutical for the treatment of dry eye disease
 - Drawbacks:
 - Delayed onset of action (90 - 180 days)
 - Potential for ocular stinging & burning (~17% of patients in Phase III)
 - Topical corticosteroids
 - Numerous studies have shown significant benefit in the short-term use of topical steroids for dry eye disease; improved not only symptomology but also ocular surface integrity, based upon goblet cell density, epithelial integrity, etc.
 - Complications of long-term corticosteroid use are well-established:
 - Ocular hypertension (up to 42% of the population)
 - ◆ “Soft steroids” e.g. **Lotemax** (loteprednol etabonate 0.5%) have been advocated by many as a “safer” alternative for dry eye therapy
 - Cataractogenesis
 - Diminished wound healing effects
 - Increased risk of secondary infection

DEWS Position Regarding the Use of Corticosteroids in Dry Eye Disease:

In the US Federal Regulations, ocular corticosteroids receiving “class labeling” are indicated for the treatment “...of steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, selected infective conjunctivides, when the inherent hazard of steroid use is accepted to obtain an advisable diminution in edema and inflammation.” We interpret that KCS is included in this list of steroid-responsive inflammatory conditions.

- “Nutraceuticals” - essential fatty acid supplements (Ω -3 ± Ω -6)
- Topical secretagogues (e.g. diquafosol) – currently experimental
- Level 3 Therapies:
 - Lacrimal Occlusion Therapy: ***Is it a good idea to ‘stop up the drain’?***
 - Rationale:
 - Prevents drainage of tears from ocular surface through nasolacrimal system
 - Prolongs contact time between tear film & ocular surface
 - Utilizes the eye’s own tears; no additives, preservatives, potential hypersensitivity

- “Downside” of punctal occlusion:
 - Potential complications can include plug displacement, foreign body sensation, pyogenic granuloma, canaliculitis and dacryocystitis
 - **“Cesspool effect”**
 - ◆ In inflammatory dry eye disease, tears are laden with cytokines; increased contact may lead to amplified symptomatology & subsequent corneal damage
 - ◆ Increased corneal stimulation can lead to nerve damage & neurosecretory block at the lacrimal gland (lacrimal functional unit)
- Oral Pharmaceutical Therapy:
 - Anticholinergic agents stimulate aqueous production in the lacrimal gland via systemic autonomic pathways
 - Used primarily to treat dry mouth associated with Sjögren’s syndrome
 - Options:
 - ◆ **Salagen**[®] (pilocarpine) 5 mg QID
 - ◆ **Evoxac**[®] (cevimeline) 15-30 mg TID
 - Side-effects may include profuse lacrimation, sweating, headache, miosis, etc.
 - ◆ Evoxac[®] has been shown to be equally effective with fewer side-effects
 - The tetracyclines (e.g. tetracycline, doxycycline, minocycline) may be beneficial in dry eye disease, particularly in those patients with meibomian gland dysfunction
 - Inhibits bacterial lipase production by normal ocular flora
 - ◆ Subsequent reduction in free fatty acid production
 - ◆ Improves consistency of meibomian gland secretions; reduces glandular dysfunction and lid margin inflammation while improving tear quality
 - Diminishes formation of matrix metalloproteinase-9, a pro-inflammatory mediator
 - Limitations / precautions for usage:
 - Dental discoloration may occur in developing children: cannot be utilized in pregnant or lactating women, or those < 10 years of age
 - Photosensitizing agent: patients must avoid excessive UV exposure
 - May not be taken within two hours of ingesting dairy products
 - Prolonged course of therapy (generally 6-12 weeks)
 - Low-dose doxycycline (e.g. Periostat[®] or Alodox[®] – 20 mg) maintains anti-inflammatory effect for lid disease but greatly diminishes side-effect profile.
- Level 4 Therapies - are reserved for the most severe patients and only rarely utilized in optometric practice. Usually entail surgical or high-risk systemic medication.

CONCLUSIONS:

Dry eye disease is an exceedingly common but frequently under-diagnosed condition. Patients are often frustrated due to chronic ocular irritation and distorted vision; management of these patients can be equally frustrating for their physicians. However, understanding the myriad of contributory factors and properly utilizing the existing therapies may help to improve many patients' symptoms, overall ocular health, and quality of life.

Optometry is uniquely positioned to be the primary care providers for patients with dry eye disease. By proactively diagnosing and prescribing for this elusive condition, we help to alleviate suffering and elevate the state of our profession.

Suggested Reading List:

- *Stern ME, Beuerman RW, Fox RI, et al. The pathology of dry eye: The interaction between ocular surface and lacrimal glands. Cornea 1998; 17:584-9.*
- *Stern ME, Beuerman RW, Fox RI, et al. A unified theory of the role of the ocular surface in dry eye. Adv Exp Med Biol. 1998;438:643-51.*
- *Mathers WD. Why the eye becomes dry: A cornea and lacrimal gland feedback model. CLAO J 2000; 26(3):159-65.*
- *Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome: A delphi approach to treatment recommendations. Cornea. 2006;25(8):900-907.*
- *The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr;5(2):75-92.*
- *The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr;5(2):93-107.*
- *Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr;5(2):163-78.*
- *Research in dry eye: report of the Research Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr;5(2):179-93.*