

**Current Treatment and Management of Dry Eye**

David I. Geffen, OD, FAAO

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**What is Dry Eye Disease (DED)?**

- Multifactorial disease of the tears and ocular surface
- Involves:
  - Increased osmolarity of the tear film
  - Inflammation in the ocular surface
  - Dysfunction of one or more tear film components
- Results in:
  - Tear film instability
  - Damage to the ocular surface
  - Discomfort (in most)
  - Visual disturbance

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**Challenges in Dry Eye Disease**

- Patients often present with conflicting signs
  - Low Schirmer (< 5 mm) with a high TBUT (> 7 seconds)
  - Evidence of staining, but normal Schirmer’s & TBUT
- Symptoms alone are not diagnostic and insufficient to determine severity
  - Questionnaires are nonspecific
  - Patients are unsatisfied with current standard of care; they move from practice to practice seeking better options
- Existing signs and tests correlate poorly with disease severity
  - Schirmer test, TBUT, staining may not correlate with each other or symptoms

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**David I Geffen, OD, FAAO**

Consultant/Advisor/Speaker

- Accufocus
- Alcon
- AMO
- Allergan
- Bausch + Lomb
- Bruder Healthcare
- EyeBrain
- Optovue
- Revision Optics
- Shire
- Tear Lab
- Tear Science
- TLC Vision

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**International Dry Eye Workshop 2007**

**Table 4**

**CORE mechanisms**

- Low Lacrimal Flow
- Tear Hypo-osmolarity
- Tear Film Instability

**Factors**

- High Air Speed
- Low Humidity

**Environment**

- High Air Speed
- Low Humidity

**Deficient or Unstable Tear Film Components**

- Lipid Layer
- Water Layer
- Thick Mucin Layer

**Tear Film**

- MGD
- Blepharitis
- Lid flora
- Lipases, esterases
- Detergents

**Low androgens**

- Ageing
- IL-1β
- TNFα
- MMPs

**Dry Eye is a Disease of the Lacrimal Functional Unit**
Dry Eye Prevalence

- NIH: 7-33% of US population has dry eye
- 63.8 Million Dry Eye Sufferers
  - At minimum: 4.5 Million in Southern California alone
- 33,100 Optometrists in the US
  - 1,927 dry eye patients per OD

Prevalence

- Data obtained from the CDC

Economic Impact

- Annual Out of Pocket Cost
- $0.00 - $3,000.00
- Average Annual Indirect Cost per Patient: $11,302.00

Patient Demographics

- Prevalence of Dry Eye with Age

New Demographics Data

- 65.6% had Definite or Probable Dry Eye Disease
  - 60.2% of Men
  - 76.5% of Women
  - 76.6% had a TBUT of 5 seconds or less
  - 74.3% of Men
  - 87.2% of Women

Estimates of DED Prevalence Vary Based on How the Disease is Defined

- Study
  - Salisbury Eye Study
  - Beaver Dam
  - Women’s Health Study
  - Blue Mountains
  - Shihpai (Asian)
  - Sumatra (Asian)
  - Allergan phone survey

Prevalence (Millions)

- Data obtained from the CDC


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Prevalence

- Data obtained from the CDC


Dry Eye Is Prevalent

- 2.5 million people in the United States\(^1\)
- A top reason for visits to EyeMDs and ODs
- Patients often dissatisfied with treatments
  - Frequent drops inconvenient
  - Limited symptomatic relief
  - Frustrated
  - Want new options


Dry Eye Patient Factors

- Older age
- Female gender
- Post-menopausal
- Tobacco smoking
- Contact lens wear
- Prolonged staring (e.g. computer work)

Environmental Factors

- Air Pollution
- Artificial, forced air
- Allergens
- Low humidity

Disease Related Factors

- Systemic:
  - Autoimmune disease (TED)
  - Neurologic disease that reduces blink
  - Vitamin A deficiency
- Local:
  - Lacrimal gland infiltration
  - Eyelid malposition, laxity, lagophthalmos
  - Ocular surface disease

Medications

- Antihistamines
- Antidepressants
- Antispasmodics
- Diuretics
- Oral contraceptives
- Hormonal therapy

Pathophysiology of Chronic Dry Eye Disease

- Disruption of normal neuronal control of tearing
- Cytokine secretion into tears
- Disruption of normal neuronal control of tearing
- Lacrimal Glands:
  - Chronic irritation
  - T cell activation
  - Cytokine secretion into tears
  - Interrupted Secretomotor Nerve Impulses
  - Tears Damage Ocular Surface

Healthy Tears

- Complex Mixture
  - Antimicrobial proteins
  - Growth factors
  - Cytokines
    - Suppress inflammation
  - Mucin secreted by goblet cells
  - Viscosity
  - Electrolytes
  - Osmolarity

Functions of a Healthy Tear Film

- Optical clarity, refractive power
- Ocular surface comfort, lubrication
- Protection from environmental and infectious insults
  - Antibacterial proteins, antibodies, complement
  - Reflex tears flush away particles
- Trophic environment for corneal epithelium
  - Necessary electrolytes maintain pH
  - Protein factors for growth and wound healing
  - Antioxidants

Tears in Chronic Dry Eye

- Decreased proteins and growth factors
- Altered cytokine balance promotes inflammation
- Proteases activated
- Increased electrolytes
- Altered viscosity

Effects of Altered Tear Composition in Chronic Dry Eye

- Ocular surface tissue environment altered
  - Lubrication compromised due to poor viscosity
  - Increased osmolarity
  - Imbalanced growth factors and cytokines fail to promote normal epithelial growth
- Ocular surface damage
  - Loss of corneal epithelial integrity
  - Squamous metaplasia of conjunctival epithelium

Most DED Is Not A Result Of Aqueous Deficiency

Two Main Subtypes of DED as Defined by DEWS
Majority of DED Patients Have Evaporative Dry Eye (EDE)

- 86% of patients with a classified DED subtype demonstrated signs of Meibomian Gland Dysfunction
- Pure Aqueous Deficient Dry Eye (ADDE) subtype represented the smallest percentage of patients (~10%)

DED Is Not Defined By Symptoms

Signs and Symptoms of DED are Poorly Correlated

<table>
<thead>
<tr>
<th>Symptoms: Normal vs Elevated Osmolarity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal osmo but Ocular Surface Irritation/complaints</td>
</tr>
<tr>
<td>Elevated &gt;308 or inter-eye difference of &gt;8 mOsm/L</td>
</tr>
<tr>
<td>Adequately treated DED</td>
</tr>
<tr>
<td>C.L. &amp;/or solution irritation</td>
</tr>
<tr>
<td>Mild allergic conjunctivitis</td>
</tr>
<tr>
<td>Epithelial Basement Membrane Dystrophy</td>
</tr>
<tr>
<td>Pinguecula/early pterygia</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Anterior Blepharitis</td>
</tr>
<tr>
<td>Demodex</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Many Asymptomatic Patients Are Hyperosmolar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population, %</td>
</tr>
<tr>
<td>Patients reporting at least one symptom of DED, %</td>
</tr>
<tr>
<td>Asymptomatic patients, %</td>
</tr>
</tbody>
</table>

¹ ≤ 308 mOsm/L
² > 308 mOsm/L

DED Can Decrease Visual Acuity
Optics Of The Tear Film

- Tear film stability is critical for the maintenance of visual quality
- Uniform reductions of tear film thickness have little effect
- Irregular thickness degrades image quality
- Patients with DED have larger optical aberrations compared with normal eyes (by a factor of ~2.5)
- Artificial tears reduce these abnormalities and improve image quality in patients with DED

The Look of Dry

Normal

Abnormal

Tear Breakup Time (TBUT)

- Tear film instability is a hallmark of dry eye
- Correlates with aqueous and evaporative tear deficiency (Pflugfelder et al, 1998)
- TBUT measures tear film quality
- Fluorescein introduced from strip, yellow filter increases sensitivity
- TBUT = time from completed blink to 1st dry spot (3 repetitions)
- TBUT < 10 seconds abnormal (Lemp, 1995)
- Anesthesia decreases TBUT (de Paiva et al, 2004)
- Abnormal corneal surface -> break-up spots

Lissamine Green Staining in Dry Eye

Exposure zone staining with limbal sparing
Exposure zone staining with limbal sparing
Intense diffuse staining of exposure zone, limbal staining

Lissamine green detects dead or degenerated conjunctival cells

Vital Stains

Fluorescein  Rose Bengal  Lissamine Green

Images from Dry Eye and Ocular Surface Disorders, 2004.

Correlated With Visual Function

Osmolarity is Very Well Correlated With Visual Function

Data Courtesy of Pisella PJ, Habay T, Nochez Y
Department of Ophthalmology University Francois Rabelais Tours, France

The Look of Dry

Tear Breakup Time (TBUT)

Lissamine Green Staining in Dry Eye

Vital Stains

Images from Dry Eye and Ocular Surface Disorders, 2004.
Consensus Treatment Algorithm Guidelines

<table>
<thead>
<tr>
<th>Dry Eye Severity Index</th>
<th>LEVEL 1</th>
<th>LEVEL 2</th>
<th>LEVEL 3</th>
<th>LEVEL 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate symptoms and no signs</td>
<td>Moderate to severe symptoms</td>
<td>Severe symptoms</td>
<td>Severe symptoms</td>
<td></td>
</tr>
<tr>
<td>Mild to moderate conjunctival signs</td>
<td>Tear film signs</td>
<td>Mild conjunctival punctate staining</td>
<td>Severe conjunctival staining</td>
<td></td>
</tr>
<tr>
<td>Corneal staining</td>
<td>Conjunctival staining</td>
<td>Corneal staining</td>
<td>Conjunctival staining</td>
<td></td>
</tr>
</tbody>
</table>

Experts recommend cyclosporine A for level 2, 3, and 4 patients when inflammation is present. Punctal plugs are not recommended until level 3.

Dry Eye Management

Mild to Moderate Symptoms
- Minimal or no signs
- Add Essential fatty acids (EFA)
  - Flaxseed oil, Hydroeye®
- Add tear replacement
  - Osmolarity
  - Viscosity
  - Combination
- Restasis
- Xiidra

Moderate to Severe Symptoms
- Signs present: Abnormal tear film, corneal and conjunctival staining
- Essential fatty acids (EFA)
  - Flaxseed oil, Hydroeye®
- Topical anti-inflammatory agents
  - Cyclosporine
  - Lifitegrast
- If dry mouth also present: consider oral cholinergics
  - Pilocarpine (Salagen®)
  - Cevimeline

Cyclosporin and / or Lifitegrast

Dosing and Administration
- Not “as needed” like traditional eye drops
- One drop each eye in morning & evening
- Vials should be discarded after each use
- Two vials per day are required, and that’s why it’s important for patients to receive 2 trays for 30 days
- Artificial tears may be used for concomitant relief (no preservatives much better!)

RESTASIS®

increases tear production in some patients
- In pivotal trials, the use of RESTASIS® twice a day for 6 months (2000)
  - Increased goblet cell density
  - Increased tear production
  - Decreased corneal staining
  - Reduced reliance on artificial tears
Xiidra

**Lifitegrast Blocks**

**The interaction of LFA-1 with ICAM-1**

*As demonstrated by in vitro study: The exact mechanism of action of Lifitegrast in dry eye disease is not known.*

**By Blocking ICAM-1/LFA-1 Interaction, Lifitegrast May Inhibit:**

- T-Cell Activation
- T-Cell Migration
- Cytokine Release

Dry Eye Surgical Management

- Punctal occlusion
- Plugs
- Cautery

Distribution of dry eye subtypes

**DEWS Dry Eye Categorization:**

- Adapted from DEWS 2007 report

**Most Common Methods of:**

- **Diagnosis:**
  - Schirmer's Testing
  - NaFl/Rose Bengal/Lissamine Green Staining
  - TBUT
  - Symptom Surveys: OSDI/SPEED Testing

- **Treatment:**
  - Artificial Tears
  - Restasis
  - Punctal Plugs
  - Warm Compresses
  - Johnson & Johnson's™ Baby Shampoo Lid Cleansing
Time for a paradigm shift

- DEWS (2007): Symptoms are an essential component to Dry Eye Disease
- 2014 Correlation Study: 43% of patients with Dry Eye are asymptomatic
- Missed Opportunities
- Early intervention

The Psychology of dry eye

- Falls into the psychology of chronic illness
  - Frustration
  - Hopelessness
  - Suffering from symptoms others can’t see

- Our most effective tool: objective in-office testing
  - Patients need proof
  - SPEED testing, Schirmer’s, Quick tear break up test

New Methods of Diagnosis:

- LipiView II Imaging
  - Interferometry
  - Blink Analysis
  - Meibography
- Miebomian Gland Evaluator
- Systemic Disease Testing

LipiView II & MGE

- Interferometry & Blink Analysis
- Meibography
- MGE

Systemic Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Type</th>
<th>Characteristic</th>
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<tbody>
<tr>
<td>SIA-P</td>
<td>Traditional</td>
<td>Not tested for dry eye disease or symptoms</td>
</tr>
<tr>
<td>SIB-4</td>
<td>Traditional</td>
<td>Not tested for dry eye disease or symptoms</td>
</tr>
<tr>
<td>Advanced TearFilm</td>
<td>Traditional</td>
<td>Not tested for dry eye disease or symptoms</td>
</tr>
<tr>
<td>PK-P</td>
<td>Traditional</td>
<td>Not tested for dry eye disease or symptoms</td>
</tr>
<tr>
<td>PK-P</td>
<td>Meibomian</td>
<td>Not tested for dry eye disease or symptoms</td>
</tr>
<tr>
<td>PK-P</td>
<td>Tearfilm</td>
<td>Not tested for dry eye disease or symptoms</td>
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New Methods of Treatment

- Problem-specific Artificial Tears
- Supplements
- Advanced Lid Hygiene
- LipiFlow
- Bio-Tissues
Problem Specific Artificial Tears
- Evaporative Dry Eye
- Multi-factoral Dry Eye
- Night time Lagophthalmos

Supplements (And Masks)

Advanced Lid Hygiene
- Dehydrated amniotic tissues
  - Aril
  - Moria
  - AmbioDisk
  - Cryo-preserved
  - BioTissues: Prokera

Bio-Tissues

Prokera Patient Outcomes
Before - 2 Days After

LipiFlow
- FDA Study Results
**Lipiflow 1 Year Study**

**LipiFlow GWSVI Outcomes**
- SPEED Scores Pre- & Post- LipiView (1 month)

**How Patients Should Prepare:**
- No drops, gels, ocular medications 4 hour prior
- No ointments for a minimum of 12 hours prior
- No moisturizers, creams, sun block, or make-up around the eye the day of

**Types of Meibum**
- Clear
- Cloudy
- Semi-Solid
- Insipissated
- Obstruction w/ Neo
- Notching

**Non-Obvious MGD**

**In Office Dry-Eye Testing:**
- Krob Meibomian Gland Evaluator
- Line of Marx Evaluation
- Transillumination Estimation of MG structure
- KB Lid-Light Test
- LipiFlow Keys to Success
Korb Meibomian Gland Evaluator

- Standardize clinical findings
- Force = deliberate blink
- How to:
  - Wipe lid margin clean
  - Press in along three zones at base of lashes
    - Temporal → Nasal
    - Angle face of MGE to be tangential to globe
  - Evaluate secretions (if no secretions, assess for 15 sec)

Transillumination Test

Complete Lid Closure

Incomplete Lid Closure

Transillumination for MG Structure

Mild

Moderate

Severe

Non-Truncated

Truncated

LipiFlow Keys to Success

- Accurate Pre- & Post-procedure measurements
- Managing patient expectations
- Improving compliance with home maintenance

Post-LipiFlow

- Managing post-procedure expectations
  - Well lubricated → Period of increased dryness
  - Maximal benefits can be seen at 9 months out
- Post-procedure inflammation management
- Re-evaluation at regular intervals
- Continued home maintenance