

**Disclosures**
William D. Toomey, O.D., F.A.A.O.
- Alcon
- CIBA
- Odyssey Medical
- Science Based Health
- Shire
- TearLab

Any product superiority mentioned during this presentation will be supported by scientific studies and papers.

**Imagine...**
- Having issues performing simple tasks like...
  - Reading
  - Computer
  - Driving
- Experiencing...
  - Tired eyes
  - Unstable vision
  - No help in sight

**Course Objectives**
- Examine quality of life issues linked to DED
- Review basic demographics of DED
- Review salient data from landmark DED studies
- Discuss diagnostic evaluation options for DED
- Review new therapy, concepts, technology DED
- Informed decisions and prescribing strategies
Do Doctors and Patients Perceive Dry Eye Differently?

Severity of Symptoms
- Symptoms are severe: Drs. 9% vs. Dry Eye Pts. 19%
- Symptoms moderate: Drs. 20% vs. Dry Eye Pts. 36%
- Symptoms mild: Drs. 47% vs. Dry Eye Pts. 23%

Summary
- Patients w/ dry eye experience more symptoms than doctors would expect from clinical signs.
- Signs & symptoms of OSD often have no correlation.


The Impact of DED on Quality of Life

210 adult subjects:
- 130 non-SKCS
- 32 with SKCS
- 48 controls


Dry Eye and Quality of Life
- QOL value for mild dry eye was roughly equivalent to that of psoriasis.
- QOL value for severe dry eye equivalent to that assigned to severe angina or disabling hip fracture.

Analyzed data from 75,000 participants in National Health and Wellness Survey

#1 - Have you ever experienced dry eye?
#2 - Have you been diagnosed by a physician
- If no, end of the evaluation
- If yes, have you experienced...
  - Pain, light sensitivity, a gritty sensation, a feeling of a foreign body or sand in the eye, itching, redness, and blurring of vision

Definition of Dry Eye

“...a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.”

1995 National Eye Institute (NEI) Industry Dry Eye Workshop

- Disorder of the tear film
- Tear deficiency
- Excessive evaporation
- Ocular surface damage
- Associated symptoms of ocular discomfort

“...a blueprint for clinical, translational, and basic research that would propel the field to the next level.”

“...identified the relevance of tear film quality as well as tear quantity.”
Definition of Dry Eye:

- 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.

1995 National Eye Institute (NEI) Industry Dry Eye Workshop

Dry Eye Workshop 2007

Definition Dry Eye:

- 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.

Dry Eye Workshop (DEWS) 2007
Definition Dry Eye

...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. Mechanisms & show how each cause may act through a common path, severity which is expected to provide a rational basis for therapy. DED represents a failure of ability to maintain homeostasis of the OC.

Multifactorial disease of tears and ocular surface
Discomfort
Visual disturbance
Tear film instability
Increased tear osmolarity
Ocular surface damage
Ocular surface inflammation
Impaired homeostasis of ocular surface

Homeostasis: the tendency toward a relatively stable equilibrium between interdependent elements, especially as maintained by physiological processes.

Inability to maintain blood glucose within a physiologic range
Diabetes represents a disruption of "energy homeostasis"
**Homeostasis: Dry Eye**

- Inability to maintain tear film osmolarity within a physiologic range
- Dry eye results in or from “disruption of ocular surface homeostasis”

**Dry Eye Workshop II 2017**

**Key Elements 1995-2017**

- Disorder of the tear film
- Tear deficiency
- Multifactorial disease
- Increased evaporation
- Visual disturbances
- Tear film instability
- Increased tear film osmolarity
- Inflammation ocular surface
- Impaired homeostasis
DED: How Prevalent is It?

- Hospital-based study, 400 subjects, mean age 56.8 years
- Questionnaire
  - Demographic, medical Hx, lifestyle Hx.
  - Symptoms
    - Dryness, grittiness, stickiness, heaviness, burning, itching, watering
- Examination:
  - SLE + TBUT


DED: How Prevalent is It?

- Incidence DED
  - Overall- 54%
  - > 71 years of age- 67%
- Gender:
  - Males 51%
  - Females 57%
- Highest incidence in outdoor workers


DED: How Prevalent is It?

- Association with systemic disease
  - Diabetes 67%
  - Hypertension 51%
  - Arthritis 55%
  - Meibomian gland blockage 18%
  - Prevalence of DED 95%*
  - Glaucoma (6%)
  - Prevalence of DED 72%

Tear break-up time (TBUT)
- Measures tear film stability
- Evaluates the relationship between tear lipids & mucins.

Conventional (fluorescein)
- Use yellow filter
- Use non-preserved, compounded fluorescein

<table>
<thead>
<tr>
<th>Presenting Symptoms</th>
<th>DE Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watering</td>
<td>89</td>
</tr>
<tr>
<td>Itching</td>
<td>43</td>
</tr>
<tr>
<td>Heaviness</td>
<td>33</td>
</tr>
<tr>
<td>Burning</td>
<td>32</td>
</tr>
<tr>
<td>Stickiness</td>
<td>20</td>
</tr>
<tr>
<td>Dryness</td>
<td>19</td>
</tr>
<tr>
<td>Grittiness</td>
<td>19</td>
</tr>
<tr>
<td>Excess mucous</td>
<td>7</td>
</tr>
</tbody>
</table>

Strategies For Diagnosis: Conventional Testing

Tear meniscus (OCT)
- Better than SLE but no definitive levels of “normal”
- Inferior meniscus correlates better than superior with w/ TBUT & fluorescein staining, Schirmer test

Corneal & conjunctival staining
- Rose Bengal- cells that have lost mucin protective layer
- Sodium fluorescein- areas cellular degeneration or death, damage to cell membranes, epithelial cell junctions
Sterile Preservative-Free Stains

- From a compounding pharmacy
- Much more consistent staining
- TBUT: No interference from preservative
- Quicker - saves time
- Easy

Tear Film Osmolarity

- 1979: Gilbard & Farris describe association between dry eye & elevated tear film osmolarity
- 1983: Gilbard & Farris propose using hypo-osmolar drops to treat dry eye syndrome
- Early dry eye studies using tear film osmolarity conducted with freezing point depression
- 2010: Tomlinson et al find good correlation between tear film osmolarity measured by electrical impedance & freezing point depression

Osmolarity in the Diagnosis of Dry Eye Disease

<table>
<thead>
<tr>
<th>Clinical Test</th>
<th>PPV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolarity</td>
<td>87%</td>
</tr>
<tr>
<td>Schirmer</td>
<td>31%</td>
</tr>
<tr>
<td>TBUT</td>
<td>25%</td>
</tr>
<tr>
<td>Staining</td>
<td>31%</td>
</tr>
<tr>
<td>Meniscus Height</td>
<td>33%</td>
</tr>
</tbody>
</table>

- Osmolarity is the “gold standard” test for Dry Eye
- 45 years peer reviewed research
- Osmolarity has been added to definition of Dry Eye
- Global marker of Dry Eye, indicating a concentrated tear film

*positive predictive value, i.e., % of time an osmolarity > 308 will actually be dry eye
Hyperosmolarity Causes Apoptosis/Inflammation

TearLab
- Composed of:
  - Base unit
  - Pens to hold test card
  - Test cards
  - Quality assurance materials
  - Test solutions
  - Standard test cards
  - Determines Tsm using tear impedance (electrical resistance measured in Ohms)

TearLab Discovery
- Determines Tsm and MMP-9
- Both markers for OSD and inflammation
- Currently in FDA approval process
- Expected availability: soon!
  - Fluctuations in tear film osmolarity are a hallmark sign of DED
  - Represent an impaired ability to maintain ocular surface homeostasis
  - Elevated osmolarity a hallmark sign of OSD/DED
Proposed mechanism for pathophysiology of MGD

Outlined specifics @ normal composition of MG secretions

Classified MGD based on secretion
- Low delivery (hypo-secretory or obstructive)
- High delivery (hyper-secretory)

Concluded that MGD is the leading cause of DED
“MGD is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease.”

**Landmark Studies in Dry Eye**

- Terminal duct obstruction
- Qualitative/quantitative changes in the glandular secretion
- Alteration of the tear film
- Symptoms of eye irritation
- Clinically apparent inflammation
- Ocular surface disease

**Pathophysiology of Meibomian Gland Disease**

- Ductal hyperkeratinization: the key event
  - Simple MGD: plugging of meibomian gland orifices
  - Cicatricial MGD: scarring of conjunctival mucosa leads to displacement of orifices
  - Meibomian keratoconjunctivitis: MKC associated with skin conditions such as seborrhea, acne rosacea
Pathophysiology of Meibomian Gland Disease

- Triggers for MGD
  - Bacterial toxins - mostly gram-positive
  - Release of pro-inflammatory mediators
  - Reduced protective function by androgens
  - Reduced access to essential fatty acids and their byproducts
  - Contact lens wear
  - Reduced blink rate

Important News @ Meibomian Glands

- Applied constant force of 1.25 g/mm²
- Location is relative to meibum output:
  - Medial > Central > Temporal
- Symptoms relative to meibum output:
  - Mild > Moderate > Severe
- Recovery of meibomian glands:
  - Total drainage by expression 20 seconds
  - Recovery to 50% = 2 hours


Meibomian Gland Evaluation

- Injection/telangiectasia
- Pouting
- Quality of secretions
- % of MG yielding lipid
- Recording
  - 40% MGYLS
  - Quality 2/4
Meibomian gland transillumination

Use standard transilluminator
Flip upper or lower lid
Position transilluminator to backlight eyelid
Maximal illumination in dark room for best viewing
Record location and loss if any of MG structures
Photo document baseline and at subsequent visits
Infrared photos gaining acceptance

Evaluation for Meibomian Gland Disease

Normal Meibomian Pano Pattern
Melomian Gland Transillumination

Normal appearance

Proximal condensation, dropout

Total loss meibomian gland structures
Therapeutic Strategies for MGD
- Renewing patency of MG orifices
- Reducing inflammation
- Thinning MG secretions
- Long-term changes to minimize recurrence of MGD

Long-term Management of Meibomian Gland Dysfunction
- Education
- Demonstration
- In office therapy
- Patient based therapy
  - Heat
  - Manual expression
- Dietary supplementation
### Long-term Management of MGD

LipiFlow
- Disposable elements
- Maintains patency up to 9 months
- Often requires periodic retreatment

### MGD and Cyclosporine A: 2013

- A 3-month prospective, randomized, double-masked trial - 70 patients
- CSA 0.05\% vs carboxymethylcellulose
- @ 3 months improvements in:
  - Study group: OSDI, NIBUT, FBUT, lid margin inflammation, MG expressibility, tarsal injection showed significant improvement from baseline group
  - Control group: only the OSDI improved

A Randomized Double-Masked Study of 0.05\% Cyclosporine Ophthalmic Emulsion in the Treatment of Meibomian Gland Dysfunction Prabhasawat
Conclusions: CSA & MGD

- CSA statistically superior to placebo
- Decreased # meibomian gland inclusions
- Improved fluorescein staining
- Improved TBUT
- Reduced inflammation
- Increased MG expressibility
- Off-label use of topical CSA appears to be beneficial in treating MGD

In our experience, it can be very useful for advanced MGD. It may take months show
1) GLA heavily favors the anti-inflammatory pathway

2) As back up, adding EPA to GLA in proper balance, blocks production of pro-inflammatory pathway

**Combination N-3 + N-6 Preparations**

**Supplement Facts**

**2017**

- IPhone introduced 10 years ago
- Since then
Moon JH et al. Smartphone use is a risk factor for pediatric dry eye disease according to region and age: a case-control study. BMC Ophthalmol. 2016 Oct 28;16(1):188.

Evaluated pediatric DED in children:
- Region (urban vs. rural)
- Age
- DED in relation to smartphone use rate

916 subjects

Rate of smartphone use in Korea
- Children 83%
- Adolescents 89.8%

---

<table>
<thead>
<tr>
<th>Diagnosis DED</th>
<th>Urban</th>
<th>Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.3%</td>
<td>2.8%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Smartphone use</th>
<th>Urban</th>
<th>Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td>61.3%</td>
<td>50.0%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis DED</th>
<th>Older children</th>
<th>Younger children</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.1%</td>
<td>4.0%</td>
<td></td>
</tr>
</tbody>
</table>

---
Smartphone Use in Children

- Daily duration of smartphone use was longer in the DED group than controls
- Daily duration of outdoor activities was shorter in the DED group than controls
- 4 weeks after D/C smartphone use: DED group
  - Subjective symptoms improved
  - Objective signs improved
- Outdoor activity protective against DED

Encourage Outdoor Activity

MGD in Children

- Just beginning to recognize severity and prevalence of MGD/DED in children!
- Management
  - Patient/parent education
  - Limit device time
  - Nutritional supplementation
  - Home-based expression
MG Loss in Children Adolescents

- Sixty-nine patients two groups
  - Children 3 to 11 years
  - Adolescents 12 to 18 years
- Meibomian glands imaged w/ IR meibography
- Results: significant meibomian gland loss
  - Found in both groups
  - Occurs in both children and adolescents


Primary issue: reduced blink rate!
- Muscle of Riolan "milks" Meibomian glands w/ every blink
- Reduced blink rate leads to stasis, ultimately loss of meibomian glands

Our Mission Statement

“To promote excellence in the care of patients and the advancement of knowledge of dry eye and ocular surface disease (OSD) for ophthalmic educators and clinicians through professional education and scientific investigation.”

OSSO’s members enjoy the benefit of the OSSO online newsletter and the opportunity to share clinical cases with our Executive Board and Members-at-large.

Membership Details

- OSSO’s goal is to serve as the “Voice of Optometry in Ocular Surface Disease”
- To join OSSO you:
  - Must have an optometric degree from an accredited school or college of optometry
  - Must be a reputable individual in good standing within their profession and community
  - Must complete and submit an application form to OSSO
  - Students, scientists, and physicians with a specific interest in dry eye and/or ocular surface disease are also welcome to join as special class members of OSSO
- Membership dues are $54.00 per year

membership@ossopt.com

Conclusion

- Dry eye represents a huge opportunity for eye care providers, especially OD’s
- Join TFOS or OSSO and connect with like minded providers who manage DES
- Give special attention to the next generation of dry eye suffers