Evidence for Technology in the Treatment of Dry Eye

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Dry eye
- Chronic
- Multifactorial
- Characterized by disturbances in tear film & ocular surface
- Females > male

Dry eye
- Environmental conditions
  - Aird
  - Computer-use
  - Contact lens wear
- Systemic disease
  - Sjogren's syndrome
  - Lupus
  - Stevens-Johnson syndrome
Doctors and Patients See Dry Eye Differently

<table>
<thead>
<tr>
<th>Severity of Dry Eye</th>
<th>Doctor Assessment</th>
<th>Patient Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>9%</td>
<td>19%</td>
</tr>
<tr>
<td>Moderate</td>
<td>20%</td>
<td>36%</td>
</tr>
<tr>
<td>Mild</td>
<td>47%</td>
<td>23%</td>
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</tbody>
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- Patients often perceive their dry eye symptoms to be more severe than their ECP suspects based on clinical signs.
- ECPs lack a gold standard clinical test for dry eye, limiting their ability to objectively assess symptoms in many patients.


Dry Eye Demographics

- Estimate of dry eye disease in Americans over 50
  - 3.23 million women
  - 1.68 million men
  - Tens of millions more have less severe dry eye
- The prevalence of severe symptoms and/or clinical diagnosis may be greater in Asian and Hispanic women.
- Public health significance of dry eye is likely to increase: US population aged 65-84 years will grow by 100% between 2000 and 2050.


Dry Eye Can Have a Marked Impact on Quality of Life

- Dry eye can have a marked impact on patients' quality of life (QoL), particularly affecting their daily roles and vitality.
- QoL in patients with severe dry eye is comparable to that in patients with severe angina or disabling hip fracture.
- Respondents in this study stated that they would be willing to give up 1.6 years of their lives to be free of severe dry eye.
- In patients with mild dry eye, the QoL value is roughly equivalent to that of psoriasis.

Dry Eye Disease

- inflammation of the ocular surface and increased osmolarity of the tear film
- common and is often under diagnosed
- Signs don’t always correlate with symptoms
- negatively impact vision quality, fluctuating vision, reduced contrast sensitivity, and increased glare
- Significant psychological impact
  - Patients have reported a willingness to trade years at the end of life to be free of dry eye disease

Crucial Factors in Dry Eye Disease

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.

Why Is the Eye Dry?

Lid aperture issues
- Lid laxity
- Lagophthalmous
- floppy eye lid syndrome

Other CAUSES OF DRY EYE symptoms
- Medications (BAK)
  - Ophthalmic
    - Glaucoma medications
    - Allergy medications

Other Causes of dry eye symptoms
- Demodex
  - Demodex follicularum
  - Demodex brevis
Causes of dry eye symptoms
- blepharitis affects millions
- upwards of 80% of those patients could have Demodex mites

- Demodex
  - Men > Women
  - The incidence of Demodex infestation increases age
    - 64% of the population at age 60
    - ~100% of the population older than 70 years of age

Other Causes of dry eye symptoms
- Diabetes
- Thyroid disease
- Autoimmune disease
Psychology of dry eye

- 89 dry eye subjects (13 Sjogren's patients & 73 control subjects)
- Zung self-rating anxiety scales (SAS)
- Zung self-rating depression scales (SDS)
- Ocular surface disease index (OSDI)

Anxiety and depression scores of the DES group were significantly higher than the control group.
SAS and SDS scores were found to be correlated with OSDI.

What are the dry eye ‘personalities’ that we are dealing with?
Psychology of the examination
- Change the single visit mentality
- Treatment is a process
- Individualized care

Patient’s thoughts?

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Patient Thought</th>
</tr>
</thead>
<tbody>
<tr>
<td>72% of patients</td>
<td>Artificial tears only</td>
</tr>
<tr>
<td>82% of patients</td>
<td>Demand “something better”</td>
</tr>
<tr>
<td>97% of patients</td>
<td>Report condition as “frustrating”</td>
</tr>
</tbody>
</table>

Lid Wiper Epitheliopathy (LWE)

New diagnosis?
- 2002 coined by Korb et al.
- Lid wiper is the portion of the eye lids that is in apposition to the ocular surface during a blink.
- LWE has been reported to occur both with and without contact lens wear.
- Correlates with symptoms for both dry eye and contact lens discomfort.

LWE is increased friction between the lid wiper and the ocular surface due to inadequate lubrication.
- The lid wiper comes into contact with the anterior ocular surface over 3,000 to 15,000 times a day.
- The lid wiper is in apposition to the globe at all times and would be constantly susceptible to mechanical trauma with poor lubrication.
- The ocular surface, in contrast, comes in contact with the lid wiper for only a fraction of a second (about frequently)."
- It would be expected that in any state of dry eye disease, the lid wiper would suffer greater trauma and epithelial compromise than would be ocular surface.

Have we been looking?
- Is this diagnosis the 'missing link'?
- How should it be detected?
Method

- Lissamine Green (or NaFl)
- Though the lid wiper can be viewed in bright white light, disturbances in the tissue and LWE can only be observed with the aid of vital dyes.
- Upper conjunctiva
- Wait ~1 minute
- Evaluate conjunctiva and lid margin (gently)
- The term epitheliopathy is used in LWE to note the uptake of vital dye(s) thereby implying that the tissue is found to have devitalized cells and/or is in the presence of neighboring cellular apoptosis.

1) Grading of Horizontal Length of Fluorescein and/or Lissamine Green Staining of the Epithelium of the Lid Wiper (Korb et al., 2010)

<table>
<thead>
<tr>
<th>Horizontal Length of Staining</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 mm</td>
<td>0</td>
</tr>
<tr>
<td>2-4 mm</td>
<td>1</td>
</tr>
<tr>
<td>5-9 mm</td>
<td>2</td>
</tr>
<tr>
<td>&gt;10 mm</td>
<td>3</td>
</tr>
</tbody>
</table>

2) Grading of Sagittal Height (Width) of Fluorescein and/or Lissamine Green Staining of the Epithelium of the Lid Wiper (Korb et al., 2010)

<table>
<thead>
<tr>
<th>Sagittal Height (Width) of Staining</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25%</td>
<td>0</td>
</tr>
<tr>
<td>25%-50%</td>
<td>1</td>
</tr>
<tr>
<td>50%-75%</td>
<td>2</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>3</td>
</tr>
</tbody>
</table>

Tear osmolarity

- Tear lab osmolarity system (tear lab)
- Single-use microchip embedded with gold electrodes
- 50 nl collected
Tear osmolarity
- Osmolarity increases with advancing dry eye disease
- Asymmetry of findings also indicative of problems

Inflammadry
- Rapid pathogen screening
  - Detects elevated MMP-9 in tears
  - Studies indicate MMP-9 as a useful biomarker for diagnosing, classifying and monitoring DED

InflammaDry
- Identifies elevated levels of MMP-9 in tear fluid
- Rapid: 10 minute results
- In-office: point-of-care immunoassay test aids in diagnosis at the time of office visit
Matrix metalloproteinases (MMP) are proteolytic enzymes that are produced by stressed epithelial cells on the ocular surface.\(^1\)

- **MMP-9 in Tears**
  - Normal range between 3-41 ng/ml
  - Correlates with clinical exam findings.\(^1\)

### Tear MMP-9 Activity in Normal Control and DTS Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>MMP-9 Activity (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 18)</td>
<td>8.39 ± 4.70</td>
</tr>
<tr>
<td>DTS1 (n = 15)</td>
<td>35.57 ± 17.04</td>
</tr>
<tr>
<td>DTS2 (n = 11)</td>
<td>46.17 ± 17.00</td>
</tr>
<tr>
<td>DTS3 (n = 9)</td>
<td>101.42 ± 70.58</td>
</tr>
<tr>
<td>DTS4 (n = 11)</td>
<td>381.24 ± 42.83</td>
</tr>
</tbody>
</table>

* Data shown are the mean ± SD.
* \( P < 0.008 \) Compared with normal.
* \( P < 0.003 \) Compared with normal and DTS1.
* \( P < 0.001 \) Compared with normal and the other DTS severity groups.

### inflamadry

- a small applicator touched to the conjunctiva
- snaps into a test cassette
- Cassette tip is submerged in solution
- results are obtained in 10 minutes
**Inflammadry**

- **Pro's**
  - Inexpensive
  - Fast
  - Identifies presence of inflammation

- **Con's**
  - Does not quantify inflammation (per se)
  - Does not identify cause

**Oculus Keratograph 5M**

- Tear film analysis by non-invasive (non-contact) scanning
  - Nictiat
  - Tear meniscus height
  - Non-contact meibomography (meiboscan)
  - Tear dynamics
  - Bulbar redness
  - Topography

**Meibomian Gland Dysfunction (MGD) is the Most Common Cause of Evaporative Dry Eye Disease**1-3

> "Meibomian gland dysfunction (MGD) may well be the leading cause of dry eye disease throughout the world."4

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### Classification of Meibomian Gland Dysfunction

Meibomian Gland Dysfunction
- Low Delivery
- Hypersecretory (Meibomian Seborrhea)
- Obstructive
- Cicatricial
- Non-Cicatricial
- Congenital
- Neoplastic
- Acute
- Other

### Meibomian Gland Dysfunction (MGD)
- Primary
- Secondary
  - Trachoma
  - Ocular Pemphigoid
  - Erythema Multiforme
  - Atopy
- Primary
- Secondary
  - Seborrheic Dermatitis
  - Acne Rosacea
  - Atopy
  - Psoriasis

### Alteration of Tear Film
- Hyposecretory
  - (Meibomian Sicca)
- Hypersecretory
  - (Meibomian Seborrhea)

### Challenges of Current MGD Therapies
- **Therapy**
  - Warm compresses
  - Eyelid scrubs
  - Manual gland expression
- **Challenges**
  - External heat application is inadequate
  - Significant discomfort
  - Limited compliance
  - Only the upper portion of the glands are treated or expressed

### LipiView
- Uses interferometry to measure lipid layer thickness between blinks
- Quantitative assessment in interferometric color units (ICU)

**Pilot study:**
- 137 consecutive patients completed SPEED test, then measured LLT by LipiView
- SPEED >10: 74% had LLT of 60nm or less
- SPEED = 0: 7% had LLT 73nm or greater

As LLT increases, symptom score decreases
microscopy
- Demodex visible at slit lamp
- Cylindrical dandruff at base of lashes
- Most common ocular parasite
- Microscopy for patient education
- Upper 1/3 has four pairs of legs that allows it to move from one follicle to the next
- Remaining body is an abdomen-tail

Demodicosis
- Demodex folliculorum
  - Buries within hair follicle (tail protrudes)
- Demodex brevis
  - Favor sebum-rich environments like Meibomian glands
- Organisms inhabit hair follicles & glands
  - Feed on sebaceous oils & dead skin cells; carry pathogenic bacteria
  - Avoid light; most active at night
- Overpopulation causes localized inflammation

Demodicosis
- Demographics:
  - More prevalent in elderly
  - Male > female
  - More common in rosacea patients
- Symptoms:
  - Grittiness and/or burning
  - Itching of eyelids
  - Crusting of eyelashes
  - Poor cosmesis (i.e. eye & eyelid redness)
Demodicosis

- Key objective findings:
  - Cylindrical dandruff ("sleeves") at lash base (especially lash line most inward)
  - Possible to see mite tails with lash manipulation

Demodicosis - Management Options

1. In-office: microblepharoexfoliation (BlephEx™)
2. In-office: Cliradex® Complete
3. Home therapy:
   - Tea-Tree oil tx

Key Reasons to Control Lid Flora and Associated Inflammation

- Blepharitis
- Rosacea / Ocular Rosacea
- MGD & secondary staph overpopulation
- Pre-op surgical prophylaxis
- Refractive
- Cataract
- Retinal
- Contact lens wear
Dr. O’Brien Recommended Pre-Op Lid Hygiene Regimen with Avenova

- No lid disease
  - 1 week prior to surgery*
- Some Blepharitis or MGD Dry Eye
  - 2 weeks prior to surgery*
- Moderate Blepharitis or MGD Dry Eye
  - 3 weeks prior to surgery*
- Severe Blepharitis or MGD Dry Eye
  - 4 weeks prior to Surgery*

* Apply to both eyelids and lid margins twice a day

Contact Lens Infiltrative Events

“...the presence of substantial (>100 colony-forming units) coagulase-negative staphylococci biofilm on lid margins was associated with about a five-fold increased risk for the development of a CIE (p = 0.04).”


“Lid hygiene should be as common place and accepted as regularly brushing your teeth”
Future Work:
Surface Health and Visual Acuity

- Disruptions in tear film can lead to wavefront aberrations and reduction in visual performance.\textsuperscript{1-3}
- Contact lenses divide the tear film into two layers, increasing tear film breakup and potentially degrading visual acuity.\textsuperscript{4}
- Tear film disruption appears to be a common factor in reducing visual acuity in contact lens patients and those with dry eye.\textsuperscript{3}

TBU, tear breakup.

Prevent papillae in CL wearers