OSD Grand Rounds: Thinking Outside the Box
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Changing Paradigms in Dry Eye

FORMER DEFINITION
Dry Eye or Keratoconjunctivitis Sicca is a disruption of the precorneal tear film caused by tear deficiency or excessive tear evaporation that results in damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.

NEW DEFINITION
Dry Eye is a multifactorial disease of the ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability and tear film disruption, and can result in ocular surface damage. It is accompanied by increased ocular inflammation of the ocular surface.

Ocular Surface Disease
- The most common clinical problems affecting the ocular surface include:
  - Dry Eye Disease
  - Blepharitis
  - Allergic Eye Disease
  - These conditions often co-exist
    - Can share contributing pathology
    - Similar signs and symptoms

Speaker Disclosures
- Alcon Speakers Bureau
- B&L KOL Speakers Bureau
- Inspire Speakers Bureau
- The author has conducted clinical studies for CIBA and Bausch & Lomb

Dry Eye Etiology & Pathophysiology
Major Etiological Causes of Dry Eye

OSD Etiology & Pathophysiology

Why Treat Ocular Surface Disease?
- "many millions" is an accurate generalization
- Can affect men and all age groups
- 5% to 35% of persons at various ages have moderate to severe dry eye symptoms
- Most common reason patients discontinue contact lenses
- "It is estimated 40% of ophthalmic visits in the US involve dry eye."

"Dry Eye and Ocular Surface Disease is the one disease process optometry can make all its own."
Prevalence of Dry Eye

Summary of Studies of Dry Eye Prevalence in the US

- Although, percent of individuals who experience signs and symptoms of dry eye at one time or another due to environmental factors = 100%

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Age</th>
<th>Criteria</th>
<th>Prevalence</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>Wisconsin</td>
<td>2732</td>
<td>48-91</td>
<td>Self-reported</td>
<td>14.4%</td>
<td>Moss, 2000</td>
</tr>
<tr>
<td>Melbourne</td>
<td>936</td>
<td>40-97</td>
<td>&gt;2 signs</td>
<td>7.4%</td>
<td>McCarty, 1998</td>
</tr>
<tr>
<td>Maryland</td>
<td>2521</td>
<td>65-84</td>
<td>Symptoms +1 sign</td>
<td>3.5%</td>
<td>Schein, 1997</td>
</tr>
<tr>
<td>Women's Health</td>
<td>33,074</td>
<td>49-84</td>
<td>Severe symptoms or clinical diagnosis</td>
<td>7.8%</td>
<td>Schaumberg, 2003</td>
</tr>
</tbody>
</table>

Epidemiology

- Women’s Health Study (WHS) & Physician's Health Study
  - 3.2 million women & 1.05 million men ≥50 yoa have clinically important dry eye
  - 5.7% to 9.8% of women ≥50 yoa have chronic dry eye
  - Prevalence increases with age

Dry Eye Etiology & Pathophysiology

- Mean 10% increase in tear film osmolarity
- Increased expression of HLA class II antigens
- Decreased conjunctival goblet cell density
- Increased conjunctival & lacrimal gland CD4 T-cell infiltration

Tear Hyperosmolality

- Tear hyperosmolality is regarded as the central mechanism causing ocular surface inflammation, damage and symptoms, and the initiation of compensatory events in dry eye
- Dry eye patients have higher tear film osmolarity
- Osmolarity is a function of tear flow rate & evaporation
- Hyperosmolality decreases goblet cell density

Human Tear Osmolarity Recorded in Studies Reported in the Literature

<table>
<thead>
<tr>
<th>Study</th>
<th>Test</th>
<th>N</th>
<th>Osmolarity (mOsm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mishima et al.</td>
<td>FPD</td>
<td>304</td>
<td>329 ± 4.7 (6)</td>
</tr>
<tr>
<td>Gilbard et al.</td>
<td>FPD</td>
<td>304</td>
<td>343 ± 32.3 (30)</td>
</tr>
<tr>
<td>Terry and Hill VP</td>
<td>FPD</td>
<td>310</td>
<td>—</td>
</tr>
<tr>
<td>Gilbard and Farris</td>
<td>FPD</td>
<td>—</td>
<td>365 ± 77 (20)</td>
</tr>
<tr>
<td>Farris et al.</td>
<td>FPD</td>
<td>304.4</td>
<td>329.6 ± 17 (123)</td>
</tr>
<tr>
<td>Farris FPD</td>
<td>—</td>
<td>302</td>
<td>324 ± 11 (51)</td>
</tr>
<tr>
<td>Gilbard FPD</td>
<td>—</td>
<td>304</td>
<td>314 ± 1.0 (31)</td>
</tr>
<tr>
<td>Mathers et al.</td>
<td>FPD</td>
<td>303</td>
<td>313.7 ± 13 (146)</td>
</tr>
<tr>
<td>Ogasawara et al.</td>
<td>Con</td>
<td>296.4</td>
<td>324 ± 41 (16)</td>
</tr>
</tbody>
</table>

Average tear osmolarity all studies: 302 ± 9.7 (815) 326.9 ± 22.1 (621)

Tear Film

- Lipid
- Aqueous
- Mucin

Ocular Environment Balance

- Production
- Evaporation
- Clearance
The Pathway to Dry Eye

- Decreased Secretion
- Increased Evaporation
- Lacrimal Gland Disease
- Decreased Corneal Sensation
- Increased Palpebral Fissure
- Meibomian Gland Dysfunction
- Increased Tear Osmolarity

Abnormal Tear Film Causes and Contributors

- Decreased tear production or increased tear evaporation increases tear osmolarity
- Conjunctival goblet-cell density and corneal glycogen levels decrease
- Corneal epithelium desquamates, peels off
- Corneal surface loses ability to "hold" tear film

- Natural History of Dry Eye
  - Elevated tear osmolarity causes the dry-eye surface changes that progress with time:
  - Decreased tear production or increased tear evaporation increases tear osmolarity
  - Conjunctival goblet-cell density and corneal glycogen levels decrease
  - Corneal epithelium desquamates, peels off
  - Corneal surface loses ability to "hold" tear film

- Dry Eye Pathophysiology

- Tear Osmolarity & Dry Eye
  - Tear osmolarity is considered "the central mechanism causing ocular surface inflammation, damage and symptoms, and the initiation of compensatory events in dry eye."

- Dry Eye Questionnaires
  - Ocular Surface Disease Index (OSDI)
  - Rapid, repeatable, and gives a quantifiable result
  - Validity has been substantiated by clinical research
  - Helpful not only diagnostically, but also as a measure of therapeutic progress
**Ocular Surface Disease Index**

OSDI: Symptoms, Functions, Environmental Triggers

**Influential Medications in Dry Eye**

- Adrenergic blocking, Anti-anginals and Anti-hypertensives
  - (e.g. Atenolol, Propranolol, Pracolol)
  - Tricyclic Anti-depressants
  - Oral Anti-histamines
- Diuretics
  - (e.g. Triamterene)

**Dry Eye Questionnaires**

- "The best-validated screening definition of dry eye probably comprises these three "?":
  - "How often do your eyes feel dry (not wet enough)?" (constantly, often, sometimes, never)
  - "How often do your eyes feel irritated?" (constantly, often, sometimes, never)
  - "Have you ever been diagnosed by a clinician as having dry eye syndrome?"

**Patient History**

- Chief complaint
- Medications
- History of Refractive Surgery/ Contact Lens Wear

**Environmental Factors**

- Visual Tasking
  - Computer use
- Systemic Medications
  - Anti-histamines
- Foods/Drink
  - Alcohol
- Arid Conditions
- Southwestern Winds
- Pollutants
  - Exhaust, smoke, smog

**Dry Eye & Contact Lenses**

- Single most common complaint among contact lens wearers
  - 34% of patients d/c contact wear
- 34% of patients d/c wear at least once, most frequently because of dry eye symptoms

**Diagnostic Tools**

- Tear Film Break-Up Time
- Lissamine Green Staining
- Fluorescein Staining
- Osmolarity
- Blink Rate
- Tear Volume Testing
- Rose Bengal Staining
- Osmolarity
- Blink Rate

**DTS Study Group**

Most Commonly Used Diagnostic Tests

Fluorescein Staining

- Helps to further accentuate corneal changes seen in the dry eye
- Sodium fluorescein is important for demonstrating punctate epitheliopathy
- Most commonly associate fluorescein with tear break up time (TBUT)
- Realize that TBUT is diminished in many, though not all, dry eye patients

Vital Dye Staining

- Sodium rose bengal is important for demonstrating corneal epithelial changes
- Helps to further accentuate corneal changes seen in the dry eye
- Rose bengal is used for key side dye

Corneal Findings

- In dry eye, the cornea commonly displays a punctate epitheliopathy, usually within the inferior one-third of the cornea
- However, ocular discomfort is significantly worse in patients with more central corneal staining
- Additional findings include mucus filaments (strands or strands adherent to the cornea) and a diminished fluorescein tear break up time in dry eye patients

Filamentary keratitis

- A corneal finding associated with dry eye
- Characterized by fine, hair-like projections on the corneal surface
- Can be seen in the inferior cornea

Tear Film Break Up Evaluation

- The tear film is evaluated by the time it takes for the dark areas to appear on the cornea
- Increased tear break up time is associated with dry eye

Timeline of a Tear

- The tear film is evaluated over time, showing the break up of the tear film and the appearance of corneal staining
- Helps to assess Tear Film Break Up Time (TBUT)
- Corneal findings can be better assessed with a healthy tear film
Symptomatic TFBUT (SBUT) or Non-Invasive Tear Break Up Time (NIBUT)

- Improved understanding of TFBUT and its relationship to ocular awareness allows for simple non-invasive test
- Procedure
  1. Obtain a stop watch or clock
  2. Blink 2 times then stare straight ahead
  3. Record time between last complete blink and the first sensation of ocular awareness
  4. The time (in seconds) is the NIBUT

Vital Dye Staining
- Rose Bengal and Lissamine Green stains reveal damaged areas of epithelium in both the cornea and conjunctiva
- More importantly, these dyes will stain mucin strands and filaments that may be difficult to distinguish otherwise
- No clinical difference between these two dyes

Vital dye staining of the ocular surface, although a measure of damage to the ocular surface, is not specific for dry eye disease, occurs in a substantial percentage of normal subjects and is present in a minority of patients with mild to moderate dry eye disease

But you have to remember...
The Schirmer Test

**Purpose:**
Measures quantity of aqueous secretion

**Procedure:**
Filter paper placed under lower eyelid to measure volume of tears

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**PRTT vs. Schirmer’s**
- Agreement between the PRTT and Schirmer test was highly significant: 78.8% of subjects had similar quantitative results.
- Drying out the lacrimal meniscus before proceeding to the PRTT provides a highly sensitive and specific method for dry eye diagnosis.
- Since the PRTT causes less discomfort and is quicker than Schirmer’s, it could be used more frequently in a daily practice for the screening of dry eye syndrome.

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Schirmer vs. Zone-Quick
- The Schirmer test is the preferred quantitative procedure for dry eye research, though it is not as useful clinically.
- Schirmer test is somewhat lengthy (5 minutes) and uncomfortable for the patient.
- Schirmer results may be quite variable.
- Phenol Red Thread Test (PRTT) is much faster (~3 seconds) and more comfortable.
- PRTT has been shown to be comparable to the Schirmer test in clinical studies.

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Other tests used to diagnose dry eyes
- Osmometers
- Interferometry
- Lactoferrin Microassay

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Interferometry is the Ophthalmoscopy of the Lipid Layer

Quantification of tear film lipid layer thickness (LLT) according to dominant color of interference pattern.


Schirmer vs. Zone-Quick

Interferometry - Lipid Layer

Blue: Thick 180 nm
Yellow: Moderate 90 nm
White: Thin ≤ 60 nm
Dry Eye = Thin Lipid Layer (LLT ≤ 60 nm)

Adequate Lipid Layer (LLT = 90 nm)

Optimal Eye = Thick Lipid Layer (LLT ≥ 150 nm)

Lipid Layer Thickness (LLT) in Action

Tear Meniscus Height

The lacrimal lake – that is, the volume of residual tears between the inferior conjunctiva and lid – may be noticeably reduced or depleted in dry eye.

Dry Eye Management

Dry eye is a chronic disease without a cure. Management is often frustrating for both the patient & the clinician.

Therapeutic Approaches

- Stabilize the tear film (subjective)
- Increase lubricity - decrease coefficient of friction
- Increase aqueous production
- Decrease inflammation
- Create a more normal tear film environment for epithelial healing

Which Patients Are Candidates for Therapy?

- No single method for determining if a patient is a candidate for dry eye therapy.
- Criteria for starting therapy may include:
  - Patient symptoms
  - Corneal & conjunctival staining
  - Decreased TBUT
  - Decreased tear meniscus height
  - Schirmer/ PRTT scores
- Patient symptoms & clinical signs should be considered when deciding on therapeutic intervention.

Levels of Dysfunctional Tear Syndrome Severity

Delphi Panel Consensus for Dry Eye Management

Current OTC Dry Eye Therapy

- Contain various active and inactive agents
- Patients view products as interchangeable
- Different mechanisms of action and efficacies
- Need exists for clearer sub-categories

"This lack of concordance between signs and symptoms presents a problem not only in the diagnosis of the disease, but also in assessment of severity and in the design of clinical trials to evaluate the clinical efficacy of drugs."  
Qualities of an Ideal Dry Eye Product

- Minimal blur
- Comfort upon instillation
- Ability of product to spread evenly over the cornea quickly and efficiently
- Prolonged retention time for extended efficacy
- Objective and subjective improvement in patient signs and symptoms

Advanced Technology

Manufacturer: Alcon, Inc.

SYSTANE® ULTRA Lubricant Eye Drops

- Active Ingredients: Polyethylene Glycol 400, Propylene Glycol
- Inactive Ingredients: boric acid, HP-Guar, potassium chloride, aminomethylpropanol, purified water, sodium chloride, and sorbitol

Composition Comparison

A Focus on pH

Advanced Technology

- Controlled Viscosity in Bottle
- Stronger Elasticity in Eye

Intelligent Delivery System

- Borate competes with calcium for cross-linking
- Lower Viscosity

Categories of Lubricant Eye Drops

- Cellulose Derivative Products
- Glycerin Containing Products
- Oil-Based Emulsion Products
- Polyethylene Glycol and Propylene Glycol Products

Composition Comparison

- SYSTANE®
- SYSTANE® ULTRA

- Active Ingredients: Polyethylene Glycol
- Inactive Ingredients: Boric Acid, Sodium Chloride, Water, POLYQUAD®

Manufacturer: Alcon, Inc.

SYSTANE® ULTRA

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SYSTANE®

- Active Ingredients: Polyethylene Glycol
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Composition Comparison

A Focus on pH

- In the bottle
- Multiphasic MOA with dynamic structure

Challenges with Current OTC Formulations

- Current Problems: Viscosity & Elasticity are out of balance
  - Viscosity = Too low
  - Elasticity = Too low
  - Retention time = Unusual

- Goal: Strive a balance between viscosity and elasticity

Mechanism of Action

- HP-Guar, Sorbitol and Borate interact to provide a delivery system to the eye

- The critical mechanism of action elements of SYSTANE® ULTRA Lubricant Eye Drops include:
  - HP-Guar and borate interaction
  - pH
  - Sorbitol
  - Divalent ions in the tears

Multifocal MOA With Dynamic Structure
Viscosity decreases Matrix rebuilds and elasticity increases protection Poly-glycol (PG) 10

Tears have a limited, palliative effect (only "For patients with moderate to severe dry eye disease, the absence of preservatives is of more critical importance than the particular polymeric agent used in ocular lubricants."

Solutions containing electrolytes and/or ions have been shown to be beneficial in treating ocular surface damage due to dry eye."

Hypo-osmotic artificial tears

Hypotonic solutions

Tear Electrolytes

Downsides of TRT

[Image]

Evaluation of Blur SYSTANE® ULTRA Lubricant Eye Drops vs. OPTIVE®

Study Design

Randomized, double masked, controlled clinical study
Two period crossover design
Single drop instillation per period
20 patients, previously diagnosed w/dry eye
Test articles
SYSTANE® ULTRA Lubricant Eye Drops
OPTIVE® Lubricant Eye Drops

Osmolarity of Various Artificial Tear Solutions

Current Treatment for Dry Eye

A majority of patients (74%) do not obtain satisfactory relief from dry eye symptoms with artificial tears
Many dry eye patients (34%) wish there was an effective therapy available for treating their dry eyes

Tear Electrolytes

Normal Electrolyte Concentration in Human Tears (mMol/Liter)

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>132</td>
</tr>
<tr>
<td>K</td>
<td>24</td>
</tr>
<tr>
<td>Mg</td>
<td>0.6</td>
</tr>
<tr>
<td>Ca</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Tear Electrolytes

Downsides of TRT

- A plethora of OTC commercial products
- Drugstore.com lists 50 products for “artificial tears”
- Tears have a limited, palliative effect (only lasting 5 minutes in some studies)
- Chronicity of use leads to decreased patient compliance
- Preservatives may have toxic effects on the ocular surface
- Avoid BAK preserved AT for chronic use
Case Report #1

46 y/o WF  
Presents c/o burning, dryness OU x 1 m  
BCVA = 20/20 OD, OS  
SLEx unremarkable (-) LG or NaFl staining,  
TBUT 12 sec, PRTT 20 mm/15 sec, normal  
tear meniscus height

Summary of the ITF Guidelines for Dry Eye Treatment

<table>
<thead>
<tr>
<th>Severity Level</th>
<th>Signs &amp; Symptoms</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mild to moderate symptoms and no signs</td>
<td>Patient counseling, preserved tears, environmental management, allergy eyedrops</td>
</tr>
<tr>
<td>2</td>
<td>Moderate to severe symptoms; tear film signs; mild corneal punctate staining; conjunctival staining; visual signs</td>
<td>Non-preserved tears, gels, ointments; cyclosporine A, topical steroids, secretagogues, nutritional support (Flaxseed oil)</td>
</tr>
</tbody>
</table>

Case Report #1

Symptomatic dry eye (DTS level 1)

Recommend artificial tears, discuss environmental modifications

Environment

Top 3 intake causes of dry eye?

- Smoking
- Caffeine (more than moderate)
- Diet (low omega 3 intake)

Artificial Tears

The rationale behind artificial tears is straightforward – replenish ocular surface moisture, and wash away accumulated debris, including antigens.

In mild to moderate cases of dry eye, most of these agents work quite well

Case Report #2

60 y/o WF  
Presents c/o burning & watery eye OU of 6 month duration. Has used “all types of artificial tears” with only minimal symptomatic improvement  
BCVA = 20/25 OD, OS  
TBUT 4 sec; (+) LG & NaFl staining of cornea + conj  
TM height decreased  
PRTT 5 mm/15 sec OU
Case Report # 2

Dx: DTS Level 2

<table>
<thead>
<tr>
<th>Severity Level</th>
<th>Signs &amp; Symptoms</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Tic: Lotemax q.i.d. x 2 wks.
- Restasis b.i.d.
- Recommend nutritional supplements
- Non-preserved artificial tears

Steroids and OSD
Symptomatic improvement in initiation symptoms in 83% and objective improvement (redness, dye staining) in 80% of 70 patients treated for 2 weeks with non-preserved methylprednisolone.

Prasasawat & Tsang BJO 1998

Ester vs. Ketone Steroids

- Loteprednol 0.2% (Alrex)
- Loteprednol 0.5% (Lotemax)
- Less side effects - M. Abelson, 88 patients 35 days
- IOP rise, secondary infection or PSC formation: 0%

Steroid Treatment

- Ester Steroids
  - Prednisolone
  - Fluorometholone
  - Dexamethasone
  - Medrysone
  - Rimexolone
  - Ester Steroids are inactivated by naturally occurring esterases, less side effects
  - Ketone Steroids are not inactivated and have propensity to remain in the anterior chamber post-breakdown as active metabolites

How Does Restasis™ Work?

- Restasis™ prevents T-cell activation
  - Activated T cells produce inflammatory cytokines that result in:
    - Recruitment of more T cells
    - More cytokine production
  - Restasis™ decreases cytokine production in the anterior chamber

Steroid Treatment

- Prednisolone
- Methylprednisolone
- Flucortisol

Restasis

- Has been shown to increase overall tear volume and goblet cell density in some patients
- Relatively slow onset of action, which can be from three to six months in most patients

How Does Restasis™ Work?

- Prevents T-cell activation
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How Does Restasis™ Work?

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How Does Restasis™ Work?

- Prevents T-cell activation
  - Activated T cells produce inflammatory cytokines that result in:
    - Recruitment of more T cells
    - More cytokine production
  - Restasis™ decreases cytokine production in the anterior chamber
Topical Cyclosporine

- **Restasis Ophthalmic Emulsion** (Allergan)
  - Useful in long-term mgmt of inflammatory DES
  - BID dosage
  - Cyclosporine A (CsA) 0.05% in castor oil vehicle
  - Mechanism of action:
    - Inhibits activation of inflammatory T-lymphocytes, & induces immune cell apoptosis, stimulating lacrimal gland tear production
    - 3-4 months to achieve clinically significant effect; 6 months for full therapeutic potential
  - 59% Patients achieved improvement from baseline Schirmer scores at 6 months
  - Excellent safety profile

Other Safety Results
- No CsA-related ocular infections
- No differences in blood chemistry, hematology (including renal and hepatic function)
- No treatment-related changes in IOP, visual acuity, or biomicroscopy
  - Sall et al, Ophthalmology 2000;107: 631

Schirmer scores increased from baseline for 59% of chronic dry eye patients treated with Restasis?

- Maximum improvement was 16 mm
- Significantly more Restasis®-treated Patients improved by ≥10 mm vs. vehicle (15% vs. 5%)

Increased Tear Production in Restasis®-treated Patients

Corticosteroids improve tear production by controlling inflammation

Corticosteroids decreases irritation associated with Restasis by 75%

Recommend a mild corticosteroid such as loteprednol qid x 2 weeks & then bid x 2 weeks for patients who complain of irritation with Restasis, high maintenance patients, and patient who want more rapid relief

Nutritional Supplements: Essential fatty acids
- Flaxseed oil (1000 mg bid if tablet form)
- Castor oil
- Fish oils
- Omega-3 fatty acids - linoleic acid

Burning and Stinging

- Not an issue if use Loteprednol simultaneously
- Also long term risks of steroid not an issue as you taper Loteprednol and maintain Restasis

Asclepius Panel Recommendations

- Loteprednol GID
- Loteprednol BID
- Loteprednol As Needed

Prescription Eye Drops

Artificial Tears

Statistically significant improvement in signs and symptoms:
- • Drying
- • Itching
- • Blurred Vision
- • Photophobia

Key signs & symptoms continue to improve

Improvement maintained with continued therapy

One Month Three Months Six Months

Sall et al, Ophthalmology 2000;107: 631

Marsh, Pflugfelder. Ophthalmology 1999

Shepard, ASCRS 2005 62

Nutritional Supplements: Essential fatty acids

- Flaxseed oil (1000 mg bid if tablet form)
- Castor oil
- Fish oils
- Omega-3 fatty acids - linoleic acid

Expectations for the First Months of Restasis® Therapy

Nutrient Tx for Dry Eye

- Omega-6 & Omega-3 Fatty acids inhibit the arachidonic acid inflammatory cascade associated with dry eye & dry eye associated allergic response.
- Nutrients have been shown to increase tear film levels of lactoferrin.
- Nutrients enhance production of acetylcholine, which triggers neural reflex loop that stimulates the lacrimal gland to produce aqueous.
- Feher et al, ARVO 2006: Omega-3 polyunsaturated fatty acids (PUFA) & enzyme CoQ10 PO improves dry eye symptoms.

Case Report #3

- 76 yo WM.
- Presents c/o severe ocular irritation (“burning and stinging”) for “several years now”.
- Using n/p AT q.2.h. + ung q.h.s without symptomatic improvement.
- “Another doc put me on that new stuff for awhile but it didn’t help either.”
- Meds: Benicar, Avandia; NKDA.

Case Report #3

- BCVA 20/20 OD, OS.
- TBUT immediate.
- TM nonexistent.
- SPK w/filaments OU / + LG staining of K.
- Atrophied meibomian glands OU.
- SLEx.

Case Report #3

- Dr: Filamentary Keratitis OU.
- MGD OU.
- Tx: Debride filaments OU.
- Lotemax q.d. OU.
- Acetylcysteine 10% (mucomyst) q.i.d.
- n/p AT q.2.h. + ung q.h.s.
- Dexamethosone 10mg p.o. q.d. x 2 wks.
- Lid hygiene.
- Consider plugs.

DEWS Report

- According to the DEWS Report:
  - Blepharitis is an important subset of Ocular Surface Disease.
  - Blepharitis often co-exists with Dry Eye Disease.
  - When a patient presents with both Dry Eye Disease and Blepharitis, treatment targeted at the lids is recommended, in addition to treatment of the Dry Eye.

The Spectrum of Lid Margin Disease

- Although Anterior Blepharitis and Meibomian Gland Disease are distinct entities, they often coexist.
- Spectrum of Lid Margin Disease.
**Blepharitis → Definitions**

- **Anterior Blepharitis**
  - Inflammatory condition of the outside portion of the eyelids.
  - Often secondary to infection or associated with acne rosacea or seborrheic dermatitis of the scalp or facial areas.

- **Meibomian Gland Disease (Posterior Blepharitis)**
  - Tissue inflammation of the inside portion of the eyelids.
  - Associated with altered composition of the meibomian gland secretions, inflammation of local tissue.

**Meibomian Gland Disease (Posterior Blepharitis)**

- Involves a change in composition of meibomian gland secretions that leads to inflammation, irritation, and an altered tear film.

**Signs & symptoms include:**
- Dilated & plugged meibomian gland orifices with "toothpaste" like material.
- Ocular surface disease signs and symptoms including: burning, foreign body sensation, contact lens intolerance.
- Lid and conjunctival hyperemia.
- Thickened lid margin.
- Foamy/soapy tear film.
- Fluctuations in visual acuity.

**Traditional Treatments for Blepharitis**

- **Non-Pharmaceutical Therapy**
  - Lid hygiene
    - Warm compresses
    - Commercial lid scrubs
  - Omega 3 nutritional supplements

- **Pharmaceutical Therapy**
  - Antibiotic ointment
  - Corticosteroids
  - Antibiotic/corticosteroid combo products
  - Oral tetracyclines

**Meibomian Gland Disease: Etiology**

- Change in composition of meibomian gland secretions that leads to inflammation, irritation, and an altered tear film.

- Normal secretions convert from unsaturated lipids (that melt at body temperature) to saturated fats.
- Involves degradation of triglycerides to mono- and diglycerides.
- Lipases appear to be involved in this degradation.
- The mono- and diglycerides are more solid in composition, leading to obstruction/plugging of the meibomian gland.
- The mono- and diglycerides are pro-inflammatory, leading to inflammation associated with MGD.

**Restasis vs. Punctal Plugs**

- While punctal plugs increase Schirmer measurement of tear production, cyclosporine is more effective in decreasing the conjunctival staining and need for artificial tears in dry eye patients.
- However, their use in combination was the most effective in relieving both the signs and symptoms of dry eyes.

**Punctal Occlusion**

- Temporary, initial treatment to monitor response to this therapy.
- Permanent.
- Cautery.

**Posterior Blepharitis Treatment**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic</td>
<td>1-2 times daily</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>1-2 times daily</td>
</tr>
<tr>
<td>Antibiotic/corticosteroid combo</td>
<td>1-2 times daily</td>
</tr>
<tr>
<td>Ointment</td>
<td>1-2 times daily</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1-2 times daily</td>
</tr>
<tr>
<td>Punctal plugs</td>
<td>1-2 times daily</td>
</tr>
</tbody>
</table>


**SmartPlug®**

- Temporary/postpermanente initial treatment to monitor response to this therapy.
Systemic Tetracyclines
- Doxycycline or tetracycline for inflammatory dry eye.
- Tetracyclines decrease circulating inflammatory mediators.
- Promotes comfort and decreased inflammation.
- Generally takes 2 or 3 months to see benefit.
- Reduce to periostat longer term (20mg doxycycline) bid or qd.

Doxycycline for OSD
- Reduces enzyme activity of bacteria—e.g., lipase activity of staphylococcus.
- Accumulation in oil glands.
- Anti-inflammatory component.

Case Report # 4
- 70 y/o WF
- Presents c/o “dry eye”; has used artificial tears in the past but not with regularity.
- Medical Hx: rheumatoid arthritis, HTN.
- Upon questioning, patient states “I have to go with a glass of water in my hands all the time b/c my mouth is so dry.”

Case Report # 4
- Meds: Diovan p.o. q.d, Naproxen, Plaquenil, carafate, NKDA.
- BCVA 20/40 OD, 20/30 OS.
- IOP 16 mm Hg OD, OS.
- TBUT 2 sec; TM nonexistent; (+) LG & NaFl staining of the cornea & conjunctiva OD, OS; PRTT 2 mm/15 sec.

Case Report # 4
- Dx: Secondary Sjogren’s Syndrome.
- Tx: Non-preserved AT q.2.h.
- Lotemax q.6 h.
- Discuss punctal occlusion.
- Discuss room humidifier.
- Recommend Panoptic sunglasses.
- Refer to rheumatologist for blood work: ANA, SSA & SSB, RF, ESR, CBC.
- Refer to dentist for evaluation.

Case Report # 4
- Lymphocytic infiltration of lacrimal & salivary glands.
- 0.4% prevalence.
- Women > Men (younger women).
- Much lower androgen counts.
- Treat underlying immune disorder.
Which of these conditions are Sjogren’s patients 46x more likely to develop?

A. Leukemia  
B. Lymphoma  
C. Meningitis  
D. Cardiac Arrhythmia

Steroids and SS Dry Eye

- Moderate (43%) or complete (57%) relief of irritation symptoms accompanied by corneal NaFl staining and resolution of filamentary keratitis in 21 SS patients treated for 2 weeks with non-preserved methylprednisolone (Marsh & Pflugfelder, 1999).
- Patients often have long lasting relief after 2 week pulse therapy.

Sjogren’s Syndrome KCS

- **Steroids Effectively Treat KCS**
- **Pre-Steroid**
- **Post-Steroid**

Case Report # 5

- 79 yo WF
- Presents c/o “skim over OU” x 2 months
- Redness, EP, photophobia, tearing OS>OD x 2 w
- Long standing hx Rheumatoid arthritis w/ Secondary Sjogren’s syndrome, currently treated w/ Lotemax + Restasis b.i.d. OU + N/P AT pm OU. LEEX 2 m.
- CVAs: 20/100 OD, CF @1’ OS, PHNI
- **Leer**

Sjogren’s Syndrome

- **Medical Treatments:**
  - Secretagogues
  - Salagen 5 mg
  - Pilocarpine tablets
  - Avoid in asthma patients, GI ulcer, acute iritis or narrow angles
  - Evoxac 30 mg – saliva stimulating drug
  - Cevimeline
  - Very effective with a lot less side effects.

Panoptx “Dry Eye Wear”

- Patented Orbital Seal creates “moisture chamber”
- New study findings demonstrate effectiveness
Case Report # 5

Dx: Secondary Sjogren’s Syndrome
Dx: Corneal Ulcer
- ? Inf/Cultures obtained: SBA, Choc, SDA Slant, Broth, Gram stain
Vigamox q.h. while awake

Case Report # 5

Added Natamycin q.h. w.a.
Continue vigamox q.h. w.a.
Patient totally resolved in 4 weeks
Albumin added to artificial tear regimen

Dry Eye & Ocular Infection

5% Albumin
- Autologous serum is difficult to formulate and expensive. Another Option: 5% albumin
- “The use of albumin as a protein supplement in artificial tear solutions is a viable approach in the treatment of ocular surface disorders associated with tear deficiency”*


Case Report # 6

17 yo WM, SDW CL wearer x 4 years
Presents c/o itchy, watery eyes of 1 week duration
Has used OTC tears & antihistamine/decongestant drops q.i.d. w/ minimal relief
No Rx meds: NKDA
Entering BCVA w/ specs: 20/20 OD, OS
Case Report # 6

- **Dx:** Seasonal Allergic Conjunctivitis
- **Tx:** Pataday q.d.
- Patient education re: decrease CL wearing time. Recommend use of non-preserved artificial tears p.r.n. and cold compresses
- Recommend OTC claritin/zyrtec for rhinitis

Seasonal Allergic Conjunctivitis

- Signs:
  - Not always present
  - Lid swelling
  - Ptosis
  - Conjunctival hyperemia
  - Chemosis
  - Papillary reaction
  - Follicular reaction

Patanol + Claritin

- Study by Lanier et al. @ University of Texas in 2001
- Compared patient’s symptoms and signs in 94 patients randomized to either receiving Claritin alone or claritin with patanol
- Concluded that patanol used in conjunction with claritin provided greater relief of signs and symptoms vs. claritin alone

Incidence of Ocular Allergies by Type of Allergic Eye Disease

- SAC/PAC: 90% - 95% of all ocular allergies are estimated to be SAC/PAC

Ocular Allergy Management

- **Non-Rx**
  - Avoidance of allergens, if possible
  - Keep car windows closed; use AC
  - Avoid outdoor activities, e.g., lawn work or gardening
  - Wash hands, face and hair often to remove allergens
  - Ice packs/cold compresses
  - Lubricants
  - DON’T RUB YOUR EYES!

- **Multiple Mechanism Products**
  - State of the art broad spectrum products
  - Combine mast cell stabilization with direct antihistamine blocking and may possibly have other effects
  - Patanol + Claritin
  - Zaditor (Ketotifen) – antihistamine w/ some mast cell stabilizing effects. Now OTC
  - Elestat (epinastine)
  - Do not require loading & can be used throughout allergy season

Ocular Allergies – Treatment Pearls

- Though ‘itching’ is the hallmark symptom of ocular allergy, about 1/3 of patients who report ‘itchy-burny’ will have ‘burning’ as their chief complaint
- When the principal symptom is actually ‘burning’, consider DRY EYE as the diagnosis vs. ocular allergy
- For this reason, always evaluate the lacrimal lake and precorneal tear film volume & function to rule out dry eye prior to beginning allergy therapy

- OSD = an opportunity to care for a segment of your patient base that may have been overlooked in the past
- OSD = an opportunity profession-wide to lay claim to a disease process we can call our own
- Can all provide this service regardless of your practice modality
- OSD = a recognized disease process with it’s own CPT-4 code, and thus reimbursable under medical insurance
OSD Is a Disease !!!

- Treat OSD like the disease process it is.
- You wouldn’t give medications to a glaucoma patient without a thorough workup & appropriate follow-up.
- Follow-up with these patients at regular intervals to monitor progress and evaluate therapeutic effects.
- And bill appropriately for your time and expertise!

Questions? Comments?

- E-mail me: drbowling@windstream.net
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- The presenter has no financial interest in ANY of the products discussed in this presentation. I’m just a poor old country eye doc with 2 kids in college...

- Thanks: Drs. Al Kabat, Paul Karpecki, Milt Honi, Bill Townsend, Chris Snyder

Thank you!