Dry Eye: A to Z
Everything you ever wanted to know about Dry Eye

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Disclaimer

• The Speaker is a member of Allergan Pharmaceuticals Dry Eye Industry Thought Leaders Panel. He also is a speaker for their Core Presentation Program.
• The Speaker has no financial interest in any of the products discussed in this lecture

Tear film function:
To maintain the integrity of the cornea & conjunctiva

• Refract light by providing a smooth, clear optical surface; improve the vision
• Wash away all the dirty materials coming onto the eye
• Moisturize and lubricate the ocular surface for comfort, eye movements, & to prevent friction during the blink
• Media transport for O₂ & CO₂ (40% from atmosphere)
• Nutrition: glucose, electrolytes, enzymes, proteins, growth factors
• Defense: Anti-microbials, antibodies, lisozymes
Tear film composition

**Mucin Layer**

- ≈ 0.02-0.05 μm
- Innermost & thinnest
- Maintains tear film stability
- Product of conjunctival Goblet cells of the bulbar conjunctiva and caruncula
- Epithelial cells produce glycocalyx to help bind mucins onto the epithelial surface

**Aqueous Layer**

- ≈ 7 μm (6.5 - 7.5 μm)
- Thickest Layer
- Alkaline and antibacterial
- Electrolytes, proteins, antibodies, oxygen, CO₂, minerals, glucose
- Secreted from lacrimal and accessory glands

**Tear film composition**

Lipid Layer \( \approx 0.1 \mu m \)
- Outermost layer
- Esters, glycerol, fatty acids
- Product of palpebral meibomian glands and glands of Zeiss
- Prevents excessive evaporation

The maintenance of a free-flowing, liquid lipid secretion is essential for maintaining a stable tear film.

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**Healthy Tears**

A complex mixture of proteins, mucin, and electrolytes
- Antimicrobial proteins: Lysozyme, lactoferrin
- Growth factors & suppressors of inflammation: EGF, IL-1RA
- Soluble mucin 5AC secreted by goblet cells for viscosity
- Electrolytes for proper osmolarity

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**Tears In Chronic Dry Eye**

- Decrease in many proteins
- Decreased growth factor concentrations
- Altered cytokine balance promotes inflammation
- Soluble mucin 5AC greatly decreased
- Due to goblet cell loss
- Impacts viscosity of tear film
- Proteases activated
- Increased electrolytes
Dry eye

- Extremely common in our daily practice
- Affects over 7 million Americans over 40
- Any age, female, male, even children
- Can be mild to severe
- Devastating and frustrating
- Life long treatment

Insert Proof slides

- Insert Proof
- Points made from those studies
- 40% of people in US have Dry Eye
- 80% of patients referred for Cataract Surgery have Dry Eye Disease BUT ONLY 20% of those are Dx and Tx before Surgery
- Fish Oil is the best source of Omega-3 fatty acids
- Artificial tears offer TEMPORARY relief of dry eye
- Computer use decreases the blink rate increasing ocular surface irritation initiating the inflammatory cascade
- Evocac 30mg TID has been approved for Sjogrens Syndrome

Insert Proof Slides

- Dry eye is a complex multifactorial disease
- Pts who have dry eye with CLS should stop CLS till DES is under control
- Restasis is the ONLY FDA approved Rx for DES
- Restasis is the cornerstone of Tx for DES
- Restasis effects the Mucin and Aqueous layer
- Doxycycline 50 MG is used because it breaks down smaller than any other oral medications
- Blepharitis in patients over 80 should be closely evaluated to make sure they do not have mites
- Lid surgery is considered a medical Tx when the lids cover the lashes
Insert Proof Slides

- Treatment options for MGD that have recently been used in many practices are Lipo-flow and IPL
- Lipoflow must be repeated one to three times a year
- IPL typically requires four monthly treatments
- IPL has a longer effect that Lipo-flow because it ablates the peripheral vascular network that occurs with maturity and allows more blood to get to the MG
- ICD-9 coding can be the disease or underlying cause so KCS not related to Sjogren's Syndrome, Blepharitis, Ptosis, are just three examples of what could be coded.

Tools to Identifying DE pts

- Allergan DE questionare OSDI
- Medical history
- Social history
- Good for hi volume practices

Influential Factors of Dry Eye

- Age
- Gender
- Arthritis
- Osteoporosis
- Gout
- Contact Lens Wear
- Blink Disorders
- Disorders of Lid Aperture
- Nutritional/Problems
- Rheumatoid Arthritis
- Thyroid Problems
- Time of Day
- Medications
- LASIK Surgery
- Cosmetic Surgery
- Mechanical Disturbances
- Exposure Keratitis
- Entropion
- Ectropion
- Systeptapheron
- Formation
- Lagophthalmos
- Lagophthalmosis
- Intermittent Blinking
- Dellen Formation
- Illumination
- Diabetes
- Temperature
- Humidity
- Air movement
- Allergies
- Change in environment
- Reading
- Computer
- Watching Movies
- Sleep
- Hormones
- Postmenopausal
- Cosmetics
- C PAP Machine

References:
Conditions Associated With Dry Eye

- **Chronic Systemic inflammation**
  - Sjogren’s Syndrome, rheumatoid arthritis, lupus
- **Ocular surface inflammation**
  - Meibomian gland disease, keratitis, infection
- **Hormonal changes**
  - Menopause, oral contraceptives, pregnancy, lactation
- **Systemic disease**
  - Diabetes, thyroid
- **Stevens Johnson’s syndrome**: severe dry eye

Environment

- **Smoke**, air pollution, wind, heat, air-conditioning, air travel, light, dry climate
- Staring at a TV, computer book, smart phone, etc (Less blinking)

Medications

- **Systemic**
  - Anti-depressants
  - Antihistamines
  - Diuretics
  - Beta-blocker
  - Antimicrobics
  - Antihypertensives
  - Nonsteroid
  - Oral Contraceptives
  - Antiparkinsonian
  - Anticholinergics
  - Antiarrhythmics
  - Isotretinoin
  - Decongestants
  - Preservatives
  - Anesthetics

- **Topical**
  - Tear film deficiencies

Tear Film Deficiencies

- **Lipid Layer Deficiency**
  - alterations in meibomian gland secretion (e.g. blepharitis, hordeolum, chalazion)

- **Aqueous Layer Deficiency**
  - aqueous deficient dry eye (e.g. inflammation, neurological defects, trauma, congenital absence, etc)

- **Mucin Layer Deficiency**
  - mucin deficient dry eye (e.g. Stevens-Johnson syndrome, pemphigoid, vitamin A deficiency, trachoma, radiation, etc.)
**Dry Eye Etiology**

- Tear Deficient
  - Sjögren's
  - Non-Sjögren's
    - Lacrimal Deficiency
      - Auto-antibodies
    - Reflex
      - Lacrimal Obstruction
  - Evaporative
    - Oil Deficient
      - Lid Related
    - Contact Lens Surface Change

**Current Triggers of Dry Eye Disease**

- Environment (Medications, Contact Lens, Surgery)
- Irritation
- Inflammation
- Tear Deficiency/Instability
- Postmenopause
- Meibomian Gland Disease

**Symptoms of Ocular Surface Disease**

**Inflammatory Cascade**

*The activation of NF-κB*

<table>
<thead>
<tr>
<th>NF-κB</th>
<th><em>Cytokines</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Chemokines</em></td>
</tr>
<tr>
<td></td>
<td><em>Tumor necrosis factor</em></td>
</tr>
<tr>
<td></td>
<td><em>Interleukin-1</em></td>
</tr>
</tbody>
</table>

Although anterior blepharitis and posterior blepharitis (MGD) are distinct entities, they are often seen coexisting in the same patient.

**The Spectrum of Blepharitis**

- **Anterior blepharitis**
- **Mixed**
- **MGD (posterior blepharitis)**

**Anterior Blepharitis**

- Inflammation outside the eyelids
- Bacterial infection (staphylococcal)
- Infection involving the lash follicles

Signs and symptoms include:
- Morning crusting
- Collarettes – scales encircling lash
- Loss of lashes
- Lid margin redness
- Conjunctival hyperemia

**Posterior Blepharitis or Meibomian Gland Disease**

- Inflammation of the inside of the eyelids
- Change in composition of meibomian gland secretions → inflammation → irritation → altered tear film

Signs and symptoms may include:
- Dilated / plugged glands
- “Toothpaste” like material
- Thickened lid margin
- Soaponification of tear film (soaps/fatty acids)
- Dry eye signs and symptoms
Any patient who has Bleph and especially those over 80 yrs old should be closely evaluated for mites.
Myth Busters

*Most* Dry Eye is linked to meibomian gland dysfunction
MGD: Study Design

- In order to determine the prevalence of 3 DE etiologies, 299 subjects were evaluated via:
  - Schirmer scores
  - MGD scores (≥5 is impaired MG function)
  - Lid inflammation: thickening, vascular engorgement, telangiectasia
  - Gland secretion: quality, expressibility, volume


MGD: Study Design

- ADDE (Aqueous Deficient Dry Eye)
  - Schirmer < 7mm and MGD score ≤ 5
- EDE (Evaporative Dry Eye)
  - Schirmer ≥ 7mm and MGD score > 5
- Mixed Mechanism Dry Eye
  - Schirmer < 7 mm and MGD score ≤ 5


MGD: Results

- Conclusions:
  - Pure EDE is 3 to 6 times more prevalent than pure ADDE (depending on schirmer cut off markers)
  - MGD in 86% of pts with DED diagnosis
  - Mixed Mech pts had greater severity of DED
  - Late progression
  - ADDE → 2° EDE due to TF instability

Myth Busters

• **Most** Dry Eye is linked to meibomian gland dysfunction
  ![FACT!]

Differential Diagnosis within Dry Eye

**Most Common Symptoms:** eye discomfort

- irritating
- Burning
- Stinging
- easily fatigue
- itchy
- foreign body sensation
- photophobia
- fluctuating vision

- contact lens intolerance
- sticky
- dryness / watering
- sleepy
- discharge
- redness
- blurred vision
- Eye rubbing
Signs

- hyperemia
- low tear meniscus
- Increase tear debris
- fast tear break up time
- conjunctival pleating
- conjunctival staining
- blepharitis
- increased cytokines
- corneal staining
- epitheliopathy
- filaments
- ulcers

Do you treat asymptomatic presentations of Dry Eye?

➢ If so – Why?

➢ If not – Why Not?

Dry Eye Diagnostic Tests

<table>
<thead>
<tr>
<th>Type of evaluation</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tear secretion</td>
<td>Schirmer, cotton thread test, dye clearance test, fluorophotometry</td>
</tr>
<tr>
<td>Tear stability</td>
<td>Invasive BUT, noninvasive BUT</td>
</tr>
<tr>
<td>Tear film integrity</td>
<td>Rose bengal staining</td>
</tr>
<tr>
<td>Epithelial integrity</td>
<td>Opsocliatity, PH, Ferri evaporation rate</td>
</tr>
<tr>
<td>Physical feature</td>
<td>Electrolytes, proteins (lysozyme, lactoferrin)</td>
</tr>
<tr>
<td>Chemistry</td>
<td>Impression cytology, acral gland biopsy, minor salivary gland biopsy, bloodwork</td>
</tr>
</tbody>
</table>
Diagnostic Tool Box

- History
  - Even if the patient does not complain of “Dry Eye” problems - a thorough Hx can reveal a problem the patient is not aware of.
- Corneal Staining
  - Dyes
    - Patterns and meaning....
  - Timing
  - What does it tell us?

Slit-Lamp Biomicroscopy
Corneal Staining

Diagnostic Tool Box

- Conjunctival staining
  - Dyes
  - Patterns and meaning
  - What does it tell us?

Lysomine Green
Diagnostic Tool Box

- Conjunctival staining
- Dyes
- Patterns and meaning
- What does it tell us?

Rose Bengal

Diagnostic Tool Box

- Conjunctival staining
- Dyes
- Patterns and meaning
- What does it tell us?

NaFL

Diagnostic Tool Box

- Conjunctival staining
- Dyes
- Patterns and meaning
- What does it tell us?

NaFL
Diagnostic Tool Box

- TBUT
  - Timing
  - What does it tell us?
  - Average Blink Rate is about 15 seconds
  - Computer Screens of any size tend to put us into a “Hypnotic Trance” decreasing our blink rate to as slow as every 23 seconds.

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Diagnostic Tool Box

- Schirmer
  - Anest vs unanest
  - What does it tell us?
  - Real value
    - Justification for plugs
    - Patient education tool: motivation for compliance and visualization of progress
Diagnostic Tool Box

• Slit Lamp exam
  • Tear film evaluation
    • Tear lake consistency
    • Most signs are noticeable without stain
  • Quality of tear film
• Lid evaluation
  • Meibomian gland evaluation
  • Blepharitis
• Pterygium
• Pinguecula

Diagnostic Tool Box

• Reeseeit
• Anterior segment camera and video
• Tear Film Assay
  • Goals
  • Limitations
  • Cost

Diagnostic Tool Box

• Keratogram
InflammaDry from RPS

- Id's pts with elevated levels of MMP-9

Dry Eye Diagnostic Tools

- Osmolality testing
- Conjunctival staining
- Corneal staining
- TBUT
- Differentiate between EDE and ADDE

Value is in establishing step one as well as deciphering which direction to go

MGD #2: Study Design

- 20 non cl wearers enrolled, age 39-55 with HEALTHY EYES
- Upper and lower lids evaluated via infrared photography for:
  - MG drop out
  - MG thickness
  - MG angle measurements
- Lipid layer analysis using TearScope Plus
- TBUT
- Ocular surface disease index (OSDI) to quantify comfort

MGD #2: Results

- LL had thicker MG, more MG drop out, less bent angles vs. UL

- Greatest DED indicator was MG loss in UL + LL
  - Strongly correlated to lipid layer analysis, TBUT, OSDI
  - Able to predict DE if ≥ 16.9% UL MG loss and ≥ 28.7% LL MG loss

Combine Results to Decipher DE Origin

- Use infrared camera, equipped topographer, or ever lid over a transilluminator tip to view MG
- Use it with schirmer testing to target your DE treatment accordingly


Insert A Patients Journey

- DEWS study

Preventive Treatment
Influential Factors of Dry Eye

- Age
- Gender
- Arthritis
- Osteoporosis
- Gout
- Cataract Surgery
- Contact Lens Wear
- Blink Disorders
- Disorders of Lid
- Aperture
- Nutritional Problems
- Rheumatoid Arthritis
- Thyroid Problems
- Time of Day
- Medications
- LASIK Surgery
- Cosmetic Surgery
- Mechanical Disruptions
- Exposure Keratitis
- Entropion
- Symblepheron
- Formation
- Large Lid Notches
- Lagophthalmos
- Incomplete Blinking
- Dellen Formation
- Illumination
- Diabetes
- Temperature
- Humidity
- Air movement
- Allergies
- Change in environment
- Reading
- Computer
- Watching Movies
- Sleep
- Hormones
- Postmenopausal
- Cosmetics
- C PAP Machine

Age and gender

- Add statistic on prevalence female age
- Treat preemptively?
- Testosterone cream
Treatment

- Add greg's slide on changing environment;
- Cpap: gel or goggles

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Treatment

- Contact lens wear
- Lens material
- Solution
- Pre/post wear treatments
Influential Factors of Dry Eye

- Age
- Gender
- Arthritis
- Osteoporosis
- Goit
- Cataract Surgery
- Contact/Lens Wear
- Blink Disorders
- Disorders of Lid Aperture
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- Thyroid Problems
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Cosmetic Considerations

THE “Raccoon Zone”

The “Raccoon Zone.”
The thinnest skin on the body is in this area.
Cosmetic Considerations

ABSOLUTELY NO

- OILS
- CREAMS
- LOTIONS
  - Make up removal pads or solutions

All Eye Make Up – SAME BRAND

No Eye Shadow that glitters or sparkles if Calcium or CA++ is on the label

Cosmetic Considerations

- Latisse is acceptable
  - Can also use eye lash dye’s (Sally’s)
  - Proper use of mascara
    - Only on tips of lashes – do not cover the whole lash
    - Used for color only – not build up
    - Most are made with fiberglass or charcoal

- NO EYE LINER
  - If patient insists- recommend using eye shadow as liner
    - will not plug meibomian glands

Cosmetic Considerations

- ALL MAKE UP
  - Hypoallergenic
  - Water Soluble

Additional Tip

- If patient plucks eyebrows have them apply Vitamin E oil directly to the eye brow
  - Kills cilia and prevents rapid re-growth
### Influential Factors of Dry Eye

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- Cosmetics
- C-PAP Machine

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### Treatment

- Oculoplastic surgeries
- Ptosis is a medical condition and as such most insurance covers Bleeroplasty
  - In addition to the usual loss of visual field two lesser known reasons insurance will approve surgery
    - If the brow is below the orbital foramen and the patient complains of frontal Head Aches
    - If the lashes lay across the lids and there is a diagnosis of KCS not related to Sjogrens Syndrome
Treatment

• Pre and post picture of a specific DE pt with dermatochalasis: aesthetically ok, functionally not ok b/c it contributed to DE. Show DE case prior to sx and post sx. Ie. staining, symptoms, etc. to increase doc awareness of lid contribution

Influential Factors of Dry Eye

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treatment

- Pts getting LASIK because cant tolerate CL wear, often bc dry
- Preparing the ocular surface prior to cat sx
- 3 month plugs, post lasik sx
- Refractive success dependent on tear film consistency

Everything Else

Influential Factors of Dry Eye

- Age
- Gender
- Arthritis
- Osteoporosis
- Cataract Surgery
- Contact Lens Wear
- Blink Disorders
- Disorders of Lid Aperture
- Nutritional Problems
- Rheumatoid Arthritis
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References:


**Treatment: Omega 3s**

- Flaxseed / blends / fish oil / lavaza
- Enteric coating $ or freeze to protect stomach discomfort
- Take with meals (breakfast)
- Start at 1000mg.
- If already using fish oil and come in with DE, increase to 2000 mg

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**Treatment: Artificial Tears**

- 1 slide—greg
- 3 columns of brands:
  - Non lipid based: preserved
  - Non lipid based: preservative free
  - Lipid based: OTC and BTC (freshkote)

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**Treatment: Artificial Tears**

- 1 slide—CB
- Which type for which patient?
- Will it work? Is there value in doing it even if you’re sure it won’t? (i.e. if first tx for pt & they need to see that they need more $ tx before you actually rx it, asymptomatic pt…)

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Treatement: AT gel

- Consistency to spread
- Timing: no risk of fall, and less blinking so no dissipation
- Amount: next morning some but not stuck

Revise …Treatment

- Majority of DE patients are affected by EDE
- Oil in water emulsion drops proven more effective than sodium hyaluronate or hydroxypropyl methylcellulose drops for EDE
  - Enhanced TF stability
  - Decreased tear osmolarity
  - Improved corneal staining scores


treatment

- IPL
- Lipoflow
Treatment: Lid scrubs

- List brands in column of with and without alcohol or Ab effect.
- Ie. alcohol free systane
- Really of use? When? Just in ant bleph…
- Vs baby shampoo. No qtip

Topical Rx Treatments

Topical Rx Treatments: Steroids

- MMP-3/9
- Pulse dosing
- Good for immediate results while waiting for restasis or Omega 3s
- Reduces insertion burn from restasis
- Builds patient confidence in treatment b/c quick relief
- Lotemax gel - no shaking - more effective patient compliance - speak to rep about coupons
Dry Eye Treatments

Efficacy of combined 0.05% cyclosporine and 1% methylprednisolone treatment for chronic dry eye
Byun YJ, Kim Ti, Kown SM, et al.

Steroid DE Tx: Background

- Steroids are increasingly being used by optometrists to treat various inflammatory conditions
- Many use them to treat dry eye signs and symptoms
- This study looks at its role with topical Cyclosporine A

Steroid DE Tx: Study Design

- 44 patients with moderate to severe dry eye were randomized to two treatment groups:
  - Study group: 21 subjects were treated with 1% methylprednisolone acetate qid and tCSA for 3 weeks and then received tCSA alone for the remainder of the 3 months
  - Control group: 23 subjects were treated with tCSA alone for 3 months

Byun YJ, Kim Ti, Kown SM, et al. Efficacy of combined 0.05% cyclosporine and 1% methylprednisolone treatment for chronic dry eye. Cornea. 2012 May; 31(5):509-13
Steroid DE Tx: Study

Design
• Evaluated at pretreatment, 1, 2 and 3 months:
  • Symptom Scores, TBUT, Schirmer Scores, Corneal and Conjunctival Fluorescein Staining
  • Proinflammatory factors, interleukin-6 and interleukin-8 tear concentrations were measured before treatment and at the end of the study in both groups


Steroid DE Tx: Results

• All clinical markers improved in both arms of the study
• There was a significant improvement in symptoms, Schirmer and corneal staining scores in the study group vs. the control group at 1 month
• There were no other differences in any measures at any time points
• IL-6 and IL-8 levels both decreased at 3 months; no statistical difference between the groups


Myth Busters: Fact or Fiction?

• Initiating dry eye treatment with a supplemental steroid in addition to Restasis improves the long term outcome of the dry eye treatment
Myth Busters: Fact or Fiction?

• Initiating dry eye treatment with a supplemental steroid in addition to Restasis improves the long term outcome of the dry eye treatment

FICTION!

Impact on Patient Care: Treatment

• Short term use of a topical steroid provides faster symptom relief and improvement of ocular signs than when treating with tCSA alone

  - Benefits of faster relief:
    - Higher patient confidence in the treatment protocol and the doctor
    - Better long term compliance
    - Happier patients
    - Less stinging with tCSA


Treatment: Restasis
Myth Busters: Fact or Fiction?

• Using Restasis once a day is not as effective as using it twice a day

Dry Eye Treatments

The effect of decreasing the dosage of Cyclosporine A 0.05% on dry eye disease after 1 year of twice-daily therapy - Su MY, et al.

tCSA qd: Background

• Cyclosporine A typically works very well for dry eye patients

• However, there are many complaints
  • Too expensive
  • Stinging / burning
  • Wasteful
  • Cumbersome

Su MY, et al. The Effect of Decreasing the Dosage of Cyclosporine A 0.05% on Dry Eye Disease After 1 Year of Twice-Daily Therapy. Cornea 2011 Oct;30(10):1098-1104
tCSA qd: **Study Design**

- 100 Dry Eye patients using tCSA bid ou, with symptom relief for at least 1 year
- Observer masked study
- Patients were randomized to continue with tCSA bid ou or reduce to qd ou

Su MY, et al. The Effect of Decreasing the Dosage of Cyclosporine A 0.05% on Dry Eye Disease After 1 Year of Twice-Daily Therapy. Cornea 2011 Oct;30(10):1098-1104

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**tCSA qd: Study Design**

Tested at baseline, 3 months, and 6 months:

- TBUT
- Fluorescein Staining
- Lissamine Green Staining
- Schirmer Tear Test (anesthetized)
- Ocular Surface Disease Index (OSDI)

Su MY, et al. The Effect of Decreasing the Dosage of Cyclosporine A 0.05% on Dry Eye Disease After 1 Year of Twice-Daily Therapy. Cornea 2011 Oct;30(10):1098-1104

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**tCSA qd: Results**

- After 3 months: study group (qd) had **better TBUT, OSDI** values, and **less** corneal staining
- After 6 months: **No statistically significant differences** between the two groups, except **OSDI scores**...
- **Study group** patients with “severe” dry eyes reported **superior OSDI scores** compared to those in the control group

Su MY, et al. The Effect of Decreasing the Dosage of Cyclosporine A 0.05% on Dry Eye Disease After 1 Year of Twice-Daily Therapy. Cornea 2011 Oct;30(10):1098-1104
Myth Busters: Fact or Fiction?

• Using Restasis once a day is not as effective as using it twice a day

FICTION!

Impact on Patient Care: Treatment

Reducing drop frequency may likely offer
• Enhanced patient compliance
• Improved therapeutic outcome
• Financial savings for the patient

• Non-FDA approved therapeutic regimen, but research supported

• Educate your patients, and monitor at 1-3 months to ensure stability

On the horizon…

Two years ago there were three different medications going through FDA trials which looked promising. None have received FDA approval.

The most promising “new” treatments are those that affect MGD
Oral Treatment Options

- Salagen
  - Oral Pilocarpine
  - Studies indicate this as beneficial in Dry Eye
  - One used 20mg (4 tablets PO QID)
  - Another used 30mg (3 tablets PO tid)
  - Proven effective in Dry Eye Associated with Radiation Therapy
- Evoxac
  - Cevimeline
  - Recommended dose 90mg/d (5 hour half life suggests 30mg tid dosing.) Most can tolerate 180mg/d
  - SE: Excessive slobbering – Titrate to 30mg BID or QD in patients that report excessive drooling while sleeping.

Treatment: Lacrisert

Treatment: Punctal Occlusion

- Dissolvable vs silicone pros and cons
- Improve quality of tears before punctal occlusion
Plugs and IOP: **Results**

- In test eyes
  - mean decrease of 1.59 mmHg
  - -6.82%
- In control eyes
  - mean increase of 0.14 mmHg
  - +1.91%
- Overall mean difference
  - 1.73 mmHg or 8.74%
- Statistically significant difference


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**Pt Care Implications: Treatment**

**MG Expression:**

- Study shows evaporative rate of tears decreases after digital meibomian expression
- In healthy individuals
- In those with sicca and MGD


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**Treatment Instrumentation**

- Lipo-flow

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Treatment Instrumentation

- Lipilow

- Lipflow treatment:
  - Automated device supplies **heat** to inner lid, **pulsating** pressure to outer lid
  - Study shows **12 min** treatment provided clinical improvement & symptomatic relief for **9 months**


Treatment: MG expression, debridement and probing

- Review of Ophthalmology 11/16/2010

The changes triggered by intense pulsed light appear to have multiple beneficial effects.

Intense Pulse Light

- Initially plan on 4 or more treatments one month apart
- Treats MGD in two ways
  - Makes Expressing Meibom abscess easier by heating the MG to as much as 108 F - which would burn the skin if done with superficial heat
  - Ablates the peripheral vascularization we develop as we age to shunt blood to thicker skin. Not Needed in lids. Permits more blood flow to MG
- Patients must understand the need for full treatment initially
  - After initial treatment patients typically need a secondary treatment q6-24mos
Intense Pulse Light

- Clinical Pearls
  - Meibom Expression does not always occur after initial treatment
  - Keep Sylvidine cream on hand because some patients may have mild superficial skin burn. Skin type is determined by Hx and patients do not always give correct answers
  - Not effective in darker skinned patients - may cause whitening of area - pigmentation of skin decreases permeability of pulsed light
  - Patients must be educated that the full effect will take multiple treatments

Extreme Treatments

- Goggles: overnight
  - Dry Eye Shields
  - Can be added to most glasses

Extreme Treatments

- Scleral lens, aka Korb Lens
Prokera

• A 16 mm PMMA ring holding amniotic membrane tissue (placental)
• Used to protect, repair, and heal damaged or inflamed ocular surface

Reduces:
• Pain
• Scarring
• Inflammation
• Healing time

Prokera

• Prokera is inserted and removed in-office
• Only FDA device that reduces inflammation and promotes healing

• Key ingredients:
  • heavy chain hyaluronic acid
  • PTX 3 (HC-HA activator)
  • Collagens (I, III, IV, V, VI)
  • Fibronectin
  • Laminin
  • Proteoglycans
  • Growth Factors

Prokera

Indicated for:
• RCE
• Infectious keratitis
• Inflammatory keratitis
• Herpes
• Superficial epithelial defects
• Severe dry eye syndrome
• Other corneal diseases
Autologous Blood Serum Treatments

THREE STUDIES

Myth Busters: Fact of Fiction?

• Autologous blood serum reduces dry eye symptoms better than artificial tears

Blood Serum vs. Tears: Background

Tears:
- Contain growth factors, fibronectin and vitamins
  • Supports cell proliferation, migration and differentiation
  • A lack of these epitheliotrophic factors can result in severe ocular surface disorders and healing deficiencies

Blood serum:
- Epitheliotrophic factors present in tears are also present in serum
- The biomechanical and biochemical properties are similar to normal tears
Blood Serum:

Background

SERUM EYE DROPS: formulated from the patient’s own blood serum (the clear part)

• Eliminates allergic reactions
• Diluted to a 20 to 50 percent w/ sterile non-preserved saline
• Compounding pharmacy: refrigeration & strict protocols required (expensive)
• Preservative free
  • kept in the freezer until use
  • one bottle is used per day

➢ Considered experimental: their role has yet to be established in large controlled clinical trials

Autologous Blood Serum
vs. Tears for Dry Eye

Randomized double-blind clinical trial of autologous serum versus artificial tears in dry eye syndrome. -Urzua CA, et al.

Myth Busters: Fact of Fiction?

• Autologous blood serum reduces dry eye symptoms better than artificial tears
Blood Serum vs. Tears: Study Design

- Double-blind randomized crossover clinical trial
- 12 adult patients, all with severe DES
- Randomly divided into 2 groups to compare 2 week (short term) topical treatments with
  - AS eye drops diluted at 20%
  - Conventional artificial tears


Blood Serum vs. Tears: Study Design

- Data Analysis
  - OSDI survey
  - Corneal fluorescein staining score
  - Conjunctival fluorescein staining score
  - Tear film break up time


Blood Serum vs. Tears: Results

- AS group showed a statistically significant larger OSDI decrease
  - 50% verses 22% with conventional tears
  - No significant difference in staining or TBUT between groups

Myth Busters: Fact of Fiction?

• Autologous blood serum reduces dry eye symptoms better than artificial tears

FACT!

Impact on Patient Care: Treatment

Consider autologous blood serum for your severe dry eye patients

➢ Good option for those unsuccessful with other treatments
➢ May deliver better symptomatic relief for your severe DES patients

AS PED Treatment

Combined application of autologous serum eye drops and silicone hydrogel lenses for the treatment of persistent epithelial defects - Choi, J. and Chung
PED: **Background**
- **Appropriate stromal adhesions** begin after the epithelium has **completely covered** a defect.
- **Poor adhesion** causes recurrent epithelial breakdown.
- PED: **Epithelium fails to regenerate steadily over a corneal wound within due course (≈ 2 weeks)**.
- PEDs may progress through the **subjacent corneal stroma** and eventually lead to stromal ulceration.

PED: **Etiologies**
- Dry eye
- Exposure keratopathy
- Limbal stem cell deficiency
- Diabetic keratopathy
- Neurotrophic keratopathy following corneal transplant surgery (involving the anterior portion of the cornea)
- Herpetic infections

PED: **Potential Consequences**
- Poor vision
- Significant discomfort
- Infection
- Scarring
- Melting
- Perforation
Myth Busters: Fact Fiction?

• HEMA and SiHy lenses work **equally** well as bandage contact lenses for PED treatment with ABS

AS PED Tx: **Study Design**

• Eight patients with PEDs lasting 30 to 240 days
  • Mean duration of 90 +/- 81.76 days
• Etiologies included:
  • Sjogran-type dry eye syndrome
  • Graft-verses-host disease
  • Toxic keratitis
  • Limbal cell deficiency
  • Superior limbic keratoconjunctivitis
  • Neurotrophic keratitis


AS PED Tx: **Study Design**

• Patients were fit with Senofilcon A (AV Oasys) SH bandage contact lens
  • SH delivers **increased O₂ needed** by compromised cornea
  • **No lens deposition** during the study
    • Better wettability, comfort, & vision
    • Hydrogel lenses cause heavy deposition, opacification, discomfort

AS PED Tx: Study Design

- Autologous serum drops were formulated at 50% dilution with sodium hyaluronate eye drops
  - Hyaluronate drops aide in epithelial proliferation & migration
  - 50% concentration: more soothing due to higher viscosity
  - Used every 2 hours while awake


AS PED Tx: Results

- 100% successful resolution within 7-20 days (mean recovery time: 11.8 +/- 4.9 days)
- Supportive treatment: Not curative in every case
  - If patient is immunocompromised, recurrence could occur
  - 1 patient had recurrence at 2 months, but resolution after repeating combined therapy


A. Before treatment:
B. After 14 days of treatment
PED x 210 days
Myth Busters: Fact Fiction?

• HEMA and SiHy lenses work equally well as bandage contact lenses for PED treatment

FICTION!

Impact on Patient Care: Treatment

➢ Using a SH lens provides
  • Extra O2 that speeds re-epithelization
  • A relatively deposit free surface for better wettability, comfort, & vision
➢ Immediate implementation of this protocol can have enormous benefit to the patient by its potential to
  • Significantly reduce the duration of the PED
  • Reduce the potential severity
  • Obtain a better visual outcome
➢ Even in the face of recurrent disease
  • Knowing this will radically shorten the course of the disease offers substantial peace of mind

Impact on Patient Care: Treatment

• Currently there are no large scale studies showing the efficacy of the MANY possible applications for autologous serum

• However, there are several small studies such as these, verifying its safety and success

Impact on Patient Care: Treatment

- Consider AS for your next patient with severe, non-infectious corneal damage such as:
  - Severe Dry Eyes / K Sicca
  - Recurrent Corneal Erosions
    - PED
    - Bullous Keratopathy
    - Sjogrens
    - Chronic graft verses host disease
    - Ocular cicatrical pemphigoid
    - Stevens-Johnson syndrome
    - Aniridic keratopathy


But What Treatment Do We Use For What Patient?
<table>
<thead>
<tr>
<th>Treatment Strategy</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tear supplementation</td>
<td>Lubricants</td>
</tr>
</tbody>
</table>
| Tear retention       | - Punctal occlusion  
|                      | - Moisture chamber spectacles  
|                      | - Contact lenses |
| Tear stimulation     | Secretagogues |
| Biologic tear substitutes | Serum  
|                      | - Salivary gland transplantation |
| Anti-inflammatory therapy | Cyclosporine  
|                      | - Corticosteroids  
|                      | - Tetracyclines |
| Essential fatty acids | Omega-3 fatty acids |
| Environmental strategies | - Avoid low humidity  
|                      | - Avoid drafts  
|                      | - VDT lowered below eye level |

<table>
<thead>
<tr>
<th>Severity level</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Mild/episodic, with stress</td>
<td>Moderate episodic/chronic, + stress</td>
<td>Severe frequent constant no stress</td>
<td>Severe and/or disabling no stress</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>None, or episodic red fatigue</td>
<td>Annoying and/or blinding + red fatigue</td>
<td>Annoying, chronic; environmenental, limiting activity</td>
<td>Constant and/or possibly disabling</td>
</tr>
<tr>
<td>Conjunctival injection</td>
<td>None to mild</td>
<td>None to mild</td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td>Conjunctival scaling</td>
<td>None to mild</td>
<td>None to mild</td>
<td>Moderate to marked</td>
<td>Marked</td>
</tr>
<tr>
<td>Corneal staining (severity/location)</td>
<td>None to mild</td>
<td>Variable</td>
<td>Moderate</td>
<td>Severe punctate erosions</td>
</tr>
<tr>
<td>Corneal signs</td>
<td>None to mild</td>
<td>Mild debris, decreased meniscus</td>
<td>Flaremary keratitis, mucus clumping, increased tear debris</td>
<td>Filamentary keratitis, mucus clumping, increased tear debris, ulceration</td>
</tr>
<tr>
<td>L/Maldeemer glands</td>
<td>Variable</td>
<td>Variable</td>
<td>Marked, central</td>
<td>Severe punctate erosions</td>
</tr>
<tr>
<td>TBUT (sec)</td>
<td>Variable</td>
<td>&gt;10</td>
<td>&gt;5</td>
<td>Immediate</td>
</tr>
<tr>
<td>Schirmer score (mm/5 min)</td>
<td>Variable</td>
<td>&lt;10</td>
<td>&lt;5</td>
<td>&lt;2</td>
</tr>
</tbody>
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</thead>
<tbody>
<tr>
<td>Treatment options</td>
<td>If no improvement to Level 1, add:</td>
<td>If no improvement to Level 2, add:</td>
<td>If no improvement to Level 3, add:</td>
<td>If no improvement to Level 3, add:</td>
</tr>
</tbody>
</table>
| - Patient education  
| - Environment/dietary modification  
| - Eliminate offending systemic medications  
| - Artificial tears/ointments/gels  
| - Lid therapy | - Nonpreserved artificial tears  
| - Anti-inflammatory Drugs:  
| | - Topical - Corticosteroids  
| | - Ocular - Cyclosporin  
| | - Oral - omega3 fatty acids  
| | - Topical - Tetracycline  
| | - Oral - Cyclosporine A  
| | - Punctal plugs  
| | - Secretagogues  
| | - Moisture goggles | - Serum  
| | - Autologous - Umbilical cord  
| | - Contact lenses | - Systemic anti-inflammatory  
| | | - Oral cyclosporine  
| | | - Antibiotics  
| | | - Moisture goggles  
| | | | Lid Surgery:  
| | | | blepharoplasty  
| | | | AMT graft  
| | | | Mucous m graft  
| | | | Salivary gland transplantation |
**Goal of Treatment**

- Alleviate symptoms
- Reduce ocular morbidity
- Prevent complications
- Improve quality of life
- Improve productivity
- Maximize benefit and relief
- Minimize cost

Consultations: rheumatologist, internal medicine, dermatologist

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**Meibomian Gland Evaluation**

Diagnosis is made by the following pathologic signs:

- Ductal orifice metaplasia
- White shafts of keratin in the orifices
- Increase turbidity and viscosity of the expressed secretions
- Reduced expressibility of secretion
- Morphologic abnormality of the gland and ductules

---

**• Dry eye is not just a disease**

_It is a complex, multi-factorial disorder_

- Regardless of the cause, all dry eye patients have in common an abnormal tear film or abnormal tear function

- Individuals who experience signs and symptoms of dry eye at one time or another due to environmental factors = 100%
Depression: Epidemiology

- Men: 5-12%
- Women: 10-25%
- Prevalence in elderly, according to setting
  - 6-10% in Primary Care setting
  - 12-20% in Nursing home setting
  - 11-45% in Inpatient setting
  - > 40% of outpatient & inpatient Psychiatry clinic
- Late-life depression: sometimes secondary to vascular etiology
Depression in the Elderly

• NOT a normal part of aging
• 2 million Americans over age 65 have depressive illness
• Often co-occurs with other serious illnesses
• Under-diagnosed and under-treated
• Suicide rates in the elderly are the highest of any age group

Depression: Biological factors

• Genetic
  • High prevalence in first degree relatives
  • High concordance with monozygotic twins
  • Short allele of serotonin transported gene
• Medical Illness:
  • Parkinson’s, Alzheimer’s, cancer, diabetes or stroke
• Vascular changes in the brain
• Chronic or severe pain
• Previous history of depression
• Substance abuse

Social & Physiological factors

• Loneliness, isolation
• Recent bereavement
• Lack of a supportive social network
• Decreased mobility
  • Due to illness or loss of driving privileges
• Traumatic experiences (abuse)
• Damage to body image
• Fear of death
• Frustration with memory loss
• Role transitions
SIG ME CAPS

- Sleep disturbance: decreased or increased
- Interest or pleasure: decreased
- Guilt or feeling worthless
- Mood: sustained low or depressed
- Energy loss or fatigue
- Concentration problems or problems with memory
- Appetite disturbance: weight loss or gain
- Psychomotor agitation or retardation
- Suicidal ideation, thoughts of death

Pseudo-Dementia

- A syndrome of cognitive impairment that mimics dementia but is actually depression
- Poor attention and concentration
- Symptoms resolve as the depression is treated effectively
- If considerable cognitive impairment remains, an underlying dementia is suspected
- Even “completely recovered” patients have higher rates of dementia (20% /year of f/u)
- This is 2.5 to 6 times higher than population risk

Aging & Dry Eye

- The most common cause of severe dry eye is aging
- Aging is directly associated with a reduction in lipid production, resulting in evaporative dry eye
- Over time, your body produces less oil
  - 60% less at age 65 than at age 18
- The incidence of severe dry eyes over the age of 65 is around 75%
Dry Eye Disease and Depression: Study Design

- 657 random patients, age 65 to 95 were compared
- Symptoms were evaluated using 2 questionnaires:
  - Short Geriatric Depression Scale
  - Dry Eye Questionnaire
- Clinical DED signs were evaluated using:
  - Schirmer scores
  - NaFl+ staining scores
  - TBUT


Geriatric Depression Scale

Choose the best answer for how you have felt over the past week:
1. Are you basically satisfied with your life? YES / NO
2. Have you dropped many of your activities and interests? YES / NO
3. Do you feel that your life is empty? YES / NO
4. Do you often get bored? YES / NO
5. Are you in good spirits most of the time? YES / NO
6. Are you afraid that something bad is going to happen to you? YES / NO
7. Do you feel happy most of the time? YES / NO
8. Do you often feel helpless? YES / NO
9. Do you prefer to stay home, rather than going out, doing new things? YES / NO
10. Do you feel you have more problems with memory than most? YES / NO
11. Do you think it is wonderful to be alive now? YES / NO
12. Do you feel pretty worthless the way you are now? YES / NO
13. Do you feel full of energy? YES / NO
14. Do you feel that your situation is hopeless? YES / NO
15. Do you think that most people are better off than you are? YES / NO

Underlined items constitute the four item scale.
Dry Eye Disease and Depression: Results

- Patients with worse depression had more DE symptoms despite minimal DED signs
- Depression is a risk factor for DED - in patients with schirmer >5mm
- Depression severity (5.63 vs 3.73) and prevalence (33.3% vs 18.1%) is worse in DE patients vs those without DE

Impact on Patient Care: Diagnosis and Management

- Sex hormones likely play a role in both
  - Being female and menopause are risk factors for both
  - Common omega 3 links in disease mechanism
  - Omega 3 supplements are an effective DE Tx
  - Reduced levels of omega 3 in pts w/ depression
  - Depression can induce cytokine production
  - Increases inflammation, therefore can exacerbate DED

Impact on Patient Care: Diagnosis and Management

- Depressed patients may have a lower pain threshold
- Up to 80% of depressed pts have symptoms w/o cause
- Decrease in VA / comfort from DED can advance depression
- Consider referring your DE patients you suspect for depression, especially those with more significant symptoms than signs
Non-Medical Interventions

- Balanced diet
- Fluids
- Exercise
- Avoid alcohol
- Family/social support
- Focus on positives
- Promote autonomy
- Promote creativity
- Pace appropriately

- Alternate therapy: Pet therapy, horticulture therapy
- Avoid stressors
- Inform about depression

Myth Busters: Fact or Fiction?

Tie Breaker…..

• This class is depressing me more than my dry eye ever did!
Questions?

THANK YOU
...for not sleeping

• IF NEED MORE TOPICS..CAN DO A SECTION ON UVEITIS AND SYSTEMIC CORRELATIONS...SEE “RED EYE KIT”