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.

Dry eye is not just a disease, it's a complex, multifactorial disorder.

Dry Eye Evaluation
- Vision care Exam
- Medical Exam
Predisposing factors

- Age
- Gender
- Environment
- Anterior Segment Disease
- Medications
- CL Wear
- Refractive surgery
- Systemic Disease

Environment

- Air conditioners or heaters
- Airline travel
- Winter months, allergy season
- Ceiling fan
- Exogenous irritants (smoking)
- Reading time/Computer

DTS: Clinical Categories

- Most common presentation: “No lid margin disease”
- Treatment decision based on severity level

Dry Eye Etiology

- Tear Deficient
- Evaporative
- Ocular Def. Lid Related Contact Lens
- Surface Change
- Sjogrens
- Non-Sjogrens
- Lacrimal Deficiency
- Lacrimal Obstruction
- Reflex
- Auto-antibodies

Tear Film Instability

- Note that a patient may have one or more of these deficiencies—they are not mutually exclusive

- Aqueous Deficiency
  - Cause: insufficient tear production by accessory and primary lacrimal glands
  - Sign: low Schirmer (tear volume/flow) score, tear meniscus height (better measurement)
Tear Film Instability (cont)

- **Mucin Deficiency**
  - *Cause*: insufficient or unhealthy mucin production
  - *Sign*: rapid tear film break-up time (TFBUT)

- **Lipid Deficiency**
  - *Cause*: meibomian gland dysfunction (MGD) causing insufficient or unhealthy lipid production
  - *Sign*: irregular meibomian gland expression, fast TFBUT

Dry Eye Evaluation

- **Vision care Exam**
  - CONVERSION

- **Medical Exam**

Tear Osmolarity

InflammaDry

RPS Technologies

Examination

- Adnexa
- Lids / Lid Margins
- Tears
- Conjunctiva
- Cornea

DIAGNOSTIC TESTS

- **TEAR EVALUATION**
  - Tear Meniscus
  - TFBUT
  - Evidence of Fluorescein Staining
  - Tear Consistency - i.e. thickness, debris, evidence of meibomian gland oil and sebaceous secretions
  - Shirmers
Tear Meniscus Evaluation

DIAGNOSTIC TESTS

- Schirmer—w/ or w/o anesthetic
- Phenol Red Thread Test
  - Zone Quick—represents fluid present in the conjunctival sac
- Fluorescein Staining
- Rose Bengal Staining
- Lissamine Green Staining
- Tear Osmolarity
- Collagen Plugs

Schirmer Test

No consensus as to which method is best

Without anesthesia
measures reflex tear secretion

With anesthesia
measures basal tear secretion

Schaeffer Shirmer

- Always do this as the last test
- Place strip in any part of the eye
- Count to three
- remove

Schirmer Testing

- Test of both tear film volume and flow rate
  - neither relevant nor reproducible
- Uses a 35 x 5-mm strip filter paper placed within temporal third of lower lid
- Normal results (measured at five minutes)
  - Unanesthetized: 15-mm or more
  - Anesthetized (basal tear secretion) 5 to 10mm
- Eyes can be open or closed
- Little variation in results with age
- Necessary for documentation
- Alternative: Zone Quick® - phenol red string

Anterior Blepharitis
What is OcuSOFT® Lid Scrub®?

- Mild eyelid cleanser that effectively removes oil, debris and desquamated (dead) skin from the eyelids
- Recommended for routine daily eyelid hygiene and maintenance
- Ocusoft lid scrubs BID 1 week preop cataract surgery eradicated Staph epidermidis equal to topical 5% Betadine intraoperatively¹

¹Jackson M. Endophthalmitis Prophylaxis: Ocusoft Lid Scrub Plus vs. Topical Betadine (ESCRS Barcelona 2010 presentation and OSN supersite)

OcuSoft Tea Tree Kit

- Contains Tea Tree Oil + Buckthorn seed oil
- Ung QHS
- OcuSoft Cleansers

Baby Shampoo......really a myth

It is the traditional method taught in school but is has disadvantages which include:

- Requires Mixing and Diluting (Convenience?)
- Poor Patient Compliance (actually is irritating to eye)
- Long Term Use Will Make the Skin Dry
- More Professional Treatments are Available

MGD

Medical treatment

- Hot compresses
- Lid hygiene
- Lipid based tears-mild/moderate
- Osmolarity lowering drops in moderate/severe

Liposome Spray

- Self-closed colloidal particles
- Membranes composed of one or more lipid bilayer(s)
- The surfaces of bilayers are hydrophilic while the interior, which contain hydrocarbon chains, are hydrophobic
- Because of the different microenvironments in their structure, liposomes can encapsulate hydrophilic molecules
- Applications for lid disease but also drug delivery, diagnostics, computer vision syndrome and nutraceuticals
**Moderate/Acute**

- Tobradex ST
- Zylet
- AzaSite
- Tobradex generic

**Long Term**

- Pulse dose medications periodically
- Restasis bid
- Essential fatty acids
  - EPA
  - DHA
  - GLA

**Potential Chronic Changes**

- Telangiectasia
- Dislocation of meibomian glands/ gland atrophy
- Scarring

**Moderate/severe or not improving**

- Add PO tetracycline
- Recommendation:
  - Doxycycline 50mg bid x 4-8 weeks then taper to qd
  - Periostat (20 mg doxycycline) bid
  - OcuSoft: ALODOX – generic 20 mg

**Tetracyclines**

- Antibiotics inhibit bacterial protein synthesis by binding 30S ribosome
- Anti-inflammatory properties
  - decreases IL-1, TNF-α
  - decreases NO production
  - decreases HLA Class II antigen expression
  - decreases metalloproteinase production and activation
- Decrease symptoms and joint destruction in RA

**Contraindications**

- Pregnant or child bearing age
- Children
**Cautions**

- Photosensitivity
- Chelates with dairy products, antacids etc.
- Minocycline may cause vestibular toxicity
- Number one drop-out reason?
- GI problems

**How to Minimize Stomach Problems with Tetracycline**

1. Do not take the second pill (bid) before going to bed
2. Do not take pills with acidic beverages
3. Take pills with food (except a high dairy meal)
4. Prescribe the lowest dose available

**Treatment**

**Recurrent Erosion**

**ABMD**

**Inflammation is the Hallmark of All Ocular Surface Diseases**

- PROKERA® utilizes the proprietary CryoTek™ cryopreservation process that maintains the active extracellular matrix of the amniotic membrane, uniquely allowing for regenerative healing.
- PROKERA® is the only FDA-cleared therapeutic device that both reduces inflammation and promotes scarless healing.
- PROKERA® can be used for a wide range of ocular surface diseases with severity ranging from mild, moderate to severe.
Insertion of Pro-Kera

- Remove from inner pouch
- Rinse with saline (prevents stinging from preservation media)
- Apply topical anesthesia
- Hold upper lid and have patient look down
- Insert into superior fornix
- Slide under lower eyelid
- Check for centration

Ocular Surface Disease: DIFFERENTIALS

Symptoms of DED but normal osmolarity, MG Expression etc.

- DED that is well controlled
- CL solutions related -PATH
- Mild allergic conjunctivitis
- EBMD - MDF dystrophy
- Pterygium
- Infection - e.g. conjunctivitis
- Anterior blepharitis – Demodex
- GPC
- Asthenopia - vertical, CI etc.
- Salzmann’s Nodular Degeneration
- Mild/mod conjunctivochalasis

Patient with epiphora will actually have osmolarity readings below normal or very low
Treatment

• Emphasis chronic nature of the condition
• Eliminate exacerbating factors
  – caffeine, air conditioner, meds.
• Drink 4-6 glasses of water per day
• Tear replacements

Treatment – AT’s

• Blink Tears & Oasis Tears
• FreshKote
• Systane Balance or Refresh Optive Advanced
• Optive/Refresh
• Systane Ultra
• Genteal gel -------> Systane gel
• TheraTears

Basic Algorithm: re AT’s

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Osmolarity</th>
<th>MG Expression</th>
<th>Staining</th>
<th>AT Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>+/-</td>
<td>&lt; 316</td>
<td>Grade 1 or less</td>
<td>minimal or -</td>
<td>Refresh, Systane etc.</td>
</tr>
<tr>
<td>+</td>
<td>&gt;316</td>
<td>Grade 1 or less</td>
<td>Central or significant</td>
<td>TheraTears, Blink, FreshKote (Consider PF), Genteal Gel</td>
</tr>
<tr>
<td>+/-</td>
<td>&lt; 316</td>
<td>Grade 2 or greater</td>
<td>Inferior or -</td>
<td>Systane Balance, Optive Advanced, Retaine MGD, Soothe XP</td>
</tr>
<tr>
<td>+/-</td>
<td>&gt;316</td>
<td>Grade 2 or greater</td>
<td>Inferior or greater</td>
<td>Retain MGD, Blink, TheraTears</td>
</tr>
</tbody>
</table>

Targeted Treatments

• Treatments aimed at local inflammatory processes
  – Topical corticosteroids (Lotemax)
    • Effective anti-inflammatory agents
    • Site specific Steroids
  – Cyclosporin A (Restasis)

Corticosteroids

• Bind to nuclear receptors that bind DNA and regulate gene expression
• Interfere with transcription regulators [e.g., AP-1 & NF-kB]
• Most inflammatory pathways
  – cytokine production
  – lipid mediators (PGs)
  – cell adhesion molecules
  – lymphocyte trafficking
  – vascular permeability
• Ring modifications alter potency and membrane stabilizing effects

Steroids and Dry Eye

Symptomatic improvement in irritation symptoms in 83% and objective improvement (✔ redness, dye staining and tarsal papillae, ⬆ FTC) in 80% of 70 patients treated for 2 weeks with non-preserved methylprednisolone

Prabhasawat & Tseng BJO 1998
Steroids and Dry Eye

- Moderate (43%) or complete (57%) relief of irritation symptoms accompanied by corneal FL 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

Sjögren’s Syndrome KCS

Steroids Effectively Treat KCS (Marsh Ophthalmology 1999)

Pre-Steroid

Post-Steroid

Ester vs. Ketone Steroids

- **Ester Steroids** are inactivated by naturally occurring esterases – less side effects
- **Ketone Steroids** are not inactivated and have propensity to remain in anterior chamber post breakdown as active metabolites

Ester vs. Ketone Steroids

Loteprednol → ester steroid

Prednisolone → ketone steroid

Fluorometholone

Dexamethasone

Medrysone

Rimexolone

Anti-inflammatory Therapy of KCS

**Corticosteroids**

- Improve signs and symptoms
- Improve tear clearance
- Normalize mucus production
- Often have sustained benefit after a 2 week pulse
- Bioengineered steroid loteprednol etabonate is effective

How Does Restasis Work?

- **Restasis** prevents T-cell activation (Kunert et al., Arch Ophthalmol. 2000;118:1489)
  - Activated T cells produce inflammatory cytokines that result in:
    - Recruitment of more T cells (Stern et al., IOVS. 2003;44:252)
    - More cytokine production (Pflugfelder et al., Curr Eye Res. 1998;18:201)
Topical Cyclosporine

- Restasis Ophthalmic Emulsion (Allergan)
  - Useful in long-term management of inflammatory DES
  - BID dosage
  - Cyclosporine A (CsA) 0.05% in castor oil vehicle
- Mechanism of action:
  - Inhibits activation of inflammatory T-lymphocytes, and 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

Nutritional Supplements: Essential fatty acids

- Omega fatty acids:
  - ALA - e.g. Flaxseed oil
  - EPA-DHA – e.g. Fish oils
  - GLA
    - Evening Primrose Oil
    - Black Currant Seed Oil etc.

HydroEye (HE) Clinical

Purpose: Evaluate HE in postmenopausal women with moderate-severe KCS & tear dysfunction

Dual Sites: Virginia Eye Consultants & Baylor University

Type: Double-blind, placebo-controlled, randomized

Duration: 6 months

Key Findings: Symptoms

HydroEye® therapy significantly decreased the mean OSDI score over the treatment period ($p=0.004$), while the OSDI score was essentially unchanged in the placebo group;

At the end of 24 weeks, OSDI scores were significantly reduced in the HydroEye® group compared to placebo ($p=0.05$).

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 TID—saliva stimulating drug
  - Very effective with a lot less side effects

Normal tears Serum

- pH = 7.4
- Osmolarity = 298
- EGF (ng/ml) = 0.2-3.0
- TGF-b (ng/ml) = 2-10
- Vitamin A (ng/ml) = 0.02
- Lysozyme (mg/ml) = 1.4
- Fibronectin (ug/ml) = 21

Autologous Serum

- pH = 7.4
- Osmolarity = 296
- EGF (ng/ml) = 0.5
- TGF-b (ng/ml) = 6-33
- Vitamin A (ng/ml) = 46
- Lysozyme (mg/ml) = 6
- Fibronectin (ug/ml) = 205
- Hepatocyte GF, NGF, IGF-1, substance p, Complement, Fibroblast GF, c GRP, other Ig, etc.
PROKERA®

Class II medical device comprising of CRYOTEK™ amniotic membrane into a thermoplastic ring set.
Combines the functionality of a symblepharon ring with the biologic actions of CRYOTEK™ amniotic membrane to create a unique treatment option for corneal and limbal wound healing.

SCLERAL LENSES

Scleral lenses are large diameter gas permeable lenses that rest beyond the limits of the cornea and extend onto the sclera.

Punctal Occlusion

• May worsen certain conditions
  – Allergies
  – MGD
  – Inflammatory dry eye?
• Treat those conditions first then plug
• Ideal FIRST treatment option for:
  – Neurotrophic keratopathy
  – Post-LASIK dry eye
  – Lagophthalmos

Expectations During the First 6 Months of Therapy

<table>
<thead>
<tr>
<th>Patients notice an onset of benefit</th>
<th>Further increase in tear production</th>
<th>Significant improvement in tear production</th>
<th>Improvements are maintained with continuation of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>3 months</td>
<td>6 months</td>
<td></td>
</tr>
</tbody>
</table>
Burning and stinging are the most important reasons that patients discontinue use of Restasis

- 17% of patients receiving Restasis experienced burning or stinging
  - Patients with dry eye have chronic ocular disease and are more sensitive to ocular insults
  - Patients with dry eye disease have anesthetic corneas
    - with return of tear function there is a return of corneal sensation, burning and stinging
  - Patients with dry eye are accustomed to treatment failure and are not willing to continue therapy which may make them feel temporarily worse

Topical Loteprednol Improves Patient Compliance and Restasis Efficacy

- Corticosteroids have been shown to improve tear production by controlling inflammation
- Corticosteroids decreases irritation associated with use of Restasis by 75%
- Recommend a mild corticosteroid such as loteprednol qid for two weeks and then bid for 2 weeks for patients who complain of irritation with Restasis, high maintenance patients, and patient who want more rapid relief

No Cyclosporine in Blood

- No detectable cyclosporine in blood of any RESTASIS® ophthalmic emulsion–treated patient
- Toxicity associated with systemic or oral cyclosporine was not observed with cyclosporine 0.05% ophthalmic emulsion

Progression of Dry Eye Disease

- Dry eye is a progressive, potentially irreversible disease
- Left untreated, the cycle of inflammation and dysfunction may cause permanent damage to the lacrimal gland

Please see slides 6 & 7 for important safety information.
MGD
Medical-Instrument Treatment

Treatment of MGD/NOMGD

At Home Therapy
- Warm compresses
- Eyelid Scrubs
- Self expression

In-Office Therapy
- Manual Expression
- Off-Label Pharmacotherapy
  - Oral tetracycline/doxycycline
  - Topical Antibiotics - erythromycin, tobramycin
  - Topical Steroids - dexamethasone

MGD TREATMENT
- Warm compresses
- Meibomian gland scrubs
- Home expression
- Blinking
- Office expression
- Secretagogues – Androgens

Additional Manual Expression

Mastrota Paddle
Jaeger Plate - modified by M. Gutierrez, OD

You can use the BIO to get a lighted slightly magnified view of the lids
Maskin Expressor

- $575
- Rhein Medical

WARNING

- Hot compresses can change the corneal tissues and structure
- Possible Link to Keratoconus
- Evidence Based Medicine

Meibomina Gland Expression

- Schaeffer Eye Protocol
  1) OSD Evaluation
     1) Includes test expression
     2) All staining
  2) RTC expression
     1) At home heat with eye medibeads
     2) 15-20 minutes in waiting room with Bruden’s heat pack (or rear wait)
     3) Expression 1 of 3
     4) RTC 2 weeks

Meibomian Gland Expression

- Fees: $289 / $25
- Out of pocket: ABN
  Covers 3 Office visits
  $68.00 Per visit after initial three visits
- 99213 / 99212
- Dry eye progress check before expression

MGD

Maskin Expressor
**Maskin Probe**

1) $158 box (10)

2) 1, 2, 4, 6 MM intraductals

3) Aluminum Handle $104

---

**Spectacles (Glasses)**

- Encourage to wear indoors-full time
- Contact lens wearers to remove lenses and use glasses when possible
- Creates a humid environment
SCLERAL LENSES

Non-Obvious MGD (NOMGD)
- MGD may be nonobvious without inflammation and without other obvious signs (NOMGD)
- NOMGD may be precursor to obvious MGD
- Highly prevalent and under-diagnosed – may be most common cause of evaporative eye disease
- In a recent dry eye study of the 52 subjects that had MGD, 48% of them had NOMGD.

L W E
Lid Wiper Epitheliopathy

LID WIPER & AUTOMOBILE WINDSHIELD WIPER

THE LID WIPER DEFINED
That aspect of the marginal conjunctiva of the upper eyelid that wipes the ocular surfaces during blinking

Korb et al., 2002–2005