DEWS

- 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.

Factors Influencing Dry Eye

- Age
- Gender
- Arthritis
- Osteoporosis
- Gout
- Lens Surgery
- Contact Lens Wear
- Blink Disorders
- Lid Disease
- Nutritional Problems
- Rheumatoid Arthritis
- Thyroid Problems
- LASIK Surgery
- Cosmetic Surgery
- Mechanical Disturbances
- Exposure Keratitis
- Entropion
- Ectropion
- Symblepharon Formation
- Large Lid Notches
- Lagophthalmos
- Incomplete Blinking
- Dellen Formation
- Illumination
- Systemic Medications
- Time of Day
- Temperature
- Humidity
- Air Movement
- Allergies
- Change in Environment
- Reading
- Preservatives in Topical Eye Medications
- Watching Movies
- Sleep

Dr Jack L. Schaeffer
financial disclosure form

- Alcon
- Allergan
- AMO / Abbott
- Bausch and Lomb
- Ciba Vision
- Cooper Vision
- Essilor
- Hoya
- Inspire
- Optos
- Optovue
- Zeiss Vision
Dry Eye Etiology

Tear Film Instability

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

DRUGS ASSOCIATED WITH DECREASED TEAR PRODUCTION

- β-Adrenergic-blocking, Anti-anginals and Anti-hypertensives (e.g. Atenolol, Practolol, Propranolol)
- Tricyclic Anti-depressants (e.g. Amitriptyline, Doxepin)
- Oral Anti-histamines (e.g. Loratadine, Clemastine, Hydroxyzine, Ceterizine, Fexofenidine)
- Alkylating Immunosuppressives (e.g. Busulfan, Cyclophosphamide)
- Diuretics

Role Of Inflammation

- Inflammation present in SS-KCS and non-SS KCS
- Inflammation present in lacrimal glands, conjunctiva and meibomian glands
- Mediated by proinflammatory cytokines in tears
- Delayed tear clearance accentuates effect
- Inflammation adversely affects neural transmission

PHYSIOLOGY OF THE DRY EYE

- Pathologic
  - Collagen vascular diseases or Autoimmune diseases
    - Rheumatoid Arthritis
    - Lupus Erythematosus
    - Sjogren’s Syndrome
      - 0.4% incidence
      - 95-98% women
      - Fibromyalgia
PHYSIOLOGY OF THE DRY EYE

Marginal
- Contact lens wear—spk
- Keratoconus
- Associated with GPC and/or blepharitis
- Meibomian gland dysfunction (mgd)
- EBM (map-dot dystrophy)
- Acne Rosacea (involves mgd, blepharitis, dry eye and leads to rosacea keratitis)

MEDICATION INDUCED
- Antihistamines
- Diuretics
- Dermatologic—i.e. Accutane
- SSRI’s (Selective Serotonin Reuptake Inhibitors—i.e. Prozac, Paxil, Zoloft, Lexapro, (Welbutrin— to a lesser degree)
- SSRI/NorEpi RI Combination—i.e. Cymbalta

HRT INDUCED
- Women on estrogen therapy (HRT) had a 69% greater risk of dry eye syndrome
- Women on estrogen plus progesterone/progestin had a 29% greater risk of dry eye syndrome
- Risk of dry eye increased 15% for every three year interval on HRT
- 38% of Postmenopausal women in the U.S. use HRT—translates into millions of women

Dry Eye Evaluation

Vision care Exam

CONVERSION

Medical Exam

Brigham and Woman’s Hosp. study—Nov. 2001, JAMA
EXAMINATION

- Adnexa
  - Dermatological Inflammation
  - Dermatochalasis
  - Rosacea
- Lids / Lid Margins
  - Infectious
  - Inflammatory
  - Allergic
  - Physiologic (Lagophthalmos)

EXAMINATION

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

Lid Disease

- Blepharitis
- Lid Wiper Epitheliopathy LWE
- Meibomian Gland Disease MGD
- GPC

- To be covered later in presentation

DIAGNOSTIC TESTS

- EXTERNAL EXAMINATION
  - THE CRANIAL NERVE FUNCTION
    - For a 7th nerve palsy w/incomplete blink on one side
      - Leads to asymmetric dry eye or exposure keratitis
  - THE HANDS
    - For typical arthritic changes suggestive of Rheumatoid or Osteoarthritis
    - Heberden’s Nodes--Nodular Swelling of Distal Joints

EXAMINATION

- CONJUNCTIVA
  - Goblet Cell function (ekc/post-op)
  - Staining
  - Mechanical abnormalities
EXAMINATION

- CORNEA
  - Staining
  - Topographical
  - Hypoxia
  - Secondary Infectious/Inflammatory
  - Dystrophy

The Economics of Dry Eye Disease

<table>
<thead>
<tr>
<th>Type of Exam</th>
<th>Average Revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyeglasses examination</td>
<td>$125-200</td>
</tr>
<tr>
<td>Contact lens examination</td>
<td>$150-200</td>
</tr>
<tr>
<td>Dry Eye care</td>
<td>$300-800</td>
</tr>
</tbody>
</table>

*Figures based on one year

The Economics of Dry Eye Disease

Medical Office Visit: OSD Evaluation

<table>
<thead>
<tr>
<th>Code</th>
<th>Amount</th>
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<tbody>
<tr>
<td>99212</td>
<td>$48.00</td>
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<tr>
<td>99213</td>
<td>$64.93</td>
</tr>
<tr>
<td>99214</td>
<td>$98.65</td>
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Medical Office Visit: Follow-up

<table>
<thead>
<tr>
<th>Code</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>99212</td>
<td>$48.00</td>
</tr>
<tr>
<td>99213</td>
<td>$64.93</td>
</tr>
<tr>
<td>99214</td>
<td>$98.65</td>
</tr>
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</table>

Follow-up Revenue per Year

<table>
<thead>
<tr>
<th>Code</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>99212(x3)</td>
<td>$144.00</td>
</tr>
<tr>
<td>99213(x3)</td>
<td>$194.79</td>
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</table>

The Economics of Dry Eye Disease

<table>
<thead>
<tr>
<th>Level of Dry Eye Disease</th>
<th>Cost of Lost Productivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Dry Eye</td>
<td>$12,686</td>
</tr>
<tr>
<td>Moderate Dry Eye</td>
<td>$12,569</td>
</tr>
<tr>
<td>Severe Dry Eye</td>
<td>$18,168</td>
</tr>
</tbody>
</table>

DIAGNOSTIC TESTS

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

Schaeffer Shirmer

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

Tear Osmolarity

Osmolarity Provides Improved Standard of Care

- Tear osmolarity is the most accurate diagnostic test for dry eye disease
- Elevated osmolarity is the central mechanism causing ocular surface damage
- Allows a physician to rapidly diagnose & classify patients with a global assessment
  - In combination with a slit lamp exam, physicians can select therapies based on mechanism of disease and severity
- Modulate therapy using a quantitative endpoint

TearLab
Ocular Surface Disease
UPDATE 2011

Zone-Quick

Red cotton thread treated with phenolsulfonphthalein
- Yellow (acidic) = water absorption indicator
- Red (basic) = tear volume indicator
Meibomian Gland Evaluator (MGE™)

The number of FUNCTIONAL Meibomian Glands correlates with dry eye symptoms.

<table>
<thead>
<tr>
<th>Symptom Score</th>
<th>Asymptomatic Healthy Eyes* (n = 10 glands)</th>
<th>Severe Symptoms</th>
<th>Moderate Symptoms</th>
<th>Minimal Symptoms</th>
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</thead>
<tbody>
<tr>
<td>≥ 10</td>
<td>14.4 ± 0.7</td>
<td>6–9</td>
<td>2.3 ± 0.2</td>
<td>0</td>
</tr>
<tr>
<td>5–9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

FUNCTIONAL MGs in the Lower Lid

- 4-6: treatment necessary, if glands present
- 5-6: intervention highly advised
- 7-9: preventive treatment (PRN)


New measurement options of the Keratograph 5M

OCULUS TF-Scan - Tear meniscus height measurement

- Overview of the curvature along the lid
- Digital measuring of the height and automatic documentation
- Automatic calibrated and digital measuring of the TMH

Lipiview

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

InflammaDry

RPS Technologies

Dry Eye Disease Cycle of Inflammation

- Dry eye is often hidden until patients have progressed and experienced symptoms
- Dry eye symptoms overlap with other ocular surface diseases, complicating diagnosis
- Numerous clinical diagnostics exist, with no single method preferred
- Most ECPs use one or multiple tests, symptom assessment and patient history to diagnose
**Dry Eye Disease and MMP-9**

Matrix metalloproteinases (MMP) are proteolytic enzymes that are produced by stressed epithelial cells on the ocular surface:
- MMP-9 in Tears
  - Non-specific inflammatory marker
  - Normal range between 3-41 ng/ml
  - More sensitive diagnostic marker than clinical signs
  - Correlates with clinical exam findings
  - Ocular surface disease (dry eye) demonstrates elevated levels of MMP-9 in tears

**InflammaDry® Limit of Detection**

Normal levels of MMP-9 in human tears ranges from 3-41 ng/ml

**InflammaDry 4-Step Process**

1. **Collect Sample**
   - Gently dab the sample collector in 6-8 locations on the palpebral conjunctiva, until the fleece glisten, to collect a tear sample.
2. **Assemble Test**
   - Snap the sample collector into the test cassette and press firmly where indicated. A double click means the test is properly assembled.
3. **Read Test**
   - Insert the absorbent tip into the provided buffer vial for 5 seconds. Replace the cap and lay the test face on a horizontal surface.
4. **Read Results**
   - After 10 minutes, read the test results.

**Patient / Busy Doctor**

- **64 YOM**
- History of Dry eye with all signs and symptoms
  - Restasis
  - UNG PM
  - PP
  - PFAT
- Signs / symptoms vary at each visit over a year
**Systemic Disease**

- Diabetes
- Rheumatoid Arthritis
- Sjogren’s syndrome
- Thyroid Eye Disease
- Rosacea
- Sleep Apnea
- Graft Vs Host Disease
- Many others

**VITAL STAINS**

- Sodium Fluorescein
  - Epithelial defects
  - Accumulates intracellularly
- Rose Bengal
  - Premier dye of conjunctiva
  - Stains devitalized cells on cornea and conjunctiva
- Stains mucin strands
- Stains unprotected tissue
- Phototoxic, sting is dose dependent, antiviral?
- Lissamine Green
  - Same purpose as RB
  - Less stinging
- Fluoromene

** Causes of Clinical Dry Eye**

- Mucin deficiency
  - Goblet cell dysfunction
  - Epithelial surface disease
- Aqueous deficiency
  - Lacrimal gland dysfunction
  - Keratoconjunctivitis sicca
- Meibum deficiency
  - Meibomian gland disease
  - Evaporative dry eye

**Developing a Specialty Ocular Surface Disease Practice**

- Lid Disease

**Lid Disease**

We cannot treat the dry eye until we understand and treat

- LWE
- MGD
- Blepharitis
- Epiphora

IT IS ALL ABOUT THE LIDS

**Case #2**

52 year old, white female

**Occupation:** Web designer

**Hobbies:** Pinterest on her iPad, reading, yoga

**Ocular history:** Dry Eye Disease, mild cataracts

**Medical history:** Occasional migraine headaches, mild hypertension

**Meds:** Lorazepam, Cymbalta, flax seed oil
Case #2

Complaint
Dry symptoms worsening, “OTC’s don’t work,”

Associated symptoms
Eye fatigue, discomfort, worsening in the evening, often matted

Effect to ADL’s
Effects work, limits reading

Medications for DED
Similasan “Dry Eye Relief” (has used “all” artificial tears), warm compresses, cold packs

Case #2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>20/20 OD 20/20 OS</td>
</tr>
<tr>
<td>EOMs</td>
<td>FROM OU</td>
</tr>
<tr>
<td>Pupils</td>
<td>ERRL</td>
</tr>
<tr>
<td>SPEED</td>
<td>14/28</td>
</tr>
<tr>
<td>OSDI</td>
<td>54/100</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Negative</td>
</tr>
<tr>
<td>NIKBUT (initial)</td>
<td>4.72 OD 4.33 OS</td>
</tr>
<tr>
<td>Osm</td>
<td>294 OD 277 OS</td>
</tr>
</tbody>
</table>

Microscopy

Demodex visible at slit lamp
- Cylindrical dandruff
- Base of lashes

Microscopy for patient education

Microscopy

Epilation maneuver
Rotation is key

Microscopy

Plate to slide
Observe under lower magnification
Increase magnification
Photograph
Demodex

• Ubiquitous obligatory ectoparasites of man
• Two forms: D. brevis and D. folliculorum
• Lifecycle of 14.5 days
• Negatively phototaxic
• Move in dark environment, stop with bright ones

Lacey N et al. Demodex Mites – Commensals, Parasites or Mutualistic Organisms? Dermatology 2011;222:128–130

Demodex

• 84% of patients at 60, 100% over 70
• Increased incidence with:
  • Age
  • Immunocompromised
  • Skin disorders (Rosacea)
  • Eye environment- increased pH and amino acids

Lacey N et al. Demodex Mites – Commensals, Parasites or Mutualistic Organisms? Dermatology 2011;222:128–130

Demodex

• Blepharitis secondary to demodex consuming epithelial cells
• Micro-abrasions causes reactive hyperkeratinization which leads to cylindrical dandruff


Demodex Treatment

• 50% TTO in-office weekly, 10% TTO wipes bid OU
• 5% TTO ointment massage


Demodex Treatment

• Commercially available:
  • Cliradex- 25% TTO wipe
  • OcuSoft Demodex kit (for in-office)
OcuSoft Tea Tree Kit

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

Lid Hygiene – Surgical Considerations

Types of Blepharitis:
- Anterior
- Staphylococcal
- Seborrheic
- Demodex
- Angular
- Posterior
- Meibomian Gland Dysfunction (MGD)

Baby Shampoo.... really a myth

It is the traditional method taught in school but 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

Case #1

84 year old, white, female
(+) severe dry eye for 1 year

Oral Medications:
- Metformin
- Lisinopril
- Glyburide
- Lovastatin
- Sertraline
- ASA
- Glucosamine
Case #1

Complaint: Chronic dryness, increasing for 1 year

Associated symptoms: Fluctuating vision, photophobia

Effect to ADL’s: Unable to read, cannot go outside comfortably

Medications for DED: Restasis BID, Non-preserved Systane, doxycycline 100mg BID, Omega 3PA

Case #1

Diagnosed with glaucoma in 1970’s

Instilling 2 glaucoma medications
- Latanoprost qhs OU
- Brimonidine BID OU

Case #1

Treatment:
- Lipflow treatment – begin Acuvail bid for 2 weeks, then qd for 2 weeks
- Lid hygiene – Cliradex wipes bid x 10 days then qhs for 20 days
- RTC 4-6 weeks

Follow up examination
- “Good days and bad days”
- Dryness less of a problem since treatment and vision is improving
- Able to read the newspaper
Case #1

Patient returned for PROKERA® at follow-up visit. S/p removal of amniotic membrane results:

<table>
<thead>
<tr>
<th>cc DVA</th>
<th>20/60 OD (PH: 20/30)</th>
<th>20/100 (PHM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOMs</td>
<td>FROM OU</td>
<td></td>
</tr>
<tr>
<td>CFV</td>
<td>FTFC OD, OS</td>
<td></td>
</tr>
<tr>
<td>PUPILS</td>
<td>ERLLJ-APDO</td>
<td></td>
</tr>
<tr>
<td>SPEED</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>OSM</td>
<td>62.5</td>
<td></td>
</tr>
<tr>
<td>Osm</td>
<td>308 OD, 308 OS</td>
<td></td>
</tr>
</tbody>
</table>

Sutureless Amniotic Membrane

- ProKera - Amniotic Membrane for wound healing
  - Cryopreserved
  - Bio Optix
  - Dry Membrane

Sutureless Amniotic Membrane

- Persistent Corneal Defect
- Recurrent Cornea Erosion
- Corneal Ulcer
- Pterygium Graft
- Bullous Keratopathy
- Band Keratopathy

Biological Scaffolding

- Helps initiate an active healing process by providing proteoglycans and growth factors
- Collagens, fibronectin and lamillin
- Cryopreserved membrane contains heavy-chain hyaluronic acid
- Inhibits proinflammatory cells
- Suppress T Cells

Sutureless Amniotic Membrane

- ProKera - Amniotic Membrane for wound healing
  - Corneal Ulcer
  - Bullous Keratopathy
  - Folds in Descemet’s
  - Chemical Burns
  - Mechanical Complications 2ary to graft
  - Disruption of surgical wound
  - Non-healing surgical wound
The Amniotic Membrane

- The amniotic membrane is the innermost lining of the placenta (amnion)
- Amniotic membrane shares the same cell origin as the fetus
  - Stem cell behavior
  - Structural similarity to all human tissue

Inflammation is the Hallmark of All Ocular Surface Diseases

- **Corneal Inflammation**
  - Keratitis
- **Conjunctival Inflammation**
  - Conjunctivitis
- **Eyelid Inflammation**
  - Blepharitis

Inflammation’s Effect on Healing

- **Inflammation**: the first sign of wound healing & is also the hallmark symptom of all ocular surface diseases
- Uncontrolled inflammation leads to:
  - Chronic pain and discomfort/irritation
  - Delayed healing, more tissue damage
  - Vision-threatening complication, e.g., scar/haze
- Effective control of inflammation is an important strategy to promote healing and minimize the risk of scar/haze

PROKERA®: BIOLOGIC CORNEAL BANDAGE

- PROKERA® utilizes the proprietary CryoTek™ cryopreservation process that maintains the active extracellular matrix of the amniotic membrane which uniquely allows 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 number 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

Devries Amniotic Membrane VEE 2016
BRUDER Dry Heat Glass Bead Sanitizer
Suitable for all metal instruments including the Bruder Meibomian Gland Expression Instruments.

Fast acting and easy to use:
- Chamber size: 1 5/8" Diameter x 2 1/2" Deep.
- Chamber with glass beads heats to 250°C in approximately 20 minutes.
- Sanitizes in 30 seconds.
- Electrical.

NOTE: Glass Bead sanitizers are not FDA approved as sterilizers. Glass Bead sanitizers are a quick, easy and accurate alternative to traditional methods of instrument sterilization.

BRUDER Instrument Trays
Autoclavable instrument trays are ideal for instrument storage or transport.

Available in two convenient sizes:

- Item #98500: Instrument Tray Small - 2.5" x 6.25" x 2.75"
- Item #98505: Instrument Tray Large - 4" x 6.25" x 2.75"

BRUDER Surgical Instrument Line

Item #98610 COILING Expression Forceps
GERMAN STAINLESS
For mild to aggressive expression of Meibomian gland, 95mm Forceps with closed paddles.

Item #98630 UVENGOOD Expression Paddle - Angled
GERMAN STAINLESS
For mild or gentle expression of the Meibomian gland, 75mm oval paddle with 12 degree angle. Non-slip knurled handle.

Item #98639 UVENGOOD Expression Paddle - Straight
GERMAN STAINLESS
For mild or gentle expression of the Meibomian gland, 95mm flat oval blades. Non-slip knurled handle.

BRUDER Surgical Instrument Line

Item #98700 S leveled Meibomian Gland Forceps
These forceps feature non-slip paddles and an easy-grip, non-slip handle for precise eyelid removal.

Item #98701 KARPECKI Eyelid Posterior Meibomian Gland Forceps
The instrument has a groove in the blade to hold the plug solidly in place during the procedure. Also, if necessary, the instrument can be turned 90 degrees to a flat side to push the plug into place. German stainless.

Item #98702 KARPECKI Eyelid Anterior Meibomian Gland Forceps
The instrument has a handle that can be released. The application of a special coating instead of serrations assures the handle will not slip when being removed. Slide the forceps under the edge of the bandage lens and easily pick it off with the eyelid.

Item #98703 KARPECKI Eyelid Desodorizer
This instrument is a slightly curved tip with a "chop" edge on both sides. The edge is just right to remove the serrations easily by sliding the instrument, curve forward, along the eyelid in a single direction. German stainless.
Sjogren’s Syndrome - Consequences

- Sjogren’s syndrome leads to:
  - Corneal abrasions and other Keratopathies
  - Blepharitis
  - Uveitis
  - Other ocular infections
  - Dental caries
  - Other infections of the mouth
- Systemic involvement in Sjogren’s syndrome may lead to:
  - Respiratory dysfunction
  - Renal dysfunction
  - Lymphoma

Sjö Testing - Research

- 26% of DED patient have autoimmune disease
- 11% have Sjogren’s syndrome
- Average delay of 10 years in receiving an accurate diagnosis
- Common Complaints:
  - Dry eye
  - Dry mouth
  - Fatigue
  - Joint pain

Sjö Testing - Research

Cataract Surgery risks:
- SPK
- Filamentary keratitis
- Conjunctivitis
- Infectious keratitis
- Recurrent epithelial defects
- Stromal keratolysis
- Corneal ulceration

Lasik surgery risks:
- Severe and difficult-to-treat dry eyes
- Refractive regression
- “Some case reports note good safety and refractive stability

Sjö Testing - Clinical

- Combines 4 traditional biomarkers with 3 novel, propriety biomarkers
- Helps detect Sjögren’s syndrome early in its disease course
- Offers significantly higher sensitivity and specificity than previous screening methods

Advanced Recalcitrant PEK

- Autologous Serum
- Amniotic Membrane
**Autologous Serum**

- Contains
  - Epithelial Growth Factor (EGF)
  - Transforming Growth Factor 8 (TGF8)
  - Fibronectin
  - Vitamin A
  - Other Cytokines

**Autologous Serum**

- Blood Draw at Lab
- Spin down to plasma @4000 rpm for 20 minutes
- Deliver to Compounding Pharmacy
- 2:1 Filtered Compounding with BSS
- 8 Bottles
- Frozen until used

**Autologous Serum**

- 1 gtt q2h from morning until bedtime
- Keep Vial Refrigerated
- Keep Additional Vials Frozen Until Use
- 8 Straight Weeks
- Evaluate After 6-8 Weeks
- Possible Additional Course

**Autologous Serum Cost**

- Lab Draw $30
- Compounding Pharmacy $120
- $150 for 8 Vials
- IF Patient delivers Serum to Pharmacy

**SCLERAL LENSES**

**Autologous Serum Cost**

- Lab Draw $30
- Compounding Pharmacy $120
- Virology Testing $210
- Freeze and Shipment To/From Compounding Pharmacy
- Approximately $450 to $550 for 8 Vials
Punctal / Lacrimal Occlusion

- Rationale for occlusion therapy:
  - Diminishes tear drainage from the ocular surface
  - Enhances contact time between tears & ocular surface
  - Utilizes "normal tears"
  - Natural complement of proteins, enzymes, buffers, etc.
- Multiple modalities, manufacturers, products
  - Collagen, silicone, acrylic polymers
  - Intracanalicular vs. punctal occlusion

LACRISERT®
(hydroxypropyl cellulose ophthalmic insert)

A Novel Approach to Treating Dry Eye Syndrome

Please see full Prescribing Information.

Case #3

68 year old, white male
Hospital-based medical researcher

Ocular history
- (+) Dry Eye – irritated, red, gritty OU
- (+) POAG OU
- (+) Retinitis pigmentosa OU

Medical history
- Rosacea
- High cholesterol
- Osteoarthritis

Meibomian Gland Dysfunction
Meibomian Gland Dysfunction

- Level one Treatment: Available to all Doctors
  - Medical:
    - In office and home Procedures
- Level two Treatment: Specialized equipment needed

Meibomian Gland Dysfunction

- 1 Manual Expression
- 2 Miboflow
- 3 Lipiflow

M G D
Meibomian Gland Disease

Meibomian Gland Dysfunction and Management

Kelly K. Nichols, OD, MPH, PhD
FERV Professor
University of Houston College of Optometry
Chair, TFOS International Meibomian Gland Workshop

Meibomian Gland Dysfunction

- The TFOS Report of the International Meibomian Gland Dysfunction Workshop
  - Etiologies
  - Definition/ Classification
  - Epidemiology
  - Clinical characteristics
  - Diagnosis/ Management
  - Contact lenses, surgical implications

Current Dry Eye Definition

“Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.”
TFOS International MGD Workshop

- Over 65 international clinicians, scientists, and industry participants
- 2+ year process
- Published in March 2011, IOVS
- #1 Most downloaded IOVS article for the last 12 months
- Downloaded over 5500 times
- All MGD workshop reports are in the "top 10"
- Translation into 12 languages

www.tearfilm.org

Anatomy, Physiology and Pathophysiology of the Meibomian Gland

Erich Knop, M.D., Ph.D. (Chair)
Nadja Knop, M.D., Ph.D.
Thomas J. Millar, Ph.D.
Hiroto Obata, M.D.
David A. Sullivan, Ph.D.

Meibomian Gland - ANATOMY

- Large sebaceous glands
- No direct contact to hair follicles
- Located in the tarsal plates
- Upper and lower eye lids

Meibomian Gland - ANATOMY

- Length
  - Follows the tarsus
- Number
  - More in upper lid (30-40)
  - Less in lower lid (20-30)
- Volume
  - Higher in upper lid (26µl vs. 13µl)
  - Relative functional contribution (upper vs. lower) to the tear film lipid layer is unknown
Meibomian Gland – PATHOLOGY
• Obstructive MGD leads to a progressive ductal DILATATION and acinar ATROPHY

Meibomian Gland Dysfunction
Definition & Classification

J. Daniel Nelson, M.D. (Co-Chair)
Jan Shimazaki, M.D., Ph.D. (Co-Chair)
Jose M. Benitez-del-Castillo, M.D., Ph.D.
Jennifer Craig, Ph.D., MCOptom
James P. McCulloy, M.D.
Seika Den, M.D., Ph.D.
Gary N. Foulks, M.D.

Evaluation, Diagnosis and Grading of Severity of Meibomian Gland Dysfunction

Alan Tomlinson, MCOpt, Ph.D. (Chair)
Anthony J. Bron, F.R.C.S.
Donald R. Karb, O.D.
Shiro Amano, M.D., Ph.D.
Jerry R. Paugh, O.D.
E. Ian Pearce, Ph.D.
Richard Nee, M.D.
Norihiro Yokoi, M.D., Ph.D.
Rahko Archa, M.D., Ph.D.
Murat Dogru, M.D.

Management and Therapy of Meibomian Gland Dysfunction

Gerd Geerling, M.D. (Chair)
Joseph Tauber, M.D.
Christophe Baudouin, M.D., Ph.D.
Eiki Goto, M.D.
Yukihiro Matsumoto, M.D.
Terrence O’Brien, M.D.
Mauricio Rolando, M.D.
Kazu Tsubota, M.D.
Kelly K. Nichols, O.D., M.P.H., Ph.D.

MGD Exposed
A new look at an old problem
The prevalence of MGD is as high as 60–70%1,2
MGD is frequently nonobvious and therefore missed3
Meibomian lipids are critical for innate tear film host defense4
MGD decreases corneal adhesiveness5
Pretreatment optimizes post-cataract surgery ocular comfort6
Evaporative stress causes MGD7 (Modern lifestyle, Contact lens wear and Chronic use of topical medications all induce evaporative stress)
MGD is progressive: Early intervention optimizes outcomes8
Identify early compromise to MG function and structure with the MGE and DMI9
Lipids Essential to Stable Tear Film

86% of dry eye patients have MGD causing instability

An Unstable Tear Film Negatively Impacts Premium Quality Vision Care

Fluctuating Vision
Ocular Discomfort
Compromised Barrier to Infection

63% of Cataract Patients (MYACD study results)
Contact Lens Intolerance and LASIK Candidates
Glaucoma and Retinal Patients

Focus on the Gland

“Meibomian Gland Dysfunction (MGD) is a chronic, diffuse abnormality of the Meibomian Glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion.”

Meibomian Gland Function

- A functional Meibomian Gland is a gland that releases its liquid contents during a deliberate blink.
- The number of functional MGs along the lower eyelid can be used to diagnose MGD and to direct therapeutic intervention

MGD is Progressive

Examples of Compromised Function and Structure

The Cycle of Inflammation
A Change in Philosophy – MGD First

Dry Eye Approach
• Wait for the onset of sequelae: The patient tells you there is a problem
• Measure and manage dry eye sequelae
• Gradually advance treatment as sequelae worsen in severity

MGD First/Root Cause Approach
• Evaluate everyone for MGD: Identify MGD at its earliest stages
• Educate patients about the front line of defense of the tear film - the lipid layer
• Offer the most efficacious MGD treatment as early as possible
• Rehabilitate the ocular surface and manage sequelae with adjunctive therapy

Goal: Treat Sequelae (primarily symptoms)
• Root cause is not identified: Promotes confusion, and patient despair

Goal: Treat Sequelae (primarily symptoms)
• Root cause is not identified: Promotes confusion, and patient despair


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.

MGD Medical treatment

Goal: Restore and optimize gland function/intervene in progression

• Root cause is not identified: Promotes confusion, and patient despair

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

MGD First: If the etiology is not treated, the Dry Eye will not resolve

MGD First does not mean that the sequelae of dry eye should be ignored.
## Moderate/Acute

<table>
<thead>
<tr>
<th>Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobradex ST</td>
</tr>
<tr>
<td>Zylet</td>
</tr>
<tr>
<td>AzaSite</td>
</tr>
<tr>
<td>Tobradex generic</td>
</tr>
</tbody>
</table>

## Long Term

<table>
<thead>
<tr>
<th>Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse dose medications periodically</td>
</tr>
<tr>
<td>Restasis bid</td>
</tr>
<tr>
<td>Essential fatty acids</td>
</tr>
<tr>
<td>- EPA</td>
</tr>
<tr>
<td>- DHA</td>
</tr>
<tr>
<td>- GLA</td>
</tr>
</tbody>
</table>

## Moderate/severe or not improving

<table>
<thead>
<tr>
<th>Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add PO tetracycline</td>
</tr>
<tr>
<td>Recommendation:</td>
</tr>
<tr>
<td>Doxycycline 50mg bid x 4-8 weeks then taper to qd</td>
</tr>
<tr>
<td>Periostat (20 mg doxycycline) bid</td>
</tr>
<tr>
<td>OcuSoft: ALODOX – generic 20 mg</td>
</tr>
</tbody>
</table>

## 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

<table>
<thead>
<tr>
<th>Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant or child bearing age</td>
</tr>
<tr>
<td>Children</td>
</tr>
</tbody>
</table>

## Cautions

<table>
<thead>
<tr>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photosensitivity</td>
</tr>
<tr>
<td>Chelates with dairy products, antacids etc.</td>
</tr>
<tr>
<td>Minocycline may cause vestibular toxicity</td>
</tr>
<tr>
<td>Number one drop-out reason?</td>
</tr>
<tr>
<td>GI problems</td>
</tr>
</tbody>
</table>
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 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

New! Ophthalmic Surgical Instruments

Collins Expressor Forceps (Item 98610)
For aggressive expression of the Meibomian gland

Livengood Expressor Paddles
Angled (Item 98620) & Flat (Item 98630)
For mild or gentle expression of the Meibomian gland

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
  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

**Maskin Probe**

1) $158 box (10)
2) 1,2,4,6 MM intraductals
3) Aluminum Handle $104

**Maskin Tube**

Meibomian gland Drug delivery system
**Maskin Probe**

Leiter Pharmacy
8% lidocaine with 25% Jojoba in ung base

**OBSTRUCTIVE MGD**

Warm Compress Treatment

*Increase in LLT Following Treatment with Warm Compresses in Patients with MGD*

Olson, Korb, Greiner, Eye & CL, 2003

| Baseline LLT | 60 nm |
| 5 minutes    | 105 nm |
| 15 minutes   | 117 nm |
| 30 minutes   | 122 nm |

Not published: 1 to 2 mins – minimal or no improvement.

Warming devices: Goto et al., 2002; Muro et al., 2003; Nagymihalyi et al., 2004; Mitra et al., 2005; Di Pascuale et al., 2005; Spiller et al., 2007

**Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire**

- Evaluates the frequency and severity of symptoms
- Developed as an easy to use fast screening tool for dry eye disease
- SPEED questionnaire is one of the tools used to identify candidates for LipiView®

**Meibomian Gland Evaluator™ (MGE)**

- The TearScience® Meibomian Gland Evaluator
  - Applies consistent, moderate pressure
  - Between 0.8 g/mm² and 1.2 g/mm²
  - Allows evaluation of secretions from Meibomian gland orifices through a slit lamp biomicroscope

<table>
<thead>
<tr>
<th>Grade</th>
<th>Secretion Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No secretion (includes capped orifices)</td>
</tr>
<tr>
<td>1</td>
<td>Inspissated (toothpaste consistency)</td>
</tr>
<tr>
<td>2</td>
<td>Colored/cloudy liquid</td>
</tr>
<tr>
<td>3</td>
<td>Clear liquid oil</td>
</tr>
</tbody>
</table>

**Indications for Use**

**Meibomian Gland Evaluator™**

- Intended for use by a clinician to evaluate meibomian gland secretions. Used to apply consistent light pressure to the outer eyelid skin of a patient while visualizing secretions from meibomian gland orifices through a slit lamp biomicroscope.
- NO KNOWN CONTRAINDICATIONS

**LipiView® Ocular Surface Interferometer**

- An ophthalmic imaging device intended for use in adult patients by a clinician to capture, archive, manipulate and store digital images of specular (interferometric) observations of the tear film, which can be visually monitored and photographically documented.
- NO KNOWN CONTRAINDITIONS

**Tear Conservation**
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

Categories of Lubricant Eye Drops

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

Tear Conservation- Therapeutics

- Artificial tears
- Ointments
- Steroids
- Cyclosporine
- Doxycycline
- Lacriserts
- Lid disease therapy
- Glasses
- Sunglasses

Tear Conservation: Surgical Intervention

- Punctal occlusion
- Lateral tarsorrhaphy
- Other procedures
  - Ectropion correction

Lifestyle Adaptations:

- Increase humidity
- Wear eye shield or goggles
- Avoid:
  - wind, air conditioning, dry heat, high altitudes
  - smog, exhaust, smoke
  - prolonged computer use
  - contact lens wear
  - medications that contribute to KCS
  - Sunglasses

Restasis™

- Ophthalmic emulsion of cyclosporine 0.05%
- Unique emulsion technology provides effective drug delivery to ocular tissue at low cyclosporine concentrations
- Cyclosporine is a complex molecule with antiinflammatory and immunomodulatory properties.
  - Inhibits T-cell mediated inflammation and cytokine driven inflammatory cell chemotaxis
- In the eye:
  - Restasis™ increases production of natural tears increases goblet cell density
**Restasis™ Dosing: BID**
- Recommended Restasis™ regimen: 1 drop in each eye every 12 hours
  - Inform patients: do not use “as needed” like traditional drops
- Concomitant therapy
  - Clinical study showed Artificial tears excellent adjunct
  - Additional emulsion may be poorly tolerated
- Contact lens users
  - Remove lenses, administer Restasis™, replace lenses after 15 minutes

**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. 2002;43:2609)

**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 BJ O 1998

**DOXYCYCLINE**
- SIDE EFFECTS
  - NVD, anorexia, dysphagia, severe photosensitivity, superinfection (fungus, vaginal candidiasis) benign IC-HTN, hepatotoxicity, pancreatitis
- WARNINGS
  - drink fluids to prevent esophagitis, use sun block, simultaneous ingestion of food OK.
  - Link to Breast CA?
- ALTERNATIVES
  - Tetracycline qid
  - Minocycline $$
  - ALODOX

**ONCE DAILY DOXYCYCLINE**
- Great for long term usage once controlled
- Blepharitis, dry eye, rosacea
- Brand Name Oracea® 40mg
- Long term —cycline therapy associated with pseudotumor cerebri
  - TCN, Doxycycline, Minocycline

**Alodox**
- 20 mg Doxycycline Hyclate
- Sub-antimicrobial dosage
  - (<50mg)
- Enzyme modulation of inflammation
- By OCuSOFT
- Kit comes with lid scrub foam
- Claims to be a more potent collagenase inhibitor than minocycline and therefore less SE
- Long term use
Contraindications
- Pregnant or child bearing age
- Children

Cautions
- Photosensitivity
- Chelates with dairy products, antacids etc.
- Minocycline may cause vestibular toxicity

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

Omega-3s and Omega-6s: Essential Fatty Acids
- Essential fatty acids
- Optimum Omega-6:Omega-3 ratio for good health varies from 3:1 up to 1:1:
- Ratio in current American Diet is about 1:10
- American diet too high in Omega-6s from dairy products, beef, vegetable oils, shortening
- American diet too low in Omega-3’s from salmon, cold-water fish, krill oil, flaxseed, walnuts, dark green leafy vegetable, beans

Omega-3 Essential Fatty Acids
- Omega-3’s
  - American diet has undergone a 6-fold reduction in Omega-3’s since 1850
  - Increases “good” prostaglandins
  - Inhibits “bad” prostaglandins
- Omega 6’s
  - US consumption of this fatty acid has doubled from what it was in 1940.
  - Excess intake can increase water retention, raise blood pressure and increase blood clotting.

L W E
Lid Wiper Epitheliopathy
That aspect of the marginal conjunctiva of the upper eyelid that wipes the ocular surfaces during blinking (Korb et al., 2002-2005)

Ocular surface

LID WIPER

LID WIPER & AUTOMOBILE WINDSHIELD WIPER

Windshield Wiper
Windshield Wiper Clearance Space
Kessing’s Space

Ocular Surface

LID WIPER EPITHELIOPATHY DEFINED

LWE is any compromise of the squamous epithelial cells or the protective coatings of the Lid Wiper

A cascade of sequelae will follow