Fall 2016 Continuing Education

Monday, October 31, 2016
The Greatest Ocular Surface Disease and Dry Eye Course

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Schaeffer Eye Center
Birmingham, Alabama

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

Membership Benefits

- Help to build the premiere organization in providing OSD education and knowledge to all optometrists.
- Access to invaluable downloadable practice management tools
- Quarterly newsletter
- Membership certificate
- New industry products and services updates
- Access to private list serve weekly conversations on ocular surface disease
- OSSOPT.com $54.00

www.ossopt.com

The OSD Wellness Symposium

- Re invent the practice
- Prevent patient problems
- White eyes
- Perfect Vision
- Patient Referrals
- Sunwear sales
- Decrease Contact lens dropout
- Look Better Feel better

The OSD Symposium

- 24 Doctors
  - 22 Ods
  - 2 MDS

- Dry Eye
  - Research
  - Lectures
  - Professors
The OSD Wellness Initiative

- OD’s
  - Need education
  - Staff Training
  - Change the culture
  - Inform the Public
- I Care

The OSD Wellness Initiative

- Pre Screening
- Diagnosis
- Treatment
- Patient Education

The OSD Wellness Initiative

Tech Driven

- OSDI / Speed questionnaire
- History
- Topography / keratometry
- Visual Acuity

The OSD Wellness Initiative

Preventive Medicine

- Dermatology
- Dentistry
- Psychology (behavior modification)

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

- Estimated 20 to 30 million people in the U.S. are thought to have early-stage signs or symptoms of dry eye
- Affects women more commonly than men
- Difficult disease to understand and treat
- Advanced dry eye effects roughly 6 million American females and 3 million American males
- More common in older individuals (45 years or older)
- Varied causes and severities
- Can be a stand-alone condition
# Schaeffer Eye Center
## Managing Your Dry Eye Condition
### Patient Instructions

<table>
<thead>
<tr>
<th>Artificial Tears</th>
<th>Dosage</th>
<th>Notes</th>
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<th>Ointment</th>
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<th>Ocular Steroid</th>
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<th>Misc Drops</th>
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<tr>
<th>Eyelid Regimen</th>
<th>Notes</th>
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<td>Hot Compresses</td>
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<tr>
<td>Beaded Heat Mask</td>
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<tr>
<td>Tranquileyes Mask</td>
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<tr>
<td>Lid Scrubs</td>
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<tr>
<th>Vitamins</th>
<th>Notes</th>
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<tr>
<td>Formula:</td>
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<tr>
<td></td>
<td>Dosage</td>
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</table>
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
- Symbiophasoph 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

Dry Eye Etiology

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)

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

Tear Film Instability (cont)

DRUGS ASSOCIATED WITH DECREASED TEAR PRODUCTION
- β-Adrenergic-blocking, Anti-anginals and Anti-hypertensives
  (e.g. Atenolol, Propranolol)
- Tricyclic Anti-depressants
  (e.g. Amitriptyline, Doxepin)
- Oral Anti-histamines
  (e.g. Loratadine, 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)
  - EBMD (map-dot dystrophy)
  - Acne Rosacea (involves mgd, blepharitis, dry eye and leads to rosacea keratitis)

PHYSIOLOGY OF THE DRY EYE
- 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—ie. Cymbalta

PHYSIOLOGY OF THE DRY EYE
- 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

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

Dry Eye Evaluation
- Vision care Exam
- Medical Exam
# Dry Eye Work-up

**Patients: please fill out form to page 2 dotted line**

**Patient Name:**

**Date:**

<table>
<thead>
<tr>
<th>Subjective: demographics and history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject's Date of Birth: ___ / ___ / ___</td>
</tr>
<tr>
<td>Sex: □ Male □ Female</td>
</tr>
</tbody>
</table>

## 1. Special considerations: please check all that apply:
- □ Pregnant or nursing
- □ Tobacco user
- □ Air travel more than 2x per month
- □ Routinely use a ceiling fan in bedroom
- □ Ocular surgery (LASIK, PRK, cataract surgery)
- □ Computer use more than 1 hour/day
- □ Allergies

## 2. Systemic medications (check all that apply):
- □ Birth control pills
- □ Beta blockers
- □ Diuretics "water pills" (LASIX)
- □ Antihistamines
- □ Anti-depressants
- □ Hormonal replacement therapy
- □ Nasal sprays
- □ Steroids
- □ Other

## 3. Ocular medications (check all that apply):
- □ Glaucoma drops
- □ Allergy drops
- □ Refract

## 4. Do you use artificial tears?:
- □ Yes □ No

## 5. If yes, how many times a day do you need them:
- □ 1x/day
- □ 2x/day
- □ 3x/day
- □ 4x/day
- □ > 4x/day

## 6. If yes, what type of artificial tears do you use?:
- □ Refresh tears
- □ Refresh Liquid
- □ Refresh Dry Eye Therapy
- □ System X
- □ System Free
- □ Steroids
- □ Other

## 7. Have you been diagnosed with dry eye?
- □ Yes □ No

## 8. Do you think you have dry eye?
- □ Yes □ No

## 9. Previous dry eye treatments:
- □ AT, punctual occlusion, lid scrubs/massages, Restasis, etc.

## 10. Successful (describe)?

## 11. Contact lens wear
- □ Yes □ No

If yes, lens and lens care information:

## 11a. Are you using contact lens solutions?
- □ Yes □ No

If yes, type of drop and how often?

## 12. Number of comfortable wearing hours: __________

## 13. Do you have dry eye symptoms when not wearing lenses?
- □ Yes □ No

## 14. Which of the following conditions have you been diagnosed with? (check all that apply):
- □ Thyroid disease
- □ Arthritis
- □ Diabetes
- □ Lupus
- □ Acne Rosacea
- □ Sleep disorders
- □ Sarcoidosis
- □ Facial Herpes Zoster (Shingles)
- □ MS
- □ Systemic syndrome: Psoriasis
- □ Acne Rosacea

## 15. How often do you experience dryness? Choose one: None Sometimes Frequently Always

**Notes:**
Dry eye work-up

Patient Name: ____________________________ Date: ____________________________

Subjective: Symptomatology

1. Do your eyes ever feel dry?
   • Never □ Rarely □ Sometimes □ Often □ All of the time □ ______

2. Do you ever feel a gritty or sandy sensation in your eye?
   • Never □ Rarely □ Sometimes □ Often □ All of the time □ ______

3. Do your eyes ever have a burning sensation?
   • Never □ Rarely □ Sometimes □ Often □ All of the time □ ______

4. Are your eyes ever red?
   • Never □ Rarely □ Sometimes □ Often □ All of the time □ ______

5. Do you notice much crusting on your lashes?
   • Never □ Rarely □ Sometimes □ Often □ All of the time □ ______

6. Do your eyes ever get stuck shut in the morning?
   • Never □ Rarely □ Sometimes □ Often □ All of the time □ ______

Total: ______
(score of greater than 7 indicates dry eye)

Scoring: Never = 0, Rarely = 1, Sometimes = 2, Often = 3, All of the time = 4.

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>AT THIS VISIT</th>
<th>WITHIN PAST 72 HRS</th>
<th>WITHIN PAST 3 MONTHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRYNESS, Grittiness or Scratching</td>
<td>YES □ NO □</td>
<td>YES □ NO □</td>
<td>YES □ NO □</td>
</tr>
<tr>
<td>Redness or irritation</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Burning or Watery</td>
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<tr>
<td>Eye Fatigue</td>
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Objective: Testing

Visual Acuity: (spectacles / unaided: circle one)

OD _______ OS _______

Fluorescein Tear Breakup Time: < 7 seconds is possibly dry / unstable

OD _____, _____, _____ Average _____ (90°) □
OS: _____, _____, _____ Average _____ (90°) □

Melbomian Gland Evaluation - Expression

OD: _______ OS: _______

Expression: 0 = normal, clear; 1 = opaque with normal viscosity; 2 = opaque with increased viscosity; 3 = severe thickening (toothpaste); 4 = no expression (glands totally blocked)

OSDI score: _______

Objective: Tear volume assessment

circle one:

Schirmer test
(amount of wetting in 5 minutes; < 5 mm = Aqueous Tear Deficiency)

without anesthesia

O.D. _______ (mm) Tape the strips/threads O.S. _______ (mm)

Phenol red thread test
(amount of wetting in 15 seconds; normal >15 mm)

with anesthesia

not for publication without permission 4/2006
Examination

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

EXAMINATION

- ADNEXA
  - Dermatological Inflammation
  - Dermatochalasis

- LIDS/ LID MARGINS
  - Infectious
  - Inflammatory
  - Allergic
  - Physiologic (Lagophthalmos)

DIAGNOSTIC TESTS

- EXTERNAL EXAMINATION

  - THE CRANIAL NERVE FUNCTION
    - For a 7th nerve palsy with 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

- SKIN
  - For Acne Rosacea
  - The nose/forehead for men
  - The cheeks for women
  - The eyelid margins for pustules, redness and teleangectasia

  - THE LID MARGINS
    - For blepharitis/meibomitis

Lid Disease

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

  - To be covered later in presentation

EXAMINATION

- CONJUNCTIVA
  - Goblet Cell function (ekc/post-op)
  - Staining
  - Mechanical abnormalities
<table>
<thead>
<tr>
<th>EXAMINATION</th>
<th>DIAGNOSTIC TESTS</th>
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<tbody>
<tr>
<td> CORNEA</td>
<td> TEAR EVALUATION</td>
</tr>
<tr>
<td> Staining</td>
<td> Tear Meniscus</td>
</tr>
<tr>
<td> Topographical</td>
<td> TFBUT</td>
</tr>
<tr>
<td> Hypoxia</td>
<td> Evidence of Fluorescein Staining</td>
</tr>
<tr>
<td> Secondary Infectious/Inflammatory</td>
<td> Tear Consistency-i.e. thickness,</td>
</tr>
<tr>
<td> Dystrophy</td>
<td>debris, evidence of meibomian</td>
</tr>
<tr>
<td></td>
<td>gland oil and sebaceous secretions</td>
</tr>
<tr>
<td></td>
<td> Shirmers</td>
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<thead>
<tr>
<th>DIAGNOSTIC TESTS</th>
<th>Schaeffer Shirmer</th>
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<tbody>
<tr>
<td> Schirmer--w/ or w/o anesthetic</td>
<td> Always do this as the last test</td>
</tr>
<tr>
<td> Phenol Red Thread Test</td>
<td> Place strip in any part of the eye</td>
</tr>
<tr>
<td> Zone Quick-represents fluid present in the conjunctival sac</td>
<td> Count to three</td>
</tr>
<tr>
<td> Fluorescein Staining</td>
<td> remove</td>
</tr>
<tr>
<td> Rose Bengal Staining</td>
<td></td>
</tr>
<tr>
<td> Lissamine Green Staining</td>
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<tr>
<td> Tear Osmolarity</td>
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<tr>
<td> Collagen Plugs</td>
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<tr>
<th>Tear Osmolarity</th>
<th>InflammaDry</th>
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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

- Increased concentrations of MMP-9 can be found in other diseases or conditions, including:
  - Ocular rosacea
  - Meibomian gland disease
  - Sjögren’s syndrome
  - Corneal ulcers
  - Corneal erosions

Importance of Detecting MMP-9

- Identifying elevated levels of MMP-9 facilitates better management of...
  - Patients who present with signs or symptoms of dry eye
  - Patients having ocular surgery such as LASIK or cataract surgery
- When elevated levels of MMP-9 are not tested, confirmed, and treated prior to ocular surgery, the following complications may occur:
  - Less accurate pre-surgical measurements lead to worse visual acuity outcomes
  - Mild dry eye becomes severe dry eye
  - Asymptomatic dry eye becomes symptomatic, chronic dry eye
  - Epithelial ingrowth or LASIK flap slippage

Normal Levels of MMP-9

<table>
<thead>
<tr>
<th>Study</th>
<th>Normal (ng/ml)</th>
<th>Elevated (ng/ml)</th>
</tr>
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<tbody>
<tr>
<td>Acera et al.</td>
<td>25.6</td>
<td>41.0</td>
</tr>
<tr>
<td>Chotikavanich et al.</td>
<td>6.7</td>
<td>14.0</td>
</tr>
<tr>
<td>Solomon et al.</td>
<td>7.2</td>
<td>8.0</td>
</tr>
<tr>
<td>Leonardo et al.</td>
<td>10.5</td>
<td>11.0</td>
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<tr>
<td>Lema et al.</td>
<td>8.9</td>
<td>8.0</td>
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<tr>
<td>Honda et al.</td>
<td>22.7</td>
<td>37.0</td>
</tr>
<tr>
<td>Velez-Fischer et al.</td>
<td>11.6</td>
<td>15.2</td>
</tr>
<tr>
<td>Total/Mean/Range</td>
<td>147</td>
<td>12.9</td>
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Literature meta-analysis supports that normal levels of MMP-9 (ng/ml) in human controls range from 3-41 ng/ml

MMP-9 and Dry Eye Severity

<table>
<thead>
<tr>
<th>Patient’s Dry Eye Dysfunction</th>
<th>Average MMP-9 Level</th>
<th>Statistical Significance vs Normal</th>
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</thead>
<tbody>
<tr>
<td>Normal (n=18)</td>
<td>8.39 ng/ml</td>
<td>No</td>
</tr>
<tr>
<td>Severity Level 1 (n=15)</td>
<td>35.57 ng/ml</td>
<td>No</td>
</tr>
<tr>
<td>Severity Level 2 (n=11)</td>
<td>66.17 ng/ml</td>
<td>Yes</td>
</tr>
<tr>
<td>Severity Level 3 (n=9)</td>
<td>101.42 ng/ml</td>
<td>Yes</td>
</tr>
<tr>
<td>Severity Level 4 (n=11)</td>
<td>381.24 ng/ml</td>
<td>Yes</td>
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</table>

If MMP-9 levels are greater than 30 ng/ml, risk of chronic dry eye is higher.

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.

1. Literature meta-analysis supports that normal levels of MMP-9 (ng/ml) in human controls range from 3-41 ng/ml
2. Matrix metalloproteinases (MMP) are proteolytic enzymes produced by stressed epithelial cells on the ocular surface.
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References:
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4. Literature meta-analysis supports that normal levels of MMP-9 (ng/ml) in human controls range from 3-41 ng/ml
5. Literature meta-analysis supports that normal levels of MMP-9 (ng/ml) in human controls range from 3-41 ng/ml
InflammaDry® Limit of Detection

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

POSITIVE TEST RESULT
MMP-9 ≥ 40 ng/ml

NEGATIVE TEST RESULT
MMP-9 < 40 ng/ml
InflammaDry 4-Step Process

Step 1 - Collect Sample
Gently dab the sample collector in 6-8 locations on the palpebral conjunctiva, until the fleece glistens, to collect a tear sample.*

Step 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.

Step 3 - Run Test
Immerse the absorbant tip into the provided buffer vial for 20 seconds. Replace the cap and lay the test flat on a horizontal surface.

Step 4 - Read Results
After 10 minutes, read the test results.

* Release the lid after every 2-3 dabs. Allow the sampling fleece to rest along the conjunctiva for 5 seconds.
InflammaDry Product Overview

- Detects elevated levels of MMP-9 in tear fluid
- Rapid: 10 minute results
- Easy to use: can be performed by a nurse or technician
- In-office: point-of-care immunoassay test aids in diagnosis at the time of office visit
- Low cost: no additional equipment required

InflammaDry Intended Use

InflammaDry is a rapid, immunoassay test for the visual, qualitative in vitro detection of elevated levels of the MMP-9 protein in human tears from patients suspected of having dry eye. InflammaDry is to be used to aid in the diagnosis of dry eye, in conjunction with other methods of clinical evaluation. This test is intended for prescription use at point-of-care sites.

Ocular Surface Disease Secondary to Systemic Disease

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

TBUT vs ABMD

Systemic Disease

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

Causes of Clinical Dry Eye
Developing a Specialty Ocular Surface Disease Practice

Lid Disease

We cannot treat the dry eye until we understand and treat
LWE
MGD
Blepharitis
Epiphora

IT IS ALL ABOUT THE LIDS

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

¹ Jackson 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

Cliradex®

• Contains the active component of Tea Tree Oil (4–Terpineol)
• Preservative-free
• Safe for daily use
• Effectively cleans lashes, eyelids, and the face
• Refreshing menthol feeling
• Great for individuals seeking to improve overall eye and skin health

BlephEx

Healthy Lids for Life!
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

Traditional Understanding of Sjögren’s
- The disease can present alone, classified as primary Sjögren’s, or subsequent to another autoimmune condition (e.g. rheumatoid arthritis), which is classified as secondary Sjögren’s.
- Sjögren’s is one of the most common autoimmune diseases.
- It currently takes 4.7 years to receive an accurate diagnosis.
- While the immune response is largely directed to the exocrine glands (lacrimal and salivary), systemic effects are seen in 30-70% of patients.

Overview and Summary

Recent Clinical Findings

The disease can present alone, classified as primary Sjögren’s, or subsequent to another autoimmune condition (e.g. rheumatoid arthritis), which is classified as secondary Sjögren’s.

It currently takes 4.7 years to receive an accurate diagnosis.

While the immune response is largely directed to the exocrine glands (lacrimal and salivary), systemic effects are seen in 30-70% of patients.

Clinical Presentation of Sjögren’s

Myth: “There are only a few patients in my practice”
- All layers of the tear film may be affected since Sjögren’s is a chronic, progressive disease.
  - Patient evaluation should include:
    - Medical and ocular history
    - Tear volume
    - Tear film distribution and stability
    - Clearance of the tear film

Traditional Serological Disease Markers for Sjögren’s

- The classical serological markers for Sjögren’s are anti-Ro/SS-A and anti-La/SS-B antibodies.
- Other antinuclear antibodies (ANA) and rheumatoid factors (RF) are also included as the more common serological markers detected.
- The combined serology sensitivity and specificity of the classical markers is around 40-60%.
- None of the currently recommended serology tests diagnose Sjögren’s early in the disease progression.
- In approximately 20-30% of cases no classic Sjögren’s antibodies are found.
**Myth:** “There are only a few patients in my practice”

- The ocular manifestation of Sjögren’s (primary or secondary) can present as aqueous-deficient dry eye alone, or in combination with evaporative dry eye\(^1,2\)
  - At least 25MM patients diagnosed with Dry Eye
  - Patients with Dry Eye symptoms see ECP first
- Major dry eye classification scheme\(^2\)

---

Prognosis for Sjögren's

- Disease progression can vary, so prognoses can also vary¹
  - Symptoms range from mild dry eyes/mouth to severe organ damage and/or lymphoma
  - Symptoms may remain stable, worsen or improve in cycles
  - As the disease progresses, debilitating fatigue and joint pain can significantly impair quality of life
- Early detection and treatment may assist in preventing complications²
- However, it currently takes 4.7 years to receive an accurate diagnosis²

 oyds range from mild dry eye/mouth to severe organ damage and/or lymphoma
- Symptoms may remain stable, worsen or improve in cycles
- As the disease progresses, debilitating fatigue and joint pain can significantly impair quality of life
- Early detection and treatment may assist in preventing complications²
- However, it currently takes 4.7 years to receive an accurate diagnosis²

Early Diagnosis/Intervention for Sjögren’s

- Ocular symptoms are frequently the first to present in patients with Sjögren’s, enabling ECP’s an opportunity to identify disease before systemic development
- Early diagnosis and treatment may delay the progression of disease¹
- Active research is ongoing for additional therapeutic options for Sjögren’s:¹,²
  - Biological therapeutic agents (e.g. monoclonal antibodies)
  - Antimalarials
  - Vitamin D supplementation
  - Immunosuppressants


Sjögren’s Syndrome

- Sjogren’s syndrome is currently defined by:
  - Ocular symptoms – dry eyes
  - Oral symptoms – dry mouth
  - Ocular signs – abnormal Schirmer’s test or Rose Bengal or Lissamine Green staining
  - Oral signs – decreased salivary gland flow
  - Histopathology showing lymphocytic infiltration of salivary or lacrimal glands
  - Autoantibodies – anti-RO antibody or anti-LA, ANA, RF
  - Exclude – hepatitis C, HIV, neck radiation, sarcoidosis, graft versus host disease, lymphoma, anti-cholinergic drugs
- Other manifestations include:
  - Lung disease – usually a lymphocytic interstitial pneumonia
  - Kidney disease – usually mild tubular disease, but may have glomerular disease
  - Peripheral neuropathy
  - Vasculitis involving skin, bowel, muscle, nerve and occasionally other organs
  - Vasculopathy, especially with secondary antiphospholipid antibodies
  - 5% of patients develop non-Hodgkin lymphoma

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

The Sjö™ In-Office Testing Kit
19 Year Old With Severe Dry Eyes?

D. B.
- 19 y. o. b. m. presents w mother c/o OU red and “infected” x 2 weeks, also very dry. Mother states last occurrence “tubes had to be put in”.
- PMHx: Mild “Behavioral” Cerebral Palsy, Epilepsy, Asthma, Deafness.
- POHx: L DCR w Crawford Tubes 2001 secondary to Dacryocystitis.

D. B.
- Allergies: Bactrim = Rash
- Meds: Depakote qd, Risperdal qd, Tylenol prn, Sudafed prn.
- Normal Pregnancy and birthweight.
- Dev. Milestones were delayed.

D. B.
- BVa: 20/40 OD, 20/50 OS
- Fundus: Normal OD, OS

Work Up
- CBC w/ Diff.
- LFTs
- Vitamin Panel

Treatment
- Pres. Free Tears q1-2h
- Topical Vitamin A ung 0.1% qid
- OTC Multi-vitamin qd
- Vitamin A 3000 mcg/d (10,000 IU)

### Lab Results

- **Vitamin A**: 22 (26-72 mcg/dL)
- **Vitamin B₁₂**: 159 (200-1100 pg/mL)
- **Vitamin D**: 12 (20-100 ng/mL)

### PCP Treatment

- Vit. B₁₂ injections
- Vit. D 400 IU qd OTC
- Continue Vit. A 10,000 IU qd

### Childhood Xerophthalmia

- Congenital
- Alacrima
- Ectodermal Dysplasia
- Allgrove Syndrome (Triple A)
- Cystic Fibrosis
- Endocrine
  - D. M.
  - Thyroid Dz

### Childhood Xerophthalmia

- Immunological
  - Sjogren Syndrome
  - GvHD
  - Juvenile Idiopathic Arthritis
- Dermatologic
  - Epidermolysis bullosa
  - Acne Rosacea
  - TEN (Toxic Epidermal Necrosis)

### Childhood Xerophthalmia

- Post Infectious
  - HTLV-1, EBV, HIV

- Medications
  - β blockers, Retinoids, Valproic acid**

- Nutritional
  - Malabsorption, Poor dietary habits**

### Vitamin A Deficiency

- Nyctalopia
- Xerophthalmia
- Bitot’s Spots
- Xerostomia
- Pruritis
- Anemia
- Humoral and Cell Med. Immune Dysfunction
- Excessive Bone Deposition
- Mortality
W. H. O.

- Most common cause of preventable blindness in the world.¹
- Est. 52,000 children go blind every year in India.²

¹. Severe malnutrition: report of a consultation to review current literature. Geneva, World Health Organization, 6-7 September 2004

Advanced Recalcitrant PEK

- Autologous Serum
- Amniotic Membrane

Autologous Serum

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

- 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 Cost

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

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
- Virology Testing $210
- Freeze and Shipment To/From Compounding Pharmacy
- Approximately $450 to $550 for 8 Vials

**Sutureless Amniotic Membrane**
- ProKera – Amniotic Membrane for wound healing
- Cryopreserved
- Bio Optix
  - Dry Membrane

**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

**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

Controlling Inflammation is Key to Preventing Tissue Damage!
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

Ocular Surface Disease

- Corneal Inflammation
  - Keratitis
- Conjunctival Inflammation
  - Conjunctivitis
- Eyelid Inflammation
  - Blepharitis
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 scar less 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

Post-Treatment Protocol

- Continue medications
- Apply Temporary Tarsorrhaphy (PRN)
- Tape:
  - "Breathe-Right" nasal strips
SCLERAL LENSES

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
  - Intracameral vs. punctal occlusion

LACRISERT®
(hydroxypropyl cellulose ophthalmic insert)

A Novel Approach to Treating Dry Eye Syndrome

Please see full Prescribing Information.

LACRISERT
(hydroxypropyl cellulose ophthalmic insert)

Indicated in patients with moderate to severe dry eye syndrome (DES), including keratoconjunctivitis sicca.

Indicated especially in patients who remain symptomatic after an adequate trial of therapy with artificial tear solutions.

Indicated for patients with exposure keratitis, decreased corneal sensitivity, and recurrent corneal erosions.

M G D
Meibomian Gland Dysfunction
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.”
DEWS—Classification of Dry Eye

- Aqueous-deficient
  - Sjogren Syndrome Dry Eye
    - Primary
    - Secondary
  - Non-Sjogren Dry Eye
    - Lacrimal Deficiency
    - Lacrimal Gland Duct Obstruction
    - Reflex Block
    - Systemic Drugs
- Evaporative
  - Intrinsic
    - Disorders of Lid Aperture
    - Low Blink Rate
    - Drug Action Accutane
  - Extrinsic
    - Meibomian Oil Deficiency
    - Vitamin A Deficiency
    - Topical Drugs Preservatives
    - Contact Lens Wear
    - Ocular Surface Disease eg, Allergy

Effect of the Environment
- Milieu Intérieur
  - Low blink rate behavior, VTU, microscopy
  - Wide lid aperture gaze position
  - Aging
  - Low androgen pool
  - Systemic Drugs: antihistamines, beta-blockers, antispasmodics, diuretics, and some psychotropic drugs
- Milieu Exterieur
  - Low relative humidity
  - High wind velocity
  - Occupational environment

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TFOS International MGD Workshop

Special Issue

The International Workshop on Meibomian Gland Dysfunction: Executive Summary

Kelly K. Nichols,1 Gary N. Foulks,2 Anthony J. Bron,3 Ben J. Glasgow,4,5 Murat Dogru,6 Kazuo Tsubota,7 Michael A. Lemp, and David A. Sullivan8,9

The 65 Most-Frequently Read Articles

Most-read rankings are recalculated at the beginning of the month and are based on full-text and pdf views.

1. Kelly K. Nichols, Gary N. Foulks, Anthony J. Bron, Ben J. Glasgow, Murat Dogru, Kazuo Tsubota, Michael A. Lemp, David A. Sullivan
   The International Workshop on Meibomian Gland Dysfunction: Executive Summary
   [in 'Special Issue'] [Full-Text] [PDF]
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2. Kelly K. Nichols
   The International Workshop on Meibomian Gland Dysfunction: Introduction
   [in 'Special Issue'] [Full-Text] [PDF]
   (Read 5318 times)

3. Edith Kneip, Takao Iio, Thomas Miller, Hidetoshi Ogita, David A. Sullivan
   [in 'Special Issue'] [PDF]
   (Read 4963 times)

   Meibomian Gland Dysfunction
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   (Read 9227 times)

5. Gest Geerling, Joseph Tauber, Christoph Beaulieu, Dik Oto, Yukihito Matsumoto, Terrence O'Brien, Mauro Ronco, Kazuo Tsubota, Kelly K. Nichols
   [in 'Special Issue'] [Full-Text] [PDF]
   (Read 3221 times)

6. J. Daniel Newton, Jun Shinagawa, Jose M. Becerra,* Carles, Jennifer P. Craig, James P. Culley, Senta Dem, Gary N. Foulks
   The International Workshop on Meibomian Gland Dysfunction: Report of the Diagnosis Classification Subcommitte
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   The International Workshop on Meibomian Gland Dysfunction: Report of the Clinical Trials Subcommittee
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8. Karl B. Green-Charles, Igne Bultynck, Mark Ruprecht, Douglas Borrmann, Friedrich Pausch, Stefan Brandt, Ben J. Glasgow
   The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittees on Sensitivity and Lipid-Protein Interactions in Health and Disease
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   (Read 2545 times)

   [in 'Special Issue'] [Full-Text] [PDF]
   (Read 2437 times)

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- 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
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

Tear Conservation

Meibomian Gland Disease

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
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 Dysfunction
Definition & Classification

J. Daniel Nelson, M.D. (Co-Chair)
Jun Shimazaki, M.D., Ph.D. (Co-Chair)
Jose M. Bentejo-del-Castillo, M.D., Ph.D.
Jennifer Craig, Ph.D., MCOptom
James P. McCulley, 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. Koh, O.D.
Shiro Anano, M.D., Ph.D.
Jarry R. Paagh, O.D.
E. Ian Irvine, Ph.D.
Richard Yee, M.D.
Norihiko Yokoi, M.D., Ph.D.
Reiko Araki, 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.
Yukito Matsumoto, M.D.
Terrence O’Brien, M.D.
Maurizio Rolandi, M.D.
Katushi Itobata, M.D.
Kelly K. Nichols, O.D., M.P.H., Ph.D.

Current Practice Patterns*

• Lid hygiene, warm compresses and lid massage
  • Cleaning of the lid margin with baby shampoo, cotton buds or wet towels, daily for 5-15 minutes
  • Lubricants in cases with additional dry eye
  • Topical antibiotic oint (moderate to severe)
  • Systemic tetracyclines/ derivatives in recurrence
  • Incision and curettage with optional steroid injection in chalazion

Meibomian Gland - ANATOMY

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


www.tearfilm.org
Meibomian Gland – PATHOLOGY

• Obstructive MGD leads to a progressive ductal DILATATION and acinar ATROPHY
What is MGD?

The Workshop defined MGD as follows:

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. This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease.
Testing Summary

- Symptoms (no validated survey)
- Expression (not widely accepted)
  - Quality/ Quantity
- Lid assessment
  - Redness (difficult to grade)
  - Irregularity
  - MG location
- Staining (fluorescein)
  - Photography
- Aq. Production (© 1903)
## Stages of MGD

<table>
<thead>
<tr>
<th>STAGE</th>
<th>CLINICAL DESCRIPTION</th>
<th>TREATMENT</th>
</tr>
</thead>
</table>
| **STAGE 1** | No symptoms of ocular discomfort, itching or photophobia  
Clinical signs of MGD based on gland expression  
Minimally altered secretions: Grade ≥2 - <4  
Expressibility: 1  
No ocular surface staining | Inform patient about MGD, the potential impact of diet and the effect of work/home environments on tear evaporation, and the possible drying effect of certain systemic medications  
Consider eyelid hygiene including warming/expression as described below (a) |
| **STAGE 2** | Minimal to mild symptoms of ocular discomfort, itching or photophobia  
Minimal to mild MGD clinical signs  
Scattered lid margin features  
Mildly altered secretions: Grade ≥4 - <8  
Expressibility: 1  
None to limited ocular surface staining (DEWS grade 0-7; Oxford grade 0-3) | Advise patient on improving ambient humidity; optimizing workstations and increasing dietary omega-3 fatty acid intake (a)  
Institute eyelid hygiene with eyelid warming (a minimum of four minutes, once or twice daily) followed by moderate to firm massage and expression of MG secretions (+)  
All the above, plus (a)  
Artificial lubricants (for frequent use, non-preserved preferred)  
Topical enollentor lubricant or liposomal spray  
Topical azithromycin  
Consider oral tetracycline derivatives |
| **STAGE 3** | Moderate symptoms of ocular discomfort, itching or photophobia with limitations of activities  
Moderate MGD clinical signs  
† lid margin features: plugging, vascularity  
Moderately altered secretions: Grade ≥8 - <13  
Expressibility: 2  
Mild to moderate conjunctival and peripheral corneal staining, often inferior (DEWS grade 8-23; Oxford grade 4-10) | All the above, plus  
Oral tetracycline derivatives (+)  
Lubricant ointment at bedtime (a)  
Anti-inflammatory therapy for dry eye as indicated (a) |
| **STAGE 4** | Marked symptoms of ocular discomfort, itching or photophobia with definite limitations of activities  
Severe MGD clinical signs  
† lid margin features: dropout, displacement  
Severely altered secretions: Grade ≥13  
Expressibility: 3  
Increased conjunctival and corneal staining, including central staining (DEWS grade 24-33; Oxford grade 11-16)  
† Signs of inflammation: e.g. ≥ moderate conjunctival hyperemia, phlyctenules | All the above, plus  
Anti-inflammatory therapy for dry eye (+) |

**Keys:**
- Meibum quality is assessed in each of 8 glands of the central third of the lower lid on a 0-3 scale for each gland: 3=clear meibum; 2=cloudy meibum; 1=cloudy with debris (granular); 0=thick, like toothpaste (range 0-24).
- Expressibility of meibum is assessed from 5 glands: 0=all glands expressible; 1=2-4 glands expressible; 2=1-2 glands expressible; 3=0 glands expressible. This can be assessed in the lower or upper lid.
- Numerical staining scores refer to a summed score of staining of the exposed cornea and conjunctiva. The Oxford scheme has a scale range of 0-15 and the DEWS scale has a scale range of 0-33.
<table>
<thead>
<tr>
<th>Stage</th>
<th>MGD grade</th>
<th>Symptoms</th>
<th>Corneal Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+ (minimally altered expressibility and secretion quality)</td>
<td>Asymptomatic</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>++ (mildly altered expressibility and secretion quality)</td>
<td>Minimal to Mild</td>
<td>None to limited</td>
</tr>
<tr>
<td>3</td>
<td>+++ (moderately altered expressibility and secretion quality)</td>
<td>Moderate</td>
<td>Mild to moderate; mainly peripheral</td>
</tr>
<tr>
<td>4</td>
<td>++++ (severely altered expressibility and secretion quality)</td>
<td>Marked</td>
<td>Marked; central in addition</td>
</tr>
</tbody>
</table>

“PLUS DISEASE” Co-existing or accompanying disorders of the ocular surface and/ or eyelids
Current Practice Patterns

- World-wide variation
  - Underreporting → difficult to assess patterns
  - Underdiagnosis common, clinical follow-up irregular
- Lid warming and hygiene common
- Many use artificial lubricants
- Most Common Rx: Systemic tetracycline or derivatives (less frequent in EU/Japan)
  – 2nd most common Rx: topical antibiotic or antibiotic-steroid combination

Recommended Staged Therapy

Stage 1

- Inform patient about dietary/environmental/medication effects
- Lid hygiene (warming/expression)

Stage 2

- Oral tetracyclines
- Ointment (pm), cyclosporine/steroid for DE
- Anti-inflammatory therapy for DE
- Steroids, CL, surgery

Stage 3

Stage 4

Existing Clinical Trials

<table>
<thead>
<tr>
<th>Key Issues</th>
<th>Findings</th>
<th>n = 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial objective</td>
<td>Majority interventional treatment trials. 1/3 comparative (hot compresses or artificial tears).</td>
<td></td>
</tr>
<tr>
<td>Trial design/Methodology</td>
<td>Primarily small trials (&lt;40 subjects) of short (&lt;3 months) duration. Most prospective, 3 randomized controlled design, 2 were double masked.</td>
<td></td>
</tr>
<tr>
<td>Study population</td>
<td>Chronic disease but selection criteria not uniformly defined; lid changes &amp; symptoms most common clinical characteristics.</td>
<td></td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>No specific and consistent criteria; most common are lid margin signs (80%), dry eye findings (50%), symptoms of discomfort/foreign body sensation (46%).</td>
<td></td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>Classification of exclusion criteria in three different categories: 1) Ocular disease related/CL wear (most common); 2) Iatrogenic (e.g. surgery, 1/3 studies); 3) Systemic disease related/pregnancy (12%).</td>
<td></td>
</tr>
</tbody>
</table>

Design and Conduct of Clinical Trials

Penny A. Asbell, M.D. (Chair)
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Kerstin Wickström, Ph.D.
Esen Akpala, M.D.
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Michael A. Lamp, M.D.
Kelly K. Nichols, O.D., M.P.H., Ph.D.

Meibomian Glands

Modified sebaceous gland
- 30-40 glands exist in upper tarsus
- 20-40 glands exist in the lower tarsus
- Secretion stimulus not fully understood
  - Secretion of meibomian oil increases with testosterone; decreases with estrogen
  - Oil expelled by mechanical force on gland during blinking
  - Not all glands secreting simultaneously

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
Structure of a Stable Tear Film

Nonpolar Lipid layer
Amphiphilic Lipid Layer  - complex - over 100 different species of lipid

Aqueous/Mucin complex  - mucins are distributed throughout this layer, rather than in distinct aqueous and mucin layers

Glycocalyx  - mucin bound complex responsible for the integration of aqueous layer with corneal epithelium

Corneal Epithelium
Structure of the Lipid Layer

Two-Phase Lipid Layer Model

- HC-Hydrocarbon
- WE- Wax Ester
- CE-Cholesterol Ester
- TG- Triglyceride
- F-Free Fatty Acid
- C-Cerebroside
- P-Phospholipid

MGD TREATMENT

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

---

**BRUDER EYE COMPRESSIONS**

*Microwave Activated*

Bruder Eye Hydrating Compress and Styre Compress conveniently provide an effective yet natural and drug-free way to help provide and maintain proper eye moisture.

**Benefits**
- Replenishes Moisture Naturally
- Relieves Dryness
- Refreshes Tired Eyes
- Provides Drug Free Relief

**Features**
- Ready in Minutes from the Microwave
- Washable & Reusable
- Clean Heat Head
- Soft Conforming Design
- Non-Allergenic
- Dust-Free

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

---

**Meibomian 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

**MGD EXPRESSION**

Fees: $189 / $25

- Out of pocket
- 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
The Greatest Anterior Segment Disease and Contact lens complications course ever

Jack Schaeffer OD FAAO

Dilation Vs Optomap

• The two together delivers the highest level of Comprehensive Eye Care

• If you have to choose just one: DILATE, DILATE, DILATE

Telephone Consultations

30 YO WF

Telephone symptoms:
sore upper lid, painful spot on lid

Internal Hordeolum??

Ready to Dx on telephone: decided to see the patient

Bacterial Conjunctivitis?

Extremely Tender Upper lid
Upper lid swelling
Excessive Mucous production

Bacterial Conjunctivitis
Orbital Cellulitis?

Tx:
PO

Augmentin PO 875 Mg Bid

Ocular
Zymaxid OS q 2 h
Day 2

Facial Pain  Headache
Fever
Referral to PCP, R/O Orbital Cellulitis
Dx Severe Sinus infection:
Contd Meds PO (Augmentin)
Antibiotic Injection in office
Sinus infection
Lid swelling with Pain

Lid Disease- Infection

Treatment
- Keflex 500 Mg BID
  - Cephalexin
- Bactrim: double strength: BID
  - Trimethoprim/ Sulfamethoxazol
- Augmentin 875 mg BID
- Miboflow
- Hot compress (Written instructions)

Caniliculitis/Dacryocystitis

MiBoFlow

Treatment
- Keflex 500 Mg BID
  - Cephalexin
- Bactrim: double strength: BID
  - Trimethoprim/ Sulfamethoxazol
- Augmentin 875 mg BID
- Hot compress (Written instructions)
- MiBo Flow
Doctor number 3

- 68 YO female
- Pain discomfort 2 years OU
- OD > OS
- 3 rd doctor

Concretions (lithiasis)

- White to yellow nodules superficially buried within and beneath the palpebral conjunctiva
- Asymptomatic unless enlarge, protrude
- Pathophysiology- inclusion cysts filled with keratin and epithelial debris- very little

<table>
<thead>
<tr>
<th>Concretions only n=35</th>
<th>Concretions + MGD n=15</th>
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</thead>
<tbody>
<tr>
<td>Severe Dry Eye</td>
<td>43%</td>
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<tr>
<td>TBUT &lt; 10 seconds</td>
<td>51%</td>
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</tbody>
</table>

Bruder Instrument Trays

Autoclavable instrument trays are ideal for instrument storage or transport. Available in two convenient sizes.

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 30 minutes.
- Sanitizes in 30 seconds.
- Electrical.

BRUDER Surgical Instrument Line

Melibomian Gland Expression Set

Item #98610 COLINGS Expressor Forceps

GERMAN STAINLESS
For mild to aggressive expression of Meibomian gland. 95mm Forceps with closed paddles.

Item #98620 LIVENGODD Expression Paddle - Angled

GERMAN STAINLESS
For mild or gentle expression of the Meibomian gland. 75mm oval blades with 12 degree angle. Non-slip knurled handle.

Item #98630 LIVENGODD Expression Paddle - Straight

GERMAN STAINLESS
For mild or gentle expression of the Meibomian gland. 75mm flat oval blades. Non-slip knurled handle.
### BRUDER Surgical Instrument Line

- Item #98703 BRUDER Jeweler Forceps 3
- Item #98704 BRUDER Jeweler Forceps 4
- Item #98705 BRUDER Jeweler Forceps 1
- Item #98707 BRUDER Jeweler Forceps 7

Broder Surgical Instruments ship in storage cases.

### ?
- We will discuss this later

### HZO
- More on Zoster later

### Allergic Dermatitis
- Elocon
- Mometasone Crème
- Lotemax ung

### Corneal Toxicity
Organic Soap splashed in eye
Moroccan Oil based soaps

### Trauma
**Corneal Abrasion**

- Debridement of the Cornea
- Techniques
- Instruments
- Bandage Contact lenses

---

**Amniotic Membrane (AM): An Emerging Clinical Option**

- Amniotic membrane is the innermost lining of the placenta and shares the same cell origin as the fetus
  - AM Contains cytokines and growth factors
- **Cryopreserved/Active** amniotic membrane is a biologic therapy that:
  - Promotes regenerative healing
  - Reduces inflammation
  - Minimizes scar formation
  - Inhibits angiogenesis
  - Minimizes pain

---

**BRUDER Surgical Instrument**

- Item #98650: **BRUDER Epilation Forceps**
  - These forceps feature non-slip jaws/tips and an easy-grip, no slip handle for precise eyelash removal. German stainless.
- Item #98651: **KARPECKI Punctal Plug Forceps**
  - This instrument has a groove on the inside tip 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 #98652: **KARPECKI Bandage Lens Forceps**
  - This instrument has a narrow, but rounded tip. The application of a special coating instead of serration assures the bandage will not slip when being removed. Slide the forceps under the edge of the bandage lens and easily pick it off the eye. German stainless.
- Item # 98653: **KARPECKI Debrider**
  - The instrument has a slightly curved tip with a “crisp” edge on both sides. The edge is just right to remove the keratin easily by sliding the instrument, curve forward, along the eyelid in a single direction. German stainless.

---

**Product Specifications**

<table>
<thead>
<tr>
<th>Product</th>
<th>Prokera®</th>
<th>Prokera®</th>
<th>Prokera® Plus</th>
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<td>Dual Ring System (polycarbonate)</td>
<td>Dual Ring System (polycarbonate)</td>
</tr>
</tbody>
</table>

---

**Key Amniotic Membrane Components**

- Extracellular matrix (ECM) components found in cryopreserved amniotic membrane regulate and promote regenerative tissue processes
  - Heavy chain hyaluronic acid
  - Proteoglycans
  - Growth factors
  - Collagens (types I, III, IV, V and VI)
  - Fibronectin
  - Laminin

---

**Recommended Treatment Tips**

**Pre-Treatment**

- Rinse PROKERA® with saline to prevent stinging from preservation media
- Topical medications may be used while the PROKERA® is place (PRN)
- Temporary Tarsorrhaphy (PRN)
  - Tape
  - “Breathe-Right”
  - Nasal Strips

**Post-Treatment**

- Follow-up within 1 week (10 day global period)
- During the healing process the membrane will thin or dissolve
- PROKERA® is easily removed in the office once the healing is completed
Developing a Specialty Practice

Cornea Disease

Recurrent Erosion

• 44 y. o. w. f. c/o 2 wk hx fbs / pain OS
• PCP tx w/ Gentamicin OS tid x 12 days
• Pain is worse today Va affected
• Pt c/o similar sx in past lasting days.
• 20/25 OD, 20/60 OS w/o Rx
• First Eye Exam!

Recurrent Erosion

EBMD / ABMD

Two unusual cases

• 1) 49 yo female
  – RCE 10 years ago OS, loss of 90% epithelium
  – Finger nail
  – 2008 OD ?? RCE vs ABMD

Case 2

• 50 YOF
• Woke up with discomfort
• Feels like something is in my eye
Case 2
- 2) 38 yo Female Pediatric Psychiatrist
  - Enjoy the slides
  - You make the choice
  - RCE vs ABMD

78 YOF
- Hx
  - Glaucoma
  - Dry Eye
  - EBMD

Case 3
- My eye really hurts!!

Treatment Strategy
- ABMD
- RCE

Recurrent Corneal Erosion
- NaCl Ung Pm
  - Muro 128

- PF AT
  - Q 1-2 hours

Recurrent Corneal Erosion
- Azasite
  - Bid 1 week
  - Qd 1 month

- Doxycycline
  - 50 mg bid 2 weeks
  - 20 mg qd 1-2 months
Recurrent Corneal Erosion
Long Term Therapy

- Restasis
  - Tid
- Fresh –Kote
  - Qid
- Lacriserts ?

• Treatment
• Nsaid
• Bandage Contact lens
  - Antibiotic??
  - How often
  - RTC daily until healed
  - Remove and fresh lens and leave in place 3 days?

Recurrent Corneal Erosion

• Bandage Contact lenses
• Antibiotic ung
• Change lens how often
• See patient how often

Bacte-viral Conjunctivitis?

- 66 y. o. b. m. c/o 3 d hx of “running, redness, soreness”, OS. AT no help.
- Bilat. Pseudophakia
- No meds., chronic sinusitis.
- 20/20 OD, 20/40 OS, IOP 16,22.
- (-) PAN

? Bacterial Conjunctivitis?

- Tx: Besivance OS qid
  Zithromax 250 mg 5 d dose pk
- 2 d F/U: 20/50 Va, dec. mucopurulent discharge, 2+ chemosis / injection, (+) PAN.
- Tx: Besivance qid, finish Zithromax
?Viral?
- 5 d F/U: OS “still swollen but not as sore”. Pt. thinks OD is “catching the infection”.
- OD 20/25, OS 20/40
- Mild follicles OU
- SEIs OU

EKC
- 7d: 20/30 OD, OS
- Resolving SEIs
- IOP: 20, 21
- 14d: 20/20, 20/25
- Mild SEI OS, OD clear
- IOP 16, 17
- D/C Durezol OU

Take Home
- Follow your instincts.
- If it looks bacterial tx it as such.
- Treat aggressively.
- If clin. pic. changes, change with it.
- Patients can have two pathological conditions at the same time.

Epidemic Keratoconjunctivitis

RPS Adeno Detector
- Prospective, masked, multi-center clinical trial in U.S. and Europe
- 186 consecutive patients examined all cases of acute conjunctivitis and compared to both cell culture and PCR
- 25% of all acute conjunctivitis confirmed as Adenovirus
- RPS Detector
- 89% Sensitive vs. 91% Cell Culture
- 94% Specificity vs. 100% Cell Culture

Four Step Test Process
- Step 1: Collect Sample
- Step 2: Transfer sample to strip
- Step 3: Dip test cassette into buffer solution for 15 seconds
- Step 4: In less than 10 minutes read test results (RPS Adeno Detector showing a positive result for Adenovirus (2 red lines))
Common Adeno Symptoms
- Colds
- Pharyngitis
- Bronchitis
- Pneumonia
- Diarrhea
- Conjunctivitis
- Fever
- Cystitis

HEKC
- A new type of acute keratoconjunctivitis developed throughout Southeast Asia*
  - Singapore in the summer of 1970.
  - It was highly contagious and probably was transmitted from person to person by the hand to eye route.
  - Sixteen cases, diagnosed by viral isolation or serologic study, or both.


Similar to EKC
* Adeno are non-enveloped, double-stranded DNA
* Non-enveloped enhances transmission by allowing prolonged survival after dissipation
* On dry surfaces, steel, viruses remain infective up to 5 weeks
* Penetrate normal barriers to infection
* Less than 5% of the US population have antibodies effective against any given serotype

Treatment EKC
- 1 lubricants
- 2 combo antimicrobial / steroid
- 3 Steroid
- 4 Betadine
- 5 Zirgan

Zirgan™ (ganciclovir ophthalmic gel) 0.15%
Indication and Usage
- Zirgan is a topical ophthalmic antiviral that is indicated for the treatment of acute herpetic keratitis (dendritic ulcers).

Important Risk Information
- Zirgan is indicated for topical ophthalmic use only.

Please see full prescribing information for Zirgan® provided at this presentation.
Zirgan™ (ganciclovir ophthalmic gel) 0.15% Dosage and Administration

- The recommended dosing regimen for Zirgan is 1 drop in the affected eye 5 times per day (approximately every 3 hours while awake) until the corneal ulcer heals, and then 1 drop 3 times per day for 7 days.

Please see full prescribing information for Zirgan® provided at this presentation.

Zirgan

- 1 drop 5x/day until ulcer “heals”
- Then 1 drop tid for 7 days
- 5 gram tube, available early 2010

EKC treatment Melton/ Thomas

- Povidone- Iodine 5% (betadine)
  - Broad spectrum microbiocide
  - Indicated for “Irrigation of the ocular surface”
  - OFF LABEL USE
    - Anesthetize with proparacaine
    - Instill 1-2 drops NSAID
    - Instill several drops of betadine in eye (close eye)
    - Swap excess over lid margin
    - After one minute irrigate with saline
    - Instill 1-2 drops NSAID
    - Rx Lotemax or Zylet or Tobadex ST qid 4 days
    - No reports of adverse reactions
    - Avoid if allergic to iodine
    - Betadine 5% ophthalmic prep soln (30 ml opaque)
    - 99070 supply code

19yoF Red Eye OD

- Red Eye x 3 days with no pain, today was the first day with irritation
- Recently had Staph infection in leg, off antibiotics less than a week ago (Bactrim)
- VA sc 20/20- OD 20/25 OS

Treatment

- Zylet qid OD
- RTC 1 day
- Some improvement over the new few days, but minimal.

Treatment

- D/c Zylet qid OD, begin Besivance q1h OD
- Differentials?

Pt showed significant improvement, at 1-day follow up.
Differentials?
- Herpes Simplex Keratitis
- Adenovirus
- Solution Hypersensitivity
- MRSA
  - Remember staph in infection leg treated with Bactrim
- Nursing student

What's Next?
- Diagnosis
- Treatment

Thygessons
- Possible Thygeson's
  When all else fails: Thygessons Vs HSV
- Discontinue ALL meds

Thygeson's SPK
- Described by Phillips Thygeson in 1950
- Slightly elevated corneal lesions, minimal staining
- Usually bilateral, Second to third decade
- Noted corneal sensitivity decreased but not as severe as herpes
- Mild conjunctival involvement, worse with exacerbations
- Appearance similar to EKC described by Fuchs

Thygeson's SPK
- Lesions in basal epithelial layer / Bowman's layer
- Debris from necrosis / degenerated epi cells
- Increased Langerhans cell density
- Part of inflammatory response - Type II
Thygeson’s SPK Treatment: Anecdotal

• Cyclosporin 2% in olive oil (8 patients)
• Supratarasal injection triamcinolone (1 case-chronic 6+ years)
• Trifluridine (6 eyes)
• PRK in myopic patient had lesions recur in periphery (untreated area) vs central (treated area)
• Rimexolone 1% for reversing dendritic cell density (4 patients)

Thygeson’s SPK

• Steroid Use
  • Loteprednol 0.2%, 0.5%
  • Cyclosporine 0.05% Long Term

Back to the case…

• D/c All meds
• Lesions healed in 1 week
• No recurrences since October

Plaquenil Keratopathy

Vortex Keratopathy or Cornea Verticillata

Clinical features:
• Symptoms: the corneal changes are rarely of any visual significance.
• Signs:
  – Symmetric, bilateral, whorl-like pattern of powdery, white, yellow or brown corneal epithelial deposits
  – Appears in a vortex fashion in the inferocentral cornea and swirls outwards sparing the limbus
• Occurs in Fabry’s disease and in patients being treated with a variety of drugs including amiodarone, chloroquine, amodiaquine, meperidine, indomethacin, chlorpromazine and tamoxifen.

Staph. Hypersensitivity

• Treatment
  – Warm compresses
  – Lid hygiene with commercial lid cleanser
  – Broad spectrum topical antibiotic
  – Antibiotic ointment
  – Topical steroid*
  – Oral tetracycline antibiotics if >10 y. o.

**Staphylococcus Hypersensitivity**

- 58 YOM
- Custom Toric Soft C/L
  - +4.00-3.00
  - +3.00-375
- Pain OS 4-5 days
- Presents wearing CL

**Phylctenular Kerato-Conjunctivitis**

**PKC / Staph. Hypersensitivity**

- Non-infectious hypersensitivity
- Phlyctenules (phlyctena)
  - histiocytes, lymphocytes, plasma cells, neutrophils
- Microbial association
  - Staph. Aureus
  - Myco. Tuberculosis
  - Chlamydia trachomatis
  - Neisseria gonorrhoea
  - Coccidiodes immitis
  - Bacillus spp.
  - Herpes simplex virus
  - Leishmaniasis Ascaris lubricoides
  - Hymenlepis nana
  - Candida spp.

**Differential Diagnosis**

- Staphylococcal keratitis with phlyctenule
- Microbial keratitis (Mycobacterium tuberculosis)
- Inflamed pterygium
- CIN (Conjunctival Intra-epithelial Neoplasia)
- Chronic FB

**Phlyctenular Kerato-Conjunctivitis**

- Tx: Pred Forte OD q2h x 2 d then qid, Gatifloxacin OD qid x 1 wk., warm compresses, lid hygiene.
- D/C topical allergy meds.
- Doxycycline 50mg bid x 2 mo.
- PPD (-)
Glaucoma

- A degenerative disease of the optic nerve characterized by ganglion cell axon death, excavation of the optic nerve, nerve fiber bundle defects and visual field loss.

- Primary vs. secondary vs. developmental
- Open angle vs. closed angle

Glaucoma in Review
Ashley M. Speilburg, OD, FAAO

### PRIMARY GLAUCOMAS

- **Open Angle Forms:**
  - Primary Open Angle Glaucoma
  - Low Tension Glaucoma

- **Closed Angle Forms:**
  - Primary Angle Closure
    - Acute Angle Closure
    - Plateau Iris Configuration
    - Plateau Iris Syndrome

### SECONDARY GLAUCOMAS

- **Open Angle Forms:**
  - Neovascular Glaucoma
    - ICE syndrome
    - Posterior polymorphous dystrophy
    - Epithelial downgrowth
    - Fibrous downgrowth
    - Inflammatory membranes
  - Malignant tumors
    - Neurofibromatosis
    - Juvenile xanthogranuloma
    - Pigmentary Glaucoma
    - Exfoliation (pseudoexfoliation)
    - Malignant melanoma
    - Uveitis
    - Lens induced glaucoma
    - Alpha-chymotrypsin
    - Vitreous in anterior chamber
    - Healon post-surgical Edema
    - Glaucomacyclitic crisis
    - Scleritis
    - Alkali Burn
    - Angle recession glaucoma
    - Intraocular foreign bodies
    - Steroid induced glaucoma
    - Carotid cavernous fistula
    - Cavernous sinus thrombosis
    - Retrobulbar tumors
    - Graves disease
    - Superior vena cava obstruction
    - Medialetal tumors
    - Senior-Wilson syndrome
    - Fuchs dystrophy, pressure rise

- **Closed Angle Forms:**
  - Neovascular Glaucoma
  - ICE syndrome
  - Posterior polymorphous dystrophy
  - Trauma
  - Uveitis
  - Aniridia
  - Miotic induced Phacomorphic
  - Subluxed lens
  - Aphakic or pseudophakic Iris bombe due to 360 degrees of posterior synechia
  - Malignant glaucoma (ciliary block glaucoma)
  - Choroidal detachment / Choroidal effusion
  - Melanoma
  - Retinoblastoma
  - Cysts of iris and ciliary body

- **DEVELOPMENTAL GLAUCOMAS**
  - **Primary developmental glaucomas:**
    - Congenital glaucoma
    - Juvenile glaucoma
  - **Secondary developmental glaucomas:**
    - Retinopathy of prematurity
    - Post-traumatic
    - Tumor related
    - Inflammatory induced
    - Neovascularization
    - Rubella
    - Sluder-Walker syndrome

### GLAUCOMA SECONDARY GLAUCOMA

- Glaucomatous damage from increased IOP that is a direct result of some other ocular or systemic abnormality.
  - Pigmentary
  - Exfoliation
  - Angle recession
  - Neovascular
  - Uveitic
  - ICE syndromes

### PRIMARY OPEN ANGLE GLAUCOMA

- Chronic Open Angle Glaucoma or Open Angle Glaucoma
- Characterized by:
  - Adult onset
  - IOP >21 mmHg
  - Open angle of normal appearance
  - Glaucomatous optic nerve damage
  - Characteristic visual field loss
Normal Tension Glaucoma

- Low Tension Glaucoma
- Characteristic optic nerve and visual field changes in the absence of IOP over 21mmHg.
- Up to 33% of open angle glaucoma
- Few unique features
  - PPA
  - Disc hemorrhages
  - h/o migraines
  - h/o reynaud's phenomenon

Ocular Hypertension

- IOP repeatedly > 21 mmHg in the absence of glaucomatous optic nerve damage, visual field loss and RNFL defects.
- 7% of population over 40 have IOP > 21 mmHg
  - Only ~1% of which have glaucoma
- 10% of OHTN will develop POAG at 5 years

Gonioscopy!

- To properly diagnose any type of glaucoma gonioscopy is key!
- Open angle vs. closed angle
- Primary vs. secondary

Risk Factors

**Ocular**

- IOP
- Pachymetry (CCT)
- Optic nerve
- Myopia (high)

**Non-ocular**

- Older age
- Race
- Family History
- Diabetes
- Hypertension (or rather over treatment of HTN)
- OPP

Age

- Prevalence for glaucoma increases with age
  - 1% < 40 yo
  - 3-8x higher > 70 yo
- Longer exposure to high IOP?
- Other factors (vascular, connective tissue integrety)

Race

- Baltimore Eye Study
  - 1.7% vs. 5.6% at 40+
  - 11% at 80+
- St. Lucia Study
  - Caribbean blacks 14%
- LALES
  - Latinos 5% (8% 60-70yo ; 15% 70+)
**Age-Specific Prevalence of OAG Among Blacks, Whites, and Hispanics**

![Graph showing age-specific prevalence of OAG among different races.](image)


**Family History**

- **Rotterdam Study:**
  - Lifetime risk of glaucoma at age 80 was 10x higher for individuals with relatives having glaucoma
  - The more family members of closer relation with glaucoma, the greater the risk to the individual

**Diabetes & Hypertension**

- DM - overall 1.35x risk
- HTN – no association to protective
  - Over-treatment real issue → low OPP

**Ocular Perfusion Pressure**

- Risk for development
- Risk for progression
- **LALES**
  - Low DPP/SPP had higher risk of POAG
  - DOPP <50 mmHg, rapid increase in prevalence

**IOP**

- Single most important risk factor
- Strongest correlation to glaucoma
  - Higher the IOP, greater the risk
- Not the whole story
  - NTG, OHTN

**“Normal” IOP**

- “Normal” = description of IOP distribution in the population.
- Mean IOP 15.4 +/- 2.5 SD
- Range: 11-21 mmHg
- Always measured via Goldmann tonometry
- Better definition: Pressure at which optic nerve damage does not occur
Characteristics of IOP

- Increases slightly with age
  - Normal change not associated with the development of glaucoma
- Symmetrical between eyes:
  - ~2-4 mmHg
  - Greater than this can be a sign of disease
- Diurnal fluctuation (4-6mmHg)
  - Exaggerated in glaucoma patients
  - Highest in overnight hours
  - Single IOP measurement in office is insufficient

Pachymetry

- Thinner CCT increases risk of POAG in patients with OHTN
  - Anatomic “weakness”?
  - True IOP higher than measured
- Still a factor in NTG
  - How much?

The Ocular Hypertension Treatment Study (OHTS)

Supported by the National Eye Institute, National Center on Minority Health and Health Disparities, Research to Prevent Blindness, and Merck Research Laboratories


OHTS

- Provided solid evidence that lowering IOP in patients with OHTN reduces the risk of developing POAG.
- Identified risk factors associated with the development of glaucoma.

OHTS and Corneal Thickness

- Treatment reduced risk of development of glaucoma from 9.5% (observation arm) to 4.4% (treatment arm) at 5 years.
- Treatment: 20% reduction and ≤24 mmHg
  - Modest goal

For all IOP’s, a thinner cornea increased the risk of developing glaucoma at 5 yrs

<table>
<thead>
<tr>
<th>CCT Microns</th>
<th>&lt;555</th>
<th>&gt;555-&lt;588</th>
<th>&gt;588</th>
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<tbody>
<tr>
<td>&gt;25.75</td>
<td>36%</td>
<td>13%</td>
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<tr>
<td>&gt;23.75-&lt;25.75</td>
<td>12%</td>
<td>10%</td>
<td>7%</td>
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<tr>
<td>&lt;23.75</td>
<td>17%</td>
<td>9%</td>
<td>2%</td>
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</table>

High risk
Low risk
OHTS Risk Factors

- **Age:** 20% to 40% increase per decade
- **IOP:** > 26 mmHg
- **Vertical C/D:** > 0.5
- **CCT:** < 555 µm

OHTS Conclusions

- **Conclusions:**
  - In patients with elevated IOP, topical ocular hypotensive treatment was effective in delaying the probability of onset of POAG.
  - For patients with a moderate to high risk of developing POAG, IOP-lowering treatment should be considered. This does not imply that all borderline or elevated IOP patients should receive treatment.
  - Some predictors of developing POAG were found to be: baseline IOP, age, vertical cup-to-disc (C/D) ratio, and lower central corneal thickness.

Optic Nerve

- **C/D ratio, RNFL, NRR**
- **Associate with increased vertical C/D ratio**
  - No single cut off for C/D
  - Larger cup in larger discs
- **Asymmetry**
- **Focus on integrity of NRR and RNFL**

Myopia?

- **2x more common among POAG**
  - Selection bias?
- **Very high myopia (>14D) are high risk**
  - Flat, obliquely inserted
  - VF confounded by retinopathy in MD

Global Risk Assessment

- **What is global risk assessment?**
  - Estimates a patient’s overall risk based on multiple rather than a single risk factor
  - Ideally based on evidence from well-controlled clinical trials and long-term studies
- **How is it used?**
  - Helps guide treatment decisions for optimal patient care

Global Risk Calculator for OHTN

- **Enhanced accuracy of identifying those most at risk for POAG**
  - Individualize who is treated
  - Developed from OHTS study data
- **Identify the global risk of developing glaucoma in next 5 years**
- **Identify who will benefit from treatment vs those who only need observation**

---

Online OHTS Risk Calculator

- 5 key risk factors considered

<table>
<thead>
<tr>
<th>FACTORS</th>
<th>RIGHT EYE MEASUREMENTS</th>
<th>LEFT EYE MEASUREMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Untinted Intraocular Pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Central Corneal Thickness (μm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Vertical Cup to Disc Ratio by Camera</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Pattern Standard Deviation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- http://ohts.wustl.edu/risk/calculator.html

Treatment Recommendations

<table>
<thead>
<tr>
<th>Expert Panel Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5%</td>
</tr>
<tr>
<td>5-15%</td>
</tr>
<tr>
<td>&gt;15%</td>
</tr>
</tbody>
</table>

**Suggested guidelines only**

Patterns of damage

- Ganglion cell axons damage at ONH
- Patterns of damage should reflect retinal anatomy of RNFL
  - Arching pattern divided by horizontal raphe
- Structural and functional change must correlate

Types of VF defects

- Pics of nasal step
- Arcuate
- Paracentral

Severity

- American Glaucoma Society staging system

<table>
<thead>
<tr>
<th>Visual Fields Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>511 MSL, No VF loss or white-on-white perimetry.</td>
</tr>
<tr>
<td>365.33, type of glaucoma</td>
</tr>
<tr>
<td>365.71</td>
</tr>
<tr>
<td>23. Moderate. VF loss in one hemisphere only and not within 5 degrees of fixation. (Whole mesh on horizontal and vertical meridians indicate 10-degree increments.)</td>
</tr>
<tr>
<td>365.72</td>
</tr>
<tr>
<td>29. Severe, with VF loss within 5 degrees of fixation.</td>
</tr>
<tr>
<td>365.23</td>
</tr>
<tr>
<td>14. Severe, with VF loss in both hemispheres.</td>
</tr>
<tr>
<td>365.73</td>
</tr>
</tbody>
</table>

VF Interpretation

- Reliability Indices
  - Fixation losses
  - False positives
  - False negatives
- Global Indices
  - Mean deviation
  - Pattern standard deviation
- Visual field index
- Glaucoma Hemifield Test
- Total deviation plot
- Pattern deviation plot
Fixation Losses

- Fixation Losses: 0/13

False Negatives

- False NEG Errors: 50%

False Positives

- False POS Errors: 64% XX

Global Indices

- Mean Deviation
  - Difference between threshold values and age-match normal value

- Pattern Standard Deviation
  - Represents localized VF loss
  - Corrects for media opacities

Global Indices

- Visual Field Index
  - Staging index
  - Less affected by cataract than MD
  - Improved correspondence to patterns of ganglion cell loss
  - Weights central points higher due to higher density of ganglion cells
    - 100% in normal VF
    - 0% in perimetrically blind VF
Glaucoma Hemifield Test

- Compares mirror-image point clusters of common glaucomatous VF loss above and below the horizontal midline

1. “Within Normal Limits”
2. “Borderline”
3. “Outside Normal Limits”
4. “Abnormally High Sensitivity”
5. “General Reduction of Sensitivity”

Single Field Analysis

- ID correct demographics
- Review Reliability Indices
- Compare TD and PD
- Review Global Indices & GHT

Single Field Analysis

- ID correct demographics
- Review Reliability Indices
- Compare TD and PD
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OCT and Glaucoma

- Excellent diagnostic tool to aide in ONH and RNFL assessment
- Mild to moderate stage disease
- Loses usefulness in severe stage disease
  - Floor effect

OCT Interpretation

- Key Parameters
  - Compared to normative data
- RNFL Thickness Map
- RNFL Deviation Map
  - Deviation from normal
  - En face fundus image
- NRR Thickness
- RNFL TSNIT Graph
- RNFL Quad & Clock Hour
  - Compared to normative data
- Bscans
  - RPE & disc black
  - ILM & cup red
OCT Interpretation

- Scan quality
  - Signal strength ≥ 7
  - No loss of signal areas
  - No motion artifacts
- Review Key Parameters
  - Color coded based on normative data base

Structure-Function Correlation

- We’ve got to have it!
  - OCT and HVF
  - HVF and ONH
  - OCT and ONH

Target IOP

- Collaborative Normal Tension Glaucoma Study
  - Showed 30% reduction in IOP reduced risk of progression
  - IDed risk factors for progression (migraine, female sex, disc here)
- Advanced Glaucoma Intervention Study
  - VF stability achieved with average IOP of 12 mmHg and always IOP <18 mmHg
- Early Manifest Glaucoma Trial
  - Tx reduces risk of progression in early POAG
  - 10% reduced risk for every 1mmHg lower
  - Risks for progression: (higher IOP, age, XFG, bilateral, worse VF)

Target IOP

- A pressure at which additional damage is considered unlikely to take place
  - Risk factors & IOP
    - How many, how strong and how high?
  - Current level of damage/ severity of disease
    - Greater the damage, the lower the IOP
  - Progression rate (if known)
- No exact method
- May (and should) be modified as needed

Treatment: Traditional Medications

<table>
<thead>
<tr>
<th>Class</th>
<th>Available medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA</td>
<td>Latanoprost, Travatan Z (travoprost), Lumigan, Zioptan</td>
</tr>
<tr>
<td>BB</td>
<td>Timolol sulf and g (Bimatoprost, IstaPiloc), Levobunolol (Betimol)</td>
</tr>
<tr>
<td>A-agonist</td>
<td>Brimonidine (Alphagan P)</td>
</tr>
<tr>
<td>CAI</td>
<td>Dorzolamide, Alopert</td>
</tr>
</tbody>
</table>

Fixed Combos

| BB + CAI | Dorzolamide-timolol, Cosopt PF |
| BB + A-agonist | Combigan |
| A-agonist + CAI | Simbrinza |
### Treatment: Traditional Medications

<table>
<thead>
<tr>
<th>Classes</th>
<th>MOA</th>
<th>Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA 30% ↓ QD</td>
<td>Increases uveoscleral outflow</td>
<td>Darkening of skin, iris, growth of lashes, loss of periorbital fat, stinging, hyperemia</td>
<td>Caution if used monocularly</td>
</tr>
<tr>
<td>BB 25% ↓ QD</td>
<td>Decreases AqH production</td>
<td>Bradycardia, bronchial constriction, arrhythmia, heart block, sexual dysfunction</td>
<td>Asthma, COPD, bradycardia, congestive heart failure</td>
</tr>
<tr>
<td>A-agonist 20-25% ↓ BID-TID</td>
<td>Decreases AqH production</td>
<td>Low BP, orthostatic hypotension, allergic reactions up to 25%</td>
<td>Children</td>
</tr>
<tr>
<td>CAI 20% ↓ BID-TID</td>
<td>Decreases AqH production</td>
<td>Allergic reactions, stinging, taste disturbances</td>
<td>Caution in true sulfonamide allergies, sickle-cell disease</td>
</tr>
</tbody>
</table>

### Treatment: Medication Selection

- Consider safety and efficacy
  - PGA first line for most
- Review history to determine best drug for patient
- Compliance and adherence are required
- Balance safety/efficacy with acceptable SE and dosing schedule

### Treatment: New Medications

- **Rho Kinase (Rock) Inhibitors**
  - Increase outflow through TM
  - Lowers episcleral venous pressure
  - NET inhibition reduces fluid production
  - May be ideal for NTG
    - Rhopressa (QD)
    - Roclatan (Rhopressa + latanoprost)

- **Vesneo (latanoprostene bunod) (QD)**
  - Latanoprost + nitric oxide donating moiety
  - Increases outflow through TM and uveoscleral
  - May positively impact perfusion pressure
  - CRL from FDA: no safety or efficacy concerns

### Treatment: Lasers

- Laser trabeculoplasty
  - ALT and SLT
  - Different lasers, different MOAs
- Similar efficacy
  - SLT may be more repeatable

### Treatment: Laser Trabeculoplasty

- Questions:
  - What is the success rate?
  - How much does it lower IOP?
  - How long does it last?
  - Does the laser matter?
  - How does it compare to medical/surgical Tx?
  - Is it repeatable?
Treatment: Laser Trabeculoplasty

- What is the success rate?
  - Effective ~70-75% of the time
- How much does it lower IOP?
  - 20-25% on average

Treatment: Laser Trabeculoplasty

- How long does the effect last?
  - ~80% success at 1 year
  - ~40% at 2 years?
  - ~50% success at 5 years
  - ~20% at 10 years
- Does the laser matter?
  - No significant difference in IOP or complications

Treatment: Lasers

- How does it compare to medical/surgical Tx?
  - SLT Med – SLT vs latanoprost same at 12 mo
  - GLT – better than timolol at 2 years; similar results at 7 years
  - Moorfields – Trabeculectomy > medical > trabeculoplasty
- Is it repeatable?
  - ALT – not already treated areas
  - SLT – yes, but probably less effective

Treatment: MIGS

- Micro Invasive Glaucoma Surgery
  - Ab interno microincision
  - Minimal trauma
  - Effective
  - High safety profile
  - Rapid recovery

Treatment: MIGS

- Newer procedures
  - iStent
  - CyPass Micro-Stent
  - Xen Gel Stent

Treatment: MIGS

- iStent (Glaukos)
  - FDA approved 2012
  - Indicated for use in conjunction with cataract surgery in adult patients with mild-moderate open-angle glaucoma currently treated with ocular hypotensive medications.
  - Allows aqueous direct route to Schlemm’s canal via bypass of TM
Treatment: MIGS

- CyPass Micro-Stent (Alcon)
  - FDA approved, late July 2016
  - Implanted at time of CE in patients with mild-moderate open-angle glaucoma
  - Reduces IOP by increasing suprachoroidal outflow

Risk Factors for Progression

- Older age
- Bilateral disease
- Higher mean IOP
- Disc hemorrhage
- Thinner CCT with higher baseline IOP
- More advanced VF loss at baseline
- Low OPP
- Exfoliation syndrome

Progression Monitoring

- Structure vs function?
- WGA Consensus → Both should be evaluated
- Assess risk factors for progression

Visual Field Progression

- Overview reports
- Changes in global indices
  - MD
  - PSD
- Progression analysis software
  - Guided Progression Analysis (HFA, Carl Zeiss Meditek)
  - Event & Trend

Visual Field Progression

- Event vs. Trend Analysis
  - Event → to identify statistically significant worsening of the VF
    - Point by point basis
    - Best for ID of small, localized change
  - Trend → quantify any observed rate of change
    - Better for overall worsening
    - Requires more tests for a reliable slope (5+)

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**Event Analysis**

- Based on progression criteria from EMGT
  - Sensitive and specific compared to expert eval
- Compares individual tests points on PD of successive tests, to the average of two baselines
- Flags points that vary by more than the expected variability of similarly damaged VFs.
- Open and shaded triangles ID statistically significant change from baseline.

**Trend Analysis**

- Linear regression analysis of the of the VFI
  - Plots VFI vs age
- Calculates rate of progression after 5+ tests
- Projects into future if 5+ tests available
  - What could happen if present trend continues

**WGA Consensus on Progression of Glaucoma 2011**

- Baseline data collection – first two years
  - In clinical practice, at least two reliable VFs is optimal in the first six months.
  - At least two further VFs should be performed within the next 18 months.
  - Repeat VFs sooner if possible progression
- Follow-up data collection - after the initial two years
  - The frequency of follow-up VFs should be based on the risk of clinically significant progression (based on extent of damage and life expectancy).
    - Low – Moderate Risk: 1x per year
    - High Risk: 2x per year

**Structural Progression**

- Serial disc and RNFL photography: still valuable
  - Disc hemorrhages, PPA, stereoscopic eval
- C/D estimates insufficient for monitoring structural change
- OCT: objective, reproducible measurements and quantitative assessment of disc and RNFL
  - Requires good image quality

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OCT Progression Analysis

- Statistical analysis of sequential OCT scans to detect progression
- Event and Trend Analysis

OCT Event Analysis

- Compares follow up scan to baselines
- IDs change when difference is greater than a predetermined threshold based on test-retest variability
- Image alignment is critical
- More susceptible to artifact

OCT Trend Analysis

- Regression line between parameter and time
- Provides rate of change
- Various parameters
  - RNFL thickness (average, inferior, superior)
  - Rim area or cup-to-disc area
- Less susceptible to artifact
- Requires large number of tests for reliable slope

OCT Progression Patterns

- Widening of a defect
- Deepening of an existing defect
- Inferior-temporal defects

Reliable baselines

- Reliable
- Free of artifact
- Ideally within 6 months of each other
- Change baselines when treatment is altered

When Progression is Suspected

- Repeat the test
  - Confirm if change is real
- Is the change typical of glaucoma?
- What is the rate of change?
- Is the rate of change acceptable compared to the patient’s life expectancy and stage of disease?
  - Not all statistically significant change is clinically meaningful
Adjusting Therapy

- Establish new target IOP
  - Rate over which progression took place
  - Additional risk factors
  - Age of patient
  - Severity of damage

Adjusting Therapy: Options

- Additional medication
  - Often jump to a fixed combination
- Laser
  - Open angle?
- MIGS
  - Mild-moderate glaucoma
  - Need CE also?
- Trabeculectomy/ GDI
  - Significant additional IOP lowering is needed on
  - Rapid progression in younger patient

Questions?

- Email: ascheurer@ico.edu