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.

Disclosures

- Disclosures
  - Douglas K. Devries
    - Consultant or Speakers Bureau for
      - Allergan
      - AMO
      - TearLab
      - MeDx
      - BVI
      - B&L

- 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 Evaluation

- Vision care Exam
  - CONVERSION

- Medical Exam
**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
- Shimmer

**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

**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

**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

**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

**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

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

Lid Disease
We cannot treat the dry eye until we understand and treat

LWE
MGD
Ephora
Etiology

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 types" of artificial tears), warm compresses, cool packs

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


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


Demodex Treatment

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


Inflammation vs. Obstruction

- MGD
- Cosmetics
- Age and Gender
- Treatments

“Volatile organic compounds (VOCs) are emitted as gases from certain solids or liquids.”

-EPA

https://www.epa.gov/indoor-air-quality/tox/volatile-organic-compounds-impact-indoor-air-quality

“VOCs include a variety of chemicals, some of which may have short- and long-term adverse health effects.”

-EPA

https://www.epa.gov/indoor-air-quality/tox/volatile-organic-compounds-impact-indoor-air-quality

Health Effects
- Headaches
- Fatigue
- Eye, nose and throat irritation
- Changes in sleep patterns
- Skin irritation
- Respiratory symptoms
- Irritation of the eyes, nose, and throat
- Some organics can cause cancer in animals, some are suspected or known to cause cancer in humans.

https://www.epa.gov/indoor-air-quality/tox/volatile-organic-compounds-impact-indoor-air-quality
“Only 11% of patients have had a conversation with their eye care provider about makeup.”


Do your eyes feel more comfortable without makeup use?

YES 41.4% (99/169)

Do your eyes itch with cosmetic use?

YES 22.5% (38/169)

Are your eyes red with cosmetic use?

YES 17.1% (29/169)

Have you ever discontinued use of makeup due to eye irritation?

YES 15.3% (26/169)

http://healthy-family.org/eyelid-rash-dry-red-itchy-skin/

US Dept HHS


Inhalational talc pneumoconiosis: radiographic and CT findings in 14 patients

Talc:


"Bismuth Oxychloride is very much like arsenic chemically, which is a poison if you ingest it."

Bismuth Oxychloride

"If your skin becomes itchy and pink after wearing mineral makeup with bismuth oxychloride you may develop a severe rash or acne over time."

Bismuth Oxychloride
“Why do cosmetic companies use bismuth oxychloride? It hides flaws, and is an inexpensive filler that helps keep the makeup sticking to your skin over the course of the day.”

http://healthy-family.org/eyelid-rash-dry-red-itchy-skin/

“Mica is colorless but has sharp edges when you see it under a microscope.”

http://healthy-family.org/eyelid-rash-dry-red-itchy-skin/

“rubbing mica on their skin can cause inflammation, redness, and itching.”

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http://healthy-family.org/eyelid-rash-dry-red-itchy-skin/

Tips
- Read the label
- Look up at US. Department HHS site (https://hap.nlm.nih.gov/index.htm)
- Not all VOCs will irritate; patient dependent
- Look at order of ingredients
- Concentrative matter
- Eye contact may increase corneal hyperemia risk
- Remove makeup nightly for greater comfort
- Avoid irritants
- Avoid allergy-known products
- Avoid allergy-known products
- Avoid eye-based mascaras
- Use water-soluble cosmetics

Disclosures
- Last 12 months:
  - Allergan
  - Bausch/Valleant
  - Shire
  - Sun

Bare Minerals
Jane Iredale
Philosophy
La Bella Donna
Youngblood

http://healthy-family.org/eyelid-rash-dry-red-itchy-skin/

253 people Wearing makeup 4.99 days/wk SPEED 8.19 (0 to 28) UNC = 3.28 (0 to 10)
O'Dell LE. et. al. Accepted for publication ARVO 2017

No eye make up remover SPEED 10.5
Use eye make up removers SPEED 7.6
P=0.0004
O'Dell LE. et. al. Accepted for publication ARVO 2017

SPEED
- Asymptomatic 2.2
- Mild 5.0
- Moderate 6.6
- Severe 9.9

MGD is currently thought to be the leading cause of dry eye.
Caroline Blackie
Donald Korb

Prevalence

MGD is currently thought to be the leading cause of dry eye.
Caroline Blackie
Donald Korb

Prevalence

Lid margin disease
Meibomian gland dysfunction (MGD)
Evaporative dry eye

Prevalence

“Overall, 86% of these qualified DED patients demonstrated signs of MGD.”
Michael Lemp

Prevalence

“Of patients with meibomian gland atrophy…60%….were asymptomatic”

What triggers you to perform a dry eye evaluation?
A. Symptoms
B. Signs
C. Both

Prevalence

“Only 30% of respondents routinely test for MGD in their comprehensive examinations”


"MGD is currently thought to be the leading cause of dry eye.”
Caroline Blackie
Donald Korb


“Overall, 86% of these qualified DED patients demonstrated signs of MGD.”
Michael Lemp

DOI: 10.13140/RG.2.1.2032.2161

Obstruction vs inflammation

Two camps: Obstruction
Inflammation

Obstruction

“Obstructive MGD is the most common form of MGD resulting in dry eye.”
Caroline Blackie
Donald Korb

Obstruction

“hyperkeratinization is one of the primary components…of obstructive MGD.”

Obstruction

Hyperkeratinization…disorder of the cells lining the inside of a hair follicle.”

Obstruction

“normal function of these cells [is] to…slough off (desquamate)…this process is interrupted…dead skin cells do not leave the follicle…[due to] excess of keratin”

Obstruction

“cohesion of cells will block or "cap"…or clog the sebaceous/oil duct.”

"changes in the composition of meibum...increase its viscosity or...can reinforce keratinization."

"The definition and involvement of inflammation in MGD have been unclear in the past for several reasons."

"Inflammatory leukocytes are not apparent [in atrophied glands]."

"inflammation...does not represent a major etiologic factor in obstructive MGD"

"inflammatory events [promoted] inside the gland, in the periglandular conjunctiva, on the lid margin, and on the ocular surface"

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

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

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 somality of the tear film and inflammation of the ocular surface."

DEWS—Classification of Dry Eye

Anatomy, Physiology and Pathophysiology of the Meibomian Gland

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

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

**Evaluation, Diagnosis and Grading of Severity of Meibomian Gland Dysfunction**

**Management and Therapy of Meibomian Gland Dysfunction**

**MGD Exposed**

A new look at an old problem

The prevalence of MGD is as high as 60-70%.

MGD is frequently transmissible and therefore missed.

Meibomian glands are critical for innate tear film host defense.

MGD increases corneal abrasion.

Prolonged epithelial exposure post-cataract surgery results in discomfort.

Exposure stress causes MGD.

Modern clinical contact lens wear and compromised tear film defenses.

MGD is progressive. Early intervention optimizes outcomes.

Identify early compromise to MG function and structure with the MGE.

**An Unstable Tear Film Negatively Impacts Premium Quality Vision Care**

**MGD**

- Fluctuating Vision
- Ocular Discomfort
- Compromised Barrier to Infection

63%+ of cataract patients experience contact lens intolerance and LASIK candidates have compromised vision.

Glucoma and Retinal Patients

[1] Adapted from work in the presentation by the authors. Reprinted with permission from the American Society of Cataract and Refractive Surgery.

[2] Adapted from work in the presentation by the authors. Reprinted with permission from the American Society of Cataract and Refractive Surgery.
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 MGD along the lower eyelid can be used to diagnose MGD and to direct therapeutic intervention.

Meibomian Gland Structure

- MGD is Progressive
- Examples of Compromised Function and Structure
- The Cycle of Inflammation
- A Change in Philosophy – MGD First

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

1. Non-Obvious MGD (NOMGD)
   - MGD may be discovered 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, 43% of them had NOMGD.

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Obstruction and inflammatory
Steroid (anti-inflammatory) + mechanical therapy

Mechanical therapy:
- Lid therapy
- Masks
- In office manual expression
- Lid margin scraping
- MiBoFlo, LipiFlow

Anti-inflammatory:
- Steroid: Loteprednol
- AzaSite
- Doxycycline
- Omegas
- Restasis

$\omega_6 : \omega_3$ ratio in the diet is approximately 4:1

Current Western diets that ratio is closer to 15:1


Greater bleeding with $\omega_3$
Not recommended for surgery

“This case reveals a significant rise in INR after the dose of concomitant fish oil was doubled”


http://www.pharmacologyweekly.com/articles/fish-oil-omega-3-fatty-acids-EPA-DHA-

MGD patients
- 30 patients -1.2g: EPA 720mg DHA 480 mg
- 30 patients -400mg Vitamin E

"grass-based diets can significantly improve the fatty acid (FA) composition and antioxidant content of beef"


Several studies suggest that grass-based diets elevate precursors for Vitamin A and E, as well as cancer fighting antioxidants.


"And where do the fish get these omega-3s? They eat it...With grass-fed cows...Omega-3s are in their meat—because they're eating grasses and clover rich in these heart-healthy fatty acids."


Meat cuts 18 cattle
Grain vs grass fed
Trimmed of visible fat & connective tissue and then minced
7 g were used for fatty acid (FA) analysis.


"Significantly higher level of total omega-3 (ω-3) in grass-fed beef (P< 0.0001) than the grain-fed groups regardless of cut types."


"Each day that an animal spends in the feedlot, its supply of omega-3s is diminished"


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

Moderate/severe or not improving

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

Contraindications

- Pregnant or child bearing age
- Children

Contraindications

- Pregnant or child bearing age
- Children

Contraindications

- Pregnant or child bearing age
- Children
MGD Treatment

Medical-Instrument Treatment

Treatment of MGD/NOMGD

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

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

At Home Therapy
- Warm compresses
- Meibomian gland scrubs
- Home expression
- Blinking
- office expression
- Secretagogues – Androgens

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) Includes test expression
4) All staining
3) 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

Maskin Expressor

In-office manual expression

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

Mechanical therapy:
- Lid therapy
- Masks
- Lid margin scraping
- MbFlo, LipiFlow
- In-office manual expression
- LEO method
n=24
Single treatment
2 wks and 1 month: OSDI and SPEED improved over control
No MG secretion improvement


n=24
Single treatment
2 wks and 1 month: OSDI and SPEED improved over control
No MG secretion improvement


O'Dell L. In-office manual expression. In press.

Pre-treatment
LEO
L=Liquify
E=Express
O=Observe

Pre-treatment
Omega 3, home warm compresses, steroids, AzaSite

Pre-treatment
Omega 3, home warm compresses, steroids, AzaSite

LEO
L=Liquify
Tranquileyes, Bruder, Bundle
10 min
Anesthesia
Lid margin scrape

LEO
L=Liquify
Tranquileyes, Bruder, Bundle
10 min
Anesthesia
Lid margin scrape

LEO
L=Liquify
Tranquileyes, Bruder, Bundle
10 min
Anesthesia
Lid margin scrape

O'Dell L. In-office manual expression. In press.
**Manual expression**

- **LEO**
  - E=Express
  - Expression forceps
  - Mastrota paddle and cotton bud
  - Collin’s expressor


**MiBoFlo**

**Pros**
- Lower cost than LipiFlow
- Not covered by insurance

**Cons**
- Not advisable in lid therapy
- Moderately invasive


**11 cases**

Single treatment
1 month: MG secretion improved over control (p=.003)
No symptomatic improvement

**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

**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
  - Cryopreserved
  - Bio Optix
  - Dry Membrane

**OBSTRUCTIVE MGD Warm Compress Treatment**

*Increase in LLT Following Treatment with Warm Compresses in Patients with MGD*  
*Olsen, Korb, Greiner, Eye & CL, 2003*

<table>
<thead>
<tr>
<th>Treatment Duration</th>
<th>LLT Increase (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>60 nm</td>
</tr>
<tr>
<td>5 minutes</td>
<td>105 nm</td>
</tr>
<tr>
<td>15 minutes</td>
<td>117 nm</td>
</tr>
<tr>
<td>30 minutes</td>
<td>122 nm</td>
</tr>
</tbody>
</table>

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

**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

**Maskin Probe**

Leiter Pharmacy
8% lidocaine with 25% Jojoba in ung base
Possible Tape Tarsorrhaphy