Disclosure

- Allergan
- Bausch and Lomb
- Bayer Canada
- I-MED pharma
- Johnson and Johnson Vision
- Labtician-Thea
- Novartis/Alcon
- Santen
- Takeda

Learning Objectives

1. Understanding the latest approaches to treatment options for meibomian gland dysfunction (MGD)
2. Overview of the multimodal approaches to managing dry eye disease (DED) and ocular surface diseases
3. Applying an interventional management strategy for DED by prevention

Can you have MGD without DED?

Gilbard JP, CLAO 1985

Figure 8: Staining electron microscopy of rabbit cornea epithelium in tissue cultures demonstrates loss of cell surface membrane or epithelium from hyperosmotic culture (left untreated), H35, right, relative to epithelium from isometric culture (H32), H35.
“Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.” TFOS DEWS II 2017
Hx: 28 y.o. female bilateral LASIK in 2015. c/o chronic dryness OD>>OS.
Topical Meds: Refresh Optive PRN
Allergies: NKDA  Oral Meds: None
SPEED symptoms: 21/28

Consultative Findings:
TDm OD 292 OS 290,
MMP OD +ve OS -ve
TBUT OD 6s OS 2s
Oxford OD -ve OS +
Meibography OD PULT1, OS PULT 2
Tear Meniscus Height (see images)

Further history:
Permanent plugs inserted post LASIK OU inferiorly. No longer present
Symptoms initially were stinging OU, visual discomfort/intermittent blur, post plugs – sticky OD>>OS

Tear Flow and Turnover

OD

TMH:
1.2mm

TMH:
0.2mm

OD

OS

Cornea (NaFl)

Meibography

OD

OS

ADDE
EDE

NSDE-KCS
NSDE Autoimmune
Lacrimal Obstruction
NLD
Lacrimal Sclerosis
MPF
Intraocular pressure
Glaucoma
Open angle
Laminar Sclerosis
Cataract
Glaucoma
Closed angle
MDD
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WHAT'S UP DOC?

Dx:
- Evaporative DED 2nd to Obstructive MGD
- NLD stenosis/obstruction (RLL)
- Neurotrophic Keratopathy (LASIK induced axonopathy)

WHY IS OSMALLITY WNL?

WHY IS MMP-9 negative OS?

WHY DID HER SYMPTOMS CHANGE FROM STINGING/BURNING TO STICKY/DISCOMFORT OD>>OS?

HOW DO I TREAT THIS?

- V1 – Dry Eye Disease circle
  - No single entry point
  - 4 contributors to DED pathophysiology
- V2 – MGD circle
  - Entry point to DED via tear film instability
Primary Care vs. Interventional

**DRY EYE FIRST**
- Wait for signs & symptoms to develop.
- Manage signs & symptoms as they present.
- *Reactive*. Late-term focus: Suppress Dry Eye.

**MGD FIRST**
- Early Diagnosis: Routinely evaluate MG function & structure
- Treat the cause of DED, not just the result
- Treat Obstruction First
- *Proactive*. Short and long-term focus: Ocular surface health

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![Graph showing normal morphological distribution by age](image)

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**MGD 6 pathophysiological mechanisms**

1. Primary obstruction – hyperkeratinization of orifice and lid margin
2. Abnormal meibum secretion
3. Eyelid Inflammation
4. Corneal and conjunctival inflammation
5. Epithelial damage
6. Microbiological changes (*Staphylococcus* spp., *P. acnes*, *Demodex* spp.)

Geerling et al. (Proceeding of the OCEAN group), OcSurf 2017

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Signs of Obstruction

![Signs of obstruction](image)

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Signs of Lipid Dysfunction

![Signs of lipid dysfunction](image)
DEWS II – Treatment (Stages)

- Treatments for tear insufficiency
  - Tear replacement
  - Tear stimulation
  - Tear conservation
- Treatment of lid abnormalities
  - Blepharitis
  - MGD
  - Blanking exposure
- Anti-inflammatory Therapy
  - Steroid
  - Redocin (CsA), Xidra (LfG)
  - Systemic
- Surgical Approaches
  - Tornado
  - CCh
  - Amnion
  - Dietary Modifications
  - General hydration
  - O3
  - Local Environmental Considerations
    - Chronic meds,
    - Desiccating conditions
    - CL use, Screen
- Complimentary Considerations
  - Herbal, Acupuncture, etc

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HOW DO I TREAT THIS?

- LipiFlow
  - 12 minute automated superior/inferior technician driven
  - 42.5 degrees vectored thermal heat
- Ilux
  - 2-4 minutes per lid handheld
  - Light emitted heat
- IPL
  - Photothermal/photothrombosis based therapy
  - Multiple sessions

LipiFlow and Biomarkers (Vaishnav, RV et al, ASCRS 2019)

Analysis of Cytokine Levels in Tears and Clinical Correlations After Intense Pulsed Light Treatment

IPL and Biomarker (Liu R, et al 2017)
**Periductal Fibrosis and Intraductal Probing (Maskin S, Cornea 2019)**

- Periductal Fibrosis
  - Partial Distal (PDO)
  - Complete Proximal (CPO)
  - Complete Distal (CDO)
- All contribute to gland atrophy

**Ocular ROSacea COnsensus (ROSCO) Grading**

Either both lid margin telangiectasia and interpalpebral injection OR Corneal abnormalities and scleral inflammation.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Features</th>
</tr>
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<tbody>
<tr>
<td>Mild</td>
<td>Mild telangiectasia with lid margin telangiectasia</td>
</tr>
<tr>
<td>Mild-to-moderate</td>
<td>Blepharitis conjunctivitis</td>
</tr>
<tr>
<td>Moderate-to-severe</td>
<td>Blepharitis conjunctivitis</td>
</tr>
<tr>
<td>Severe</td>
<td>Sclerokeratitis, anterior uveitis</td>
</tr>
</tbody>
</table>

Table 4 Grading of ophthalmological abnormalities in ocular rosacea, based on the clinical opinion of the ROSea COncensus panel ophthalmologists. Ocular manifestations may present with or without skin disease.

**Skin rosacea and MGD are closely related**

- 80% of skin Rosacea patients suffer from MGD.\(^1\)
- MGD patients with skin rosacea have a worse prognosis: WE NEED MORE TOOLS\(^2\)
- 86% of OSD patients have an MGD component.\(^2\)
- 20% of ocular rosacea (MGD) precedes skin rosacea.\(^3\)
- Both conditions have significant QoL and psychosocial impacts

1. Viso et al., 2014; 2. Lemp et al., 2012; 3. Ghanem et al., 2003

**Interventional MGD Framework**

**Prescribing for DED**

- Steroids, Lifitegrast, Cyclosporine A, Tacrolimus, NSAIDS
- Mucin Secretagogues, Lifitegrast

Brad Persig, MD, MPH, FACS

**Dry Eye Disease - Rx**

ADD IPL/IDP/LF IF FURTHER CLINICAL INDICATIONS WARRANT

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ADD IPL/IDP/LF IF FURTHER CLINICAL INDICATIONS WARRANT
### Lifitegrast MOA
- **Lifitegrast** inhibits integrin, lymphocyte function-associated antigen 1 (LFA-1), from binding to intercellular adhesion molecule 1 (ICAM-1).
- This mechanism down-regulates inflammation mediated by T lymphocytes.

### Interventional MGD Framework
- **MGD**
- **LID TENDERNESS ON PALPATION**
  - **YES**
  - **NO**
- **ADD**
  - **IPL**
  - **IDP**
  - **LF**
- **Add LIG** (anti-ICAM 1, anti-IL 17, Th17)
- **Reverse if MMP-9 is negative**

### Pre and Post LF TPS
- **Pre-LipFlow**
- **Post-LipFlow (Immediate)**

### LipiFlow® Uniquely Manages Meibomian Gland Obstruction
- **Directly Treats** Obstruction
- **Heats** the Inner lid surface to 42.5°C.
- **Simultaneously** evacuates gland contents.
- **Protects** the cornea and globe from heat and pressure.
- **Automated:** limits user variability
Intense Pulsed Light MOA

1. Anti-Inflammatory: Cellular and molecular mechanisms
2. Thrombolytic: Destruction of abnormal blood vessels
3. Sanitizing: Destruction of skin parasites and reduction of bacterial load (Demodex, B. oleronius)
4. Photomodulating: Cellular activation by increasing mitochondrial output
5. Rejuvenating: Collagen remodeling

MGD Therapy Tools (Dr. Laura Periman MD)

<table>
<thead>
<tr>
<th>Tool</th>
<th>CnA</th>
<th>LSG</th>
<th>Lipflow</th>
<th>IPL</th>
<th>Hypochlorous acid</th>
<th>Omega 3/6</th>
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<tbody>
<tr>
<td>Obstructive hyperostesation</td>
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<td>Bacterial bacteria load</td>
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<td>Inflammation</td>
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Restore Surface Homeostasis...

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HOW DO I TREAT THIS?

Tear Outflow

PREMIUM SURGERY, SUBOPTIMAL SURFACE?

“22% of preoperative cataract patients come in with DED, 80% will have evidence on pre-op examination of ITF level 1, 2, 3 DED” W. Trattler – PHACO study
The Economics of MGD

- 33 Million Americans have Dry Eye
- 86% have a component of MGD

Dwarfs cataract surgeries (4 M), glaucoma (2 M), diabetic retinopathy (1.5 M)


Diagnostics
1. Tear chemistry (Osmolarity/MMP-9)
2. Meibography (1. LipiView/LipiScan best image quality
2. KSM comprehensive DE suite
3. Melbox

Treatments
1. LipiFlow Thermal Pulsation
2. ILux
3. IPL (Lumenis, E-Eye, Eye-Light)

Get Your Checklist On...

"The volume and complexity of what we know has exceeded our individual ability to deliver its benefits correctly, safely, or reliably. Knowledge has both saved us and burdened us."

Simple problems have basic, but necessary steps to solve

Simple problems: eg. Baking a dessert
Solution: Follow a recipe, which is often tested to assure easy replication without the need for any particular expertise

Complicated problems require expertise, consistency and high level of experience

Complicated Problems: eg. Landing 2 rockets simultaneously back on earth
Solution:
- For new or recipes are necessary to resolve them but are often not sufficient
- High levels of expertise in a variety of fields necessary for success
- eg. Sending one rocket increases assurance that the next mission will be a success
- In some critical ways, rockets are similar to each other and because of this there can be a relatively high degree of certainty of outcome

Complex problems require a process and patience

Complex Problems: eg. Raising a child
Solution:
- Here, formulae have a much more limited application.
- Raising one child provides experience but no assurance of success with the next mission
- High levels of expertise in a variety of fields necessary for success
- As a result there is always some uncertainty of the outcome
- To some extent this is because every child is unique and must be understood as an individual
- In some critical ways, rockets are similar to each other and because of this there can be a relatively high degree of certainty of outcome
What does your DED checklist look like?

- The DED work up is a SIMPLE problem
  - Apply a methodical work-up that includes the exact same tests in the exact same order (e.g., DEQ-5, TOSm, NaFl, TIBUT)
- The DED diagnosis is a COMPLICATED problem
  - Analyzing the findings from the work-up using the DED workflow will provide repeatable answers to drive the diagnosis. It requires your expertise, knowledge and the SIMPLE steps completed in the initial work-up
- The DED Management is a COMPLEX problem
  - Each patient has multiple variables to consider and thus treatments will have variable results – however we have a finite number of tools and by treating the diagnosis, you are in the best position to intervene appropriately and sufficiently

Summary

- Unlearn evaporative vs. aqueous deficient dry eye
  - Consider the Vicious Circles in guiding diagnosis and treatment
  - evidence supports multi-modal therapy
  - LIG in MGD cases
  - Objectively measure symptoms, osmolarity and meibography
  - Always consider tear production AND outflow

- Look early and apply preventative model of care
  - Interventional MGD management is a paradigm shift in primary care philosophy (think dental)
  - Think of what would happen if every patient had meibography routinely?

Thank you
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Photo Credit: Dr. Jessica Dixon Heinke