Advancement in Dry Eye Treatment-

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May Eye Care – Hanover, PA
US Ophthalmic Disease Prevalence

Approximately 30%-40% of patients in ophthalmic practices
Dry eye facts

- Prevalence increases with age
- 2-3 x more common in females
- 20-30 million Americans have mild/moderate dry eye
- #1 cause for eye exams
- Negative impact on one’s life
  - Decreased quality of life
  - Reduced work capacity
  - Decreased visual function- reading/driving/computer
Dry Eye Defined

- 1995- NEI

  Dry eye is a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.
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.
“...a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative and quantitative changes in the glandular secretion. It may result in alteration of the tear film, eye irritation, clinically apparent inflammation, and ocular surface disease.”

—The International Workshop on Meibomian Gland Dysfunction: Executive Summary
Evaporative Dry Eye Is the Most Common Cause of Dry Eye

In a recent study by Lemp et al, 86% of patients evaluated had Evaporative Dry Eye

159 patients

23/159 aqueous deficient
14%

79/159 MGD
50%

57/159 MGD and aqueous deficient
36%

86% of patients have MGD
These tests are used to diagnose or rule out any of the major causes of ‘Dry Eye’ and direct the treatment plan.

- Lipid layer thickness (LV)
- MG function (MGE)
- Gland structure (imaging)
- Partial Blink (LV)
- Lagophthalmos (Staining)
- Inadequate lid seal (KB Light test)

- Schirmer Test
- Phenol Red Thread Test
- Any lacrimal output test

- Blood tests
- History
- Sjö™
These tests are used to identify key signs of dry eye. The tests may or may not correlate with each other. Each is testing a different aspect of the ocular surface or tear film.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Tear Film Stability</th>
<th>Tear Volume</th>
<th>Tear Chemistry</th>
<th>Tissue Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• History</td>
<td>• TBUT</td>
<td>• Schirmer</td>
<td>• Osmolarity</td>
<td>• Hyperemia</td>
</tr>
<tr>
<td>• Questionnaire</td>
<td>• NIBUT</td>
<td>• Red thread test</td>
<td>• Inflammadry</td>
<td>• Corneal staining</td>
</tr>
<tr>
<td></td>
<td>• Tear Stability Analysis</td>
<td>• Tear meniscus height</td>
<td>• Lactoferrin</td>
<td>• Conj. staining</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Tear meniscus dimensions (OCT)</td>
<td></td>
<td>• LWE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Line of Marx</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• OCT</td>
</tr>
</tbody>
</table>
Tear Film Composition

- Schirmer testing
  - Normal >10mm at 5 min
  - Excessive tearing >25 mm

- Phenol Red Thread test- 15 sec
  - Normal 9-20mm
  - Dry eye <9 mm

- Osmolarity

- TearScan
Evaluating the lipid layer

- Meibometry
  - Lipiview

- TBUT
  - < 10 sec abnormal
  - > 15 sec normal

Tear film break up viewed with fluorescein stain on a patient with dry eye. Dry spots (tear film break up) are indicated by the dark areas that appear on the cornea.
Ocular surface evaluation

- Fluorescein
- Rose Bengal
- Lissamine Green
Are you waiting long enough?

- Instill strip (Fl or Lissamine) to inferior fornix while patient is looking up
- Wait 90 seconds for initial evaluation of cornea or conjunctiva
- After 5 min instill a second strip of dye
- Wait 1 min- evaluate for lid wiper epitheliopathy
Treatment Options- Aqueous Deficiency

- OTC- Hypotonic
- Rx- Restasis
- Conservation- Plugs
- Anti-inflammatory

Figure 1. Insertion of the Parasol Punctal Occluder.
Restasis

- Clinically proven to treat AQUEOUS deficient dry eye
- Long-term data
- Pt using AT’s 2+/daily
Survey Results Show Patients Are Satisfied With RESTASIS®

Will continue to use RESTASIS® ophthalmic emulsion?  
Would recommend to others?

- 94% of patients will or may continue RESTASIS® ophthalmic emulsion
- More than three fourths would definitely recommend RESTASIS®
MGD is the leading cause of dry eye

MGD is chronic

MGD is progressive

Determining MG functionality requires physical expression

MG functionality is not equally distributed across the lid margin

All MGD is NON OBVIOUS prior to the cascade resulting in anatomical and functional changes
The Etiology of the majority of all dry eye signs and diagnoses, dry eye symptoms and contact lens related dry eye is Evaporative dry eye.

The treatment of MGD should be both palliative and restorative.

The role of Lipiflow.
Use a questionnaire

The role of the lid wiper

The role of interferometry

The line of Marx

Transillumination and meibography

Lagophthalmos
Meibomian Gland Dysfunction (MGD) Is the Most Common Cause of Evaporative Dry Eye Disease\textsuperscript{1-3}

“Meibomian gland dysfunction (MGD) may well be the leading cause of dry eye disease throughout the world.”\textsuperscript{4}

\textit{—The International Workshop on Meibomian Gland Dysfunction: Executive Summary}

Current Treatments- evaporative dry eye

- Warm Compresses
- Lid Massage- RISK of keratoconus
- Lid Scrubs
- Drugs
- Manual expression
- IPL
- Mibo
Dry eye Cascade

- Visible Changes
  - Inflammation- blepharitis
  - Staining- cornea/conj
  - Lid Wiper epitheliopathy
  - Conjunctival inflammation
  - Infections
  - Anatomical Changes to line of Marx

- Non-visible changes- confocal
  - Cornea
  - Lids
  - MG
DRY EYE CASCADE

Korb & Blackie

Stasis – Obstruction
  ↓
Decrease in lipid secretions and LLT
  ↓
Evaporation increases – minimal to 4 - 16 x
  ↓
Decrease in aqueous layer thickness
  ↓
Unstable tear film & evaporative stress

Stare Test

Is inflammation the cause or a sequelae of dry eye?
Consequences of MGD

Partial obstruction

Total obstruction

Decreased availability of Meibomian lipids at the lid margin and tear film
MGD Can Lead to a Downstream Cycle of Inflammation

Meibomian gland obstruction
↓
Decrease in Meibomian secretions (↓ Lipid layer thickness)
↓
Increase in evaporation (↓ Aqueous layer thickness)
↓
Unstable tear film

SYMPTOMS START

Critical intervention point

Ocular surface and lubricity compromised
↓
Ocular surface exposure (between blinks) and microtrauma (during blinking)
↓
INFLAMMATION

SYMPTOMS INCREASE

OCULAR CHANGES
Visible/nonvisible

Potential long-term damage

Are the Meibomian gland functional

- Is it secreting?
- 2005- studies began to determine the force of the blink
- 1 gram/sq mm to secrete – forced blink .3PSI
- MGD expressor
  - Applied to eyelash margin apply for 5-10 seconds
HOW IS MG FUNCTIONALITY DETERMINED?

Requires physical expression to determine if secretion present

Manual expression on surface overlying meibomian glands

**Problem**
An art form and difficult to quantify

**Functional**
(expresses clear sebum)

**Optimal**
(expresses copious clear sebum)


Digital expression is an art form, not a science. It cannot be standardized.

MGE: Applies standardized force of ~ 1.25 g/mm² to mimic blink forces and provides a metric for evaluation.

Korb & Blackie, Cornea, 2008

Korb & Henriquez, 1980

The TearScience® Meibomian Gland Evaluator

- Applies consistent, moderate pressure
  - Between 0.8 g/mm² and 1.2 g/mm²

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

Number of Meibomian Glands Yielding Liquid Secretion (MGYLS)
By Symptom Categories

<table>
<thead>
<tr>
<th></th>
<th>Severe Symptoms</th>
<th>Moderate Symptoms</th>
<th>Minimal Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom Score, SPEED questionnaire (0-28)</td>
<td>≥10 (14.39 ± 0.69)</td>
<td>6–9 (7.26 ± 0.17)</td>
<td>≤5 (2.30 ± 0.23)</td>
</tr>
<tr>
<td>Number of MGYLS for entire lower eyelid</td>
<td>4.14 ± 0.56</td>
<td>5.14 ± 0.41</td>
<td>6.25 ± 0.35</td>
</tr>
</tbody>
</table>

DRY  |

0 - 4 \| 5 \| 6 \| 7 \| 8 - 10+  

NOT DRY
MG functionality is not equally distributed across the lid margin

- The NASAL glands are the most efficacious
- The TEMPORAL glands are rarely secreting
- Glands alternate functionality from one day to the next
MG Functionality

**MG FUNCTIONALITY IS NOT EQUALLY DISTRIBUTED ACROSS THE LID MARGIN**

The nasal glands are the most efficacious. The temporal glands are rarely efficacious.

<table>
<thead>
<tr>
<th>Third</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal Third</td>
<td>0.27 ± 0.06</td>
</tr>
<tr>
<td>Central Third</td>
<td>2.14 ± 0.13</td>
</tr>
<tr>
<td>Nasal Third</td>
<td>3.10 ± 0.15</td>
</tr>
</tbody>
</table>

*Korb & Blackie, Cornea, 2008*
Why do glands obstruct? Multifactorial

- Root cause - BLINKING
- Age
- Hormones
- Drugs
- Seborrhea
- Epithelial overgrowth
1. The number of functional meibomian glands varies by location on the lower eyelid.

2. The number of functional meibomian glands is correlated with dry eye symptoms.

3. **Contact lens success correlates to functional MG**
   - RGP wearers for over 30 years – 8 or more glands open
   - SCL wearers – high correlation to success

A new metric to evaluate MG function and monitor status and progress of treatment.
In the absence of a paradigm and an objective method of evaluation, fact-gathering and development are severely impeded.

Formulated from writings of Thomas S. Kuhn

The first metric to allow standardized quantification of MG function

Diagnosis, Monitoring, Tx, Research
It is critical to understand that MGD is frequently present without obvious lid signs or inflammation.

Meibomitis must have MGD

THERE IS MORE NON-OBVIOUS THAN OBVIOUS MGD

Korb and Henriquez, 1980
Blackie, Korb, Knop et al., 2010
NON - OBVIOUS OBSTRUCTIVE MGD

WITHOUT OBVIOUS INFLAMMATION OR SIGNS

REQUIRES EXPRESSION FOR DIAGNOSIS

May appear normal without expression

Total obstruction
NO SECRETIONS or MATERIAL
despite extreme pressure

Korb & Henriquez
J Am Opt Assoc, 1980
**Mechanism of MG Obstruction - Multifactorial**

Keratotic clusters and bacterial proliferation

*Korb and Henriquez, 1980*

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**Blinking inhibition**

- Age
- Epithelial overgrowth
- Line Marx movement
- Drugs
- Eczema
- Hormones
- Lipid Profiles
- Seborrhea
- Surfactants Phospholipids

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**Ductal hyperkeratinization**

*Sullivan, 2009 – Androgens*

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**Dental Plaque Analog**

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**Why no chalazia when gland obstructed?**

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**Partial blinking is the primary reason for failure in Tx**
TREATMENT OF MG

- PALLIATIVE
- RESTORATIVE

GOALS
Reduce Evaporation & Evaporative Stress
Provide Lubrication

THE FUTURE – PREVENTIVE
The Dental Model
TREATMENT TO IMPROVE MG FUNCTION

Epithelial overgrowth

ROOT CAUSE
REMOVE OBSTRUCTION

Obstruction of duct

Dilated duct

1980 Korb & Henriquez, J Am Opt Assoc
TREATMENT TO IMPROVE MG FUNCTION

PATIENT
• warm compresses
  8-10 mins effective
• massage = risk
• self expression
• lid scrubs

The limits of home therapy: compliance, severity, duration
WARM COMPRESS Tx

**Warm compress at 45°C (113°F)**
Temp measured with infrared pyrometer
- outer lid: 35.5 to 42 - 43°C (2 - 3 mins)
- inner lid: 36 to 40°C (6 - 10 mins)

**Goal:**
Liquefy obstructive material

**Risk – Corneal deformation and irreversible keratoconus**

**The role of heat in rubbing and massage-related corneal deformation**
McMonnies, Korb, Blackie, CL&E 2012
MGD is Progressive

Meibomian function and structure changes over time

<table>
<thead>
<tr>
<th>Normal Function</th>
<th>Nonobvious MGD</th>
<th>Obvious MGD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Function</td>
<td>Structure</td>
<td>Normal Structure</td>
</tr>
</tbody>
</table>

An Increasing Problem

With new technology we stare even more and blink even less
A Change in Philosophy

Dry Eye Approach

- Await the onset of symptoms to commence treatment
- Lead with the most conservative treatment
- Gradually advance treatment as symptoms increase in severity\(^1,2\)

Goal: Treat Symptomology

- When treatments are unsuccessful this approach promotes confusion, and patient despair.

MGD Root Cause Approach

- Identify MGD
- Commence treatment when gland dysfunction is identified
- Lead with the most efficacious MGD treatment
- Rehabilitate the ocular surface and symptoms with adjunctive therapy

Goal: Intervene in Progression/Restore Gland Function

- This approach promotes patient and physician confidence in MGD management.

Meibomian Gland Structure

Visualization Prioritizes Therapy

Now MGD is diagnosed and managed with ability to also Visualize Structure
Meibomian Gland Dysfunction Progression

<table>
<thead>
<tr>
<th>Meiboscale</th>
<th>Area of Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Degree 0</td>
</tr>
<tr>
<td></td>
<td>≈0%</td>
</tr>
<tr>
<td></td>
<td>Degree 1</td>
</tr>
<tr>
<td></td>
<td>≤25%</td>
</tr>
<tr>
<td></td>
<td>Degree 2</td>
</tr>
<tr>
<td></td>
<td>26% - 50%</td>
</tr>
<tr>
<td></td>
<td>Degree 3</td>
</tr>
<tr>
<td></td>
<td>51% - 75%</td>
</tr>
<tr>
<td></td>
<td>Degree 4</td>
</tr>
<tr>
<td></td>
<td>&gt;75%</td>
</tr>
</tbody>
</table>

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LipiView II with DMI vs. Meibography

Meibomian glands that appear to be dropped out in traditional, static meibography can be seen with Dual-Mode DMI
LipiView II: Simple Procedure

- LipiView II imaging can be performed by one tech through the use of the keyboard at the top of the device.
- Lid everter ensures consistent and accurate (all glands visible) imaging.
Challenges of Current MGD Therapies

Therapy
- Warm compresses
- Eyelid scrubs
- Manual gland expression

Challenges
- External heat application is inadequate
- Significant discomfort
- Limited compliance
- Only the upper portion of the glands are treated or expressed
Warm Compresses Have Limited Efficacy

- Anterior lid is highly vascular; therefore, difficult for heat application to reach gland contents

- Adequate temperatures cannot easily and safely be achieved by the use of external warm compresses

Survey including ~550 patients diagnosed with Dry Eye:

- Those using artificial tears, lubricants, or punctal plugs report little to no success
Lipid/oil-Based Lubricant Eye Drops

Palliative – None treat the cause

Downside can be blurring & stinging with castor oil emulsions
Obstruction

Expression utilizing a hard surface against palpebral conjunctiva has been the only professional method until LipiFlow

- Pain tolerance = 10-20 PSI
- Pressure for effective expression = 20-30 PSI
- Limitation – Pain despite topical anesthesia

1994) Increase in tear film lipid layer thickness following treatment of meibomian gland dysfunction
KORB, GREINER

(2011) MG therapeutic expression — Quantifying pressure and pain
Korb & Blackie, Eye & CL
Problems with forceful expression against a hard surface

- Topical anesthesia not effective – **Painful**
- Requires multiple Tx: monthly – quarterly (3 - 6 per year)
- Trauma results in transient edema & inflammation (black and blue)
- Effective expression may require 2 - 5 minutes each lid – variable efficacy
The device applies **controlled heat** to the upper and lower *(inner)* palpebral conjunctival surfaces and lid margins, while simultaneously applying pulsating pressure over the upper and lower *(outer)* eyelids.

**Heat applied to both inner lid surfaces**

**Pulsatile pressure applied to outer lids**
Each eye receives a single 12-minute treatment with the treatment device at the same office visit.
Indications For Use

- The LipiFlow® System is intended for the application of localized heat and pressure therapy in adult patients with chronic cystic conditions of the eyelids, including meibomian gland dysfunction (MGD), also known as evaporative dry eye or lipid deficiency dry eye.
LipiFlow® Contraindications

Do not use the LipiFlow System in patients with the following conditions:

- Ocular surgery, ocular injury, ocular herpes of eye or eyelid within prior 3 months

- Active ocular infection or inflammation or history of chronic, recurrent ocular inflammation within prior 3 months

- Eyelid abnormalities or ocular surface abnormalities that may affect/compromise corneal integrity or lid function
# FDA STUDY – TREATMENT RESULTS WITH LIPIFLOW

<table>
<thead>
<tr>
<th>Effectiveness Parameter</th>
<th>LIPIFLOW (9 Site Study)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (n=130)</td>
</tr>
<tr>
<td>Meibomian Gland Assessment</td>
<td>1.9 (1.6)</td>
</tr>
<tr>
<td>Tear Break-up Time (0 to 20)</td>
<td>5.5 (2.9)</td>
</tr>
<tr>
<td>Dry Eye Symptom Questionnaire</td>
<td></td>
</tr>
<tr>
<td>Total SPEED Score (0 to 28)</td>
<td>14.3 (4.8)</td>
</tr>
<tr>
<td>Total OSDI Score (0 to 100)</td>
<td>32.0 (20.0)</td>
</tr>
</tbody>
</table>

**15 OF 25 GLANDS STUDIED**

*p < 0.0001, change from baseline to 2 weeks*

Control Group: *iHeat* standardized warm compresses – 5 minutes, QD x 2w
NO SIGNIFICANT IMPROVEMENT

One Year Duration Study
Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment.

PURPOSE: To determine the 1-year post-treatment dry eye status of subjects with meibomian gland dysfunction (MGD) and dry eye symptoms after receiving a single LipiFlow® Thermal Pulsation System (LTPS) treatment.

DESIGN: Single-center, prospective, observational, open-label, 1-month registered clinical trial with a 1-year follow-up examination.

PARTICIPANTS: Patients with evaporative dry eye disease with MGD and dry eye symptoms who had participated in the registered 1-month clinical trial and who were available for follow-up at 1-year.

METHODS: 18 of 30 subjects initially enrolled were able to return for a 1-year follow-up. Both eyes of all patients were treated with a single 12-minute treatment using the LTPS that liquefies and expresses the secretory contents of the meibomian glands. Meibomian gland function, tear break-up time (TBUT) and dry eye symptoms were measured. Data are presented for pre-treatment (baseline), and 1-month and 1-year post-treatment.

MAIN OUTCOME MEASURES: Meibomian gland secretion scores and TBUT and dry eye symptoms.

RESULTS: Significant improvement in meibomian gland secretion scores from baseline measurements (4.0±3.4) to 1-month post-treatment (11.3±4.7; p<0.0005) was maintained at 1-year (7.3±4.6; p<0.05). Baseline TBUT (4.9±3.0) was significantly increased at 1-month (9.5±6.9; p<0.05), however, this improvement was no longer evident at 1-year post-treatment (6.0±4.4). The significant improvement in symptom scores on OSDI and SPEED questionnaires observed at 1-month (p<0.0005) was maintained at 1-year [OSDI (p<0.05); SPEED (p<0.0005)].

CONCLUSION: A single 12-minute treatment with the LTPS offers an effective treatment for evaporative dry eye and MGD resulting in significant and sustained improvement in signs and symptoms for up to 1 year.
Long-Term (3 Year) Effects of A Single LipiFlow Thermal Pulsation System Treatment on Meibomian Gland Function and Dry Eye Symptoms

Conclusion: LipiFlow thermal pulsation system (LTPS) treatment provides an extended duration of efficacy in patients with evaporative dry eye disease with significantly improved meibomian gland function and significantly reduced dry eye symptoms for up to 3-years after a single treatment. This unexpected observation is further supported by 9-month, 7 12-month, 13 and 24-month14 post-LPTS studies. These findings involve simultaneous applications of regulated levels of heat and pressure applied to the upper and lower eyelids.
The Role of Ocular Surface In Vision Care

How to identify MGD during a medical exam

• Inspect lid margins & meibomian gland orifices
• Ask…“how do your eyes feel ?”
• Set appropriate expectations: Our primary goal is to intervene in MGD progression
• “Treatment is in your Future”
Treat MGD Aggressively

MGD is common and under-diagnosed

- Obvious signs may be absent
- Non-obvious MGD (NOMGD) is CLINICALLY SIGNIFICANT and may progress to classical MGD

Know when to refer

- Optometry needs to refer to one another
- Embrace the skill set of your fellow OD and lose the fear of losing a patient
- Working together to develop best outcomes for our patients with strengthen the doctor-patient and doctor-doctor relationship
Thank you

Co-manage patients with dry eye and formulate better treatment plans
Let’s work together to make our patient’s happy.
helpmydryeyes@gmail.com