"The Role of Meibomian Gland Dysfunction and Lid Wiper Epitheliopathy in Dry Eye Disease"

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SPONSORING SECTION: Cornea, Contact Lenses, and Refractive Technology

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OVERVIEW

According to *Contact Lens Spectrum*, the "Contact Lens Event of 2011" was the Tear Film and Ocular Surface Society's Meibomian Gland Dysfunction Workshop Report. Therefore, the Section on Cornea, Contact Lenses, and Refractive Technologies will devote the 2012 Section Symposium to this important and timely topic. The information presented in this Symposium will assist the contact lens practitioner and the general optometrist alike in the management of one of the most prevalent and morbid conditions seen in eye care—dry eye disease.

The faculty for this Symposium includes the Chair and the Vice Chair of the TFOS International MGD Workshop Steering Committee, Kelly Nichols, OD, MPH, PhD, FAAO and Gary Foulks, MD, FACS. The Symposium will also include a discussion of the recently identified entity, Lid Wiper Epitheliopathy. Caroline Blackie, OD, PhD, FAAO is one of the leading researchers in Lid Wiper disease, and she will detail the pathogenesis, diagnosis, and treatment of this condition.

PROGRAM

Moderator: Clarke Newman, OD, FAAO

"Changing Practice Patterns: 1.5 Years After the TFOS Meibomian Gland Dysfunction Report" (30 min + 5 min Q & A)
Kelly Nichols, OD, MPH, FAAO
Houston, TX

"What Do We Really Know About Lipid…Time-Tested and Emerging Therapies for Dry Eye/MGD" (30 min + 5 min Q & A)
Gary Foulks, MD, FACS
Louisville, KY

"Let's Translate Anatomy to Diagnostic Clinical Care: LWE and Marx's Line" (30 min + 5 min Q & A)
Caroline Blackie, OD, PhD, FAAO
North Andover, MA

Meibomian gland dysfunction
What is it, why does it occur and how may it be treated?

Kelly K. Nichols, Gary N. Foulks, Anthony J. Bron and David A. Sullivan, on behalf of the participants in the International Workshop on Meibomian Gland Dysfunction

Introduction

Although meibomian gland dysfunction (MGD) is a common, chronic, disabling disorder that influences the health and well-being of millions of people worldwide, there has been no global consensus on its definition, classification, diagnosis or therapy. To achieve this, the Tear Film & Ocular Surface Society (TFOS) sponsored the International Workshop on Meibomian Gland Dysfunction (www.TearFilm.org). This Workshop required over two years to complete and involved more than 50 leading experts from around the world. The Workshop Report is now published in IOVS 2011; Vol. 52, No. 4. Some highlights of the Workshop and its recommendations appear below.

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.

MGD is classified into two major types based on meibomian secretion: 1) Low Delivery States – the most frequent cause, and 2) High Delivery States (Figure 1). Ultimately, MGD can lead to alterations of the tear film, symptoms of eye irritation, inflammation of the ocular surface and dry eye.

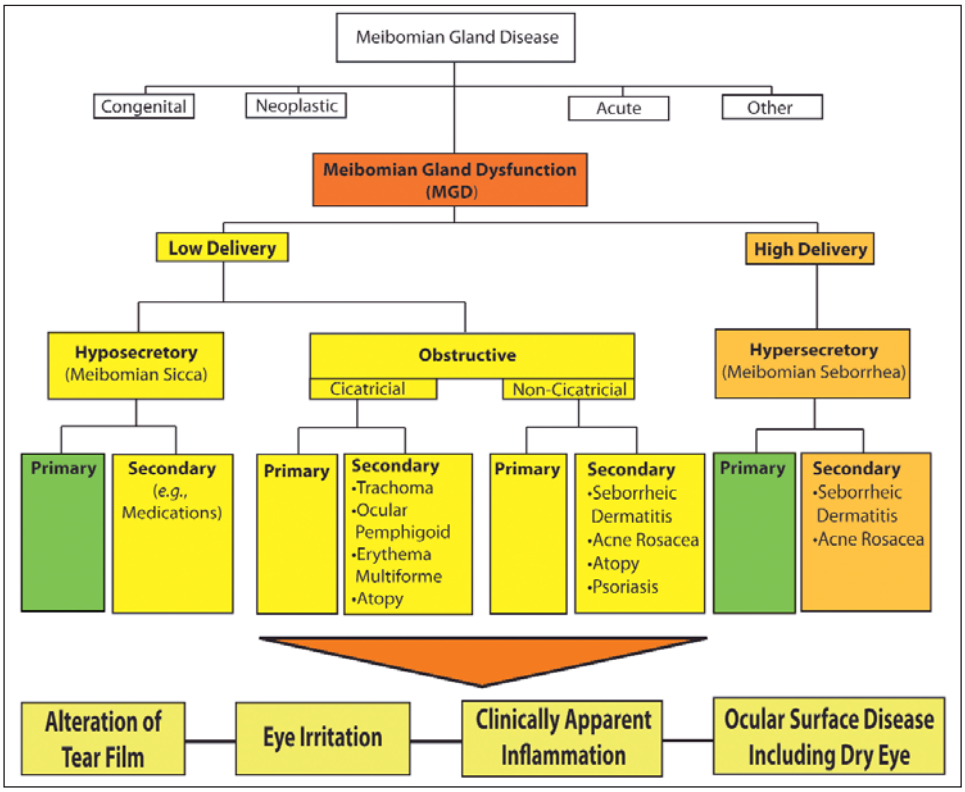


Figure 1. *Classification of MGD*

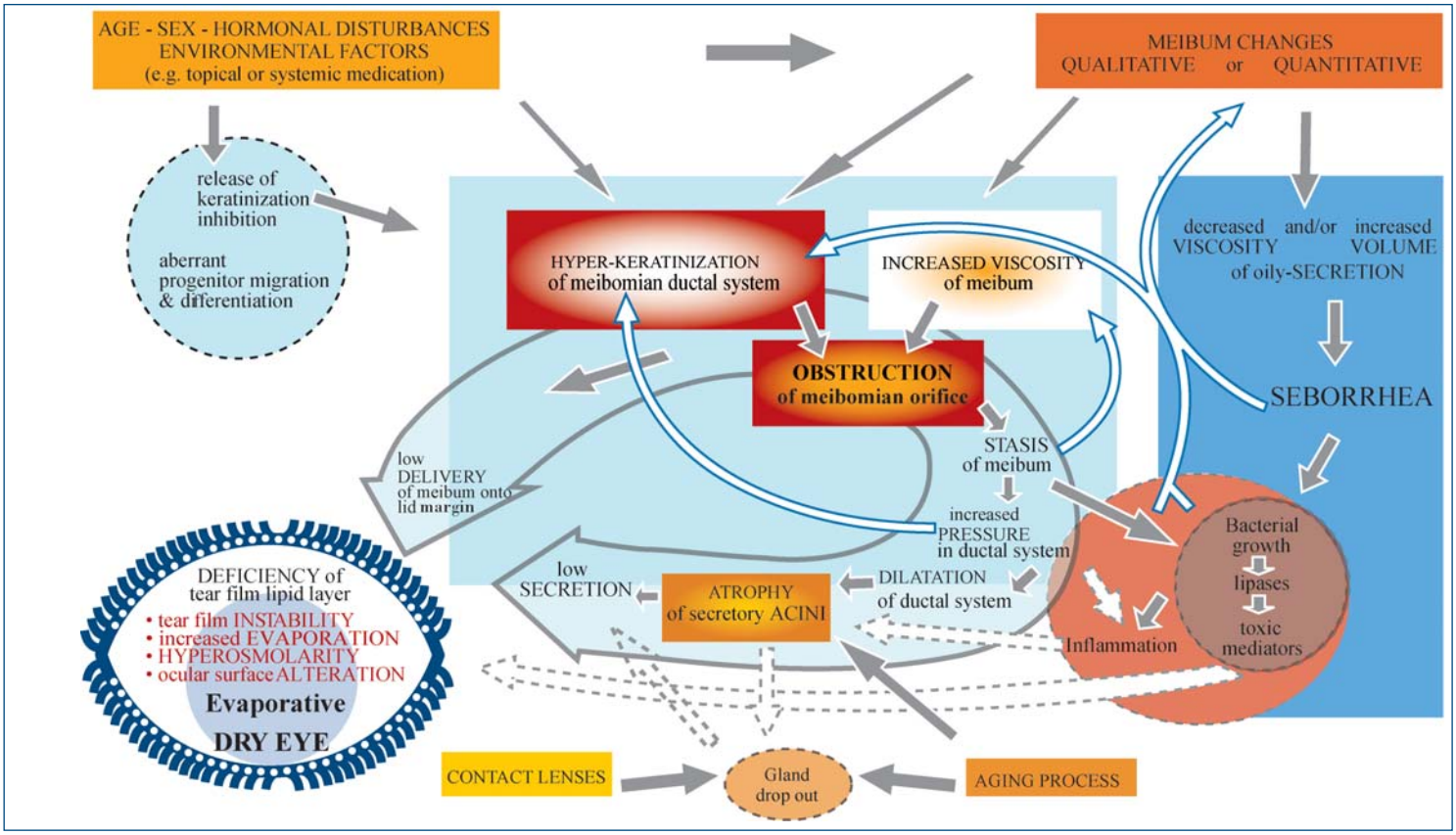


Figure 2. *Pathophysiology of obstructive MGD*

Why does MGD occur?

Low delivery, obstructive MGD is caused primarily by terminal duct obstruction, due to hyperkeratinization of the ductal epithelium, keratinized cell debris and increased meibum viscosity (Figure 2). A cicatricial form is also important.

The obstructive process is influenced by endogenous factors such as age, sex and hormonal disturbances, as well as by exogenous factors such as systemic agents (e.g. retinoids) and possibly contact lens wear. Important secondary associations are skin diseases (e.g. acne rosacea; atopic and seborrhoeic dermatitis) and cicatricial conjunctivitis (e.g. *Erythema multiforme; trachoma*). The obstruction may lead to intraglandular cystic dilatation, meibocyte atrophy, gland dropout and low secretion, effects that do not typically involve inflammation.

The end result is a reduced delivery of meibum to the lid magin and tear film lipid layer, leading to tear film instability, increased evaporation, tear hyperosmolarity, evaporative dry eye and ocular surface inflammation and damage.

Overall, MGD is an important, under-estimated condition, and is very likely the most frequent cause of dry eye disease.

How may MGD be treated?

An evidence-based approach to the management of MGD is shown below. At each treatment level, lack of response to therapy advances treatment to the next level. A [±] sign means that the evidence to support the use of the treatment at that level is limited or emerging, thus use should be based on clinical judgment. A [+] sign indicates the treatment is supported by the evidence at that stage of disease. The quality of expressed meibum and meibum expressibility are key features in the clinical assessment of MGD.

Further details of the management of MGD and MGD-related diseases are discussed in the full Report.

STAGE	CLINICAL DESCRIPTION	TREATMENT
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 (±)
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 (±) *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* (±) Artificial lubricants (for frequent use, non-preserved preferred) Topical emollient 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 (±) Anti-inflammatory therapy for dry eye as indicated (±)
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 11-15] ↑ Signs of inflammation: e.g. ≥ moderate conjunctival hyperemia, phlyctenules	*All the above, plus* Anti-inflammatory therapy for dry eye (+) **Key:** **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: 0=clear meibum; 1=cloudy meibum; 2=cloudy with debris (granular); 3=thick, like toothpaste [range 0-24]. **Expressibility of meibum** is assessed from 5 glands: 0= all glands expressible; 1=3-4 glands expressible; 2= 1-2 glands expressible; 3=no 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.

Acknowledgments: We thank Michelle Dalton (www.dalton-and-associates.com) and Sabrina Zappia and CITYNet (www.citynetonline.it) for their professional assistance with this Workshop highlight report. A listing of Workshop participants, as well as a direct link to the entire TFOS report in IOVS, may be found at: www.tearfilm.org

What we really know about meibum lipid: time-tested and emerging therapies for MGD and dry eye.

Gary N Foulks, MD, FACS
Emeritus Professor of Ophthalmology
University of Louisville School of Medicine

I. Lipid chemistry of meibum
   a. Composition
   b. Behavior of lipids
II. Lipid changes with age
   a. Composition
   b. Behavior
   c. Effect on tear film stability
III. Lipid changes with MGD
IV. Time tested therapy of MGD
   a. Lid massage after hot compress
   b. Oral doxycycline
V. Emerging therapy of MGD
   a. When it's the lipid problem
      i. Topical azithromycin
      ii. Topical cyclosporine
   b. When it's the epithelial plugging problem
      i. Lid expression
      ii. Controlled thermal pulsatile compression
      iii. Cannulation of the orifice and duct

Let's translate anatomy to diagnostic clinical care:
Lid Wiper Epitheliopathy (LWE) and the Line of Marx.

Caroline Blackie OD, PhD, FAAO

Lid Wiper Epitheliopathy (LWE) is an important dry eye sign frequently correlated with dry eye symptoms. It has been referred to as 'a missing link' in dry eye diagnosis and treatment. LWE occurs with all types of dry eye conditions, and is also a frequent consequence of contact lens wear.

The Line of Marx (LOM) is a normal anatomical feature of the upper and lower eyelids. Research has shown the LOM to undergo age related changes in its appearance. Research also shows that changes in the appearance of the LOM maybe indicative of MGD and dry eye states.

The purpose of this lecture is to review LWE and LOM. The importance of understanding each finding as separate entities in the maintenance of ocular surface health will be reviewed and methods for the diagnosis and management of dry eye disease with also be addressed.

As meibomian gland dysfunction (MGD) is recognized as a leading contributor to both dry eye and lack of lubrication, and in fact may be the leading cause of dry eye syndrome throughout the world. The role of MGD, and particularly obstructive MGD in LWE and changes to the LOM will be presented.

A. ANATOMY

- A review of the anatomy of the upper and lower lids – special attention is given to Kessing's Space, The Lid Wiper and The Line of Marx
- Kessing's Space defined: Kessing's space is the space separating the surface of the tarsal palpebral conjunctiva of the upper eyelid from the ocular surface.
- Lid Wiper is that aspect of the marginal conjunctiva of the upper eyelid that wipes the ocular surface during blinking.
- The Line of Marx represents the surface of the ocular mucocutaneous junction.
- Reasons why the Lid Wiper and the Line of Marx are not the same structure.

B. Lid Wiper Epitheliopathy (LWE) is defined as compromise to the lid wiper's epithelia.

- LWE, first described in 2002, is correlated to dry eye symptoms and may occur with or without contact lenses.
- Diagnosis of LWE requires careful eversion of the upper lid and observation of this specific area for the width of the upper lid.
- LWE diagnosis requires the use of a vital dye for diagnosis.
- Best diagnoses with two dyes: fluorescein and either rose Bengal or lissamine green

C. Prevalence of LWE

- 80% of symptomatic CL wearers demonstrated LWE vs. 13% for asymptomatic controls
- LWE with SCL and RGP wearers

D. Prevalence of LWE when dry eye symptoms present, but no signs in non-CL wearers (Korb et al., 2005)

- 76% of symptomatic non-CL wearers demonstrated LWE vs. 12% for asymptomatic controls
- Conclusion: A significant proportion of the population with dry eye exhibits lid wiper epitheliopathy.

E. Prevalence of LWE when both dry eye symptoms and signs are present in non-Cl wearers (Korb et al., 2005 – 2009)

- 88% of symptomatic non-CL wearers had LWE compared to 16% for asymptomatic patients. The prevalence of LWE was 6 times greater for those with symptoms compared to the control group, and the prevalence of LWE ≥ grade 2 was 16 times greater for the symptomatic group than for the control group. (Scale 0 – 3)

F. Causative factors:

- Inflammation – the primary cause or sequelae
- Lubrication – boundary *vs.* hydrodynamic
- Mechanical – ocular surface or contact lens surface abnormalities leading to epithelial trauma
- Protective coatings of the epithelia of the LW
- Meibomian Gland Dysfunction

G. Meibomian Gland Dysfunction

- Review the expanding role of meibomian glands: Meibomian gland dysfunction may be the leading cause of dry eye syndrome throughout the world.

- We need to understanding MGD and how to evaluate MG functionality.
- MGD defined by the MGD workshop 2011:

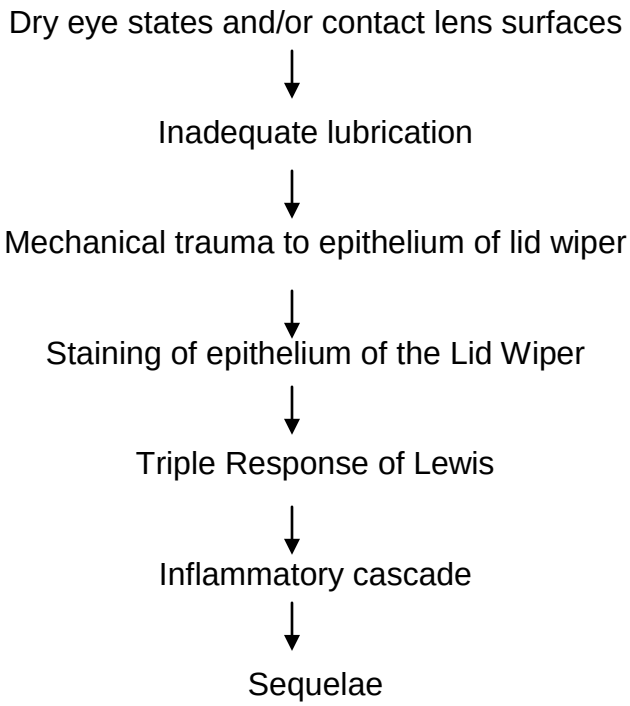
> *Meibomian gland dysfunction* (*MGD*) *is a chronic*, *diffuse abnormality of the meibomian glands*, *commonly characterized by terminal duct obstruction and/or qualitative/ quantitative changes in the glandular secretion*. *It may result in alteration of the tear film*, *symptoms of eye irritation, clinically apparent inflammation*, *and ocular surface disease.*

- MG function can be determined through standardized diagnostic meibomian gland expression.

H. Treatment of LWE

- Philosophy for treatment of LWE
  - LWE is a sequela of a dry eye state
  - Treat the specific dry eye state
  - Treat inflammation as required
- Specific treatment of LWE
  - Ointment at night
  - Lubrication during day
  - Medications for dry eye (Restasis)
  - Topical Steroids
  - MGD
    - Meds
    - Heat (warm compresses, heated face masks, etc.)
    - Expression
    - LipiFlow

I. Pathophysiology of LWE



J. Conclusions

- The squamous epithelia of the lid wiper are designed for the movement and rubbing actions of the upper lid, but require an adequate tear film and lubrication to prevent LWE.
- LWE is an alteration of the epithelia of the lid wiper and or their protective physiological coatings.
- LWE is diagnosed by staining with specific techniques.
- LWE is frequently present with any dry eye states, depending on the severity.
- LWE is frequently present in contact lens wearers symptomatic for dry eye.
- LOM and LWE are not the same entity.
- Changes in the LOM can be and indicator of MGD.
- Treatment is required for LWE.