A New Paradigm for Confronting and Overcoming Failure in the Treatment of Ocular Surface Disease: A Review of My Most Challenging Cases

Donald R. Korb, OD (Boston, MA)
Caroline A Blackie, OD, PhD (Boston, MA)

American Academy of Optometry
Seattle, October 2013
2-Hour Course

FINANCIAL DISCLOSURES: Dr. Korb is a founder of Korb Associates of Boston, and a co-founder of both Ocular Research of Boston and TearScience (Morrisville, NC). Korb Associates and TearScience have supported Dr. Korb’s research. Dr. Korb has a financial interest in all 3 organizations. Dr. Blackie receives funding from TearScience.

ABSTRACT

Dry eye is the leading reason for visits to optometrists and ophthalmologists in the US and the leading cause of contact lens intolerance and discontinuation of wear. A change in direction from an aqueous to a lipid etiologic model was highlighted by the 2011 Report of the International Workshop on Meibomian Gland Dysfunction’s summary statement: “MGD may well be the leading cause of dry eye disease throughout the world.” (IOVS, 2011)

This paradigm shift from the traditional aqueous and mucous-based models for dry eye to inclusion and emphasis of MGD has resulted in an explosion of interest and research. This course will focus on 16 concepts and diagnostic tools including the evidence based data to support this new paradigm of dry eye etiology, its diagnosis and treatment. Illustrative case reports will be presented.

The following topics will be emphasized:

- MGD is usually non obvious prior to anatomical and functional changes resulting from a MGD induced inflammatory
- Differentiating between palliative and restorative treatment of MGD
- The role of new treatments; the role of the lid wiper in the dry eye cascade
- The role of interferometry
- The importance of the Line of Marx and a new treatment, debridement of the Line of Marx
- Understanding the dry eye cascade, a consequence of MGD, and the data establishing that it is responsible for the majority of all dry eye signs, dry eye symptoms and contact lens related dry eye
- Why MG functionality is critical to diagnosis and treatment
- The relevance of the multiple types of physical expression
- The relevance of transillumination and meibography
• The importance of the Korb-Blackie Light Test, a new test for diagnosis of exposure of the ocular surfaces to air while sleeping despite apparent optimal lid closure, and indicated treatments
• Hidden or non obvious inflammation of cornea and lids, requiring in vivo confocal microscopy for diagnosis

Emphasis will be placed on how this research provides a practical clinical approach for the diagnosis and management of dry eye patients in clinical practice, and how to specifically confront and overcome failure. Illustrative case reports of the latter will be presented including how dichotomies and anomalous findings encountered in dry eye conditions and disease can be explained by considering how to differentiate between the relative contributions of aqueous vs. evaporative dry eye.

INTRODUCTION:

Dry Eye in 2013: Dry eye is the leading reason for visits to optometrists and ophthalmologists in the US. Dry eye is also the leading cause of contact lens intolerance leading to discontinuation of contact lens wearing. Treatment of dry eye has proven to be less than optimal.

A New Direction for Dry Eye: A change in direction for the understanding of dry eye etiology and treatment was established by the 2011 Report of the International Workshop on Meibomian Gland Dysfunction summary statement:

“MGD may well be the leading cause of dry eye disease throughout the world.” (IOVS, 2011)

This dramatic shift from the traditional aqueous and mucous-based models for dry eye to inclusion and emphasis of meibomian gland dysfunction resulted in an explosion of interest and research and qualifies as a true paradigm shift, as defined by the nomenclator of the term paradigm shift, Thomas S. Kuhn

Why do we care about Dry Eye?

• High prevalence
• Rapidly changing non-blinking environment with ever increasing use of electronic mobile media and computers – the world of the 21st century
• Average age of onset is decreasing due to lifestyle – now includes children
• A public health issue
• Aging population
• Dietary concerns
• Contact lens wear
• Surgical outcomes – LASIK – cataract extraction
• Dry eye has come looking for us …. with today’s lifestyle we cannot ignore dry eye.
16 OBJECTIVES — NEW PARADIGM CONCEPTS AND TOOLS

1. MGD IS THE LEADING CAUSE OF DRY EYE, NOT LACRIMAL GLAND AQUEOUS DEFICIENCY

2. MGD IS CHRONIC AND PROGRESSIVE INVOLVING A DRY EYE CASCADE

*Definition:* "Meibomian gland dysfunction 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.*" (Report of the International Workshop on Meibomian Gland Dysfunction, IOVS, 2011)

*Progressive:* The author’s new model for the **Dry Eye Cascade**, including a proposed mechanism of action to explain how minimal hyposecretory MGD, frequently non-obvious, cascades into anatomical and atrophic changes of the lids, meibomian glands, cornea, mucous secretory system and lacrimal gland until the magnitude of the changes obscure the root cause – meibomian gland obstruction. This model provides an understanding for the treatment and prevention of the most prevalent form of dry eye.

3. MG FUNCTIONALITY – Dx REQUIRES DIAGNOSTIC PHYSICAL EXPRESSION

*Definition:* "Meibomian gland dysfunction is a *chronic*, diffuse abnormality of the meibomian glands, *commonly characterized by terminal duct obstruction* and/or qualitative/quantitative changes in the glandular secretion.

Obstruction of the meibomian gland ducts and orifices results from keratinized epithelial cells and secretory material aggregating in keratotic clusters, altering MG secretion & the tear film.

*Case report — Evaluation of only the central glands led to misdiagnosis and ineffectual treatment.*

4. MG FUNCTIONALITY – NOT EQUALLY DISTRIBUTED ACROSS THE LID MARGIN
5. NON OBVIOUS MGD – ALL MGD IS NON OBVIOUS PRIOR TO THE CASCADE, RESULTING IN ANATOMICAL AND FUNCTIONAL CHANGES

Expanded classification and understanding of MGD should include:

- **Obstructive MGD without obvious inflammation but with signs of MGD**
- **Non-obvious Obstructive MGD, possibly the most common form of MGD — requires physical expression for Dx**

*Case report — Evaluation of the lids with conventional methods, but without expression, resulted in a misdiagnosis of aqueous deficiency and not lipid deficiency and evaporative dry eye, leading to ineffectual treatment.*

6. EVAPORATIVE DRY EYE – THE ETIOLOGY OF THE MAJORITY OF ALL DRY EYE SIGNS & DIAGNOSES, DRY EYE SYMPTOMS & CONTACT LENS RELATED DRY EYE IS EVAPORATIVE DRY EYE

The Goggle Test is very effective for diagnosis of evaporative dry eye

7. TREATMENT OF MGD: SHOULD BE BOTH PALLIATIVE AND RESTORATIVE

- Lipid Eye Drops – Sprays
- Warm compresses
- Blinking exercises
- Self expression
- Professional Office Physical Expression
- LipiFlow

8. THE ROLE OF THE LIPIFLOW

- Liquefy, express and evacuate ductal obstruction and gland contents
- 12 minute treatment
- No pain
- THE FUTURE SHOULD ALSO BE PREVENTATIVE (*DENTAL MODEL*)

9. USE A QUESTIONNAIRE

- The SPEED questionnaire – validated
10. THE ROLE OF THE LID WIPER IN THE DRY EYE CASCADE

Lid Wiper Epitheliopathy (LWE) – Frequently the Missing Link

*Definition*: Lid Wiper is that aspect of the marginal conjunctiva of the upper eyelid that wipes the ocular surfaces during blinking

- A missing link in dry eye diagnosis, treatment and contact lens comfort
- Windshield wiper analogy
- Prevalence
- Diagnosis and grading of LWE – the use of stains in diagnosis
- Correlation of LWE to dry eye signs and symptoms
- Evidence based medicine for LWE – the studies
- Causative factors of LWE – inflammation, lubrication, mechanical
- The role of the lid wiper in ocular sensation and symptoms
- The lid wiper and lid wiper epitheliopathy in contact lens practice
- The role of the lid wiper in exacerbating dry eye and inflammation
- Treatment of LWE
- **FOCUS ON LUBRICITY OF TEAR FILM AND LWE**

*Case report* – Evaluation of a severe dry eye condition with conventional methods, but without either examination of the lid wiper or diagnostic expression of the meibomian glands, resulted in a misdiagnosis of aqueous deficiency, leading to ineffectual treatment.

11. The Role of Interferometry

- Instrumentation – Interferometers
- The LipiView – a new computerized interferometer
- Measurement of lipid layer thickness and characteristics
- Correlation of lipid layer thickness to dry eye symptoms
- Correlation to meibomian gland expressibility and function
- **Role in diagnosis and treatment**

12. BLINKING:

- **The world of the 21st century** – Rapidly changing non-blinking environment
- Ever increasing use of electronic mobile media and computers
- Inhibition of blinking
- Stasis – obstruction of Meibomian glands
- Dry eye cascade
- Evaporative Dry Eye
- Blink rehabilitation to meet the 21st century requirements
13. THE LINE OF MARX, THE LID MARGIN AND DEBRIDEMENT

Case report — Evaluation of the lids with careful attention to the Line of Marx and diagnostic meibomian gland expression led to both treatment of the Line of Marx and lid margins with debridement and treatment of MGD with expression. The result was effectual treatment in a previously refractory dry eye condition.

14. TRANSILLUMINATION AND MEIBOGRAPHY

Case report - Evaluation of the lids with both transillumination and meibography resulted in an understanding of the magnitude of the dropout, allowing for the both patient understanding and the design of a treatment program to provide comfort despite the loss of over 90% of all MG function.

15. SURFACE EXPOSURE TO AIR WHILE SLEEPING DESPITE APPARENT OPTIMAL LID CLOSURE

Case report – Evaluation with the Korb-Blackie Light Test within 30 seconds provided the diagnosis and allowed the design of a program to protect the ocular surfaces while sleeping, controlling inflammation and providing patient comfort and dramatic cosmetic appearance.

16. Hidden inflammation – a consequence of Chronic MGD
(Requires In Vivo Confocal Microscopy for diagnosis)

- In vivo confocal microscopy (800 magnification) required to diagnose inflammation and other changes to cornea and eyelids
- Corneal pathological findings
  - Changes to corneal cells
  - Changes to corneal nerves
  - Inflammatory cells
- MG pathological findings
  - Subepithelial eyelid fibrosis
  - Periglandular inflammatory cells
  - Thickening of ductal basement membrane
A NEW TREATMENT PHILOSOPHY

To understand the new treatment philosophy, it is helpful to characterize treatment into three separate areas:

1. **Reactive treatment** – reactive treatment is primarily in response to patient symptoms and usually for severe dry eye or dry eye which has been present for a significant length of time – i.e., over one year. The patient usually presents with symptoms, although some present with blurred vision and ocular fatigue as their chief complaint.

24-hour a day approach to treatment

The Korb/Blackie Light Test is valuable in establishing whether inflammation occurs during sleep. This inflammation can prevent symptom improvement post LipiFlow treatment.

Debridement is helpful with the majority of patients, as it not only removes excess tissue (analogous to dental scaling), but also prepares the lid margins to better deliver the increased Meibomian secretion resulting from LipiFlow treatment to the tear film

2. **Maintenance treatment** – Treatment post successful treatment of MG obstruction

- Further increases the efficacy of treatment and prevent regression
- Maintenance treatment – either office or home treatment, or both
- Debridement would be performed in the office
- Home therapy tailored to the individual and might include blinking exercises, warm compresses, lid and lash scrubs, and Meibomian orifice and Line of Marx scrubs.
- Consider fee structure – private and insurance

3. **Preventive treatment** - A new area dedicated to preventing evaporative dry eye

- Embrace a dental model
- Routine visits to the dentist and hygienist provide maintenance of the gums and teeth, and also more significant intervention such as coating on the teeth to prevent decay and the need for orthodontics
- The dental analogy applied to Dry Eye and to intervention is that the patient should undergo specialized ocular examinations at routine intervals to prevent dry eye
SUMMARY: THE DRY EYE CASCADE IS INITIATED BY A DECREASE IN MG FUNCTIONALITY, RESULTING IN A DECREASE IN LIPID SECRETION AND RESULTING LLT AND QUALITY. WHEN THE RATE OF EVAPORATION OF THE AQUEOUS EXCEEDS THAT THRESHOLD REQUIRED TO MAINTAIN TEAR FILM STABILITY, A SERIES OF SEQUELAE RESULT IN DRY EYE.

IMPLICATIONS OF MGD DRY EYE CASCADE

Stasis – Obstruction
Decrease in lipid secretions
Evaporation increases
Decrease in aqueous layer thickness
Unstable tear film

Lubricity compromised
Microtrauma
Lid Wiper Epitheliopathy
Triple Response of Lewis
Inflammation

Sequelae of a compromised lipid layer
Visible changes
Inflammation
Palpebral and bulbar conjunctivitis
Anatomical changes to external surfaces, lid margins, Line of Marx

Sequelae of a compromised lipid layer
Not Visible Changes – Specular Microscopy – 800 X
Cornea: Cells altered, nerve density, branching, tortuosity, neuromas, dendritic cells
Lids: Fibrosis, inflammatory cells, MG damage
SEVERE INTERNAL INFLAMMATION, FIBROSIS & ATROPHY

Sequelae of a compromised lipid layer
• Does lacrimal gland up-regulate, overwork leading to atrophy?
• Diabetic & adrenal analogues

Treat MGD early to:
Prevent visible and non-visible lid and corneal changes
Prevent MGD & Dry Eye

Ocular surface compromised
Dry eye Inflammation

Sjögren’s Syndrome
JRA
SUMMARY OF DRY EYE CASCADE

- Lipid deficiency & not aqueous deficiency is usually the catalyst for the DRY EYE & inflammatory cascade

Backward to conventional models and treatment

- MGD and MG OBSTRUCTION may be obvious or non-obvious, most frequently non-obvious, particularly in contact lens practice
- Stasis and obstruction of the meibomian glands leads to decreased secretion and increased evaporation with the sequela of dry eye
- Dx of MG functionality requires expression
- Treat MG obstruction and MGD aggressively