MEIBOMIAN GLAND DYSFUNCTION: “WHERE DRY EYE BEGINS”

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FINANCIAL DISCLOSURES

I am a paid consultant for the following companies:
- Konan Medical
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DRY EYE DISEASE

“It 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.”

To determine a diagnosis of dry eye disease, symptoms that suggest the presence of dry eye syndrome must be present and positive scores in any of the following three measurements must be present
- Tear film stability
- Tear film osmolarity
- Ocular surface staining

Severe dry eye disease with major impact on quality of life can affect up to 10% of the population over 50 years old


NATURAL HISTORY OF DRY EYE DISEASE

The disease evolves in a sequence of four milestones:
1. Loss of water from the tear film with an increase in tear osmolarity
2. Decreased conjunctival goblet cell density and decrease corneal glycogen produce increased conjunctival epithelial desquamation
3. Increased corneal epithelial desquamation
4. Destabilization of the corneal-tear interface

LOSS OF WATER FROM THE TEAR FILM

- Loss of water from the precorneal tear film results in decreased tear film volume and is associated with debris in the tear film
- Dehydrated mucus that has precipitated in to the inferior fornix indicates severe loss of water from the tear film

CONJUNCTIVAL DESQUAMATION

- Abnormal increase in conjunctival sloughing results in immature conjunctival epithelial cells moving onto the surface of the eye
- As the desquamation accelerates, the damaged cells release inflammatory mediators onto the surface of the eye and the inflammatory process begins
MEIBOMIAN GLAND DYSFUNCTION

"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 glandular secretions, if they result in obstruction of the tear film, symptoms of eye irritation, clinical apparent inflammation, and ocular surface damage."

- Most prominent clinical aspects of meibomian gland dysfunction
  - Obstruction of meibomian gland orifices and terminal ducts
  - Synthesis and quantitative changes in meibomian gland secretions such as increased viscosity or loss of meibum transparency
  - Consequence of insufficient lipids in the precorneal tear film
  - Increased tear-film evaporation with subsequent hyperosmolarity
  - Tear film instability
  - Increased bacterial growth on the eyelid margin
  - Ocular surface damage and discomfort

Risk Factors for MGD

- The number of meibomian glands declines with age
- Medications such as
  - Statin therapy
- Contact lens wear
- Allergic conjunctivitis and other external ocular diseases
- Long-term use of eyedrops for dry eye syndrome
- Autoimmune diseases
- Smoking
OBSTRUCTIVE MEIBOMIAN GLAND DYSFUNCTION

Requirements for a clinical diagnosis of obstructive meibomian gland dysfunction

- Medical and ophthalmic history
- Biomicroscopy
- Eyelid margin, tarsal hyperemia
- Eyelid margin telangiectasia
- Eyelid margin thickening
- Gland orifice metaplasia
- External examination
- Eyelid tenderness

Clinical appearance of severe obstructive meibomian gland dysfunction

- Eyelid margin hyperemia
- Tarsal hyperemia
- Eyelid margin telangiectasia
- Obstruction of gland orifices
- Irregularity of eyelid margin
- Partial meibomian gland dropout

EYELID MARGIN ABNORMALITIES

- Irregular eyelid margins
- Plugged meibomian gland orifices
- Vascular engorgement
- Anteroror postero-replacement of the MCJ

GLAND EXPRESSION PEARLS

- The gland will initially become obstructed or plugged
- A patent medium outflow tract through the natural orifice is not always achieved
- The location of the damage is dependent upon the location of the ductal obstruction
- Treatment is focused on re-establishing a patent duct/orifice system

- Obstruction just inside the orifice abuts the ductular process
- If the obstruction is proximal to the first acinus and there remains a communication between the acinus and the orifice, the gland would demonstrate expressible meibum even though there is proximal obstruction
- In these glands, if the proximal obstruction is not relieved, the gland tissue behind the obstruction would show elevated intraductal pressure with subsequent atrophy leading to a truncated gland

MEIBOMIAN GLAND ATROPHY

Untreated obstructive meibomian gland dysfunction will lead to atrophy of the glands and is characterized by the following abnormal morphologic features

- Segments of discontinuous meibomian gland tissue
- Shortening of glands (i.e., truncated)
- Whole or partial gland dropout
- Fading or poorly defined glands
- Loss of all meibomian gland tissue

CONTACT LENS-INDUCED MEIBOMIAN GLAND ATROPHY

Although the mechanisms responsible for gland atrophy in contact lens wearers is unclear, researchers have found that shortening of the glands in lens wearers is likely detectable at the lateral side of the glands rather than horizontally

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**MEIBOMIAN GLAND ATROPHY**

Dark area on tarsal plate indicates total acinar-ductular atrophy.

- Obstruction of gland orifice or central duct death in ducts of meibum
- Increased intraductal pressure
- Atrophy over time
- Obstructive function of the central duct
- Atrophy of the secretory duct is characterized by gland dropout

**WHY IS THE EYELID INFLAMED?**

The International Workshop on Meibomian Gland Dysfunction

- Bacteria on the lid margin produce enzymes that inactivate and lyse the outermost meibum lipids and a terminal duct epithelium
- Meibum glands obstruct due to keratinized and material mixed with the biofilm
- Obstructive process is influenced by the following factors:
  1. Age
  2. Sex
  3. Emotional stress
  4. Topical medications

**Biofilm Theory**

In dry eye blepharitis syndrome (DEBS), meibomian gland dysfunction involves six steps, which are related to bacterial changes causing inflammation.

1. Biofilm formation
2. Biofilm colonization
3. Quorum-sensing gene activation
4. Virulence factor production
5. Inflammation

**DRY EYE BLEPHARITIS SYNDROME**

The disease evolves through a series of four milestones over several decades

- Stage 1: Follicular Inflammation
- Stage 2: Meibomian Gland Dysfunction
- Stage 3: Aqueous Deficiency
- Stage 4: Eyelid Deformity

**FOLLICULITIS**

- Small lash bulb becomes inflamed after virulence factor production begins from a bacterial biofilm
- The inflammation is characterized by edematous follicular tissue swelling up around the base of the eyelash in a "volcano" sign
- As the eyelash grows, small pieces of biofilm adherent to the eyelash will be pulled off of the eyelid margin resulting in what is known as coloboma

**WHY IS THE EYELID INFLAMED?**

The newly activated genes produce a wide variety of virulence factors, many of which are extremely inflammatory

- Virulence factors cause bleb-grade classic inflammation on the eyelid surface and eventually within the structures of the margin such as lash follicles, glands and connective tissue, eventually affecting the accessory glands and promoting a chronic inflammatory response continuing.
"Cylindrical Dandruff" is a manifestation of folliculitis.

Biofilm accesses the potential space between the lash and the surrounding follicle by extending down along the inert eyelash.

The biofilm accumulates around the eyelash while still deep within the follicle, effectively sheathing the slow-growing eyelash. Because the follicle is usually damaged at this point, the rate of lash growth is slower and the biofilm accumulation effectively results in a "pipe-stemming" of the eyelash.

A layer of biofilm within the gland.

Inflammatory damage has begun.

The ductile is probably blocked and decreased lipid or abnormal lipid now makes up the secretions.

Abnormal lipids are characterized by an increased melting point and the secretions become thickened. When these glands are expressed, you may see copious amounts of "meibofilm" (biofilm and abnormal meibomian secretions).

A systematic and long-term program of eyelid margin hygiene is the basis of treatment for obstructive meibomian gland disease.

1. Application of heat to liquify the meibum
   - Electromechanical or light-based device with manual expression
   - Home-based warm compresses with digital massage or heated masks

2. Eyelid margin is cleaned mechanically
   - Topical or oral antibiotic/anti-inflammatory therapy

A thermoelectric device for evacuation of the meibomian glands that brings glandular secretions to their melting point and expresses the softened meibum via digital massage.

An automated technique for evacuation of the meibomian glands using heat and intermittent pressure.

An automated technique for evacuation of the meibomian glands using heat and intermittent pressure.
EYELID MARGIN IS CLEANED MECHANICALLY

Mechanical Debridement with Spatula

A technique for debridement using a pool, spatula or electromechanical device to scrape the eyelid margin
- Bacterial overgrowth is removed
- Meibomian glands are unroofed
- Potential complication is structural microtrauma to the eyelid margin

 Destruction of the biofilm on the eyelid margin can result in the following benefits:
- Removes the source of eyelid inflammation
- Improves the lipid layer of the tear film
- Allows the eyelids and the glands to begin the healing process

Clinical Applications
- Dry eye disease
- Contact lens patients
- Surgical patients
- Chronic conjunctivitis

CONCLUSION
A multimodal treatment program is the best way to treat dry eye blepharitis syndrome
- Remove the bacterial biofilm that is causing the inflammatory response in the structures of the eyelid
- Reduce or eliminate meibomian gland obstruction
- Reduce or eliminate inflammation on the ocular surface
- Treat tear film insufficiency with topical lubrication and/or punctal occlusion
- Design a treatment program to maintain eyelid health
- Clean the eyelid margin
- Anti-inflammatory and/or antibiotic therapy

ANTI-INFLAMMATORY & ANTIBIOTIC TREATMENT

Topical Therapies
- Lipid-based artificial tears or hypotonic artificial tears
- Steroid/antibiotic drops
- AZITHROMYCIN drops
- Steroid drops
- STEROID drops
- HYPOCHLOROUS acid drops, gels, sprays
- Other eyelid hygiene products

Oral Therapies
- Doxycycline or AZITHROMYCIN
- Omega-3 essential fatty acid nutritional supplementation