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MILLENNIALEYE

MEIBOMIAN GLAND DYSFUNCTION:

A Dermatologic Perspective



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This is a summary of a paper recently published in *Clinical Ophthalmology* by the featured authors.

Meibomian gland dysfunction (MGD) was first named as a key contributor to evaporative dry eye in the first formal attempt to define and classify dry eye in 1995.¹ Despite this initial mention, MGD wasn't clearly defined until 2011 when the International Workshop on Meibomian Gland Dysfunction proposed the following definition: "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."² The significant negative impact of MGD and its high prevalence make it worthwhile to better understand the underlying etiology and pathogenesis (Figure 1).

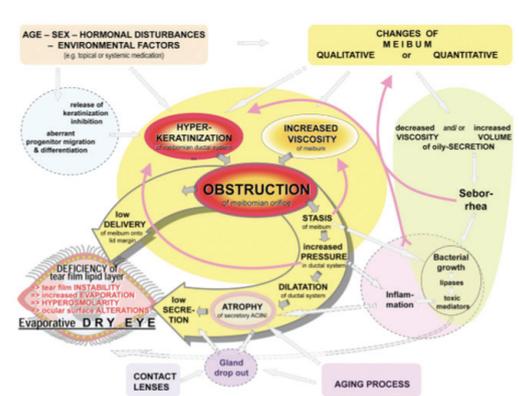
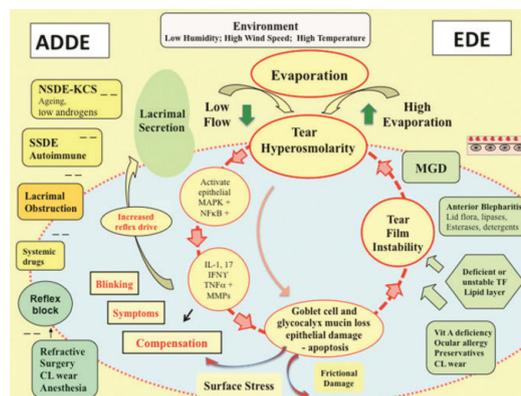


Figure 1. The negative impact of MGD and its high prevalence make it worthwhile to better understand the underlying etiology and pathogenesis.

UNDERSTANDING THE MEIBOMIAN GLAND

An individual meibomian gland consists of multiple acini, which are continuously synthesizing hundreds of different lipids in addition to various proteins and forms of keratin which make up meibum (Figure 2).³⁻⁵ This meibum, moved by the mechanical pressure of blinking, is driven into the central duct of the gland and out of the gland orifice to become a key component of the tear film. The central duct of the meibomian gland is lined with modified keratinized epithelial cells.⁶

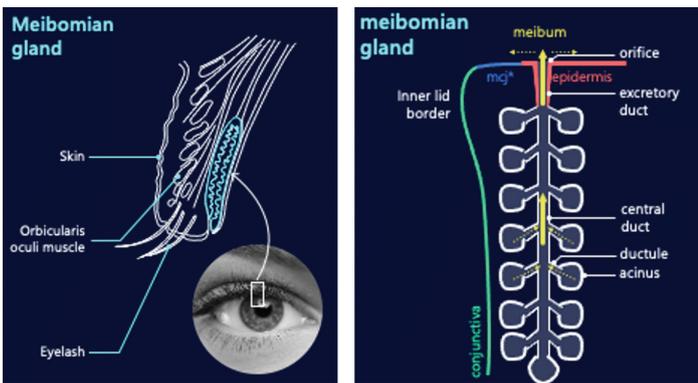


Figure 2. The meibomian gland.

MGD occurs when there are pathological alterations to the quantity and composition of the meibum. This may be an increase in heavier wax and saturated cholesteryl esters, or an alteration of the keratin proteins within the meibum. Incorporation of keratin into the meibum can make it more rigid and unable to incorporate into the lipid layer of the tear film and can raise its melting point so that it is a solid at body temperature.⁷⁻¹⁰

OXIDATIVE STRESS

In healthy tissue, disulfide bonds form between keratin when a single healthy protein has reached its final location. In oxidizing conditions, there is significantly less control in

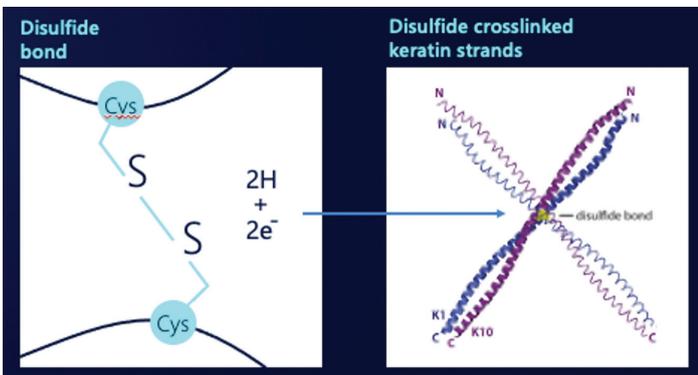


Figure 3. Oxidative stress contributes to the pathology of MGD¹¹ and the formation of aberrant disulfide bonds.

the formation of disulfide bonds that leads to aggregates in uncontrolled locations (Figure 3). Reactive oxygen species that are present in MGD may be promoting this formation of disulfide bonds.¹¹

THE PROCESS OF HYPERKERATINIZATION

Meibomian glands are similar to sebaceous glands, in that they both involve a process that requires continual cell turnover. In meibomian glands, epithelial cells transform to become keratinocytes, and dead keratinocytes are bound together by an intracellular lipid bilayer that includes keratin filaments to allow the skin to function as a barrier. Healthy epithelial cells shed at regular intervals. When these cells do not shed at a sustainable rate, it results in an excess of keratin formation and cell accumulation known as hyperkeratinization.¹² Hyperkeratinization is a fundamental cause of acne and a common finding in other dermatologic diseases, such as psoriasis and atopic dermatitis (Figure 4).



Figure 4. Hyperkeratinization in the gland orifice (top) and central duct (bottom).

Significant study has led to our current understanding that both hyperkeratinization within the meibomian glands and excess protein within the meibum itself are present in patients with MGD.^{7,13} Blackie and colleagues published a review of the data and stated, “Despite the potentially coexisting roles of bacteria, tear film osmolarity, and inflammation, it is critical to recognize that the primary mechanism for obstructive MGD is keratinization of the meibomian gland ducts. Thus, the success of any therapy for all forms of obstructive MGD is primarily dependent upon relief of the obstruction and secondarily upon the management of other factors such as inflammation and/or infection.”

SELENIUM SULFIDE: A KERATOLYTIC AGENT

Keratolytic agents (agents that soften keratin) are commonly used in dermatology, both water-soluble alpha hydroxy acids (AHAs) and lipid-soluble beta hydroxy acids (BHAs). Selenium sulfide is one potent keratolytic agent that slows the production and development of keratinocytes. It is used as an antifungal for the treatment of dandruff, seborrheic dermatitis, and a fungal skin infection called tinea versicolor. The pathogenesis of dandruff involves hyperkeratinization,

Selenium sulfide has also been found to decrease hyperkeratinization of the meibomian gland ducts by retarding the proliferation of keratinocytes and the production of keratin. It may also break down disulfide bonds, further loosening meibomian gland blockages.

resulting in corneocytes that clump together and manifest as large flakes of skin.¹⁴ Keratolytics, such as selenium sulfide, loosen the attachments between the corneocytes and allow them to be washed off.

Selenium sulfide has also been found to decrease hyperkeratinization of the meibomian gland ducts by retarding the proliferation of keratinocytes and the production of keratin. It may also break down disulfide bonds, further loosening meibomian gland blockages. Furthermore, selenium sulfide has a potential lipogenic effect, stimulating an increase in the quantity of lipids secreted by the meibomian glands.¹⁵ Selenium sulfide has also been applied to the lid margin as a successful treatment for seborrheic blepharitis.^{16,17}

RETHINKING MGD TREATMENT

Current therapies for MGD focus on removing blockages in the glands to restore a normal flow and quality of meibum. The most common methods for achieving this include warm compresses and gentle lid massage, gland probing, thermal pulsation, and microblepharoexfoliation. While all of these approaches aim to clear out the hardened meibum that is obstructing the gland, none of them attempt to address the underlying cause for the altered composition of the meibum. Research was recently presented that addresses hyperkeratinization as a core mechanism of the pathophysiology of MGD, demonstrating successful treatment with a keratolytic agent.¹⁵ An ophthalmic preparation of selenium sulfide applied to the meibomian glands over several weeks caused blocked glands to reopen and lipid quality to improve. It is thought that selenium sulfide opens obstructed meibomian glands, stimulates lipid production, and prevents further keratin deposits. Selenium sulfide has also been applied to the lid margin as a successful treatment for seborrheic blepharitis.^{16,17} (It should be noted that dermal keratolytics tested in a rabbit toxicology study caused extreme chemosis, redness, corneal clouding, and edema).¹⁸

Similar to acne, MGD may be the result of hyperkeratinization that alters the flow of meibum and allows the creation of a plug in the central duct of the meibomian gland. Modifying the keratin is a novel approach to the treatment of MGD which may address the underlying pathophysiology of the disease. ■

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