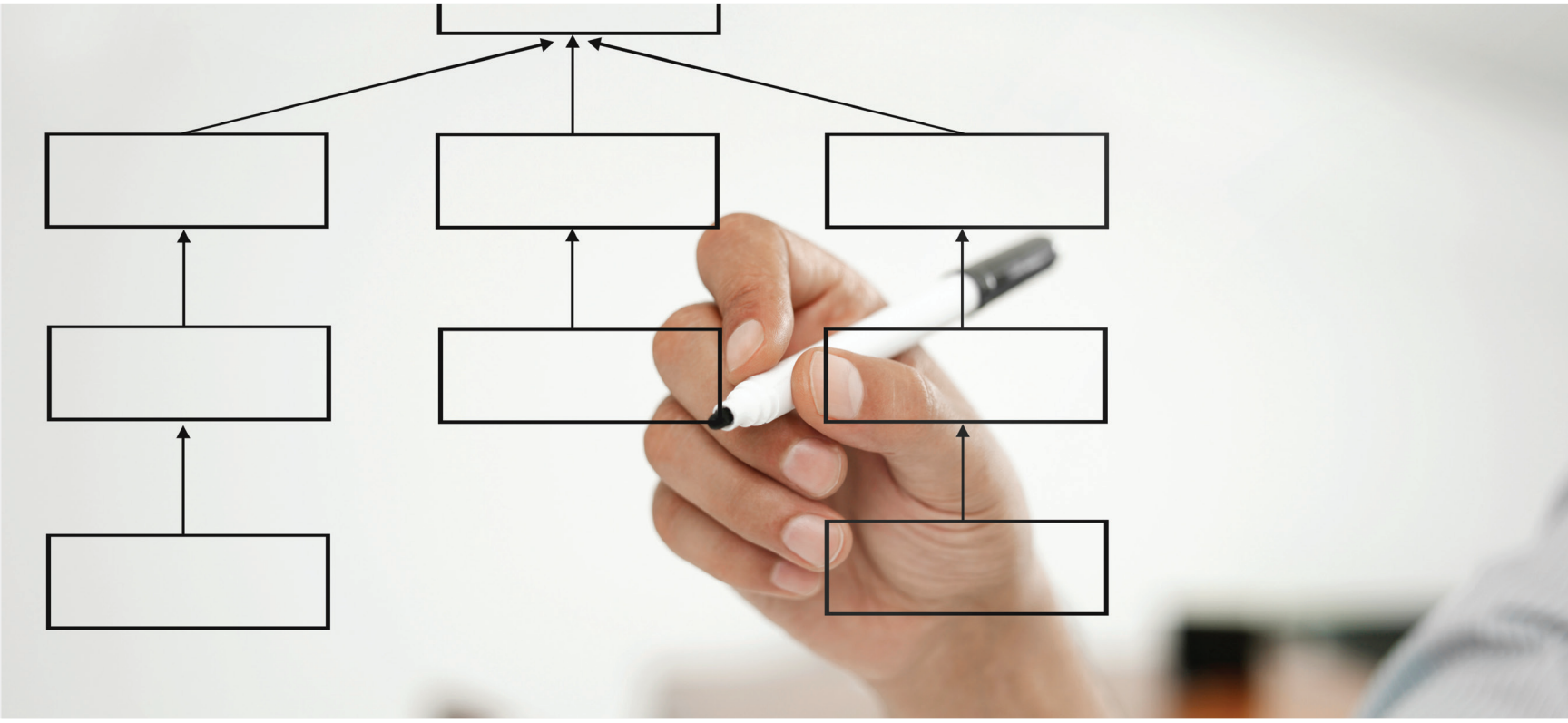

BREAKING DOWN MEIBOMIAN GLAND DYSFUNCTION


Different clinical manifestations require different treatment approaches for the best results.

BY STEVEN J. FERGUSON, OD, AND TANNER J. FERGUSON, MD

Meibomian glands are essential pieces of the homeostatic machinery that help maintain a clean, healthy, and well-lubricated ocular surface. Functional abnormalities of these glands lead to a multifactorial disease known as meibomian gland dysfunction (MGD). Clinical manifestations of MGD vary widely, and the signs of MGD often do not correlate with its symptoms. Patients with MGD often present with an array of findings, such as abnormal meibum secretions, meibomian orifice plugging and gland dropout, a frothy tear film, and telangiectasias. However, many patients present with a clinical picture consistent with MGD without obvious examination findings. This article proposes a subclassification of MGD to help guide clinical and treatment decision-making.

SPECIFICALLY SPEAKING

The International Workshop on Meibomian Gland Dysfunction emphasized the need to address MGD to improve tear film stability and ocular surface health.[1] However, the term *MGD* may be too broad for day-to-day clinical use and should be subcategorized according to case-by-case clinical manifestations of MGD (see Table).

In addition to the hallmark sign of altered meibomian gland secretions, the presence or absence of lid margin telangiectasia helps subclassify MGD into non-telangiectatic and telangiectatic cases. Patients with MGD demonstrating lid margin telangiectasia at an early stage should be assessed for the presence of skin conditions, such as rosacea. Prior studies have shown that 90% of patients with ocular rosacea have eyelid changes similar to those with MGD.[2] Thus, it is essential

to differentiate between cases of MGD without rosacea and rosacea-associated MGD, as the latter form can be more difficult to treat and may require a multifaceted approach to treatment.[2] For this reason, the workup of patients with ocular surface-related symptoms should include rosacea as a possible associated diagnosis, especially in those with signs of MGD and telangiectasia.[3] MGD in patients with rosacea is also commonly associated with inflammation of the lid margin and conjunctiva.[4,5]

We routinely perform meibography on all of our patients. We have observed that loss of meibomian glands occurs not only in patients with clinical signs and symptoms of MGD, but also in those with no clinical manifestations of MGD (ie, normal meibum secretions). We have found that many of these subclinical patients are young contact lens wearers who report frequent and/or extended digital device use. Even though these patients have normal meibum expression, we have observed that many worsen over time and will experience further gland dropout. This subgroup of patients with meibomian gland atrophy without clinical manifestations of MGD can be classified as having *primary atrophic MGD*.

A previously published study in a population of patients younger than 18 years of age with no history or clinical diagnosis of MGD reported meibomian gland atrophy (meiboscore ≥ 1) in 42% of cases.[6] The study authors proposed that meibomian gland atrophy is common and can occur in patients who are asymptomatic. Most of these patients had mild atrophy, and the team suggested that some degree of low-grade atrophy might be a natural variant of meibomian gland anatomy in some patients, not solely due to long-standing disease. Meibum expression scores were not reported in this paper; thus, it remains unclear if meibomian gland loss in these patients resulted from meibum gland obstruction. The proposed subclass of primary atrophic MGD involves meibomian gland atrophy with normal meibum expression ruling out obstruction as a cause. Although the etiology of primary atrophic MGD is not yet clear, we believe that poor and/or reduced blinking plays a meaningful role in reducing meibomian gland activation.

AT A GLANCE

- Meibomian gland dysfunction (MGD) may be too broad a term for daily clinical use and should be subcategorized based on case-by-case clinical manifestations to help guide approaches to treatment and dictate the need for alternate or adjuvant therapies.
- MGD can be subclassified into non-telangiectatic and telangiectatic cases based on the presence or absence of lid margin telangiectasia.
- It is essential to differentiate between cases of MGD without rosacea and rosacea-associated MGD, as the latter form can be more difficult to treat and may require a multifaceted approach to treatment.
- The authors' experience treating these patients has led to a clinical approach based on MGD subclass that combines frontline treatment targeting the underlying etiologies contributing to AMD with supportive adjuvant therapies for treatment maintenance to promote long-term stability.

MGD TREATMENT

The treatment of MGD will typically involve a combination of different therapies. Our experience treating these patients has led to a clinical approach based on MGD subclass that combines frontline treatment targeting the underlying etiologies contributing to MGD with supportive adjuvant therapies for treatment maintenance to promote long-term stability.

Frontline Therapy

Because patients with primary atrophic MGD do not exhibit signs or symptoms of altered meibomian gland secretions, treatments aimed at clearing meibomian gland obstruction may not help. These patients may benefit from regular blinking exercises and eyelid activation alerts that help stimulate frequent blinking. In addition, reducing visual display time may also help prevent further meibomian gland loss.

When MGD is associated with altered meibomian secretions and there is no telangiectatic vessel formation (non-telangiectatic MGD), our treatment pathway primarily targets alleviating meibomian gland obstruction and improving meibum expression. Meibomian gland treatment with precision-controlled heat and mechanical expression is vital in relieving gland obstruction and clearing the glands with altered meibum expression. In cases where meibomian excreta and epithelium

TABLE. Proposed MGD Subclasses and Their Characteristics

	PRIMARY ATROPHIC MGD	NON-TELANGIECTATIC MGD	TELANGIECTATIC MGD	ROSACEA-ASSOCIATED MGD
Telangiectasia on lid margin	No	No	Yes	Yes
Hyperplasia of line of Marx	No	Often	Often	Yes
Saponification	No	Yes	Yes	Yes
Meibomian gland expression	Normal	Turbid or congested	Turbid or congested	Turbid or congested
Pain on lid palpation	No	Rare	Rare	Yes
Tear breakup time	Normal	Reduced	Reduced	Reduced
Tear osmolarity	Normal	Elevated	Elevated	Elevated
MMP-9	Negative	May be positive	May be positive	Positive
Gland atrophy and dropout	Yes	Yes	Yes	Yes

plugs cap the meibomian orifices, microexfoliation of the lid margin or manual debridement to remove the microbial biofilm is vital for adequate meibomian gland clearance. Repeat biofilm removal may be necessary at follow-up visits, and antiinflammatory agents may be prescribed to suppress possible inflammation.

When MGD is associated with ocular surface inflammation (eg, raised matrix metalloproteinase-9 [MMP-9] activity, corneal and conjunctival vital dye staining, telangiectatic MGD, ocular rosacea), blocking the inflammatory cascade using either corticosteroids or other immunomodulating ophthalmic agents, including cyclosporine A and lifitegrast ophthalmic solution 5% (Xiidra, Novartis), is often necessary before prescribing MGD treatment and blepharoexfoliation to rehabilitate the tear film.

For patients in whom obstructive MGD is accompanied by telangiectatic vessel formation (particularly those with rosacea-associated MGD who may develop aggressive telangiectatic vessels along the lid margins), intense pulsed light (IPL) may serve as an effective adjuvant therapy to photocoagulate the telangiectatic vessels.

Adjuvant Therapy

Although precision-controlled heat and mechanical expression are the mainstays for clearing meibomian gland obstruction, adjuvant therapies to address contributing etiologies in individual MGD patients can help augment treatment.

Microbial flora of the eyelid can produce inflammatory virulence factors, which persist on the lid margin and produce lipase. Excessive lipase production from the colonized flora can degrade meibum on the surface and within the gland, causing saponification. This biochemical transformation breaks down tear lipids into soaps and free fatty acids, causing tear frothing and symptoms of burning. The use of oral medications, such as azithromycin (pulse dosing) or tetracycline derivatives, may help control MMP-9 activity both within the glands and along the ocular surface. These oral adjuvant therapies should be repeated as needed to help reduce or control saponification, improving MGD treatment stability and aiding ocular surface homeostasis. Also consider saponification control with topical azithromycin drops and omega-3 complex supplementation.

Adjuvant Maintenance Therapy

Eyelid margin inflammation caused by microorganism overgrowth can be controlled with daily lid hygiene therapy. Studies support the positive affect of continued daily lid care on MGD stability. All patients with MGD can benefit from a targeted flora-specific daily maintenance plan. Lid margin treatment may include tea tree oil, medicated pads, or hypochlorous acid spray to reduce

eyelid flora overload, primarily *Staphylococcus* or *Demodex*.

We've found that residual or exacerbated ocular surface inflammation persists early in the posttreatment phase up to 3 months as the tears rehabilitate from the gland clearance and respond to lid margin hygiene therapy. Immunomodulation is often used to control ocular surface inflammation during the recovery period.

Adding omega-3-based supplementation to the regimen may also be an effective adjuvant therapy for patients with MGD because of its purported antiinflammatory properties. Although the literature is mixed on the value of omega-3 supplements, we routinely recommend their use in our practice and believe it holds value as an adjuvant therapy.

Blinking exercises can modify poor blinking patterns and improve dry eye symptoms while keeping the meibomian glands active and offering improved lid wiping of tears across the ocular surface.

Adjuvant Advanced Therapy

Dry eye disease is often classified as mild, moderate, or severe. With advanced dry eye disease, advanced supportive therapy beyond standard adjuvant therapy is required. Applying MGD subclassification can guide best practice patterns to improve the longevity of MGD treatment while addressing other ocular surface disease comorbidities.

Patients with dry eye disease often have clinical manifestations of MGD and low aqueous production. Addressing MGD first with ocular surface treatment is essential to improving tear physiology and ocular surface health. Immunomodulation (cyclosporine or lifitegrast) offers the potential to alter the physiological immune response on the ocular surface and effectively combat inflammation that impairs the stability of the tear film and causes tear hyperosmolarity. Tear retention by punctal plug occlusion or cauterization of punctums helps to optimize tear levels.

IPL, in addition to photomodulation of the telangiectatic vessels, has been proposed to play a vital role in meibum heating and liquefaction and inflammation suppression.[7] *Demodex* eradication also plays a critical role, and the recently introduced lotilaner ophthalmic solution 0.25% (Xdemvy, Tarsus Pharmaceuticals), the first FDA-approved drop for the treatment of *Demodex*, represents an exciting addition to the treatment armamentarium.[8] In our limited experience thus far with the topical medication, lotilaner has been an effective and well-tolerated option for treating blepharitis associated with *Demodex*.

Neuromodulation is another new development in dry eye and acts directly on the nervous system to alter the physiologic response to a targeted area. Two treatment options to stimulate natural tear production include varenicline solution nasal spray 0.03 mg (Tyrvaya, Viatris) and the iTEAR100 (Olympic Ophthalmics) neurostimulator device. Neurostimulators may be a pivotal adjuvant therapy to keep meibomian glands active and increase the aqueous mucin layer of the tear film.

PATIENT EDUCATION

MGD is a chronic condition; therefore, it is important to take the time to educate and counsel patients appropriately. Patients should first and foremost understand that the disease is progressive, with the potential for degeneration. As such, following their maintenance therapy regimen, including regular blinking exercises, omega-3 supplementation, and warm compresses, may help reduce the frequency of disease episodes. Proper lid margin hygiene and use of scrubs can decrease the pathogenic flora load, reducing the potential of biofilm and excess endotoxins and stimulating meibomian gland health.

Diagnostically evaluating the state of ocular surface disease, including lid margin pathogens, presence or absence of eyelid telangiectatic vessels, degree of saponification, meibum expression, tear volume, and level of gland atrophy, provides a more consistent diagnostic roadmap for effective tear film treatment and ocular surface homeostasis.

SPECIFICATION ALLOWS CUSTOMIZATION

MGD is a major contributing factor to dry eye disease. We hope our subclassification suggestions can help guide treatment decisions, as a more individualized treatment approach can improve long-term outcomes. ■

1. Nichols KK, Foulks GN, Bron AJ, et al. The International Workshop on Meibomian Gland Dysfunction: executive summary. *Invest Ophthalmol Vis Sci*. 2011;52:1922-1929.
2. Geerling G, Baudouin C, Aragona P, et al. Emerging strategies for the diagnosis and treatment of meibomian gland dysfunction: proceedings of the OCEAN group meeting. *Ocul Surf*. 2017;15(2):179-192.
3. Viso E, Millán AC, Rodríguez-Ares MT. Rosacea-associated meibomian gland dysfunction—an epidemiological perspective. *European Ophthalmic Review*. 2014;8(1):13-16.
4. Akpek EK, Merchant A, Pinar V, Foster CS. Ocular rosacea: patient characteristics and follow-up. *Ophthalmology*. 1997;104(11):1863-1867.
5. Ghanem VC, Mehra N, Wong S, Mannis MJ. The prevalence of ocular signs in acne rosacea: comparing patients from ophthalmology and dermatology clinics. *Cornea*. 2003;22(3):230-233.
6. Gupta PK, Stevens MN, Kashyap N, Priestley Y. Prevalence of meibomian gland atrophy in a pediatric population. *Cornea*. 2018;37(4):426-430.
7. Dell SJ. Intense pulsed light for evaporative dry eye disease. *Clin Ophthalmol*. 2017;11:1167-1173.
8. FDA approves Xdemvy (lotilaner ophthalmic solution) 0.25% for the treatment of Demodex blepharitis. Tarsus. July 25, 2023. Accessed December 28, 2023. ir.tarsusrx.com/news-releases/news-release-details/fda-approves-xdemvytm-lotilaner-ophthalmic-solution-025

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