

# Meibomian Gland Dysfunction

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Dry eyes is a common, chronic condition that has a prevalence of about 5- 50%.<sup>1</sup> According to the Dry Eye Workshop II report (DEWS II report), published in 2017, the updated definition of Dry Eye Disease is, “a multifactorial disease of the ocular surface characterised 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.” The Tear Film & Ocular Surface Society (TFOS) released their report on the international work on Meibomian Gland Dysfunction (MGD)<sup>2</sup> in 2011, which defined MGD, classified it and *considered it as the primary cause of dry eye disease worldwide*. Previously dry eye disease was considered as an aqueous deficiency problem, but after this report by TFOS, there is a paradigm shift towards “not producing enough lipids to retain the tears that are being produced”. This has led to a huge impact on the treatment protocols which were previously focused on managing the sequelae and symptoms of dry eyes rather than targeting directly on the underlying cause, the MGD. It has now been accepted worldwide that dry eye occurs when the ocular surface system cannot adequately protect itself from the desiccating stress due to the lack of a healthy meibomian gland secretion. This article is mainly focussed on the Meibomian Gland Dysfunction, discussing the normal anatomy of the glands, how they are affected by disease, its implications on the ocular surface and finally, the various treatment strategies.

**Key words:** Blepharitis, Dry eyes, Meibomian gland dysfunction, blepharospasm.

The term meibomian gland dysfunction (MGD) was described for the first time by Korb and Henriquez in the early 1980s<sup>3</sup>. Its prevalence appears to be much higher in Asian populations<sup>4</sup>, i.e. greater than 60% while in Caucasians, it spans from 3.5% to 19.9%. There was no firmly established definition of MGD before 2011 when the International Workshop on MGD defined it<sup>5</sup> as “a chronic, diffuse abnormality of the meibomian glands, characterised by the terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in an alteration of the tear film, symptoms of ocular irritation, clinically apparent inflammation, and ocular surface disease”.

MGD is generally considered by the clinicians as posterior blepharitis<sup>6</sup>. The term “Blepharitis” means inflammation of the eyelids. As the eyelid is anatomically

made up of two lamellae, anterior and posterior, the blepharitis is also divided into an anterior and a posterior variety. The term “anterior blepharitis” is referred to as the inflammation of lid-margin anterior to the grey line i.e. of the skin, eyelashes, and lash follicles. The term “posterior Blepharitis” means the inflammation of structures posterior to the grey line; that includes the meibomian duct orifices, meibomian glands, tarsal plate, and the blepharo-conjunctival junction. Frequently, a mixed variety may be seen as the inflammatory process spreads from one structure to the next.

## Anatomy & Physiology of Meibomian Glands

The meibomian glands were first described in detail by Heinrich Meibom<sup>7</sup> in 1666. They are modified seba-

ceous glands<sup>8</sup> with a tubulo-acinar structure. Each gland consists of a cluster of 10-15 secretory acini opening into a long central duct via tiny ductules. There are 30-40 glands in the upper tarsal plate, each gland about 5.5 mm long while there are 25 glands in the lower tarsal plate, each being 2 mm long. They are densely innervated by the sympathetic and parasympathetic nerves (via the V nerve) as supplying the lacrimal and accessory lacrimal glands, thereby ensuring an optimal composition of the tear film. There is also a strong hormonal control mediated by estrogens, androgens, progesterins, retinoic acid, growth factors and neurotransmitters.

The secretion of meibomian glands is called meibum<sup>9</sup> which is primarily made up of nonpolar lipids (about 90%, comprising of wax, sterol-esters and triacylglycerols), while less than 10% are polar amphiphilic lipids (hydroxy fatty acids), and a small amount of proteins and electrolytes. The tear film lipid is a multilayered structure comprising of a thin layer of polar lipids that resides at the aqueous-lipid interface and acts as a surfactant (essential for the uniform spreading and stability of the tear film). This is covered by a thick layer of non-polar lipids that forms the lipid-air interface and resists the evaporation of aqueous component of the tear film.

The mode of meibum secretion is Holocrine, which means that the secretions are produced in the cytoplasm of a cell; the cell membrane ruptures to release the secretion into the gland's lumen while the cell itself is destroyed in the process. The secretion from multiple acini are poured via tiny ductules into the central duct that opens at the grey line of the lid margin. A thin strip of orbicularis muscle fibres, called the Riolan's muscle, surrounds the terminal part of the central duct and the few terminal acini present close to the lid margin.<sup>10,11</sup> During a blink, the pre-tarsal orbicularis muscle generates a uniform compression of the tarsal plate and of the enclosed meibomian glands, thereby promoting the flow of secretion towards the duct opening by a milking action. Meibum is squirted out of the duct openings by the contraction of Riolan muscle.

Meibum is normally liquid at body temperature and coats the lid margins thus making their movement smooth over the ocular surface and is delivered to the tear meniscus. From there it is picked up by the upper lid margin (as it comes down during a blink and picks up the tear meniscus) and is spread uniformly over the aqueous layer of the tear-film thus preventing its thinning and evaporation in-between the blinks, and mak-

ing the tear film stable. After an absence of blinking, meibum accumulates within the ducts and is delivered in increased amounts when a person wakes up in the morning<sup>12</sup>. This accounts for the diurnal variation in meibum secretion and the excess amount of oil in the pre corneal tear film makes the vision misty and blurred in the morning.

To summarise, the functions of healthy meibomian lipids are:<sup>13</sup>

- i: To make the optical surface of the cornea smooth at the air-lipid interface.
- ii: They reduce the evaporation of the tear film.
- iii: They enhance the stability of the tear film.
- iv: They allow a uniform spread of the tear film over the cornea.
- v: They prevent the spillover of tears from the lower meniscus over the lid margin.
- vi: They prevent contamination of the tear film by sebum.
- vii: The lipids help seal the apposing lid margins during sleep.

#### Pathophysiology of MGD

MGD is a complex disease that is caused by the interplay of hormonal, microbial, metabolic and environmental factors<sup>14</sup>. It is classified according to the rate of gland secretion:

**A: Hypo-secretion of meibum** occurs due to:

- 1: *Obstruction of meibomian duct opening by conjunctival scarring* seen in Ocular Pemphigoid, chemical burns, Stevens Johnson's Syndrome.
- 2: *Duct obstruction by desquamated epithelial cells, clumped together forming plaques, due to hyperkeratinisation of the lid margin.* This results in stasis of meibum within the duct; the back pressure produces cystic dilation of the glands, the pressure compresses the acini and causes their atrophy. This results in further hypo-secretion. Hyperkeratinisation is commonly the result of hormonal imbalance as a part of the ageing process, decreased expression of androgen receptors (hormonal therapy), blink abnormality, contact lens wear or medications.
- 3: *Hypo-secretion with thick, altered meibum* may be produced in seborrheic dermatitis, acne rosacea and as a side-effect of medications (anti-

histamines, anti-depressants, hormone replacement therapy, Isotretinoin for Acne).

It is important to keep in mind the double vicious cycle<sup>14</sup> in which obstruction due to a thick, viscous meibum or hyper-keratinisation of Meibomian ducts leads to back pressure and atrophy of acini, with a further decreased secretion of meibum; this makes the meibum more viscid and enhances further obstruction. In addition, stasis of meibum inside the ducts promotes the growth of commensal bacteria, which produce lipases that cause meibum degradation and release of toxic chemicals. These factors aggravate the primary hyper-keratinisation and compositional disturbance of meibum and result in a progressive MGD. Chronic obstruction leads to degeneration of the secretory gland tissue and even if the primary obstruction is later resolved by therapeutic approaches, the damage is permanent.

**B: Hyper-secretion of meibum:** is seen in meibomitis (meibomian gland inflammation) in which excessive amount of meibum is produced that has an altered chemical composition and is toxic to the ocular surface.

This is due to meibocyte abnormalities seen as result of ageing, Staph aureus or Demodex folliculorum infection, environmental factors (hot, dry climate). Moreover nutritional disorders such as generalised malnutrition, a diet low in omega-3 fatty acids, protein deficiency, vitamin A deficiency have all been associated with the production of a poor quality meibum.

#### Risk Factors for MGD<sup>15</sup>

**1: Ageing & Hormonal Imbalance:** this is the most common cause of MGD. Receptors for sex hormones (androgen and estrogen) are present within the meibomian glands while meibocytes (the epithelial cells lining the acini) contain enzymes which are necessary for the synthesis and metabolism of sex steroids. Androgens stimulate the secretion of meibum by promoting the synthesis of lipids and proteins, suppress meibomian gland inflammation and keratinisation of the ducts, while estrogens reduce/thicken the secretion and promote inflammation.

With increasing age, there is a decline in androgen production in both genders. Similarly in autoimmune disease like rheumatoid arthritis, Sjögren's syndrome and systemic lupus erythematosus, androgen production is reduced in the body.

In post-menopausal women, the level of androgen production declines by the ovaries and adrenal glands causing meibomian glands to atrophy.<sup>16</sup> Ageing of the meibomian glands results in a decreased cell renewal and differentiation of meibocytes, with reduced gland size, and an increased infiltration of inflammatory cell. These changes lead to generalised atrophy of meibomian glands and deficiency of meibum. Similar changes in meibomian glands have been observed in androgen-depleted states in individuals on anti-androgen therapy for benign prostatic hypertrophy or prostate cancer.

**2: Gender:** More common in women<sup>17</sup> particularly with oily skin conditions, post-menopausal state and hormonal imbalance due to polycystic ovaries.

The key ingredient of many anti-ageing cosmetics that are used for peri-ocular skin is retinoid acid<sup>18</sup>. It suppresses the action of androgens on meibomian glands leading to their atrophy.

**3: Environment:** Hot, dry environment with low humidity results in structural and functional changes in meibocytes; there is an excessive proliferation of basal cells of the acini, a high protein/lipid ratio in the meibum that increases its viscosity and has a negative impact on the stability of the tear film. Increased production of meibum causes dilation of ducts as well as depletion of the number of functioning meibocytes (being a holocrine secretion), with subsequent gland atrophy and hypo-secretion. Exhaustion of the basal cells leads to the atrophy of acini and meibomian gland dropout.

**4: Topical Medications<sup>19,20</sup>:** All topical medications contain preservatives to enhance their shelf life. The most commonly used preservative is Benzalkonium Chloride, which is most toxic to the ocular surface. In addition, anti-Glaucoma medications like beta blockers, prostaglandin analogs, carbonic anhydrase inhibitors result in an altered morphology of meibomian glands and a decrease in the number of meibocytes. Chemical formulations containing Adrenaline or phenylephrine promote keratinisation of the lid margin and blockage of meibomian ducts. Retinoic acid reduces meibum production and alters its quality.

**5: Dietary Factors:** malnutrition (explained above) alters quality of meibum.

The use of oral fatty acids improves the quality and expressibility of meibum. Specifically, the intake

of omega-3 fatty acids improves the quality of meibum with a decrease in the saturated fatty acid content of meibum. It decreases the ocular surface inflammation. Foods rich in omega-3 fatty acids are flaxseed oil, and olive oil and oily fish like tuna and cod.

**6: Microbial infection:** Cholesterol esters present in meibum promote the growth of commensal organisms on the eyelid margin, in particular *Staphylococcus aureus*. The bacterial lipases, in turn, break down the neutral fats and cholesterol esters, releasing glycerides and free fatty acids into the tear film, destroying the mucin layer and making the cornea hydrophobic. This makes the tear film unstable. The free fatty acids also stimulate hyperkeratinisation of the lid margins, with keratin plugs adding to the blockage of meibomian ducts.

**7: Infestation with the Demodex mite:** Demodex mite is a microscopic ectoparasite of the human skin and constitutes a part of the normal flora. It produces disease when its cell population increases which has been detected in about 46.8% of MGD patients.<sup>21,22</sup> It is of two distinct varieties: *demodex folliculorum* that infests the eyelash follicles, and *demodex brevis* that burrows deep into the sebaceous and meibomian glands. It causes a direct mechanical damage to the epithelial cells of eyelash follicles (by feeding on them), and by laying eggs at the base of eyelashes, causing follicular distention and misdirected lashes. *D. brevis* mechanically blocks the orifice of meibomian ducts and produces a granulomatous reaction inside the glands resulting in a chlamydia.<sup>23</sup> Therefore, it should be considered in the differential diagnosis of every ocular surface disease.

Diagnosis can be made by random epilation of nonadjacent eyelashes placed on a glass slide, mounted with a coverslip with the addition of a drop of oil, sodium fluorescein, peanut oil, or 75% alcohol which helps release embedded Demodex in the hair follicles.

**8: Contact Lens Wear**<sup>24</sup>: The pre-corneal tear film is approximately 3 microns thick; the average central thickness of a contact lens is 30 microns. When the contact lens is worn, the tear film is split both above and below the lens, its thickness is altered resulting in excessive evaporation and further thinning.

Contact lenses cause a direct mechanical trauma to the lid margin by constant rubbing, desquamating the epithelium, plugging the meibomian duct orifices

resulting in gland atrophy.

Also, chronic ocular surface inflammation affects the gland morphology and function, with secretion of altered meibum that adds to the ocular surface inflammation. All these changes worsen as the duration of contact lens wear increases.

**9: Congenital anomalies of meibomian glands:** A reduction in the number or complete absence of meibomian glands maybe seen in Turner syndrome, ectodermal dysplasia with cleft-lip/palate (ECC syndrome). Rudimentary meibomian glands maybe visible as yellow streaks on the conjunctival surface of the tarsal plate.

Dystichiasis (aberrant row of eyelashes) maybe present at birth in which meibomian glands are replaced by an extra row of eyelashes at the grey line. The misdirected eye lashes cause ocular surface trauma as well as meibum deficiency. Dystichiasis can also occur secondary to repeated rubbing of eyelids that occurs in VKC, chronic allergic conjunctivitis or in the autosomal dominant lymphoedema. Rubbing induces metaplasia of meibocytes to form eyelash follicles.

### Clinical Presentation of MGD

MGD, in its early stages, is asymptomatic and may remain undiagnosed. It only becomes symptomatic when it has worsened enough to cause tear-film instability or eyelid inflammation. Its symptoms and signs are varied and include changes due to:

- a: Altered morphology of the lid margin, altered meibum secretion, bacterial overgrowth and gland dropout.
- b: Tear film instability.
- c: Ocular surface inflammation

### Symptoms & Signs

The most common symptom is visual fluctuation that occurs during visual tasks associated with decreased blinking, such as driving, reading, staring at a computer screen or watching television. This results in blurred vision, reduced focusing ability, and diplopia. Despite the presence of a dry eye, a foreign body sensation and paradoxical reflex tearing may occur (as the lacrimal gland function is normal and dry spots on cornea stimulate the reflex), particularly when patients are exposed to low environmental humidity and blowing air.

Chronic lid margin inflammation is manifested by

symptoms of lid discomfort, pain, redness and irritation.

The symptoms related to ocular surface inflammation are burning, itching, frequent blinking and photophobia which gradually worsens to severe blepharospasm.<sup>25</sup> In a study, MGD and dry eyes were the most common causative factors for blepharospasm.<sup>26</sup> The symptoms of ocular irritation tend to be worse in the morning because of prolonged exposure of the ocular surface to toxic meibum and hyper-osmolar tears (due to poor clearance of the tear film) during sleep. These symptoms also get worsened after the insertion of punctal plugs due to poor tear clearance. The most troublesome symptom is chronic burning with or without associated photophobia. This is presumably attributable to the presence of inflammatory mediators or to increased tear osmolarity in the pre-corneal tear film. Itching of eyelids is more commonly present in atopic patients.

Morphological changes should be assessed on slit lamp examination and documented<sup>27</sup>.

- i: Lid margin:** thickening, hyperaemia, telangiectasia, keratinisation, foaminess or frothing at the canthal angles and along the lid margin. Presence of scales along eyelash follicles should be noted (keeping in mind Demodex infestation).
- ii: Meibomian duct orifice:** plugging with thick meibum, notching (indicating lost/atrophic glands), distichiasis.
- iii: Meibum quality** is assessed by gently pressing the lid margin with a finger or a cotton-tipped applicator, and noting the ease with which meibum is expressed and its texture.

Meibomian gland expressibility (MGE) is a clinical score<sup>28</sup> that helps in assessing the severity of disease at initial presentation, and how it improves with treatment. This is calculated by finding the number of glands that can be expressed with mild pressure either with a cotton-tipped swab or a commercially available device that is specifically formulated for this purpose. Five glands in the nasal, middle, and lateral thirds of the lower eyelid (total 15 glands) are expressed and scored at each visit. A score of zero indicates a complete blockage of ducts and total absence of meibum. A score of 15 indicates that the glands are expressible throughout the lower eyelid. Patients with MGE score 0-5 are always symptomatic, and those with a score of 7 or more, are usually asymptomatic. The quality of secretion is noted whether clear, opaque, viciid, cheesy.

*MGD is graded accordingly:*<sup>29</sup>

**Grade 0:** Normal, clear meibum is seen squirting out of the duct orifices with each blink and can be easily expressed by lightly touching the lid margin.

**Grade 1 MGD:** meibum looking opaque, viscous and needs pressure on the lid margin to be expressed. Patient is asymptomatic at this stage and has no corneal staining. MGE score is more than 7.

**Grade 2 MGD:** meibum becomes more thick, cheese like, expressed with difficulty; frothing may be noted at the lid margins (indicates lipid breakdown by bacterial lipases). Patient may be asymptomatic or may have slight discomfort of lid margins, mild conjunctival hyperaemia, mild corneal staining detected by fluorescein at the inferior limbus and an MGE score of 7.

**Grade 3 MGD:** plugging of ducts with thick meibum that cannot be expressed by pressure. MGE score is 3-7. Excessive frothing at the canthal angles or the lid margins is noted. Patient is moderately symptomatic with irritable lid margins, injected, watery eyes with inferior corneal and conjunctival staining.

**Grade 4 MGD:** Meibomian gland dropout is detected by the presence of notching at the grey line and by transillumination with a pen-light through everted eyelids or by infrared photography. MGE score 0-3. At this stage patient presents with severe dry eye symptoms and corneal staining.

**iv: Ocular Surface Signs:** Damage to the ocular surface can result from a variety of closely linked factors like increased tear-film evaporation that causes hyper-osmolar tears and mediates the release of pro-inflammatory mediators in the tear-film like cytokines, leukotriens, as well as decreased lubrication of the conjunctival surface of the eyelids prevent their smooth excursion over the eyeball. These result in an irritable eye and the symptoms overlap with the dry eye disease. MGD is considered as the main contributor to an evaporative dry eye disease, but an increased tear production (measured with Schirmer's test) may be noted in patients with MGD. This is due to a compensatory reflex tearing due to ocular surface abnormalities and discomfort.

**Diagnostic tests:**<sup>30</sup>

- 1: **Administer a symptoms questionnaire, Ocular surface Disease Index (OSDI).**<sup>31</sup> This questionnaire assesses symptoms of photophobia, ocular/eyelid pain, blurring of vision, problems with reading/driving/watching TV.

- 2: **Measure blink rate and blink interval:** Blinking normally occurs once every 3-4 seconds (15-20 times /minute) in most people. However, during reading or staring at a computer/cellphone screen, the blink rate slows to 4.5 per minute, or once every 13.5 seconds. Blinking has a significant role in the secretion of meibum into the tear film, as already explained. If the blink rate is slowed or blinks are incomplete (the upper lid fails to close onto the lower lid), the lipid layer will build up at the lid margin and meibomian glands will be used less over time. This could lead to meibomian gland atrophy if unidentified.
- 3: **Measure lower tear meniscus height** and its clarity. Normal lower tear meniscus is 1.00-2.00 mm. It can simply be measured by narrowing the vertical beam of a slit lamp or by Meniscometry: an instrument measures the tear meniscus height, its radius and cross-sectional area.
- 4: **MGE score:** Expressibility of meibum, noting its quality and grading the MGD.
- 5: **Measure tear osmolarity:**<sup>32</sup> (*measuring the concentration of solutes/salts*). As the aqueous component of the tear-film evaporates, the concentration of solutes (mainly salts) increases. This test has become a critical part of dry eye management. It requires only a microlitre sample of tears (0.2 µL) collected by a micro-pen from the lateral canthal tear meniscus. It is placed in an instrument, called the osmometer, which gives the reading in a minute. The disadvantages are the need for an expensive equipment and its constant maintenance.

The osmolarity of both eyes is measured; a difference of 8 mOsm/L or more in the tear osmolarity between the two eyes is considered abnormal.

The osmolarity score of 300 mOsm/L or greater in the higher scoring eye is considered abnormal. From 300-320 mOsm/L, is graded as mild; from 320-340 mOsm/L, is graded as moderate; and greater than 340 mOsm/L, is graded as a severe dry eye disease.

- 6: **Ocular surface staining by Fluorescein:** It stains the corneal stroma under the desquamated epithelium but does not stain a dry spot (it becomes hydrophobic after losing its mucin coating), and appears as a blue spot in the uniform green fluorescence of the tear film. Fluorescein pools in the areas of epithelial erosions/thinning. The area of ocular surface stained should be noted as an interpalpebral staining is due to excess evaporation of aqueous while an inferior limbal staining is due to

a toxic meibum production.

Rose bengal and lissamine green stain dead / devitalised epithelial cells and healthy cells that have lost their mucin coating. The conjunctiva is more intensely stained than the cornea. Therefore, early or mild cases of dry eye disease can be detected more easily with these dyes.

- 7: **Tear-film Break up time (TFBUT):** It is assessed by instilling a drop of fluorescein stain in the conjunctival sac and using a slit lamp with cobalt blue illumination. Time is noted between the last blink and the appearance of a black island in the normal green fluorescence of the tear film, or the first dry spot on the cornea. The test is performed prior to the instillation of anaesthetic eye drops (as they are toxic to the corneal epithelium and produce dry spots). Normal TFBUT is 15-45 seconds. If it is > 5 seconds, the patient is usually asymptomatic, but when it becomes less than 2 seconds, the patients are almost invariably symptomatic.
- 8: **Blink dynamics need to be noted:** The examiner evaluates, by inspection on a slit-lamp, whether the upper lid closes on to the lower lid with a blink, the frequency of partial and complete blinks, the area of ocular surface (cornea and conjunctiva) that remains exposed with each complete blink.
- 9: **Schirmer's test:**<sup>33</sup> It is of two types: Schirmer I performed without the topical anaesthesia and Schirmer I performed after topical anaesthesia.

S I test performed *after topical anaesthesia* measures only the basal lacrimal secretion. *It is highly specific and sensitive for a dry eye disease due to aqueous deficiency.* After instilling a topical anaesthetic, a thin strip of filter paper (5 x 35 mm) is placed in the inferior cul-de-sac in the lateral canthus. The excess tears should be wiped off prior to measuring the basal aqueous production. This distinguishes a dry eye due to less aqueous production from the one due to excess aqueous evaporation (due to MGD).

*S I test can be performed without the anaesthesia:* this measures the basal tear secretion (which is from the accessory lacrimal glands) as well as the reflex secretion from the main lacrimal gland which is stimulated by the irritating nature of the filter paper. Less than 10 mm of wetting after 5 minutes is diagnostic of ATD. The test is relatively specific, but it is poorly sensitive.

Schirmer II test is performed without the anaesthesia. The nasal mucosa is stimulated by a cotton

wisp or a pungent odour and the amount of tear production (both reflex and basal) are noted. This should only be performed in patients in whom Schirmer I test fails to demonstrate tear production (in KCS).

10: **Meibography:** Document morphology and meibomian gland count in upper and lower lids by infra-red camera, confocal microscopy, spectral-domain optical coherence tomography. Normal meibomian glands are long, vertical, extending from the lid margin to the end of tarsal plate. They become dilated and tortuous in early/mild disease. In disease of intermediate duration/ moderate severity, the gland dropout increases with loss of identifiable gland architecture. In prolonged / severe disease, all glands are markedly shortened or absent.

### Management and Treatment of MGD<sup>34</sup>

- i: **Patient education:** this is the most important part of treatment in order to ensure compliance to therapy. Patients need to be educated regarding the chronic nature MGD, its prolonged therapy, affect of diet (flaxseed oil, fish oil, and olive oil), environment dryness/humidity and the drying effects of topical or systemic medications.
- ii: **Lid hygiene:** lids should be scrubbed gently with diluted baby shampoo applied on cotton-tipped applicator, and rinsed with lukewarm water. This removes toxic foamy meibum and reduces microbial load.
- iii: **Warm compresses** or application of heat is the mainstay of therapy. Normal meibum is liquid at body temperature, but denatured meibum becomes thick, dry and hard. It blocks the duct opening as well as the whole lumen of the ducts. Heat therapy dissolves the thick meibum, and to be effective, the glands have to be consistently heated to at least 45°C (113°F). This can be done with application of a warm wet towel or cotton pads, soaked in hot (not boiling) water; with the eyes closed, the hot towels held onto the eyelids for 2 minutes. It is made wet again with hot water and the process repeated five times, so that total heat application is for 10 minutes. This needs to be done daily for at least a month. It can also be done with commercially available heat masks, or devices (Lipi Flow Thermal Pulsation System, MiBo Thermaflow)<sup>35</sup> that helps the liquefaction of meibum and massages it upwards towards the ducts from where it can be easily expressed.
- iii: **Gentle massage:** after the application of heat, upper eyelid should be massaged downwards with the fingers, while the lower lid massaged upwards to establish meibum flow out of the glands.
- iv: **Blinking exercises:** they help improve meibum flow and tear-film spread over the ocular surface by contraction of pre-tarsal orbicularis and Riolan muscle. Patients should be advised to do 10 good blinks at a time; the eyes should be fully closed for 2 seconds, then squeezed for another 2 seconds. This should be done for every hour of digital device use.
- iv: **Topical lubricants:** They help to relieve ocular surface irritation by replenishing the tear film. Preservative-free preparations should be preferred to prevent further damage to the ocular surface.
- v: **Topical or systemic antibiotics** to control infections: low-dose oral doxycycline (50-100 mg/day for 6 weeks) helps to reduce inflammation in the eyelid tissue, it is anti-angiogenic and helps in restoring healthy meibum secretion. Azithromycin 250 mg once daily is also effective in patients allergic to doxycycline.
- vi: **Topical Cyclosporin eyedrops (0.5%)<sup>36</sup> or Tacrolimus** ointment / skin cream 0.03%: Cyclosporine as well as Tacrolimus are highly specific immunomodulator drugs that primarily affects T-lymphocytes. They are used as steroid-sparing agents as they have all the anti-inflammatory affects but without the side-effects of prolonged steroid use. They increase the production of aqueous, improve goblet cell count and reduce meibomian gland inflammation. In addition, Tacrolimus cream applied to the lid margin reduces vascular congestion, telangiectasia, and improves the quality of meibum produced. To have these affects, therapy has to be continued for 2-4 months. The tear-film break-up time has shown to improve with this therapy.
- vi: **Treating Demodex mite infestation:<sup>37</sup>** Management involves reduction in the number of Demodex mites; total eradication is not required as it is a part of the normal skin flora. This can be achieved by a combination of lid scrubs (scrubbing the eyelids twice daily with baby shampoo diluted with water to yield a 50% dilution and applying an antibiotic ointment at night until resolution of symptoms) and removal of the eyelash collarettes with the use of a cotton-tipped applicator and lid foam. Demodex mites are resistant to a wide range of an-

tiseptic agents including 10% povidone-iodine, 75% alcohol and erythromycin. The most effective and commonly used treatment is tea tree oil. Chemically, it is Terpinen-4-oil –a terpene with antimicrobial, antifungal, and antiseptic properties. There are many commercially available products that contain tea tree oil like shampoo, soap, ointment, skin cream. Hypochlorous acid and mercury oxide 1% ointment is also effective. Patients should be instructed to avoid oil-based cleansers and greasy makeup as they can provide further "food" for the mites. They should discard the previously used make-up, use hot water to wash their clothes, and a hot dryer to dry them.

**vii: Intra-ductal Probing:** it clears the obstruction of the ducts and allows the meibum to flow thereby reducing the intra-ductal pressure (IDP), inflammation, lid congestion with improvement of symptoms.

**viii: Intense pulsed light (IPL):** this also liquifies the meibum and improves its drainage by delivering a combination of heat and gentle pressure to the eyelids. It is an in-office therapy and requires 1-2 sessions.

The International Workshop on MGD recommended a Staged Treatment Algorithm, depending upon the grade of MGD.

Grade 1:

- i: Patient education regarding MGD, diet, environment.
- ii: Lid hygiene.
- iii: Warm compresses.

Grade 2:

- i: Advise patient to use humidifiers in air-conditioned rooms, and increase dietary intake of Omega 3 fatty acids, or use dietary supplements containing linoleic acid (vegetables, fruits, nuts, grains and seeds; linseed oil) or docosahexaenoic acid (DHA) 1000 mg daily.
- ii: Warm compresses followed by firm lid massage .
- iii: Blinking exercises.
- iv: Topical Lubricants.
- v: Topical tetracycline / azithromycin eye ointment massaged to lid margin<sup>38</sup>.

VI: Oral tetracycline, 50-100 mg or azithromycin, 250 mg daily for a month<sup>39</sup>.

Grade 3: All in Grade 2 plus:

- i: Add anti-inflammatory therapy for dry eyes (Topical Cyclosporin 0.5%, Tacrolimus 0.03%)<sup>40,41</sup>
- ii: Ductal probing.

Grade 4: All of Grade 3 therapy.

## CONCLUSION

MGD is an extremely common clinical entity and is the leading cause of an evaporative dry eye. It should be specifically looked for and treated in its early stages even in an asymptomatic patient; if untreated, it progresses to meibomian gland atrophy and drop out which is an irreversible stage. The goal of therapy is to improve the flow and the quality of meibum so as to restore the stability of the tear film. Since the therapy has to be continued for 2-3 months, patient education is mandatory to ensure compliance.

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## Author's Contribution

Dr. Sameera Irfan  
Literature review, Manuscript writing & review.

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