A Diagnostic & Treatment Strategy for Dry Eye Associated With MGD

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A Diagnostic & Treatment Strategy for Dry Eye Associated With Meibomian Gland Dysfunction (MGD)

Is the burgeoning instance of dry eye in the aging population adequately served by existing treatment approaches? Might clinicians benefit from a review of the etiology of blepharitis and additional options now available for its diagnosis and treatment? Recently, an expert panel convened to explore this multifactorial condition and assess the science that may yield symptom relief.

CURRENT STATE OF DRY EYE DIAGNOSIS & TREATMENT

**TOPIC:** Is the classical three-compartment model (conjunctival cul-de-sac, precorneal tear film, tear meniscus) of tear distribution and the three-part composition of the tear film (lipid, aqueous, mucin) still useful for clinicians? How about the distinctions between different forms of dry eye as lipid deficiency, including meibomian gland dysfunction versus aqueous deficiency? How do these distinctions affect the clinical evaluation and management of dry eye?
**Dr. Foulks:** We really can’t separate three “compartments.” There is a dynamic distribution of meibum from the cul-de-sac into the tear meniscus and across the tear film with blinking of the lids.

As for layers of the tear film, there are multiple interactions: proteins interact with the aqueous, the lipids, the mucins, and so on. There is the glycochalyx associated with the corneal epithelium; then the mucin layer, which has membrane-associated mucins that break off and contribute to a junctional layer with the aqueous layer, which has electrolytes and some proteins; then the lipid layer which then has two segments: one with proteins interacting with lipids within the aqueous layer and the other primarily lipids on the surface of the tear film.

Some of the distinctions about the different forms of dry eye are more useful than others. Also, some of them overlap. For example, the lipid profile may not play the same role in posterior blepharitis versus anterior blepharitis. (See sidebar.)

**TOPIC:** How does MGD fit into the categorization of blepharitis as anterior, posterior or mixed (Figure 1), and how does that factor into the choice of pharmacologic therapy?

**Dr. Asbell:** When we examine patients, there are many who have MGD but not anterior blepharitis.

**Dr. Foulks:** That’s why I keep them separate. I’m not sure that one leads to the other. There are

**Meibomian Gland Function:**

**Thumbnail Review & Update**

**Mcculley et al have noted** that “There is growing laboratory and clinical evidence implicating the meibomian glands… as playing a critical role in the pathogenesis of various ocular surface disorders such as chronic blepharitis and dry eye.”

Meibomian glands are large sebaceous glands seen as parallel strands across the central margin of the tarsal plates of the upper and lower eyelids. These glands secrete an “oily” substance (meibum) composed primarily of lipids and proteins. Meibum is transported through a ductule to enter the tear meniscus at the inner lid border. Meibomian glands are regulated by sex hormones: agonistically by androgens and antagonistically by estrogens.

The complex mixture of lipids and proteins that comprises meibum is normally a clear liquid at body temperature, and it passes through the meibomian glands onto the posterior lid margin by secretory pressure and is pulled from the tear meniscus as a thin layer across the preocular tear film during blinking. The lipid components of the meibum are partly water soluble (polar lipids) and partly insoluble (non-polar lipids), whose interactions are not yet well described, although they seem to have different roles in posterior blepharitis. These secretions may also be affected by lipases produced by ocular bacteria.

In a recent review, Knop et al noted that, although meibomian gland dysfunction is often considered to be synonymous with posterior blepharitis, it typically appears without prominent inflammatory alterations of the lid margin. “It is a discrete disease entity,” they wrote, “and a frequent cause of wetting deficiencies of the ocular surface leading to dry eye disease that deserves increased recognition by clinicians.” They recommended inspection of the eyelids and lid margins with eversion to check for gland atrophy. Inspection of the meibomian orifices should include expression by mild mechanical compression of the lid to assess patency of the orifices and the quality of the meibum.

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**Dr. Foulks:** That’s why I keep them separate. I’m not sure that one leads to the other. There are
situations where you can argue that it does, but epidemiologic studies show that they occur separately as well.7

**DR. MAH:** I agree that there is a group of patients that have both forms, but both are not necessarily from infection.

**DR. CHUCK:** To me, MGD falls into the category of posterior blepharitis. However, it can often be seen as part of a “mixed” picture.

**DR. PAUGH:** To my personal way of thinking, only anterior blepharitis is a distinct clinical entity, characterized by significant injection of the anterior eyelid margin. Posterior blepharitis and mixed blepharitis are not distinct sub-types.

**DR. Foulks:** It’s possible that inflammation of the anterior lid causes secondary changes of the meibomian gland. However, the debate continues about the role of bacteria in MGD. You can culture bacteria and identify it in anterior blepharitis, but you’re hard-pressed to find anything in the literature providing evidence of bacterial presence in the meibomian secretion in patients with anterior blepharitis.

McCulley’s group has worked for years showing that bacteria do have a place and a role in the pathogenesis of both posterior and anterior blepharitis.8,9 They have connected MGD with dry eye,1,10 but I don’t know of a study that connects bacterial infection to MGD. When I was a fellow, Stephen Foster used to be constantly expressing the meibomian glands and culturing the secretions looking for staph. He didn’t find it.

**DR. PAUGH:** I believe that MGD is characterized by a continuum of clinical severity, with gland secretions often compromised, becoming more viscous and turbid or opaque as the condition worsens.

I support the idea of “hypersecretory” and “hyposecretory” situations where you can argue that it does, but epidemiologic studies show that they occur separately as well.7

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MGD. Hypersecretory MGD, where there is copious oil but poor biochemical composition, is what used to be called by the general term "blepharitis," meaning eyelid inflammation.

Classic blepharitis was thoroughly studied by McCulley and coworkers from the late 1970s through the early 1980s. They noted that 4 of the 6 sub-types they described had meibomian seborrhea as a major sign. Seborrhea is an over-secretion of oil.

Conversely, the less inflamed hyposecretory form of MGD that results from blockage of meibomian gland ducts or atrophy of glandular tissue is probably what most clinicians view as MGD, as it is much more common.

**DR. FOUJKS:** Anti-inflammatory therapy can be useful in posterior blepharitis. However, the present guidelines from the American Academy of Ophthalmology and the American Optometric Association don't reflect that.

**TOPIC:** A new paradigm for dry eye treatment is being suggested under the acronym SET, which stands for:

- **S** = Symptoms from patient history
- **E** = Express the meibomian glands
- **T** = Treat the patient

What do you think are the important elements of this approach to dry eye assessment (Figure 1) and management, especially in lipid-deficiency dry eye can be identified by reduced tear film break-up time.

If untreated, dry eye can lead to damage of the corneal epithelium. These tests are widely used in the assessment of dry eye by both optometrists and ophthalmologists.

*Photos courtesy of Marianne Anderson, OD, Alcon Research, Ltd.*

*“The recommendation for expression of the glands will increase the actual diagnosis of patients suffering from MGD-related dry eye.”*

—ROY S. CHUCK, MD, PHD
Meibomian Gland Expression: The Paugh Procedure

**Physical Setup**

**The Subject Is Seated**, with the head resting comfortably at the slit-lamp. The examiner scans along both lower lids, using 10x to 16x magnification. The slit lamp illumination is used at a moderate level (essentially a “white” beam color).

A sterile, wooden-stemmed, cotton-tipped applicator is used to press the lids against the globe right at the margin to express the gland contents. Wood is preferred rather than fiber or paper because it is more rigid. The tip of the applicator will cover approximately 5 glands at a time.

The glands are expressed starting from the temporal aspect of the right eye and continuing to the extreme nasal extent. Nasal to temporal expression is undertaken for the left eye.

**Technique**

**The Examiner Applies** pressure at the tip of the applicator for 5 to 10 seconds, watching for the excreta to emerge through the slit lamp. Often there will be observed a sudden expulsion, akin to a small volcano erupting.

**Grading & Interpretation**

**The Color and Viscosity** of the excreta are observed. The examiner records a global “average” or summation of the appearance of the excreta from all glands from each lid. If the excreta are clear, it is helpful to observe the excreta against the relatively darker background of the iris as the excreta becomes invested into the tear film. A 4-point scale is useful, with at least 0.5 unit increments, as follows:

- **Grade 0** = Normal, Clear Oil Expressed
- **Grade 1** = Opaque, Diffusely Turbid, Normal Viscosity
- **Grade 2** = Opaque, Increased Viscosity
- **Grade 3** = Inspissated (i.e., like toothpaste)

Using this 4-point scale, Grade 1 or higher suggests Meibomian Gland Dysfunction.

Procedure developed by Jerry R. Paugh, OD, PhD
is the most important indicator of MGD. Examination of the glands by meiboscopy is certainly helpful to identify atrophy, but the technique may be too onerous for the majority of practitioners.

I think Steve Pflugfelder wrote one of the best papers ever on clinical assessment of dry eye. He describes two categories of aqueous tear deficiency (ATD): Sjögren’s and non-Sjögren’s, and two categories of MGD: inflammatory and atrophic. It was based on a small sample size, but we have followed that idea since about 2001 in our clinic and found it very useful.

Most patients will basically fall into one of those four categories. The one other category I would add is a mixture of ATD and MGD. It’s possible that, in some cases, the MGD stems from the inflammation due to ATD, but there are a number of patients that have major signs of both.

Then we have the “T” for treatment. In mild to moderate cases of hyposecretory MGD, it makes sense to undertake warm compresses and eyelid massage to try to revitalize the natural function of the meibomian glands, but it is also useful to supplement the missing oils with a viable external supply. In more severe cases, the combination of eyelid massage, oil supplementation, and systemic tetracycline therapy (doxycycline, minocycline) is necessary.

**OCULAR EXAMINATION — TO EXPRESS OR NOT TO EXPRESS?**

**DR. ASBELL:** If you have a patient with MGD and don’t
express the gland during the exam, you’ll miss it, right?

**DR. PEREZ:** Yes, and that’s an important point. In addition to looking for meibomian gland atrophy (Figure 3) you have to express the meibomian gland to identify MGD, which epidemiological studies show will be present but not obvious in some of your dry eye patients. 16-18

It’s something like a stress test. People can have serious cardiovascular disease that you’ll never see until they get on the treadmill.

**DR. MAH:** It’s a good, efficient approach to add gland expression to what we do already. If I were to add one test, I think gland expression is probably the best choice.

**DR. HERNÁNDEZ-QUINTELA:** I would like to stress the importance of the epidemiology. One study states: “obstructive meibomian gland dysfunction is the most common cause of evaporative dry eye.” 22 So, that’s something that the general practitioner must know. Next, we need to teach all of our residents and colleagues exactly what we’re saying here today.

**DR. ASBELL:** I would recommend expressing the glands in the middle of the lower lid. The upper lid is too hard to get to.

**DR. CHUCK:** There are probably as many ways to express the meibomian glands as there are eye care practitioners. However, at the very least, physical pressure — be it via device or finger — needs to be applied to the glands.

One mistake that people make is that they’ll sometimes press on the lid and stop because they don’t see anything. You really need to do the old “press and pause” for 5 or 6 seconds before you start seeing anything coming out (Figure 4).

**DR. PAUGH:** Gland expression is paramount in making a diagnosis, and I have developed a procedure that I teach to all my students at Southern California College of Optometry and to any practitioners who ask for advice. (See sidebar.)

**DR. FOULKES:** It is important for the clinician not only in evaluating dry eye, but also in any patient with any ocular surface complaints, to carefully examine the meibomian glands and express the glands with a maintained pressure to produce secretions. Without applying pressure, you can’t evaluate what
is going on with the glands. Once you start doing this more often, you might find MGD in patients who have not been complaining about dry eye. MGD is actually quite common, and it is often missed.

**DR. MAH:** I have a question related to that. If you have anesthetized the eye for a Goldman tonometry as part of the normal examination, would that be a good time to do the expression?

**DR. ASBELL:** It is typical that that’s been done by the time you would be ready to do the lid expression.

**DR. HERNÁNDEZ-QUINTELA:** I would also recommend not delegating the gland expression to the technician, even if he or she is putting in the anesthetic. The time saved would not be worth the clinical information lost.

**TREATING THE PATIENT**

**TOPIC:** Both lid hygiene and antibiotics (oral or topical) are recommended for both anterior and posterior blepharitis, but anti-inflammatories are only recommended for anterior blepharitis in the Preferred Practice Patterns of the American Academy of Ophthalmology, and similar recommendations are made in the Optometric Clinical Practice Guidelines of the American Optometric Association. Is this what you see in actual practice?

**DR. ASBELL:** I think people do use anti-inflammatories in posterior blepharitis as well as for anterior, or at least, it is considered.

**DR. FOUJKS:** That seems to be increasingly true when choosing topical treatment of posterior blepharitis rather than oral doxycycline. I think that the use of anti-inflammatories and antibacterials in both types of blepharitis are now part of the continuum of practice.

**DR. CHUCK:** We use anti-inflammatories for posterior blepharitis as well, and they are very effective.

“The formulation facilitates a very rapid and uniform coverage of the ocular surface with comfort upon insertion as well as minimal blur.”

—MIKE T. CHRISTENSEN, OD, PHD

**FIGURE 5**

**EMULSION COMPOSITION OF SYSTANE® BALANCE LUBRICANT EYE DROPS**

The SYSTANE® BALANCE formulation is different from SYSTANE® and SYSTANE® ULTRA Lubricant Eye Drops in the addition of mineral oil and a proprietary anionic phospholipid which are emulsified and combined with the HP-Guar/borate technology used in previous SYSTANE® products. This new formulation is specifically designed to provide ocular surface protection, stabilise the tear film, and supplement meibum secretions with lipid. Illustration courtesy of Alcon Research, Ltd.
**DR. PAUGH:** In severe cases of MGD-related anterior blepharitis (very rare in our clinical setting) and MGD-related posterior blepharitis (much more common, i.e., cases in which there is greater than grade 3 on a 4-point scale of corneal fluorescein staining), we use anti-inflammatory drugs and systemic tetracycline therapy. Sometimes, all this is still ineffective.

**DR. FOULKS:** In terms of emulsion eye drops available in the UK, we currently have the SYSTANE® lubricant eye drop for which there is a new formulation called SYSTANE® BALANCE Lubricant Eye Drops.

In addition to the propylene glycol, the emulsion composition of SYSTANE® BALANCE Lubricant Eye Drops has some components that other lubricant eye drops don’t. These include HP-Guar/borate, which helps reduce friction and coat the surface of the cornea, as well as an anionic phospholipid to help stabilize the tear film lipid layer. That is something new, and it seems to offer some significant advantages over what we’ve had until now.

I have had some experience with it, and found it effective in controlling both the signs and symptoms of dry eye in MGD patients.

**A NEW THERAPEUTIC OPTION — SYSTANE® BALANCE LUBRICANT EYE DROPS**

**DR. CHRISTENSEN:** SYSTANE® BALANCE Lubricant Eye Drops is a combination of lipids with other compounds homogenized in a process that produces a sub-micron particle emulsion that both remains stable and avoids coalescence (Figure 5).19,20

This formulation was developed to address dry eye symptoms associated with meibomian gland dysfunction. The components of this formulation have been combined to provide superior ocular surface protection,20,21 stabilize the tear film,20 and supplement the natural meibum.19

In vitro rheology data (Figure 6) simulates the change in viscosity of SYSTANE® BALANCE Lubricant Eye Drops after a drop is administered to the eye. Upon instillation in the eye, viscosity decreases as a function of shear rate, which is indicative of rapid mixing or thinning. After several “blinks,” as pH increases and sorbitol is diluted, there is enhanced viscosity from strengthening of the HP-Guar crosslinking.19

The blue line represents what would happen after several blinks as you have an equilibration of the pH of the formulation. So, it’s formulated at pH 7.0, but we know that, over several blinks, since the tear film is slightly alkaline, you have a slight increase in the pH and you get a dilution of the sorbitol (sorbitol is highly water soluble), enhanced viscosity, and a muco-mimetic layer on the ocular surface.19

The relevance of this experimental data is that the formulation facilitates a very rapid and uniform coverage of the ocular surface with comfort upon insertion as well as minimal blur. With the combination of the excellent rheology, improvement in TFBUT, and the haze profile, the formulation of SYSTANE® BALANCE Lubricant Eye Drops will be a good option for those MGD patients whose needs have not been met. ◀

**Disclosures**

Dr. Christensen is employed by, and Drs. Asbell, Chuck, Foulks, Mah, Paugh and Perez are paid consultants for and/or receive research support from, Alcon Laboratories, Inc. Dr. Hernández-Quintela has no relevant disclosures.
REFERENCES


A new twist for your patients with dry eye associated with MGD

SYSTANE® BALANCE Lubricant Eye Drops

- Unique formulation with the LipiTech™ System restores the lipid layer. (1)
- Stabilizes the natural tear film for extended TFBUT. (2)
- Decreased dosing from baseline. (3)