Dr. Alan G. Kabat, O.D., F.A.A.O.

What is the role of lipids in the fight against DED and the maintenance of normal tear stability?

Dry eye disease (DED) represents one of the most challenging disorders that today’s eye-care practitioners face. Few other conditions are so ubiquitous and yet so poorly understood. The multifactorial nature of DED combined with the tremendous variation of inconsistent symptoms often makes for a frustrating experience with regard to adequate detection and management.

The Facts

According to the National Women’s Health Resource Center, about 20 to 30 million Americans suffer from dry eye; roughly one-third of these individuals present with moderate or severe symptoms. The incidence of DED appears to be higher in women, possibly due to hormonal impact on lacrimal and meibomian secretions, and the elderly. Also, patients over the age of 50 may be as much as six times more likely than younger patients to experience this condition. Many elements other than gender or age may contribute to or exacerbate DED. Systemic disorders (e.g., diabetes, rheumatoid arthritis), contact lens wear, medications, diet, environmental humidity and temperature, and even daily activities like computer use or driving can influence the tendency to manifest DED.

With the recent publication of the Dry Eye WorkShop (DEWS) report in April 2007, practitioners have gained additional insight concerning dry eye classification and man-
But, the most important contributory element in evaporative DED is undoubtedly lid margin disease, or blepharitis. To understand how lid margin disease impacts DED, we must first recognize the role of lipids in maintaining tear stability.

The Role of Lipids

Tear film lipids originate primarily from the meibomian glands, located within the tarsal plate; to a lesser degree, lipids are also derived from the accessory sebaceous glands of Zeiss, found along the eyelid margin. These secretions consist of a variety of both polar and non-polar oils, including wax and sterol esters, triglycerides, hydrocarbons and phospholipids. With each blink, lipid secretions are expressed along the ocular surface, forming the most distal aspect of the tear film. In this capacity, the lipids serve to provide several essential functions, including lubrication of the ocular surface, which diminishes lid-globe friction; reduction of tear film surface tension, which allows for more even tear distribution; and establishment of a superficial barrier to aqueous tear evaporation.

Posterior blepharitis, also known as meibomian gland dysfunction (MGD), is a significant cause of tear lipid deficiency and evaporative DED. Chronic inflammation within the meibomian glands leads to stagnation of lipid flow and altered composition/consistency of the polar lipids. The result of MGD on the ocular surface is a diminished quantity and/or quality of lipids, which is why patients with this condition experience more rapid tear evaporation and increased ocular surface friction. Ultimately, chronic MGD can lead to significant inflammation of the ocular surface and symptoms of DED.

To effectively manage MGD and lipid-deficient DED, we must first accurately identify this condition. Evaluation must include inspection of the lid margins. Look for irregularities, telangiectatic blood vessels, and madarosis (e.g., extensive loss of lash follicles). Also, observe the expression of the meibomian glands; apply moderate but firm pressure with a finger or cotton-tipped applicator just proximal to the glands, and the secretions should flow easily (figure 1). The expressed lipids should be clear—not turbid—and have the consistency and color of a light cooking oil. Glands that do not express easily with digital pressure or secretions that are thick and “cheesy” are indicative of MGD.

Treatment Options

Treatment of MGD aims to restore the glands to normal, healthy function. Patients are typically advised to use warm compresses and digitally massage or express the lid margins several times daily, as this helps to thin the secretions and promote improved meibomian flow (figure 2). Another commonly employed therapy involves the use of oral supplements containing high levels of essential fatty acids (EFAs). EFAs, which tend to be deficient in the typical Western diet, purportedly have the capacity to improve meibomian secretions by stimulating tear-specific anti-inflammatory prostaglandins. Likewise, tetracycline drugs (including doxycycline and minocycline) have been shown to be beneficial in cases of severe MGD. It is believed that these drugs hinder the production of bacterial lipases, which alter the consistency of the meibomian oils. Additionally, tetracyclines

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are now recognized to be potent anti-inflammatory agents, inhibiting the production of matrix metalloproteinases and other cytokines.8

While the aforementioned treatment options may help improve MGD, it may take weeks or even months before patients experience significant relief. And while lubrication therapy with artificial tears can help to provide substantial short-term improvement of symptoms, very few commercially available tear products incorporate a lipid component, which is the key element that is deficient in MGD. For this reason, rapid tear evaporation may still be a significant problem in these individuals, despite the copious use of eye drops. Conversely, excessive application of these agents may flush away crucial constituents of the natural tear film, including lipids.9

Over the last few years, however, manufacturers have begun to recognize the significance of lipids in maintaining a stable tear film, and several lipid-containing products have been introduced to the U.S. market. The first of these was Refresh Endura (Allergan), a preservative-free, castor oil-in-water emulsion. Endura was created partially because early studies on cyclosporine ophthalmic solution (Restasis) had found that patients treated with the castor oil vehicle alone also experienced substantial symptomatic improvement from baseline.9 The researchers concluded that the sustained residence time on the ocular surface of a lipid emulsion may help to reduce evaporation of the limited volume of natural tears present in patients with dry eyes.10,11

Lid Hygiene and Massage


If tear glands get clogged or do not function properly, you may experience burning, stinging or even watering of your eyes. The meibum (the fluid secreted from the meibomian glands) should be the consistency of vegetable oil. If it hardens, it becomes more like margarine and cannot excrete the glands properly. By placing moist heat over the eyes, the hardened gland material softens (just as if you were melting butter).

Lid massage with warm washcloth (Can also be done in shower)
1. Use small, clean washcloth.
2. Rinse the cloth with warm water.
3. Gently massage the upper and lower lids for 30 seconds.
4. Rinse the cloth again with warm water.
5. Repeat massage; the oil in the glands can be waxy and needs to be warmed up before it can come out.

Lid Expression
1. Follow steps for lid massage as above.
2. Close your eyes.
3. Gently press the lower lid in. Squeeze the oil upwards with a rolling motion.
4. Start with the side closest to the nose and move out toward the ears.
5. Repeat with upper lid, try to squeeze the oil downwards with a rolling motion.

Lid massage with rice and sock
1. Measure about one cup of uncooked white rice (or flaxseed) and pour it into a clean sock.
2. Sock should be long enough to create a surface area of at minimum six inches when a knot is tied in the end.
3. Microwave the uncooked rice and sock for about 30 seconds (microwave times may vary).
4. Place a wet sterile gauze between the sock and eye for moist heat.
5. Gently massage the upper and lower lids for 30 seconds.
6. Re-warm the sock and repeat.
7. Optional step: Gently press the upper and lower lids with a circular motion to squeeze the oil out of the glands (just like lid expression above; only done with the sock).

Remember: the above procedures must be done at least twice a day to be effective.

2. These lid hygiene instructions can help patients to control meibomian gland dysfunction, along with targeted oral and/or topical therapy.
Elements Associated With Dry Eye Disease

- Reduced blink rate (e.g., during excessive computer use, reading, driving)
- Wide lid aperture
- Other ocular surface disease (e.g., allergy, meibomian gland dysfunction)
- Systemic medications (e.g., antihistamines, beta-blockers, diuretics, anxiolytics)
- Systemic disease (e.g., Sjögren’s syndrome, diabetes, rheumatoid arthritis)
- Aging
- Contact lenses
- Low androgen pool
- Low relative humidity
- High wind velocity
- Occupational environment
- Contact lens wear

Another recent addition to this lineup of artificial tears is Soothe XP (Bausch & Lomb). This oil-in-water emulsion contains restoryl, a proprietary combination of mineral oils designed to mimic the natural tear lipids. Also unique is the fact that the emulsion is “metastable;” it maintains its integrity in the bottle, but under the forces of lid action in the eye, it rapidly breaks into its component elements. Studies have shown that Soothe XP may help to increase tear lipid layer thickness in dry eye patients by approximately 100% from baseline and provide sustained relief from dry eye symptoms for up to eight hours.12,13

The latest tear product to address the issue of deficient tear lipids is FreshKote (Focus Laboratories). This distinctive formulation contains an exclusive ingredient—a proprietary combination of phospholipids, polysorbate-80, glycerin and ethanol, called Amisol Clear. Amisol Clear acts as a dispensing agent for the solution and also serves to simulate the lipid layer, helping to retard tear evaporation. Additionally, FreshKote contains several demulcents, such as polyvinyl alcohol and polyvinyl pyrrolidone, which help to enhance wettability of the ocular surface and bind moisture to the corneal epithelium. Another extremely unique property of FreshKote is its high oncotic pressure, which results from the presence of large particles (colloids) in the solution that induce an osmotic flow.

Theories suggest that the epithelial layer of the cornea in DED is often damaged, causing a loss of permeability and allowing for an influx of fluid.14 The cells become “water-logged” due to edema and are prone to incomplete wettability and basement membrane damage. Only solutions with high oncotic pressure can safely remove this excess water; hypertonic sodium chloride solutions (e.g., Muro 128) can damage stromal keratocytes due to excess salt accumulation.13 Although few prospective clinical studies on FreshKote have been published, significant anecdotal experience exists to suggest that this product may be extremely helpful in a variety of ocular surface disorders, including evaporative DED.

The Future

While dry eye has been recognized as a clinical entity for many years, researchers are only now beginning to comprehend the nuances and intricacies of this complex ocular surface disorder. As more information becomes available, clinicians are gaining a better understanding of the disease and the need for more appropriate and proactive therapy. Evaporative DED accounts for a substantial portion of our patients with dry eye-related complaints and pathology. By recognizing the contributory elements and prescribing targeted therapies, we can provide our patients with enhanced relief and improved quality of life.

Disclosure: Dr. Kabat is a member of Alcon’s Speakers Alliance and the Board of Optometric Consultants for CYNACON/OCuSOFT. He has no direct financial interest in any of the products mentioned in this article.