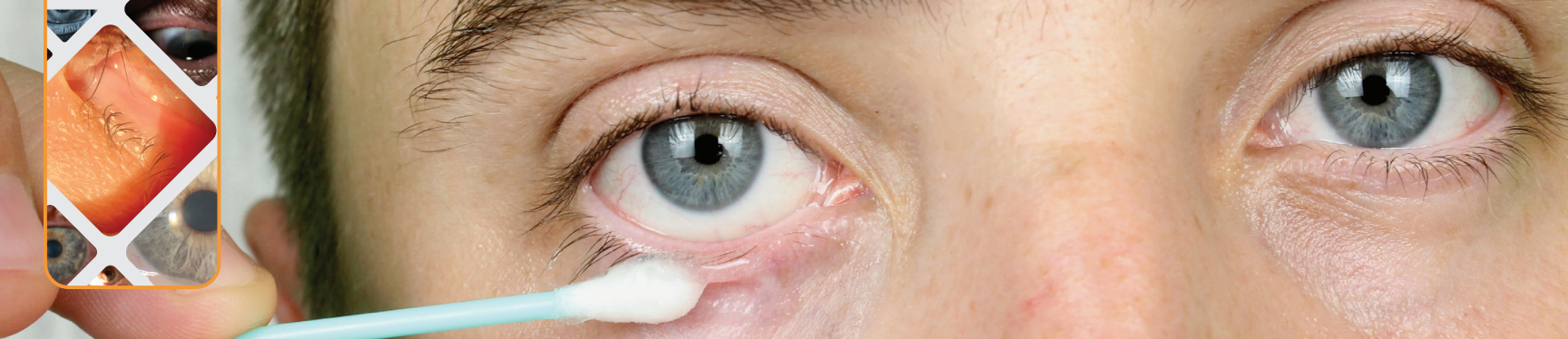




SURVEYING THE OPTIONS FOR TREATING *DEMODOX*



What's available, what's coming, and the attributes of each.

BY LESLIE E. O'DELL, OD, FAAO

Demodex is associated systemically with acne vulgaris, folliculitis, rosacea, seborrheic dermatitis, perioral, and scalp hair loss, as well as basal cell carcinoma.¹ For decades, eye care professionals have been aware of the problems caused by *Demodex* blepharitis. *Demodex* overpopulation, or *demodicosis* contributes to diseases of the lid and lid margin, blepharitis, and meibomian gland dysfunction (MGD), and if left untreated, can lead to recurrent chalazia, pterygia, blepharokeratitis, and possibly meibomian gland atrophy.¹ However, there are no FDA-approved therapies available to help control the overpopulation of *Demodex folliculorum* and *Demodex brevis*, which are the common residents found in the lash follicles and meibomian glands of our patients.

In this article, I offer a brief review of what has been used to help patients manage *Demodex* blepharitis from the past to the present and take a look at what's in the pipeline.

THE OLD STANDARDS

In the past, *Demodex* blepharitis and other forms of resistant blepharitis were treated with topical ointments such as sulfuric ointment and yellow mercuric ointment, and antibiotic ointments such as erythromycin, anticholinesterase, and antifungal drugs with marginal improvement of clinical presentation.² Sulphuric ointment or yellow mercury treatments were poorly supported and are now obsolete with research of these products dating from 2 decades ago.

Pilocarpine is a miotic and has been used to treat glaucoma by allowing excess fluid to drain from the eye. More recently, pilocarpine HCl ophthalmic solution 1.25% (Vuity, Allergan) has been approved by the FDA to treat presbyopia³ and has shown interesting antiparasitic results in a gel form, thought to be due to its parasympathomimetic action, resulting in paralysis of mite respiration and mobility.⁴ The use of 4% pilocarpine gel demonstrated complete resolution of *Demodex* blepharitis in 37.5% of cases, and partial cure

in 40.6% of cases⁵—perhaps another treatment that needs future research.

In addition to treatment, lid hygiene is another area of focus for managing *D. folliculorum*, with both in-office (microexfoliation) and at-home options recommended. For many providers, at home care with warm compresses to soften the debris and surfactant cleansers, such as diluted baby shampoo, is recommended. Hypochlorous acid lid cleansing products are also gaining use more recently. The method of heating the lid varies, from warm washcloths to standardized heat masks. Of note, baby shampoo has been proven to have no effect on the survival time of *D. folliculorum*. A 50% concentration of baby shampoo showed that mites exposed for longer than 150 minutes were still living, and there was no change in quantity over the course of 350 days.⁶

The in-office procedure microblepharoexfoliation (MBE) of the eyelid margin can improve patient outcomes. One study showed that MBE with lid hygiene significantly reduced the *Demodex* mite count compared with lid hygiene alone (a decrease of 3.88 vs. 0.04 organisms, $P < .001$) in adults with *Demodex* blepharitis.⁷ A second study demonstrated significant reduction in the levels of *Demodex* with a combination of MBE and lid scrubs containing T-40.⁸

Tea Tree Oil

Tea tree oil (TTO) is an essential oil from the *Melaleuca alternifolia* plant that has been found to be effective at reducing the number of *Demodex* mites and the associated ocular surface inflammation in patients with *Demodex* blepharitis, but only at concentrations of 50% or more, which is irritating to the ocular surface.⁶ TTO has nearly 100 components, and scientists have identified terpinen-4-ol (T-40) as its most active ingredient and isolated it for



► COVER FOCUS **OSD FROM A TO Z**

treatment of *Demodex*. The formulation of T-40 with the highest concentration is Cliradex (Bio-Tissue), which has been shown to effectively kill adult mites within 40 minutes of exposure.⁹ Oust *Demodex* (Ocusoft) is another commercially available eyelid wipe that is well tolerated, but contains only 1% TTO.

Another OTC product that contains TTO is Blephadex Eyelid Wipes (Lunovus). A pilot study demonstrated no changes in ocular microbiota, tear film characteristics, or bacterial lipase in eyes tested after 1 month of daily use with Blephadex Eyelid Wipes, however a statistically significant reduction in *Demodex* count was observed in eyes treated with Blephadex Eyelid Wipes despite the overall numbers of *Demodex* being low in both groups studied.¹⁰

Although T-40 can effectively reduce a *Demodex* population, new research states that T-40, even at low levels, is toxic to human meibomian gland epithelial cells.¹¹ Chen et al recently found a dose and time-dependent decrease in the cell survival of human meibomian gland epithelial cells, with changes noted 15 minutes after exposure to 1% T-40 and cell death after 90 minutes.¹¹

Off-Label Use of Medications

Over the past 3 decades, off-label use of anthelmintics, such as ivermectin or metronidazole, were used empirically to treat *Demodex* blepharitis.¹² Ivermectin is orally administered as an effective antiparasitic drug. It has selective activity against glutamate-gated chloride ion channels from the peripheral nervous system of invertebrates. The acaricidal effect of metronidazole on the *Demodex* mite is unknown.¹²

THE PROMISE OF NEW OPTIONS

A few alternative treatments have become available in recent years, with limited research.

Manuka Honey

Manuka honey has been thought of as an alternate treatment for *Demodex*

blepharitis. One study has demonstrated that cyclodextrin-complexed Manuka honey was comparable to the anti-demodectic efficacy to 50% TTO.¹³ Complexed honey with proven in vivo tolerability shows promise as a possible alternative to TTO for *Demodex* eradication.

IPL

IPL therapy has been considered off-label when used in patients with rosacea, MGD, and *Demodex* blepharitis with successful outcomes.¹⁴ Treatment was performed three consecutive times every 3 weeks. Zhang et al suggested that IPL may affect the germ of the mites to inhibit their reproductive ability, and the high temperature may damage the environment in which the mites live.¹⁵ A recent study showed that intense pulsed light (IPL) caused mite death during application in vitro.¹⁶

New Therapy on the Horizon

Lotilaner ophthalmic solution 0.25% (TP-03, Tarsus Pharmaceuticals) administered one drop twice daily in each eye for a 6-week duration has proven to be effective at reducing collarettes and mite counts in patients with *Demodex* blepharitis.¹⁷ This medication is thought to paralyze the mites nervous system thru parasite-specific GABA inhibition.¹⁷ Saturn-1 (phase 2b/3) was a randomized, controlled, multicenter, double-masked pivotal trial evaluating the safety and efficacy of TP-03 in adults with *Demodex* blepharitis, which met each of its primary and secondary endpoints with high statistical significance and demonstrated positive and clinically significant improvements within 2 weeks for patients treated with lotilaner.¹⁷ Lotilaner was found to be comfortable and had a good safety profile with no treatment-related serious adverse events. Recently results of the Saturn-2 phase 3 trial recently were released. TP-03 was found to have clinically meaningful collarette cure in 89% of subjects and mite eradication in 52% of patients studied.¹⁸

THE TREATMENT QUEST CONTINUES

Demodex blepharitis contributes to the negative impact of the overall ocular surface health as well as the quality of life of patients. Current treatment options can reduce mite count, but not effectively kill eggs, and they typically last between 1 and 3 months. Patients find treatment options difficult to adhere to, and they come with a potential risk for further complications. Continued research to expand treatment options for patients with *Demodex* blepharitis can improve patient outcomes. ■

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