

induced Stevens-Johnson syndrome.^{96,97} Tetracyclines can sensitize the skin to the sun and result in greater likelihood of sunburn with exposure. Minocycline has been reported to stain skin, nails, sclera, teeth, conjunctiva, tongue, and bone.¹¹¹⁻¹¹³

Oral azithromycin (off label) has been used successfully in the management of acne rosacea as an alternative to oral tetracyclines and can be combined with 0.1% topical tacrolimus.^{114, 115} Similarly, oral azithromycin 500 mg per day for 3 days in three cycles with 7-day intervals yielded good clinical improvement in 13 patients with blepharitis in an open-label single-center prospective case series.¹¹⁶ Another acceptable dosing regimen for pulsed oral azithromycin in adults is 1 g per week for 3 weeks.¹¹⁷ Another study found efficacy with topical azithromycin as well as systemic azithromycin in both the signs and symptoms of posterior blepharitis.¹¹⁸ Importantly, a Medicaid cohort in Tennessee showed a small but absolute increase in cardiovascular deaths (hazard ratio, 2.88; 95% confidence interval, 1.79–4.63; $P < 0.001$), which was most pronounced among patients who had a high baseline risk of cardiovascular disease and were treated with a 5-day oral azithromycin therapy.¹¹⁹ In March 2013, the FDA issued a warning that oral azithromycin may lead to abnormalities in the electrical activity of the heart, with the potential to create serious irregularities in heart rhythm.¹²⁰ However, the use of oral azithromycin for 5 days may actually be more efficacious with fewer side effects than 30 days of doxycycline.¹²¹ A Cochrane study showed a small benefit of oral doxycycline in improving clinical signs, but may cause more adverse events.¹²² More studies are necessary to evaluate the efficacy of oral antibiotics in blepharitis.

Currently, there is only high-quality evidence to support topical azelaic acid, topical ivermectin,^{123, 124} brimonidine, doxycycline, and isotretinoin as effective treatments for patients with systemic rosacea. Additional studies must be performed to determine the effectiveness of topical metronidazole, oral tetracycline, low-dose minocycline, or topical cyclosporine for ocular rosacea.¹²⁵

A brief course of topical corticosteroids may be helpful for eyelid or ocular surface inflammation, including marginal keratitis or phlyctenules. Corticosteroid eye drops or ointments are typically applied several times daily to the eyelids or ocular surface. Once the inflammation is controlled, the corticosteroid can be tapered and discontinued and then used intermittently to maintain patient comfort. The minimal effective dose of corticosteroids should be used, and long-term corticosteroid therapy should be avoided if possible. Patients should be informed of the potential adverse effects of corticosteroid use, including the risk for developing increased intraocular pressure and cataract. These adverse effects may be minimized by using a site-specific corticosteroid such as loteprednol etabonate and corticosteroids with limited ocular penetration, such as fluorometholone phosphate. Guidelines for maintenance therapy should be discussed. Topical cyclosporine may be helpful in some patients with posterior blepharitis.¹²⁶

Diet modification has been a traditional (though not well-documented) way of managing acne rosacea. The role of dietary supplementation with essential fatty acids in the management of blepharitis was evaluated in a 1-year study in which patients took two 1000-mg capsules of essential fatty acids three times a day. Those receiving the supplement demonstrated an improvement in the tear film break-up time, dry eye symptoms, and meibum score, suggesting a potential benefit for this treatment in some blepharitis patients.¹²⁷ A prospective, multicenter, double-blind clinical trial funded by the National Eye Institute and National Institutes of Health, studied the use of oral omega-3 supplements by patients with moderate to severe dry eye disease. Patients who were randomly assigned to receive supplements containing 3000 mg of omega-3 fatty acids for 12 months did not have significantly better outcomes than patients assigned to receive placebo (olive oil).¹²⁸ These two conflicting outcomes may indicate differences in patient population, formulations of the supplements, dosing, and/or the disease process being examined (i.e., blepharitis vs. moderate to severe dry eye disease). There may be a treatment effect of the olive oil placebo, which could explain the lack of significant benefit of omega-3 fatty acids in the multicenter trial. One review showed a benefit of oral omega-3 supplementation in MGD.¹²⁹ More studies are needed to clearly define the role of omega-3 supplements in ocular surface disease.

Artificial tears, especially those containing oil or lipid-based products, can be helpful for posterior blepharitis. Because many blepharitis patients have tear film instability, artificial tears may improve symptoms when used as an adjunct to eyelid cleansing and medications. If artificial tears are used more than four times per day, nonpreserved tears should be used to avoid