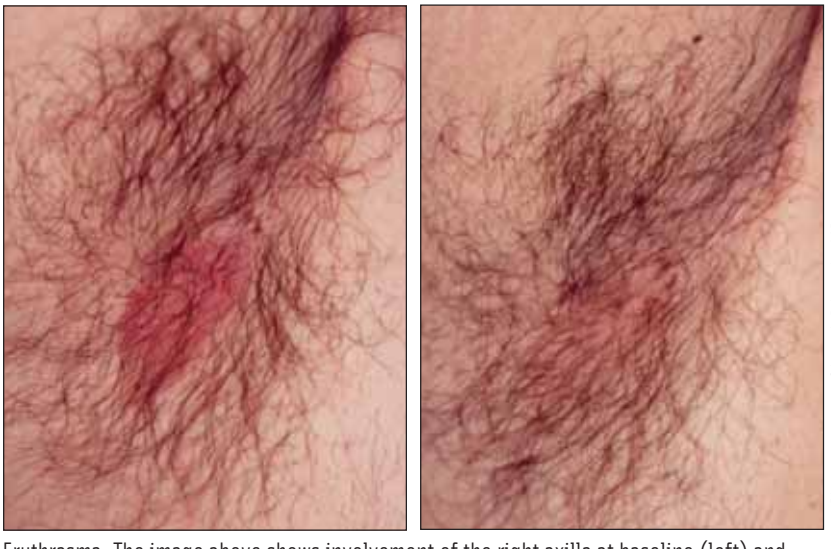
Update on Diagnosis and Topical Management of Erythrasma

This under-diagnosed cutaneous infection is caused by a bacterium but may respond to anti-fungal therapies.

By Joseph Bikowski, MD

Erythrasma is a frequently under-diagnosed cutaneous infection caused by *Corynebacterium minutissimum*. It commonly affects body folds, particularly the groin, and has been identified as one of the leading causes of interdigital foot infections.[1] Traditionally, erythrasma has been considered to more frequently affect individuals living in warmer climates, though it can occur at any lattitude. Along with candidiasis, intertrigo, candida folliculitis, furunculosis, tinea cruris, and folliculitis, erythrasma has been reported to occur with increased incidence among obese individuals[2] and those with diabetes.[1] However, the infection may also be common among athletes, particularly when affecting the toe webs.[3]



Photos courtesy of Joseph Bikowski, MD

Erythrasma. The image above shows involvement of the right axilla at baseline (left) and improvement following four weeks of once-daily application of ketoconazole foam (right).

Among other cutaneous diseases, the differential diagnosis of erythrasma includes cutaneous fungal infections, including pityriasis rotunda, tinea corporis/cruris,[4] tinea pedis, and pityriasis versicolor.[5] Importantly, erythrasma may coexist

with cutaneous dermatophyte infections.[6] Proper diagnosis of erythrasma and any concomitant skin infection(s) is essential to allow initiation of appropriate therapy targeted at all causative organisms. Topical anti-infective therapy, including broad-spectrum ketoconazole, is typically sufficient to manage the condition, although systemic antibiotics have traditionally been advocated for erythrasma and may be indicated for severe or refractive cases.

Presentation and Prevalence

Erythrasma is a bacterially mediated scaly skin eruption typically localized to warm, moist skin folds. The rash tends to be deep red to brown in color and is not typically associated with significant pruritus. Erythrasma was once improperly considered a fungal infection, though research over the past 50 years has confirmed the role of *C. minutissimum* in its pathogenesis. [7,8] These gram-positive bacteria are typically part of the normal resident flora of human skin. In 1965, Montes, et al. evaluated biopsied skin from patients with erythrasma absent any concomitant fungal etiology.[8] They found *C. minutissimum* dispersed over the skin surface, between and penetrating superficial cornified cells, and within keratinized cells. Their investigation showed that the stratum corneum of affected patients was hyperkeratotic and identified likely keratolytic processes associated with the presence of intracellular bacteria.

Erythrasma generally is diagnosed through visualization, but it may be mistaken for candidiasis, intertrigo, psoriasis, seborrheic dermatitis, contact dermatitis, or dermatophytosis.[1] Luminecescence with a Wood's Lamp reveals a coral pink fluorescence that confirms the presence of *C. minutissimum* and supports the diagnosis. The diagnosis may be missed if the patient has bathed within the preceeding 24 hours; bathing may wash away coproporphyrin III, the pigment produced by *C. minutissimum* that causes fluorescence. Fungal culture may be used to rule out concomitant fungal infection.

Erythrasma has been found to have a higher prevalence in diabetics and the obese.[1,2]

Treatment Options

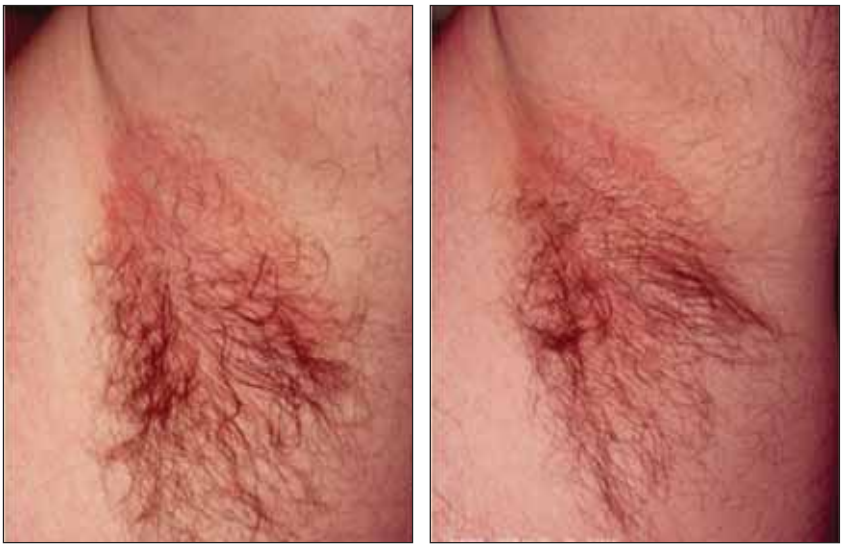
Systemic antibiotics offer proven efficacy and have been used for the management of erythrasma; Erythromycin 250mg four times daily for 14 days has been recommended as the systemic antibiotic treatment of choice.[1] Yet systemic antibiotics are currently described as a third-line treatment option for erythrasma, and they are known to confer limited efficacy for affected toe-webs.[9,10] As dermatologists and other physicians have become increasingly aware of antibiotic resistance and its potential long-term impact on patient care, there have been efforts to reduce the use of systemic antibiotics. Furthermore, systemic medications in general tend to present a greater risk of side effects and/or drug interactions compared to topical agents. Given that erythrasma is a generally benign condition, the use of systemic antibiotics as first-line therapy becomes questionable.

Topical antimicrobial therapies are second-line choices for erythrasma management.[9] Topical preparations containing antibiotics have not been shown in the published literatureto be very effective for treating erythrasma. However, antimicrobial fusidic acid ointment 2% has demonstrated efficacy, as has Whitfield's ointment (salicylic acid and benzoic acid).[1,9] Whitfield's ointment reportedly has similar efficacy to systemic erythromycin for erythrasma affecting the axillae and groin and is superior to the oral agent in the interdigital areas.[1]

Despite the potential efficacy of the topical antimicrobial ointment preparations, they are not ideal in the clinical setting. They may lack cosmetic elegance and thus be associated with low compliance. Most patients are unwilling to apply thick, greasy preparations to intertriginous areas or toe webs.

Although a role for dermatophytes, yeasts, and molds in the pathogenesis of pure erythrasma has been disproven, topical antifungal formulations

have been used with success to manage the condition and are described as first-line treatment options.[9] Topical miconazole,[11,12] clotrimazole,[12] and econazole[9] have all been shown effective for erythrasma. In one trial involving 61 patients with fungal infection or erythrasma, subjects were randomized to use topical tioconazole base 1% w/w or econazole nitrate 1% creams for a mean treatment period of 40 and 38 days respectively.[13] All but two patients in each arm achieved clinical and mycologic cure and described treatment as generally acceptable, though mild intermittent pruritus was reported with econazole. Again, creams may not be ideal for use in skin folds and interdigital spaces.



Photos courtesy of Joseph Bikowski, MD

The patient above is shown at baseline (left) and following 10 days of once-daily application of ketoconazole foam.

In my clinical experience, a new ketoconazole foam 2% formulation (Extina, Stiefel), has been a welcome new treatment option for erythrasma. The foam vehicle (VersaFoam HF) is a hydroethanolic formulation that is neither hydrating nor drying. It is designed to rapidly dissolve at skin temperature leaving little to no residue. As such, it is ideal for application to skin folds. The foam can be easily applied to various body sites large and small and is readily applied to hair-bearing skin, making it suitable for use in the axilla and hair-bearing chest and abdomen. It is also easily and comfortably applied to the toe webs.

Ketoconazole has long been recognized as having a broad spectrum of activity.[14] It confers documented anti-inflammatory and antibacterial effects.[15] Researchers demonstrated the agent's anti-inflammatory and antibacterial properties in a guinea pig model.[12] First, either living or killed *Staphylococcus aureus* was applied to the backs of the animals, which then received either ketoconazole 0.5% ointment alone or with hydrocortisone acetate 1%, ketoconazole 2% ointment alone or with hydrocortisone acetate 1%, no therapy, ointment vehicle alone, or hydrocortisone acetate alone. For the killed bacteria (i.e., no infection) groups, topical ketoconazole had anti-inflammatory activity comparable to that of hydrocortisone acetate. For infected animals, ketoconazole was superior to hydrocortisone. Combination therapy was beneficial in both groups.

An added benefit of topical ketoconazole for the management of erythrasma is that the broad-spectrum antifungal will address any concomitant fungal component of the presentation, eliminating the need for culture and optimizing the likelihood of complete cutaneous clearance.

Prevention

To reduce the likelihood of recurrence of erythrasma, patients must make efforts to reduce bacterial colonization and minimize moisture in the skin folds. The use of antibacterial washes has been recommended, though no published data are available. Advise patients to thoroughly dry the skin after bathing.

Although standard laundering practices are expected to prevent bacterial colonization of clothing, bacteria may, like dermatophytes, colonize

Cutaneous Infections Associated with Obesity

Common cutaneous infections:	*Less common infections:*
Candidiasis	Cellulitis
Intertigo	Necrotizing fasciitis
Candida folliculitis	Gas gangrene
Furunculosis	
Erythrasma	
Tinea cruris	
Folliculitis	

–Scheinfeld NS
Clin Dermatol. 22(4):303-9

moist footwear.[3] Patients with erythrasma involving the toe webs may need to disinfect or replace shoes to eliminate exposure to bacteria. Once clear, patients should be advised to allow their shoes to thoroughly dry between wearing, perhaps alternating footwear every-other-day, if needed, to allow drying.

Patients with a history of recalcitrant or recurrent erythrasma may be directed to prophylactically apply topical ketaconozole foam to previously affected areas once daily.

Multi-Targeted Intervention

The ability to manage a generally benign, bacterially-mediated cutaneous eruption with a topical formulation that poses minimal risk of side effects and no risk of bacterial resistance is ideal. As with all dermatologic presentations, therapeutic outcomes are optimized when patients are compliant with therapy. In light of these considerations, ketoconazole foam 2% represents a new treatment option for the management of erythrasma that may increase compliance.

Topical ketoconazole provides both anti-inflammatory and antibacterial properties that directly target the underlying bacterial cause of erythrasma. It also provides broad-spectrum antifungal effects that eradicate the fungal component that frequently co-exists with erythrasma. The foam vehicle is particularly suited for application to skin folds, toe webs, and hair-bearing skin without greasy residue, supporting patient compliance with therapy. ■ ☑

Dr. Bikowski has served on the advisory board, served as a consultant, received honoraria, and/or served on the speaker's bureau for Allergan, Barrier, CollaGenex, Coria, Galderma, Intendis, Medicis, OrthoNeutrogena, PharmaDerm, Quinnova, Ranbaxy, Sanofi-Aventis, SkinMedica, Stiefel, UCB, and Warner Chilcott.

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