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Fungal Toenail Infections

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Fungal toenail infection (onychomycosis) is characterized as infection of part or all of the toenail unit, which includes the nail plate, the nail bed, and the nail matrix. Over time, the infection causes discoloration and distortion of part or all of the nail unit.

- Fungal infections are reported to cause 23% of foot diseases and 50% of nail conditions in persons seen by dermatologists, but are less common in the general population, affecting 3% to 12% of persons.
- Infection can cause discomfort in walking, pain, or limitation of activities.

Persons taking oral antifungal drugs reported greater satisfaction and fewer onychomycosis-related problems, such as embarrassment, self-consciousness, and being perceived as unclean by others, compared with persons using topical antifungals.

- Oral antifungals have general adverse effects, including gastrointestinal symptoms (such as diarrhea), rash, and respiratory problems. It was rare for persons to withdraw from a randomized controlled trial because of adverse effects.

Both oral itraconazole and oral terbinafine effectively increase cure rates; terbinafine seems slightly more effective.

- Adverse effects unique to terbinafine include sensory loss, such as taste, smell, or hearing disturbance. This is usually temporary and reversible.

An alternative oral antifungal treatment is fluconazole, which seems to modestly improve cure rates, but the evidence is insufficient to allow us to say for certain.

Topical ciclopirox seems to modestly improve symptoms compared with placebo.

- We found no evidence examining the effectiveness of other topical agents such as ketoconazole, fluconazole, amorolfine, terbinafine, tioconazole, or butenafine.

Definition

Fungal toenail infection (onychomycosis) is characterized as infection of part or all of the nail unit, which includes the nail plate, the nail bed, and the nail matrix. Over time, the infection causes discoloration and distortion of part or all of the nail unit. The tissue under and around the nail may also thicken. This review deals exclusively with dermatophyte toenail infections (see Etiology) and excludes candidal or yeast infections.

Incidence and Prevalence

Fungal infections are reported to cause 23% of foot diseases and 50% of nail conditions in persons seen by dermatologists, but are less common in the general population, affecting 3% to 12% of persons. The prevalence varies among populations, which may be because of differences in screening techniques. In one large European project (Achilles project; 13,695 persons with a range of foot conditions), 35% had a fungal infection diagnosed by microscopy/culture. One prospective study in Spain (1,000 adults older than 20 years) reported the prevalence of fungal toenail infection as 2.7% (infection defined as clinically abnormal nails with positive microscopy and culture). In Denmark, one study (5,755 adults older than 18 years) reported the prevalence of fungal toenail infection as 4.0% (determined by positive fungal cultures).

The incidence of mycotic nail infections may have increased in the past few years, perhaps because of increasing use of systemic antibiotics, immunosuppressive treatment, more advanced surgical techniques, and the increasing incidence of human immunodeficiency virus infection. However, this was contradicted by one study in an outpatient department in Eastern Croatia, which compared the prevalence of fungal infections

between two periods (1986 to 1988, 47,832 persons; 1997 to 2001, 75,691 persons). It found that the prevalence of fungal infection overall had increased greatly over the 10 years, but that the percentage of fungal infections affecting the nails had decreased by 1% (fungal infections overall: 0.26% in 1986 to 1988 vs. 0.73% in 1997 to 2001; nail: 10.31% in 1986 to 1988 vs. 9.31% in 1997 to 2001).

Etiology/Risk Factors

Fungal nail infections are most commonly caused by anthropophilic fungi called dermatophytes. The genera *Trichophyton*, *Epidermophyton*, and *Microsporum* are typically involved, specifically *Trichophyton rubrum*, *Trichophyton mentagrophytes var. interdigitale*, and *Epidermophyton floccosum*. Other fungi, molds, or yeasts may be isolated, such as *Scopulariopsis brevicaulis*, *Aspergillus*, *Fusarium*, and *Candida albicans*. *Trichophyton rubrum* is now regarded as the most common cause of onychomycosis worldwide.

Several factors that increase the risk of developing a fungal nail infection have been identified. One survey found that 26% of persons with diabetes had onychomycosis and that diabetes increased the risk of infection, but the type and severity of diabetes was not correlated with infection (odds ratio [OR] = 2.77; 95% confidence interval [CI], 2.15 to 3.57). A further study also found that the condition was not correlated with the severity of diabetes mellitus, but found a lower prevalence of onychomycosis in persons with diabetes (7.8%) and the causative organism was more typically yeast rather than dermatophyte. Another survey found that peripheral vascular disease (OR = 1.78; 95% CI, 1.68 to 1.88) and immunosuppression (OR = 1.19; 95% CI, 1.01 to 1.40) increased the risk of infection. These factors may explain the general increase in prevalence of onychomycosis in the older population.

Environmental exposures such as occlusive footwear or warm, damp conditions and close living conditions have been cited as risk factors, as has trauma. Fungal skin infection has been proposed as a risk factor. However, one large observational study, which included 5,413 persons with positive mycology, found that only a small proportion (21.3%) had both skin and toenail infections.

Clinical Questions

What are the effects of oral treatments for fungal toenail infections in adults?

Beneficial	Itraconazole (more effective than placebo, but probably less effective than terbinafine)
	Terbinafine
Likely to be beneficial	Fluconazole (although benefits are modest, even after long-term treatment)

What are the effects of topical treatments for fungal toenail infections in adults?

Likely to be beneficial	Ciclopirox (although benefits are modest, even after long-term treatment)
Unknown effectiveness	Amorolfine
	Butenafine
	Fluconazole
	Ketoconazole
	Terbinafine
	Tioconazole

Prognosis

Onychomycosis does not have serious consequences in otherwise healthy persons. However, the Achilles project (involving 846 persons with fungal toenail infection) found that many have discomfort in walking (51%), pain (33%), or limitation of their work or other activities (13%). Gross distortion and dystrophy of the nail may cause trauma to the adjacent skin, and may lead to secondary bacterial infection. In immunocompromised persons, there is a risk that this infection will disseminate. Quality-of-life measures specific to onychomycosis have been developed. Studies using these indicators suggest that onychomycosis has negative physical and psychosocial effects.

EDITOR'S NOTE: Amorolfine is not available in the United States.

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