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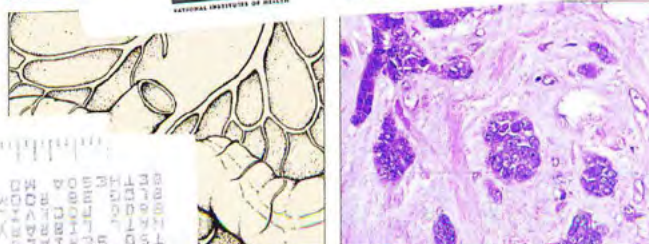
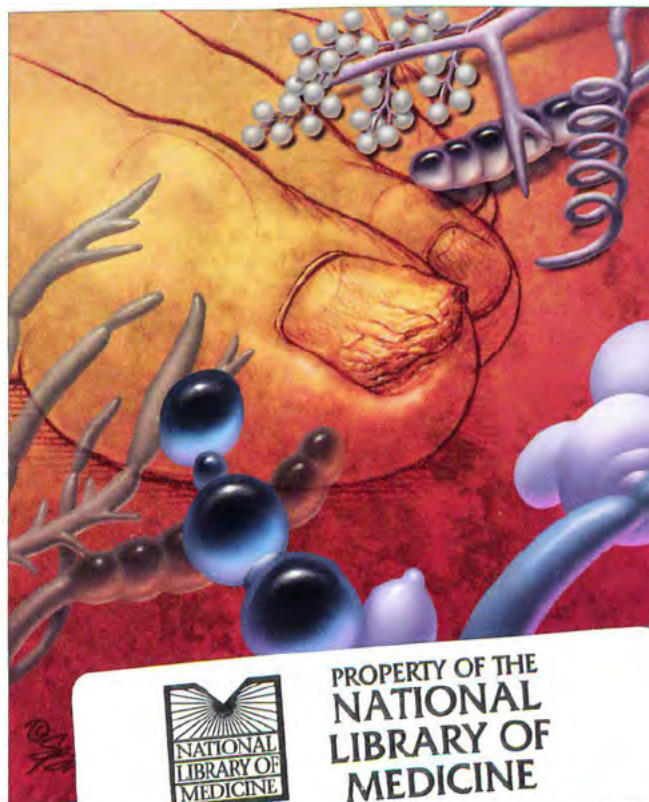
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# Advances in the diagnosis and treatment of onychomycosis

With a new pharmacologic armamentarium available, you can now cure many fungal infections of the fingernail and toenail.

**Richard K. Scher, MD, and Lisa Marie Coppa, MD**

**O**nychomycosis refers to a fungal infection of the nail unit—the nail matrix, bed, or plate. The incidence of onychomycosis is reported to be 2% to 14%,<sup>1</sup> but the actual incidence is probably much higher. Onychomycosis accounts for one-third of all fungal skin infections and one-half of all nail disease. It affects toes—usually the hallux—much more frequently than fingers.

Fungal infections of the nail are notoriously difficult to treat. Spontaneous remission is rare and recurrence after treatment is common. The incidence of onychomycosis is 30 times higher in adults than in children, afflicting 15% to 20% of adults aged 40 to 60 years and 25% to 40% of adults older than 60 years, but only up to 2.6% of children under the age of 18 years.<sup>2</sup> The disease occurs worldwide and its incidence has been steadily increasing. The following factors have contributed to its proliferation:<sup>3</sup>

- Growing elderly population
- Spread of HIV infection/AIDS
- Immunosuppressives and other drugs (eg, corticosteroids, antibiotics)
- Occlusive footwear
- Vigorous physical activity
- Communal bathing facilities



Illustration by Scott Bodell

*Dr Scher is Professor of Clinical Dermatology and Dr Coppa is a Dermatopharmacology Fellow, Department of Dermatology, Columbia University College of Physicians and Surgeons, New York, New York.*



Onychomycosis is more than just a cosmetic problem. The nail unit serves many different functions, including pincer grasp, scratching, enhancement of fine touch, and protection of the digit. Any disease of the nail unit can have a negative impact on quality of life and interfere with the activities of daily living. Thickened painful nails may limit mobility, affect peripheral circulation, delay healing, exacerbate diabetic foot ulcers, and serve as a fungal reservoir.<sup>3</sup>

### CAUSATIVE AGENTS

Onychomycosis is caused by dermatophytes, yeast, and nondermatophytic moulds. The incidence of each type of infection varies with geographic region. In temperate zones, the most common causative agents are dermatophytes, a group of closely related fungi that can invade keratinous tissue—skin, hair, nails, or fur. Therefore, dermatophytes are primary causative agents of onychomycosis. The three genera of dermatophytes are *Epidermophyton*, *Microsporum*, and *Trichophyton*.<sup>4</sup> *Trichophyton rubrum* accounts for 80% of all dermatophyte nail infections and 46% of all nail infections.<sup>5</sup>

The incidence of yeast-related onychomycosis ranges from 5.4% to 6.3%. Yeast is most likely to be a causative agent in tropical areas. *Candida albicans*, the most common isolate, has been cultured in 70% of cases of onychomycosis attributed to yeast. Candidal infections are more common in fingernails than toenails and in women than in men.<sup>6</sup> Yeast as a causative agent in onychomycosis is actually a controversial topic; some maintain that *Candida* is not a primary pathogen in healthy patients, whereas others assert that candidal infection is the primary process. Yeast are not keratinolytic and no mechanism for their primary

### KEY PRACTICE POINTS

Characteristic signs of distal subungual onychomycosis include nail bed hyperkeratosis, nail plate thickening, discoloration, and onycholysis.



In white superficial onychomycosis, the nail looks white and crumbly, in a speckled pattern, but the patches may eventually coalesce to involve the whole nail surface.



Before instituting oral antifungal therapy, make sure to confirm the diagnosis of onychomycosis via KOH, fungal culture, and any additional modalities that are necessary.

invasion into nails has been clearly established.<sup>6</sup> In one report, chronic paronychia and onycholysis (separation of the nail plate from the nail bed) were attributed to trauma or contact irritants; *Candida* only aggravated the problem. In some patients with immunodeficiency disorders and mucocutaneous candidiasis, *C. albicans* clearly is the primary offending pathogen.

Nondermatophytic moulds (eg, *Scopulariopsis brevicaulis*, *Aspergillus niger*) are typically found in subtropical and tropical climates. Like yeast, they are not keratolytic; instead, they invade nails that have suffered prior damage. The usual site is a single toenail.<sup>5</sup> Again, like yeast, even when grown on culture, nondermatophytic moulds are not always considered primary causative agents.<sup>6</sup>

### IMMUNOLOGY

Dermatophyte colonization, generally limited to the dead keratinized tissue of the stratum corneum, results in an inflammatory reaction of mild to severe intensity. Both humoral- and cell-mediated immunity and specific and nonspecific host defense mechanisms respond and eventually eliminate the fungus. Humoral immunity is responsible for producing antibodies, but it is the development of cell-mediated immunity that is associated with clinical cure and ridding the stratum corneum of the offending dermatophyte. Patients with recurrent or chronic onychomycosis have high antibody levels but impaired cell-mediated immunity.

### CLASSIFICATION

The four clinical types of fungal nail disease—each with its own host-parasite relationship—are distal subungual onychomycosis (DSO), white superficial onychomycosis (WSO), proximal subungual onychomycosis (PSO), and *Candida* onychomycosis.<sup>7</sup>

**Distal subungual onychomycosis.** DSO, the most common subtype, begins with fungal penetration into the hyponychium (the area just proximal to where the nail plate begins to separate from the nail bed) and the distal or lateral nail bed (Figure 1, p 13). Characteristic signs include nail bed hyperkeratosis, nail plate thickening, discoloration, and onycholysis. Other dermatologic findings usually accompany these signs. In a series of 2,000 patients with distolateral subungual onychomycosis (DLSO), 98% had asymptomatic microvesicles with little or no erythema on their soles,<sup>8</sup> suggesting that the infection was transmitted from the soles to the nails rather than vice versa. Transmission of DLSO may also occur in an autosomal dominant pattern within families.<sup>9</sup>



**White superficial onychomycosis.** In cases of WSO, the fungi directly invade the nail plate and may proceed to the nail bed and hyponychium (Figure 2, right). Initially, the nail looks white and crumbly, in a speckled pattern, but the patches may eventually coalesce to involve the whole nail surface. The most common causative agent is *Trichophyton mentagrophytes*.

**Proximal subungual onychomycosis.** PSO, the least common presentation of onychomycosis in healthy persons, affects fingernails and toenails in similar frequency. It is usually caused by *T. rubrum*.<sup>10</sup> The fungi invade the proximal nail fold and subsequently penetrate the newly formed nail plate. The distal portion of the nail remains normal until late in the course of the disease, when the entire nail plate is affected.<sup>11</sup> The proximal white subungual onychomycosis (PWSO) subtype affects immunocompromised persons. In a recent case series, 87.1% of patients with AIDS had PWSO.<sup>12</sup>

**Candida onychomycosis.** *Candida* causes three different patterns of infection: mucocutaneous candidiasis, *Candida* paronychia, and *Candida* onycholysis. In chronic mucocutaneous candidiasis, the yeast organism directly invades the nail plate, after which the proximal and lateral nail folds thicken increasingly until the nail becomes totally dystrophic.<sup>11</sup> *Candida* paronychia, characterized by swelling and erythema of the nail folds, usually occurs in persons who frequently immerse their hands in water, such as dishwashers.<sup>11</sup> The seal between the nail plate and nail fold is broken, allowing *Candida* to secondarily populate the area and retard the "re-sealing" of the nail unit.<sup>10</sup> In nails previously damaged by infection or trauma, *Candida* can act as a secondary pathogen causing onychomycosis.

*Candida* onycholysis may or may not be a distinct entity; the organism may be the cause of the onycholysis or it may colonize onycholytic nails secondarily.

#### MAKING THE DIAGNOSIS

First, cleanse the nails, using alcohol to eliminate bacterial contamination.

**Collecting a specimen.** For each type of onychomycosis, collect a specimen as follows: For DSO, clip the distal nail plate and use a curette to obtain debris from the nail bed at a site as proximal to the cuticle as possible, where the number of viable hyphae is greatest. Nail clippings or portions of the nail that have been

**Figure 1. Distal subungual onychomycosis**



DSO, the most common subtype of fungal nail disease, begins with fungal penetration into the hyponychium and the distal or lateral nail bed. Characteristic signs include nail bed hyperkeratosis, nail plate thickening, discoloration, and onycholysis.

**Figure 2. White superficial onychomycosis**



In WSO, the fungi directly invade the nail plate and may proceed directly to the nail bed and hyponychium. Initially the nail looks white and crumbly, in a speckled pattern, but the patches may eventually coalesce to involve the whole nail surface.

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