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ONYCHOMYCOSIS; A FUNGAL INFECTION OF NAIL CAUSED BY DERMATOPHYTES

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ABSTRACT
Onychomycosis is a fungal infection of the nail unit. When dermatophytes cause onychomycosis, this condition is called tinea unguium. The term onychomycosis encompasses the dermatophytes, yeasts, and saprophytic mold infections. An abnormal nail not caused by a fungal infection is a dystrophic nail. The dermatophyte *Trichophyton rubrum* is the major cause of tinea pedis and onychomycosis.

KEYWORDS: nail fungus, dermatophyte, tinea pedis.

OVERVIEW

Athlete's foot is a form of dermatophytosis (fungal infection of the skin), caused by dermatophytes, funguses (most of which are mold) which inhabit dead layers of skin and digest keratin. Dermatophytes are anthropophilic, meaning these parasitic funguses prefer human hosts. Athlete's foot is most commonly caused by the molds known as *Trichophyton rubrum* and *Trichophyton mentagrophytes*, but may also be caused by *Epidermophyton floccosum*. Most cases of athlete's foot in the general population are caused by *Trichophyton rubrum*; however, the majority of athlete's foot cases in athletes are caused by *Trichophyton mentagrophytes*.[1]

Figure 1: Athlete's Foot & Fungus SEM.

You paint it on your infected nails and surrounding skin once a day. After seven days, you wipe the piled-on layers clean with alcohol and begin fresh applications. Instead of medications or debridement, offers a laser therapy treatment with an 80% success rate at permanently treating nail fungus. It's painless and performed in-office with three 10-minute procedures every four weeks. For some patients, additional treatments may be required. Keep your nails trimmed. Cut nails straight across, smooth the edges with a file and file down thickened areas. Disinfect your nail clippers after each use. Letting your nails grow long creates more places for the fungus to grow. Nail fungus doesn't go away by itself. And if you don't treat it, there's a chance it could get worse and cause pain when you walk. It could also spread to other nails or through your body. Luckily, there are a number of ways to take care of it. You can spread the fungus to someone else through direct contact. You can also get toenail fungus by touching an infected surface. For diagnosis and testing, JDD recommends that: confirmatory laboratory testing should be performed using one or more of the following: microscopic examination (e.g., potassium hydroxide [KOH], periodic acid, Schiff test [PAS]), or fungal culture.[2]

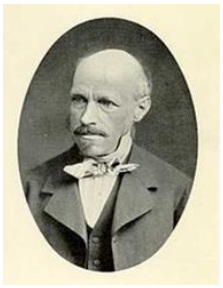

Figure 2: George Meissner [Inventor of Athlete's foot]

In 1853, onychomycosis was first described and reported by Meissner, a German medical student. George Meissner (19 November 1829 – 30 March 1905) was a German anatomist and physiologist born in Hanover. The history of onychomycosis is analogous to that of *Trychophyton rubrum*, the major causative fungal pathogen involved in the pathogenesis of onychomycosis and tinea pedis. Tiny, microscopic organisms called fungi (the plural of fungus) cause a fungal nail infection. Many people pick up the fungi when they have skin-to-skin contact with someone who has a fungal infection such as athlete's foot or ringworm on their hands. There are topical drugs that work to get rid of nail fungus.

Drugs: Terbinafine [CAS: 91161-71-6; IUPAC: [(2E)-6,6-dimethylhept-2-en-4-yn-1-yl](methyl)(naphthalen-1-ylmethyl)amine] has the highest effectiveness of any available therapy and should be recommended as first-line therapy for most patients without contraindications. Topical therapy can be used to treat patients with superficial onychomycosis or early distal lateral sublingual onychomycosis. Your health care provider may prescribe an antifungal nail polish called Ciclopirox (Penlac) [CAS: 29342-05-0; IUPAC: 6-cyclohexyl-1-hydroxy-4-methylpyridin-2(1H)-one].

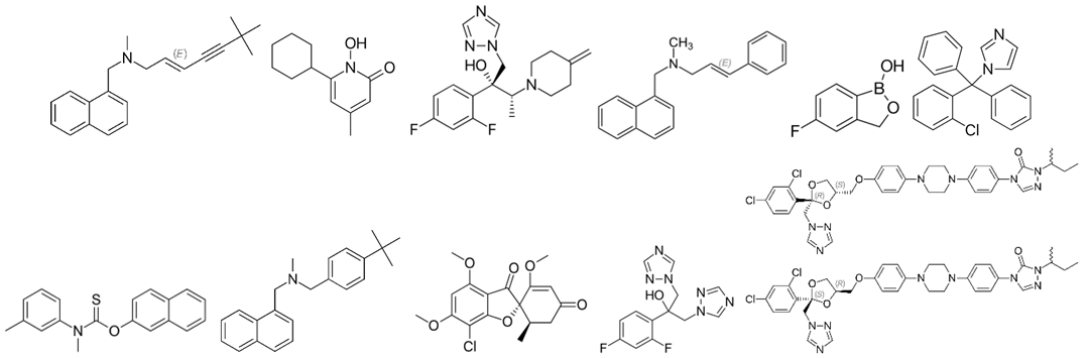

Figure 3: Antifungal Drugs.

Ciclopirox (Ciclodan, Penlac, Loprox)
Efinaconazole (Jublia) [CAS: 164650-44-6; IUPAC: (2R,3R)-2-(2,4-Difluorophenyl)-3-(4-methylene-1-piperidinyl)-1-(1H-1,2,4-triazol-1-yl)-2-butanol]
Naftifine (Naftin) [CAS: 65472-88-0; IUPAC: (2E)-N-methyl-N-(1-naphthylmethyl)-3-phenylprop-2-en-1-amine]
Tavaborole (Kerydin) [CAS: 174671-46-6; IUPAC: 5-Fluoro-2,1-benzoxaborol-1(3H)-ol]
Terbinafine (Lamisil)
Stop the stubborn cycle of toenail fungus with SteriShoe®

Figure 4: SteriShoe.

The innovative SteriShoe® kills the germs that reside inside shoes with a special germicidal, ultraviolet light. The treatment destroys up to 99.9% of the micro-organisms in shoes. Tinea pedis, commonly known as

athlete's foot, results from fungal infections on the skin of the feet caused by dermatophytes, including *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton interdigitale*, and *Epidermophyton floccosum*. Athlete's foot, known medically as tinea pedis, is a common skin infection of the feet caused by a fungus. Signs and symptoms often include itching, scaling, cracking and redness. In rare cases the skin may blister. Athlete's foot fungus may infect any part of the foot, but most often grows between the toes. The next most common area is the bottom of the foot. The same fungus may also affect the nails or the hands. It is a member of the group of diseases known as tinea.[3]

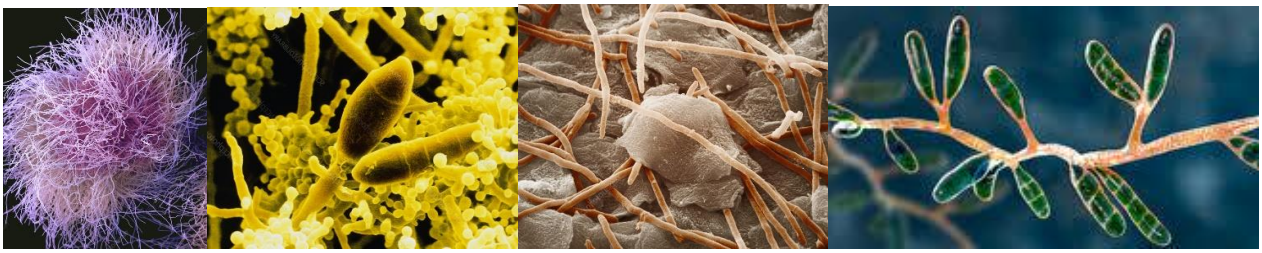

Figure 5: SEM of Fungus.

Wash your hands regularly to prevent an infection. Use a clean washcloth to help reach beneath your nails. Use antifungal or antimicrobial soaks to help prevent infection. Antimicrobial soaks may include lemon juice, vinegar, hydrogen peroxide and tea tree, orange or lemongrass essential oils. Athlete's foot is caused by a number of different funguses, including species of Trichophyton, Epidermophyton, and Microsporum. The condition is typically acquired by coming into contact with infected skin, or fungus in the environment. Common places where the funguses can survive are around swimming pools and in locker rooms. They may also be spread from other animals. Usually diagnosis is made based on signs and symptoms; however, it can be confirmed either by culture or seeing hyphae using a microscope.[4]

Athlete's foot is not limited to just athletes: it can be caused by going barefoot in public showers, letting toenails grow too long, wearing shoes that are too tight, or not changing socks daily. It can be treated with topical antifungal medications such as Clotrimazole [CAS: 23593-75-1; IUPAC: 1-[(2-Chlorophenyl)(diphenyl)methyl]-1H-imidazole] or, for persistent infections, using oral antifungal medications such as terbinafine. Topical creams are typically recommended to be used for four weeks. Keeping infected feet dry and wearing sandals also assists with treatment.

Athlete's foot was first medically described in 1908. Globally, athlete's foot affects about 15% of the population. Males are more often affected than females. It occurs most frequently in older children or younger adults. Historically it is believed to have been a rare condition that became more frequent in the 20th century due to the greater use of shoes, health clubs, war, and travel.[5]

Signs and symptoms

Athlete's foot: Athlete's foot is divided into four categories or presentations: chronic interdigital, plantar (chronic scaly; aka "moccasin foot"), acute ulcerative, and vesiculobullous. "Interdigital" means between the toes. "Plantar" here refers to the sole of the foot.

Figure 6: Moccasin Foot, Interdigital Foot and Plantar Foot.

The ulcerative condition includes macerated lesions with scaly borders. Maceration is the softening and breaking down of skin due to extensive exposure to moisture. A vesiculobullous disease is a type of mucocutaneous disease characterized by vesicles and bullae (blisters). Both vesicles and bullae are fluid-filled lesions, and they are distinguished by size (vesicles being less than 5 mm and bulla being larger than 5 mm, depending upon what definition is used).

Athlete's foot occurs most often between the toes (interdigital), with the space between the fourth and fifth

digits (the little toe and the fore toe) most commonly affected. Cases of interdigital athlete's foot caused by *Trichophyton rubrum* may be symptomless, it may itch, or the skin between the toes may appear red or ulcerative (scaly, flaky, with soft and white if skin has been kept wet), with or without itching. An acute ulcerative variant of interdigital athlete's foot caused by *Trichophyton mentagrophytes* is characterized by pain, maceration of the skin, erosions and fissuring of the skin, crusting, and an odor due to secondary bacterial infection. Plantar athlete's foot (moccasin foot) is also caused by *Trichophyton rubrum* which typically causes asymptomatic, slightly erythematous plaques (areas of redness of the skin) to form on the plantar surface (sole) of the foot that are often covered by fine, powdery hyperkeratotic scales. The vesiculobullous type of athlete's foot is less common and is usually caused by *Trichophyton mentagrophytes* and is characterized by a sudden outbreak of itchy blisters and vesicles on an erythematous base, usually appearing on the sole of the foot. This subtype of athlete's foot is often complicated by secondary bacterial infection by *Streptococcus pyogenes* or *Staphylococcus aureus*.[6]

Complications: As the disease progresses, the skin may crack, leading to bacterial skin infection and inflammation of the lymphatic vessels. If allowed to grow for too long, athlete's foot fungus may spread to infect the toenails, feeding on the keratin in them, a condition called onychomycosis. Because athlete's foot may itch, it may also elicit the scratch reflex, causing the host to scratch the infected area before they realize it. Scratching can further damage the skin and worsen the condition by allowing the fungus to more easily spread and thrive. The itching sensation associated with athlete's foot can be so severe that it may cause hosts to scratch vigorously enough to inflict excoriations (open wounds), which are susceptible to bacterial infection. Further scratching may remove scabs, inhibiting the healing process. Scratching infected areas may also spread the fungus to the fingers and under the fingernails. If not washed away soon enough, it can infect the fingers and fingernails, growing in the skin and in the nails (not just underneath). After scratching, it can be spread to wherever the person touches, including other parts of the body and to one's environment. Scratching also causes infected skin scales to fall off into one's environment, leading to further possible spread. When athlete's foot fungus or infested skin particles spread to one's environment (such as to clothes, shoes, bathroom, etc.) whether through scratching, falling, or rubbing off, not only can they infect other people, they can also reinfect (or further infect) the host they came from. For example, infected feet infest one's socks and shoes which further expose the feet to the fungus and its spores when worn again. The ease with which the fungus spreads to other areas of the body (on one's fingers) poses another complication. When the fungus is spread to other parts of the body, it can easily be spread back to the feet after the feet have been treated. And because the condition is called something else in each place it takes hold (e.g., *Tinea corporis* (ringworm) or *Tinea cruris* (jock itch)), persons infected may not be aware it is the same disease. Some individuals may experience an allergic response to the fungus called an id reaction in which blisters or vesicles can appear in areas such as the hands, chest, and arms. Treatment of the underlying infection typically results in the disappearance of the id reaction.[7]

Figure 7: Onychomycosis Medications.

Causes

Transmission: Athlete's foot is very contagious and can be spread through direct and indirect contact. The disease may spread to others directly when they touch the infection. People can contract the disease indirectly by coming into contact with contaminated items (clothes, towels, etc.) or surfaces (such as bathroom, shower, or locker room floors). The funguses that cause athlete's foot can easily spread to one's environment. Funguses rub off of fingers and bare feet, but also travel on the dead skin cells that continually fall off the body. Athlete's foot funguses and infected skin particles and flakes may spread to socks, shoes, clothes, to other people, pets (via petting), bed sheets, bathtubs, showers, sinks, counters, towels, rugs, floors, and carpets. When the fungus has spread to pets, it can subsequently spread to the hands and fingers of people who pet them. If a pet frequently gnaws upon itself, it might not be fleas it is reacting to, it may be the insatiable itch of tinea.[8] One way to contract athlete's foot is to get a fungal infection somewhere else on the body first. The funguses causing athlete's foot may spread from other areas of the body to the feet, usually by touching or scratching the affected area, thereby getting the fungus on the fingers, and then touching or scratching the feet. While the fungus remains the same, the name of the condition changes based on where on the body the infection is located. For example, the infection is known as tinea corporis ("ringworm") when the torso or limbs are affected or tinea cruris (jock itch or dhobi itch) when the groin is affected. Clothes (or shoes), body heat, and sweat can keep the skin warm and moist, just the environment the fungus needs to thrive.

Diagnosis: When visiting a doctor, the basic diagnosis procedure applies. This includes checking the patient's medical history and medical record for risk factors, a medical interview during which the doctor asks questions (such as about itching and scratching), and a physical examination. Athlete's foot can usually be diagnosed by visual inspection of the skin and by identifying less obvious symptoms such as itching of the affected area. If the diagnosis is uncertain, direct microscopy of a potassium hydroxide preparation of a skin scraping (known as a KOH test) can confirm the diagnosis of athlete's foot and help rule out other possible causes, such as candidiasis, pitted keratolysis, erythrasma, contact dermatitis, eczema, or psoriasis. Dermatophytes known to cause athlete's foot will demonstrate multiple septate branching hyphae on microscopy.

A Wood's lamp (black light), although useful in diagnosing fungal infections of the scalp (tinea capitis), is not usually helpful in diagnosing athlete's foot, since the common dermatophytes that cause this disease do not fluoresce under ultraviolet light.[9]

Prevention: There are several preventive foot hygiene measures that can prevent athlete's foot and reduce recurrence. Some of these include: keeping the feet dry; clipping toenails short; using a separate nail clipper for infected toenails; using socks made from well-ventilated cotton or synthetic moisture wicking materials (to soak moisture away from the skin to help keep it dry); avoiding tight-fitting footwear; changing socks frequently; and wearing sandals while walking through communal areas such as gym showers and locker rooms. According to the Centers for Disease Control and Prevention, "Nails should be clipped short and kept clean. Nails can house and spread the infection." Recurrence of athlete's foot can be prevented with the use of antifungal powder on the feet. The funguses (molds) that cause athlete's foot require warmth and moisture to survive and grow. There is an increased risk of infection with exposure to warm, moist environments (e.g., occlusive footwear—shoes or boots that enclose the feet) and in shared humid environments such as communal showers, shared pools, and treatment tubs. Chlorine bleach is a disinfectant and common household cleaner that kills mold. Cleaning surfaces with a chlorine bleach solution prevents the disease from spreading from subsequent contact. Cleaning bathtubs, showers, bathroom floors, sinks, and counters with bleach helps prevent the spread of the disease, including reinfection.

Keeping socks and shoes clean (using bleach in the wash) is one way to prevent funguses from taking hold and spreading. Avoiding the sharing of boots and shoes is another way to prevent transmission. Athlete's foot can be transmitted by sharing footwear with an infected person. Not sharing also applies to towels, because, though less common, funguses can be passed along on towels, especially damp ones.[10]

Treatment: Athlete's foot resolves without medication in 30 to 40% of cases. Topical antifungal medication consistently produces much higher rates of cure. Conventional treatment typically involves thoroughly washing the feet daily or twice daily, followed by the application of a topical medication. Because the outer

skin layers are damaged and susceptible to reinfection, topical treatment generally continues until all layers of the skin are replaced, about 2 to 6 weeks after symptoms disappear. Keeping feet dry and practicing good hygiene (as described in the above section on prevention) is crucial for killing the fungus and preventing reinfection. Treating the feet is not always enough. Once socks or shoes are infested with funguses, wearing them again can reinfect (or further infect) the feet. Socks can be effectively cleaned in the wash by adding bleach or by washing in water 60°C (140°F). To be effective, treatment includes all infected areas (such as toenails, hands, torso, etc.). Otherwise, the infection may continue to spread, including back to treated areas. For example, leaving fungal infection of the nail untreated may allow it to spread back to the rest of the foot, to become athlete's foot once again. Allylamines such as terbinafine are considered more efficacious than azoles for the treatment of athlete's foot. Severe or prolonged fungal skin infections may require treatment with oral antifungal medication.[11]

Topical treatments: There are many topical antifungal drugs useful in the treatment of athlete's foot including: Miconazole nitrate, Clotrimazole, Tolnaftate [CAS: 2398-96-1; IUPAC: O-2-Naphthyl methyl (3-methylphenyl)thiocarbamate] (a synthetic thiocarbamate), Terbinafine hydrochloride, Butenafine hydrochloride and Undecylenic acid. The fungal infection may be treated with topical antifungal agents, which can take the form of a spray, powder, cream, or gel. Topical application of an antifungal cream such as Butenafine [CAS: 101828-21-1; IUPAC: [(4-tert-butylphenyl)methyl](methyl)(naphthalen-1-ylmethyl) amine] once daily for one week or terbinafine once daily for two weeks is effective in most cases of athlete's foot and is more effective than application of miconazole or clotrimazole. Plantar-type athlete's foot is more resistant to topical treatments due to the presence of thickened hyperkeratotic skin on the sole of the foot. Keratolytic and humectant medications such as urea, salicylic acid (Whitfield's ointment), and lactic acid are useful adjunct medications and improve penetration of antifungal agents into the thickened skin. Topical glucocorticoids are sometimes prescribed to alleviate inflammation and itching associated with the infection. A solution of 1% potassium permanganate dissolved in hot water is an alternative to antifungal drugs. Potassium permanganate is a salt and a strong oxidizing agent.[12]

Oral treatments: For severe or refractory cases of athlete's foot oral Terbinafine is more effective than Griseofulvin [CAS: 126-07-8; IUPAC: (2S,6'R)-7-chloro-2',4,6-trimethoxy-6'-methyl-3H,4'H-spiro [1-benzofuran- 2,1'-cyclohex[2]ene]-3,4'-dione], Fluconazole [CAS: 86386-73-4; IUPAC: 2-(2,4-Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)propan-2-ol] or Itraconazole [CAS: 84625-61-6; IUPAC: (±)-1-[(RS)-sec-butyl]-4-[p-[4-[p-[[(2R,4S)-rel-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]phenyl]-Δ2-1,2,4-triazolin-5-one] may also be taken orally for severe athlete's foot infections. The most commonly reported adverse effect from these medications is gastrointestinal upset.

CONCLUSION

An infected nail may separate from the nail bed. Nail fungus is a common infection of the nail. It begins as a white or yellow-brown spot under the tip of your fingernail or toenail. As the fungal infection goes deeper, the nail may discolor, thicken and crumble at the edge. Oral antifungal drugs. These drugs are often the first choice. Medicated nail polish. Your health care provider may prescribe an antifungal nail polish called ciclopirox. Medicated nail cream. Terbinafine and itraconazole are the 2 medicines most commonly prescribed for fungal nail infections. These usually need to be taken once or twice a day for several months to ensure the infection has completely cleared up. If you stop taking the medication too early, the infection may return. There are multiple treatments for toenail fungus, though some are faster than others. The fastest way to eliminate the infection is through toenail laser treatment. Tiny, microscopic organisms called fungi (the plural of fungus) cause a fungal nail infection. Many people pick up the fungi when they have skin-to-skin contact with someone who has a fungal infection such as athlete's foot or ringworm on their hands. Usually three months of treatment cures a toenail fungal infection. Antifungal pills, however, can cause side effects. Your dermatologist will watch you closely. You'll also need to have blood tests every month to check for problems. To treat fungal nail infections from inside the body, you can take tablets that inhibit the growth of fungi or kill them. They are all prescription-only. Terbinafine and itraconazole are typically used for this purpose. Terbinafine is preferred if the nail fungus is caused by a skin fungus (dermatophyte). Ciclopirox topical solution is used along with regular nail trimming to treat fungal infections of the fingernails and toenails (an infection that may cause nail discoloration, splitting and pain). Ciclopirox is in a class of medications called antifungals. It works by stopping the growth of nail fungus.

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