

Tropical Fungal Infections

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- Antifungal therapy

Fungal infections in humans are more prevalent and diverse in the tropics and subtropics,¹ likely because warm and humid climates are more conducive for the growth and dissemination of fungi. Several of the dimorphic and geographically delimited fungi such as *Lacazia loboi* are found only in the tropical zone, but infections by these organisms may present anywhere in the world owing to the increasing frequency of human migration and travel.^{2,3} In global surveys of travel-related diseases, fungal infections are invariably among the most common causes of dermatologic disorders in returning travelers.⁴

One commonly used classification for fungal infections is based on the tissue that is initially colonized.^{1,5} Superficial mycoses are restricted to the outermost layer of the epidermis (stratum corneum) and do not cause any inflammation. Cutaneous mycoses involve the integumentary system, including nails and hair, and generally elicit inflammation of the skin. Subcutaneous mycoses describe infection of the deeper layers of tissue, with the fungi usually being directly implanted following minor trauma. Unlike the previously mentioned mycoses, these infections may invade beyond the initial colonized area, involving muscle, deep fascia, and even bone. The respiratory and gastrointestinal tracts are the main portals of entry for systemic mycoses, which can be further classified into primary and opportunistic mycoses based on whether the fungus in question is able to cause an infection in a normal host.⁵ Several fungi, such as *Sporothrix schenckii* and certain dematiaceous molds, are able to manifest as either subcutaneous or systemic mycoses depending on the portal of entry and the immune status of the human host.

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In this review, the authors briefly discuss superficial and subcutaneous mycoses that are far more prevalent or restricted to the tropics (**Fig. 1, Table 1**), as well as fungal infections in returning travelers. Systemic mycoses caused by dimorphic fungi have been extensively reviewed recently⁶⁻⁸ and are not further discussed except in the context of travel-related infections.

SUPERFICIAL AND CUTANEOUS MYCOSES

These very common mycoses affect up to 25% of the global population and occur predominantly in the tropics, although they have a worldwide distribution.⁹

The most common superficial mycoses are pityriasis versicolor, tinea nigra, and the piedras. Pityriasis versicolor is caused by various *Malassezia* spp and is characterized by the presence of asymptomatic (rarely, mild itch) fine hyperchromic or hypochromic macules on the torso, neck, and arms, occasionally extending to face, groin, and thighs.¹⁰ Major risk factors include warm and humid environments, corticosteroids, and tanning lotions. Young adults are more frequently affected, with no gender bias.¹⁰ Differential diagnoses include pityriasis alba and rosea, solar dermatitis, and postlesional melanodermas.^{10,11} Laboratory diagnosis is made by finding clusters of round budding yeast cells on microscopy of skin scrapings with 10% potassium hydroxide solution. Woods (ultraviolet) light is useful in the clinic setting, with macules emitting a characteristic yellow-green fluorescence.¹² Treatment comprises topical therapy (imidazoles, allylamines, ciclopirox olamine, 20% sodium hypochlorite, or 50% propylene glycol) for 2 to 4 weeks for limited/initial cases and systemic azoles for extensive/recurrent cases. Avoiding or removing risk factors is helpful in preventing relapse.^{10,12}

Tinea nigra presents as chronic, asymptomatic, irregular, scaly, hyperpigmented (tan, brown, or black) patches or spots on the palms, occasionally involving soles, arms, and torso. It is caused by the pigmented yeast *Hortaea werneckii*, occurring predominantly in children and young adults in coastal tropical regions, with the

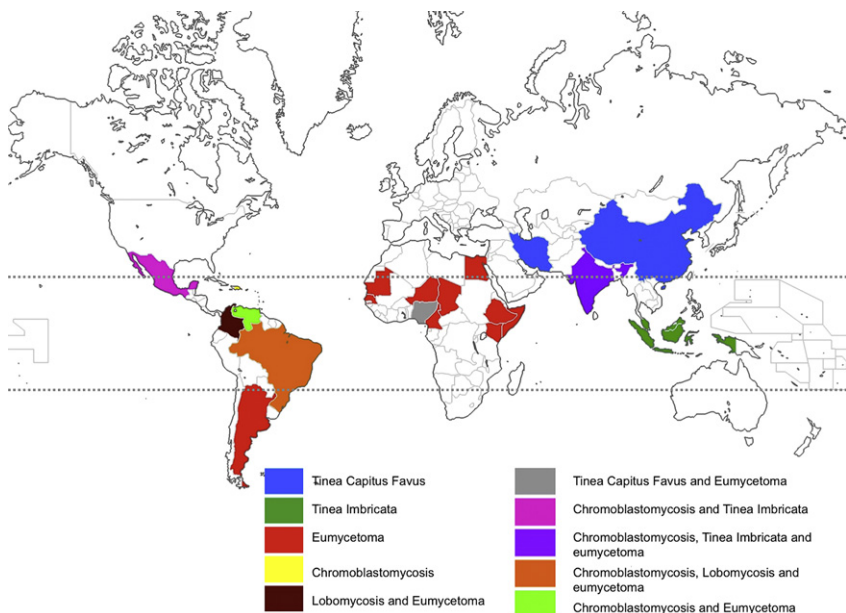


Fig. 1. Geographic distribution of major superficial, cutaneous, and subcutaneous mycoses.

most important predisposing factor being hyperhidrosis of hands and feet.^{12,13} Laboratory diagnosis is made by finding dark septate hyphae with clusters of blastoconidia on microscopy, whereas dermatoscopy in the clinic setting, showing hyperchromic fungal growth, may be helpful in differentiating this condition from nevi and melanoma.^{12,14} Control of hyperhidrosis is sufficient for treating tinea nigra, although keratolytics and topical antifungals may also be used.¹²

White and black piedra are caused by *Trichosporon* spp and *Piedraia hortae*, respectively, which are chronic asymptomatic infections of the hair shafts (scalp and, less commonly, beard, axilla, and pubic hair) in children and young adults. Predominant risk factors are humidity and poor personal hygiene. Soft white concretions or nodules are seen in white piedra, whereas black hard nodules are seen in black piedra. Laboratory diagnosis is made via observation of masses of septate hyphae and arthroconidia on microscopy of infected hair, and treatment is identical for both conditions, involving clipping of infected hair followed by application of topical antifungals or keratolytics, one effective option being 2% ketoconazole shampoo.¹²

Cutaneous mycoses and onychomycoses are predominantly caused by dermatophytes, with *Candida* spp being the most common nondermatophyte cause. Dermatophytosis is somewhat inappropriately named tinea (ie, ringworm in Latin) followed by the body part affected, whereas onychomycosis is another term for tinea unguium or fungal nail infection.¹ The major pathogenic dermatophyte genera are *Trichophyton*, *Microsporum*, and *Epidermophyton*, with different species being transmitted between humans (anthropophilic), from animals (zoophilic), or from soil (geophilic).^{1,5} Ameen¹⁵ has recently described the global epidemiology of the causative species, highlighting the changing epidemiology as a consequence of migration and socioeconomic conditions. In general, the clinical presentation is that of a circumscribed scaly and itchy rash, with interdigital erosive changes in tinea pedis and hair loss in tinea capitis. In tinea unguium, affected nail plates have a thickened, dirty, and granular appearance.^{1,5}

As with superficial mycoses, laboratory diagnosis is made via observation of fungal organisms in skin scrapings or hair on microscopy, mounted in 10% potassium hydroxide. Cultures are unnecessary for making a diagnosis. However, it is impossible to distinguish the various dermatophytes by microscopy alone, and cultures are therefore useful for epidemiologic trending.^{1,5} Therapy is site specific, with topical antifungals or Whitfield ointment (salicylic acid and benzoic acid in a suitable base) being successful in most cases of tinea corporis, cruris, or pedis, whereas oral antifungals remain the mainstay of therapy for tinea capitis and onychomycosis as well as extensive tinea corporis and tinea pedis.^{1,16} A couple of the more unusual tropical dermatophytoses are briefly described.

Tinea capitis favosa or favus is a specific chronic scalp dermatophytosis caused almost primarily by *Trichophyton schoenleinii*, although cases have rarely been attributed to other dermatophytes.^{1,17} The fungus, and therefore the disease, is currently geographically restricted to Iran, some parts of Africa, and China, although sporadic cases are seen in various parts of the world.¹⁷ The prevalence of favus is higher in boys and in children aged between 6 and 10 years, and few individuals are infected after puberty. The disease has 3 stages of severity, with the classic lesion being that of a cup-shaped yellow crust on the scalp termed the scutulum.¹⁷ The fungus can be seen on microscopy of affected hair, but culturing on Sabouraud agar is required for definite identification of *T schoenleinii*. Treatment is identical to that of tinea capitis; *T schoenleinii* remains susceptible to griseofulvin unlike other dermatophytes for which resistance may be increasing.^{1,16,17}

Tinea imbricata or Tokelau is caused by the strict anthropophilic dermatophyte *Trichophyton concentricum* and is restricted to Polynesian and Melanesian archipelagoes

Table 1
Cutaneous and subcutaneous mycoses that are more prevalent in the tropics

Mycoses	Pathogens	Distribution	Diagnosis	Therapy
Superficial mycoses				
Pityriasis versicolor	<i>Malassezia</i> spp	Global (more common in the tropics)	<ul style="list-style-type: none"> • Woods light (clinic) • Microscopy of skin scrapings 	Topical antifungals, systemic antifungals for severe/ recurrent cases
Tinea nigra	<i>Hortaea werneckii</i>	Tropical coastal regions	<ul style="list-style-type: none"> • Dermatoscopy (clinic) • Microscopy of skin scrapings 	Control of hyperhidrosis; rarely, keratolytics or topical antifungals
White piedra	<i>Trichosporon</i> spp	Global (more common in the tropics)	Microscopy of infected hair	Removal of infected hair, then topical antifungals or keratolytics
Black piedra	<i>Piedraia hortae</i>	Global (more common in the tropics)	Microscopy of infected hair	Removal of infected hair, then topical antifungals or keratolytics
Cutaneous mycoses				
Dermatophytosis (including favus and tinea imbricata)	<i>Trichophyton</i> spp, <i>Microsporon</i> spp, <i>Epidermophyton</i> spp	Global (more common in the tropics); <i>Trichophyton schoenleinii</i> virtually restricted to Iran, Africa, and China; <i>Trichophyton concentricum</i> restricted to Polynesian and Melanesian archipelagos and Central and South America	<ul style="list-style-type: none"> • Clinical presentation • Microscopy of skin scraping 	Site specific with topical antifungals or Whitfield ointment; oral antifungals for extensive disease <ul style="list-style-type: none"> • Favus: griseofulvin • Tinea imbricata: griseofulvin or terbinafine

Subcutaneous mycoses				
Chromoblastomycosis	Dematiaceous molds, especially <i>Fonsecaea</i> spp, <i>Cladophialophora</i> spp, and <i>Phialophora</i> spp	Global (most common in India, Thailand, Madagascar, Amazonian regions, Dominican Republic)	<ul style="list-style-type: none"> • Microscopy of skin scrapings • Fungal cultures (slow growth) • Serology and PCR, experimental 	<ul style="list-style-type: none"> • Small lesions: surgical excision or liquid nitrogen, thermotherapy • Extensive lesions: itraconazole, terbinafine, newer azoles
Eumycetoma	Various fungal species (most commonly <i>Madurella mycetomatis</i> and <i>Scedosporium apiospermum</i>)	Global (more common in India and Africa)	<ul style="list-style-type: none"> • Clinical presentation • Ultrasonography or magnetic resonance imaging appearance • Fine-needle aspiration cytology (early lesions) • Deep surgical biopsy 	<ul style="list-style-type: none"> • Surgical excision • Systemic antifungals (itraconazole or terbinafine) • Newer azoles may be useful for recurrent disease
Lobomycosis	<i>L. loboi</i>	Amazon rainforest	<ul style="list-style-type: none"> • Microscopy of tissue samples 	<ul style="list-style-type: none"> • Surgical excision • Cryosurgery for isolated lesions • Clofazimine
Sporotrichosis	<i>S. schenckii</i> complex	Global (more common in tropical and subtropical regions)	<ul style="list-style-type: none"> • Tissue culture • ELISA (limited use) • PCR, experimental 	<ul style="list-style-type: none"> • Itraconazole (terbinafine and potassium iodide for nonresponders)

Abbreviations: ELISA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction.

of South Pacific, Southeast Asia, and Central and South America, areas with high humidity. Susceptibility to the disease is inherited in either an autosomal recessive manner or an autosomal dominant manner with incomplete penetrance, with the disease most often beginning in childhood. The clinical appearance is characteristic, comprising thick, concentric, scaly plaques covering the skin surface; palms, hair-bearing areas, and nails are rarely affected. Diagnosis is based on clinical appearance, confirmed by direct microscopic examination of skin scrapings showing thin branching filaments with few arthroconidia. However, culturing in Sabouraud media or polymerase chain reaction (PCR) testing is necessary for identifying the fungus. Treatment is with oral griseofulvin or terbinafine, with azoles generally demonstrating poorer response. Nonetheless, recurrence rates are high no matter what agent is prescribed.¹⁸

SUBCUTANEOUS MYCOSES

There are several distinct clinical syndromes in the mycoses of implantation, some of which may be caused by a variety of different fungi. Because subcutaneous zygomycosis and phaeohyphomycosis are found worldwide, with no significant increased prevalence in the tropics, they are not discussed further.

Chromoblastomycosis

Chromoblastomycosis is a term encompassing a group of chronic subcutaneous mycoses caused by specific species of dematiaceous molds, mainly those belonging to the genera *Fonsecaea*, *Cladophialophora*, and *Phialophora*. Although these fungi are present worldwide, chromoblastomycosis is more common in parts of India, Thailand, Madagascar, Amazonian Latin America (particularly Brazil), and the Dominican Republic.^{19–22} The most commonly implicated fungus is *Fonsecaea pedrosoi* in Amazonian and temperate regions of Latin America, whereas *Cladophialophora carrionii* is commonly found in drier climates, including the subtropical parts of India and Thailand.^{20–22}

Unlike other subcutaneous infections caused by dematiaceous molds, the lesions of chromoblastomycosis are unique in having thick-walled hyperpigmented multicellular structures called muriform cells or sclerotic bodies.^{21,23} Certain dematiaceous molds such as *Exophiala jeanselmei* may separately cause chromoblastomycosis, eumycetoma, and subcutaneous phaeohyphomycosis,²³ but it remains unclear at present whether it is host or pathogen-associated factors that result in the type of subcutaneous mycosis manifested.

Because the fungi are inoculated via puncture wounds, those infected tend to be rural workers, belong to the lower socioeconomic classes, and are barefoot, with the distal limbs being most commonly affected.^{19–23} Men are more commonly affected in Latin America and parts of Asia, whereas women are predominantly affected in southern Africa, and children younger than 15 years are rarely affected.²⁴ Disease progression is very slow and may be asymptomatic at the start, appearing as small skin-colored papules that insidiously enlarge to form verrucose warty growth complexes.²¹ More rapid growth of lesions, albeit still in term of months, has been described.²² Satellite lesions may develop as a result of autoinoculation or lymphatic dissemination, and complications include secondary bacterial infection and lymphedema; keloidal scarring; and, rarely, neoplastic transformation to squamous cell carcinoma. Disease extension to underlying muscle or bone is rare unless there is concomitant immunosuppression.²⁵

The diagnosis is readily confirmed by direct microscopy (in 10% potassium hydroxide) of skin scrapings taken from characteristic black dots present on the

lesions, showing the typical muriform cells. Fungal cultures are slow because the organisms generally take weeks to grow.^{21,25} Serologic and PCR tests are available but are used almost exclusively for research purposes at present.

Treatment of chromoblastomycosis is difficult, complicated by the lack of comparative trials and variable rates of treatment failure, ranging up to 85% in line with the extent of disease.²⁵ Surgical excision or cryosurgery with liquid nitrogen should be limited to small lesions, with wide surgical margins, as remnant infecting fungus may spread within the scar tissue.^{26,27} Thermotherapy using devices such as benzene pocket warmers, either as monotherapy or in combination with antifungals, has been successfully but not systematically assayed in Japan.^{26,28} The mainstay of therapy remains high-dose, long-term (minimum 6–12 months) oral antifungals. Itraconazole, terbinafine, and 5-flucytosine in combination have been variously prescribed in the past.^{25,26} The new azoles, particularly posaconazole, show great promise for the treatment of extensive and/or refractory chromoblastomycosis²⁹ but are highly expensive.

Eumycetoma

Eumycetoma is a chronic, granulomatous, suppurative fungal infection of the subcutaneous and deeper tissues, usually of the foot and lower limbs (**Fig. 2**). English physicians first described the condition in Madura, India, in 1842, giving rise to the term Madura foot or maduromycosis.³⁰ It has a wider distribution than chromoblastomycosis, being endemic in equatorial Africa, India, Mexico, and the Middle East, although sporadic cases have been described from most tropical and temperate countries.^{21,23,31} A diverse and large group of fungi cause eumycetomas, with the most common being *Madurella mycetomatis* (black grain eumycetomas in India and Africa), *Magnaporthe grisea*, *Acremonium* spp, and *Scedosporium apiospermum* (white grain eumycetomas in temperate countries, including the United States).^{21,31} The predisposing factors are virtually identical to that of chromoblastomycosis.

As with chromoblastomycosis and other subcutaneous mycoses, the fungi are introduced via penetrating trauma and present initially as an asymptomatic subcutaneous mass that gradually progresses, forming multiple sinuses that drain out pus and aggregated fungi (grains).^{21,23,31} These aggregated fungi are also known as sclerotia and are a multicellular version of the muriform cells in chromoblastomycosis. They vary in color depending on the fungus and are also found within the lesions in granulomata that are formed as a result of the host neutrophilic inflammatory response.³¹ Unlike chromoblastomycosis, the infection frequently involves the muscle and bone if left untreated, although tendons and nerves are spared until the disease is advanced.²³ Enlarged regional lymph nodes are also unusual in this disease.

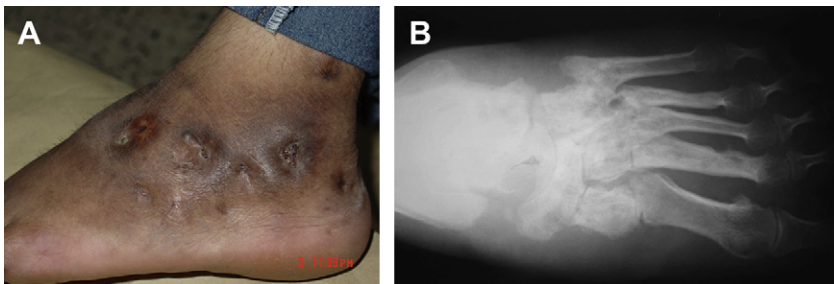


Fig. 2. Eumycetoma. (A) Multiple chronic sinuses and skin hyperpigmentation from an underlying eumycetoma. (B) Underlying osteomyelitis from eumycetoma.

Diagnosis is traditionally dependent on clinical presentation; the classical triad of subcutaneous mass, sinuses, and fungal grains; and laboratory identification of the infecting fungus, the laboratory identification being vital for treatment success.^{31,32} During the early stages, eumycetomas are difficult to distinguish clinically from chromoblastomycosis. Subsequently, other clinical differentials include chronic osteomyelitis, actinomycosis (which forms identical mycetomas), botryomycosis, tuberculosis, and certain skin tumors.^{21,23,30,31} Ultrasonography is a noninvasive technique of differentiating the possible diagnoses; fungal grains produce sharp hyperreflective echoes, and numerous thick-walled cavities without acoustic enhancement are seen.³² Actinomycetomas appear similar, but the smaller and less consistent grains are less distinct.³² Magnetic resonance imaging shows promise as a useful diagnostic adjunct for those patients who can afford it and is helpful for planning surgery; fungal grains appear as minute hypointense foci within the hyperintense signals given off by the surrounding granulomata (dots-in-circles).^{31,33,34} Fine-needle aspiration cytology is useful even in early disease and can distinguish between eumycetomas and actinomycetomas.³⁵ It is cheap, rapid, and well tolerated. However, deep surgical biopsies tend to have better yield in terms of fungal cultures because these avoid picking up surface bacterial contamination that may interfere with the slower growth of the fungi. Molecular methods of fungal identification show future promise but are currently research based only.³⁶

Aggressive surgical excision combined with systemic antifungals is the mainstay of therapy for eumycetoma, with limb amputation for advanced cases.^{21,31-33} As with chromoblastomycosis, treatment success is very much dependent on extent and duration of disease, with local and regional lymph node recurrences being frequent.^{21,31} Itraconazole and terbinafine are the current drugs of choice for eumycetoma, with the more expensive voriconazole and posaconazole as alternative options.³¹ Criteria for cure include complete clinical and radiologic (ultrasound absence of hyperreflective echoes and cavities) resolution of the lesions as well as repeating negative serology tests if this has been performed.^{21,37,38} Treatment recommendations are based on case series and noncomparative studies because there has been no randomized controlled trial to date.

Lobomycosis

First described in 1930 by Brazilian dermatologist Jorge Lobo,³⁹ lobomycosis or laceriosis is an uncommon chronic subcutaneous mycosis caused by *L. loboi*.⁴⁰ Human disease is geographically restricted to natives of and travelers to the Amazon rainforest in South America, although sporadic cases have been reported from Mexico, Central America, the United States, and France.²¹ Besides humans, bottlenose dolphins are the only other known animals that are infected in the wild.⁴¹ The incubation period is long, ranging from several months to years, as is evidenced by individuals developing the disease years after their visits to endemic regions.⁴² The disease is more common in young men aged between 21 and 40 years who work in the forest.⁴³ The natural reservoir of the fungus is unknown but is presumed to be in the rural environment in view of disease distribution.^{21,43}

The most common clinical presentation is that of chronic keloidal lesions in exposed skin, with occasional regional lymph node involvement but no systemic involvement.⁴³ The most frequently affected area is the pinna of the ear (**Fig. 3**), followed by the limbs, with new lesions arising locally or via lymphatic dissemination.^{21,43} Infiltrative, gummatous, macular, and/or disseminated lesions may also present occasionally, representing the other end of the clinical spectrum.⁴³ Patients are generally well, with no symptoms other than pruritus and possible restriction of movements at affected sites,



Fig. 3. Lobomycosis of the pinna.

except when rare complications such as secondary bacterial infection or carcinomatous change develop.⁴³ Clinical differential diagnoses include keloids, xanthomas, and dermatofibrosarcoma protuberans.²¹

Diagnosis is confirmed via direct microscopy of tissue samples in 10% potassium hydroxide, showing abundant chains of round hyaline cells with thick and birefringent cell walls.^{21,43} There has been no successful attempts at culturing *L. loboi* in vitro. Serologic testing is complicated by cross-reactions with *Paracoccidioides brasiliensis*, which shares similar geographic endemicity.⁴⁴

Wide surgical excision of the affected area remains the treatment of choice.^{21,43} As with other subcutaneous mycoses, relapses are common in extensive disease. Cryosurgery and electrodissection are options for isolated lesions.^{21,43} Experience with medical therapy is limited, with success reported for clofazimine (for at least 2 years) and mixed results for itraconazole.^{21,43,45,46}

Sporotrichosis

The *S. schenckii* complex, the rapidly growing group of related dimorphic fungi causing sporotrichosis, has a worldwide distribution, although the disease is primarily reported from tropical and warmer temperate regions.^{47,48} Unlike other subcutaneous mycoses, large clusters of cases and outbreaks have occurred with regard to sporotrichosis, generally caused by contact with the same contaminated environmental source, that is, wooden pit props in the South Africa Rand gold mines outbreak, sphagnum moss, and even cats, among others.⁴⁹

Most cases of sporotrichosis involve the subcutaneous and cutaneous tissues, with osteoarticular, pulmonary, and meningeal disease occurring rarely and disseminated infection occurring mainly in the setting of immunosuppression.^{21,50} Subcutaneous infections are subdivided into 2 categories: fixed cutaneous and lymphocutaneous diseases.⁵¹ The former is less common, with infection confined entirely to the site of inoculation, presenting as a scaly, verrucous, or ulcerative nodule.⁵¹ The latter results from lymphatic spread of infection, with an initial subcutaneous nodule at the site of inoculation that may ulcerate to form a nontender sporotrichotic chancre. Satellite lesions appear along a lymphatic chain, followed by lymphadenopathy (Fig. 4).^{21,51,52} The major clinical differentials are leishmaniasis, nontuberculous mycobacterial (especially *Mycobacterium marinum*) infections, nocardiosis, and tuberculoid Hansen disease.^{21,53} Spontaneous healing seldom occurs.



Fig. 4. Sporotrichotic chancre with satellite nodules.

Unlike other subcutaneous mycoses, microscopy of tissue biopsy specimens is not sensitive, although, rarely, finding extracellular asteroid bodies of eosinophilic spicules surrounding a central yeast is diagnostic.^{21,54} More commonly, a nonspecific granulomatous reaction with pseudoepitheliomatous hyperplasia is seen.^{21,54} The gold standard for making a diagnosis is tissue culture, with *S schenckii* grown in mycelial phase at 25°C and converted to yeast form at 37°C.⁵⁵ In most cases, the organism grows within 8 days after initiating cultures.⁵⁰ A recent enzyme-linked immunosorbent assay test directed toward detecting antibodies to SsCBF, a cell wall antigen of *S schenckii*, was developed in Brazil and demonstrated fairly high sensitivity and specificity⁵⁶ but has seen limited use to date, whereas older serologic tests have not been commercialized. Similarly, molecular (PCR based) techniques are research based at present but seem to be promising for rapid diagnosis in the future.⁵⁷

Consensus guidelines for the treatment of sporotrichosis were published 4 years ago by the Infectious Diseases Society of America.⁵⁰ For cutaneous and lymphocutaneous sporotrichosis, the recommended first-line agent was itraconazole to be given for up to 3 to 6 months, with terbinafine and saturated solution of potassium iodide considered for nonresponders. Fluconazole and local hyperthermia were reserved for patients who could not be safely prescribed the previous antifungals. Amphotericin B was not recommended because of toxicity and inconvenience of administration and also because these were non-life-threatening infections.⁵⁰ A recently published open-label study showed that terbinafine at a lower dose (250 mg daily) had equivalent outcomes compared with oral itraconazole for cutaneous sporotrichosis.⁵⁸ In contrast to other subcutaneous mycoses, treatment outcomes are generally excellent for cutaneous and lymphocutaneous sporotrichosis, and surgery is usually unnecessary. The fungi are susceptible to the newer azoles *in vitro*, but there have been no clinical studies to date.⁵⁰

FUNGAL INFECTIONS IN RETURNING TRAVELERS

Travelers, particularly those to the tropics, are at risk for a wide range of infectious diseases. Except for superficial and cutaneous mycoses, however, other forms of fungal infections are rare. Dermatophytosis accounts for 4% of all dermatologic conditions in travelers,^{59–61} but there are surveillance limitations because individuals who do not view their symptoms as significant may not seek medical advice.

Systemic and endemic mycoses have been reported in areas of nonendemicity because travelers are involved in a range of activities that increase their risks for acquiring such infections. Most infections manifest soon after travel, although delayed presentations are seen among migrants and long stayers from endemic regions. Histoplasmosis is the most commonly reported endemic mycosis affecting travelers, followed by coccidioidomycosis and scattered cases of paracoccidioidomycosis, blastomycosis, and cryptococcosis.

Histoplasmosis in travelers can be difficult to diagnose, presenting most frequently as a self-limiting illness of fever, dry cough, and headache in immunocompetent individuals. Severe pulmonary symptoms can occur in high-inoculum exposure, and immunocompromised individuals may present with disseminated disease. Clusters and outbreaks have been reported among groups that have gone spelunking in Costa Rica, Ecuador, and Peru.^{62–69} Immigrants or expatriates from endemic countries tend to present with disease reactivation, often associated with immunosuppressive conditions such as human immunodeficiency virus (HIV) infection.^{70,71} The number of reported cases of histoplasmosis in travelers is likely an underestimate because of the self-limiting nature of acute pulmonary histoplasmosis. Case clusters highlight the lack of awareness of risks of this disease among more adventurous travelers. Potential spelunkers and cave explorers should be informed about the risks of acquiring histoplasmosis, with the use of face/surgical masks during cave exploration being the most important preventive strategy.⁶ Immigrants with HIV infection and undifferentiated fever from endemic countries should be investigated for histoplasmosis.

Coccidioidomycosis is caused by inhalation of the fungi in areas where it is endemic.⁶ Around 40% of those infected develop symptomatic illness, the most common of which is a nondescript flulike illness. Immunocompromised individuals such as those with HIV infection or who are on immunosuppressive drugs are at risk of disseminated disease, whereas African Americans, pregnant women, and diabetic patients may develop severe pulmonary disease.⁷² Outbreaks of coccidioidomycosis have been reported in travelers who have returned from endemic areas.^{73,74} Sporadic cases have been reported in travelers from Japan, Australia, and India,^{75,76} whereas some Indian nationals who had previously resided in endemic parts of Arizona have also been diagnosed with the disease.^{77,78} Common risk factors were activities related to construction or working in a dusty environment in endemic areas. During the Model Airplane Flying World Championship in Lost Hills, California, in 2001, several participants from various parts of the world, including Australia, United Kingdom, and Finland, developed coccidioidomycosis.⁷⁹

Penicillium marneffe is endemic in Southeast Asia, with most cases being reported from northern Thailand.⁸⁰ Global travel and migration have resulted in cases of penicilliosis exported from these countries among individuals with HIV infection.^{81–84} Antinori and coworkers⁸² reviewed 36 cases of penicilliosis reported outside endemic regions from 1998 to 2004. These were mainly in travelers to and from endemic regions such as Thailand and Myanmar. There were few cases with no links to an endemic region, an African patient who had spent 4 months in a microbiology laboratory in Paris, and an HIV-infected Ghanaian who was diagnosed in Germany.⁸⁴

Paracoccidioidomycosis is endemic in South America, in rural areas surrounding the Amazon River. As with the other endemic mycoses, infections have been reported in Netherlands, Austria, Spain, and Germany, primarily in individuals who are either migrants from South America or who have resided in an endemic area for a prolonged period.^{71,85–87}

Cryptococcal infections are rarely seen in travelers. However, sporadic cases of *Cryptococcus gattii* have been reported from travel to Vancouver Island in Canada, where the fungus is now considered endemic following an outbreak since 1999.^{88–90} Blastomycosis is also rare in travelers; imported cases with pulmonary or cutaneous disease have been described, however.^{91,92}

SUMMARY

The spectrum of fungal infections is greater in the tropics, as is the burden of disease. For many conditions, especially the subcutaneous mycoses, the best treatment strategies remain unclear because of the lack of proper therapeutic trials. The export of tropical fungal infections via travelers and migrants is increasingly prevalent as international travel becomes easier. Travelers and physicians need to be aware of the risk factors for infection, and the prolonged latency of illness in conditions such as paracoccidioidomycosis highlights the need for detailed travel history. Enhanced surveillance for fungal infections can lead to early diagnosis and an understanding of the epidemiology of the fungal infections among travelers.

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