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Review Article

Mycoses of implantation in Latin America: an overview of epidemiology, clinical manifestations, diagnosis and treatment

FLAVIO QUEIROZ-TELLES*, MARCIO NUCCI†, ARNALDO LOPES COLOMBO‡, ANGELA TOBÓN§ & ANGELA RESTREPO§

**Division of Infectious Diseases, Department of Public Health, Hospital de Clinicas, Universidade Federal do Paraná, Curitiba, Brazil, †University Hospital, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, ‡Division of Infectious Diseases, Department of Medicine, São Paulo, Brazil, and §Corporación para Investigaciones Biológicas, Medellín, Colombia*

Implantation or subcutaneous mycoses are a frequent health problem in Latin American countries and other tropical and subtropical areas. Although such infections rarely cause disseminated or invasive disease, they have an important impact on public health, and timely diagnosis and appropriate treatment remain important. Although some implantation mycoses are found in immunocompromised persons, the immunocompetent population is the principal target in Latin America. Most etiologic agents are found in soil, vegetation, and decaying matter in tropical, subtropical, and humid environments and infection is commonly the result of penetrating injury. Infections primarily occur (1) among low socioeconomic groups, (2) among those living in rural areas or involved in farming, hunting, or other outdoor activities, and (3) particularly among adult men. This review focuses on the epidemiology of the most clinically significant implantation mycoses in Latin America, i.e., sporotrichosis, eumycetoma, chromoblastomycosis, subcutaneous phaeohyphomycosis, subcutaneous zygomycosis, and lacaziosis. Main epidemiologic findings, clinical manifestations, diagnosis, and treatment options are also discussed.

Keywords subcutaneous mycoses, endemic mycoses, posaconazole, itraconazole

Introduction

Implantation mycoses include a heterogeneous group of fungal diseases that develop at the site of transcutaneous trauma. They are also known as 'subcutaneous mycoses', but some of them (sporotrichosis and mycetoma) may also involve muscles, fascia, cartilage and bones, beyond the skin and the subcutaneous tissues. These infections are a frequent health problem in Latin American countries and other tropical and subtropical areas [1]. Although such infections rarely cause disseminated or invasive disease, they have an important impact on public health, may be difficult to control, and often recur [2,3]. The objective of this paper was to review the epidemiology of the most clinically significant implantation mycoses in Latin America, i.e., sporotrichosis, eumycetoma, chromoblastomycosis, subcutaneous phaeohyphomycosis, subcutaneous zygomycosis, and lacaziosis. An overview of these implantation mycoses with respect to the populations typically affected, main clinical manifestations, and suggestions for diagnosis and treatment is presented in Table 1. Data particularly supporting the potential use of some newer antifungal agents in the treatment of some of these infections are presented in Table 2.

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Correspondence: Flavio Queiroz-Telles, Infectious Diseases Unit, Hospital de Clinicas, Universidade Federal do Paraná, Rua General Carneiro, 181, Curitiba, PR, Brazil, 80060-90. Tel: +55 41 3360 1809; fax: +55 41 3363 6090; E-mail: Queiroz.telles@uol.com.br

Sporotrichosis

Sporotrichosis is caused by *Sporothrix schenckii*, a thermally dimorphic fungus that grows optimally in the presence of

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Table 1 Subcutaneous mycoses prevalent in Latin America.

Disease	Population typically affected	Main clinical manifestations	Suggestions for diagnosis	Treatment
Sporotrichosis	*Lymphocutaneous:* immunocompetent persons engaged in agriculture, gardening, mining, or other outdoor activities; zoonotic spread from infected domestic cats or scratches from digging animals such as armadillos; variable sex and age distribution *Disseminated (cutaneous or extra-cutaneous):* persons with history of alcohol abuse, chronic steroid therapy, AIDS [7,89]	*Lymphocutaneous:* chronic subcutaneous nodular lesion arising at site of minor skin trauma and spreading proximally along lymphatic channels *Fixed cutaneous or disseminated:* less common; occasional hematogenous dissemination to lungs, central nervous system, or genitourinary tract [29]	*Culture:* intradermal sporotrichin skin test (in endemic areas); tube and latex particle agglutination (not widely available) [8,29,89]; Montenegro skin test to distinguish from cutaneous leishmaniasis [90] *Histopathology:* yeast cells and asteroid bodies are depicted in one-third of cases	*Lymphocutaneous:* itraconazole 200 mg/d po for 2–4 wk after lesions resolve, usually for total of 3–6 mo *Nonresponders:* itraconazole 200 mg po bid, terbinafine 500 mg po bid, SSKI 40-50 drops tid, fluconazole 400-800 mg/d po (only in patients who cannot tolerate other agents) *Options for other clinical presentations:* terbinafine, amphotericin B [89,91,93]
Eumycetoma	Men aged 20–40 who work as herders, farmers, or other field laborers [26]; increasingly in travelers to tropical endemic areas [3]	Local chronic, progressive, multifistulous, suppurative, tumoral lesions discharging grains. Infection involves cutaneous and subcutaneous tissues, fascia, and eventually muscle and bone [29]	Observation of grain color and texture; deep surgical biopsies containing grains that can be cultured or fixed for histopathology; immunodiffusion, ELISA, PCR with DNA sequencing; MRI or CT to determine bone involvement [2,3,26,46,93]	Surgery and antifungal therapy with itraconazole (400 mg/ po) or ketoconazole (400–800 mg/d po), often given for 7–12 mo; posaconazole (400 mg po bid) in patients with disease refractory to itraconazole or who are intolerant of itraconazole [26,30,94]
Chromoblasto-mycosis	Usually in men aged 30–50 who work as farm laborers, lumberjacks, or sellers of farm products; affected persons usually poor, without adequate protective footwear and clothing [37,42]	Slowly progressive disorder usually limited to the skin and subcutaneous layer in which initial erythematous papular lesions may gradually evolve to display varying morphologies, such as nodular, tumoral (cauliflower-like), plaque, verrucous, and cicatricial lesions; affects feet and legs most frequently; may transform into squamous cell carcinoma [3,42]	Microscopic finding of muriform cells (sclerotic bodies) is the hallmark of this disease. Examination of scrapings or vinyl adhesive tape preparations, wet mount, histology, culture [37,95–98]	Surgery effective in early stages; itraconazole (100–400 mg/d), terbinafine (250–500 mg/d), terbinafine (500 mg/d) plus itraconazole (50–100 mg/d); combination therapy (itraconazole with terbinafine or 5-flucytosine) for severe cases, posaconazole (400 mg po bid) in patients with disease refractory to itraconazole or who are intolerant of itraconazole; cryotherapy [3,37–41,94,99]
Phaeohypho-mycosis	Occurs sporadically, often in older men who work in farming, carpentry, or other occupations that expose them to plant materials; usually occurs in both immunocompetent and in immunocompromised persons [48,50]	Chronic localized infection of deep dermis and subcutaneous tissues; single asymptomatic mass or nodule at trauma site gradually evolving to form painless cystic abscess; erythematous plaques possibly also present; lesion usually remaining localized with overlying skin staying intact *Most common sites of infection:* feet, legs, hands, arms, head [48,49]	Microscopic examination of biopsy material from cyst, with hematoxylin-eosin or Fontana-Masson staining; culture; PCR [2,95,96,100]	Complete surgical excision; itraconazole (100-600 mg/d), amphotericin B (0.5–1 mg/kg/d), often for several months; immunosuppressant doses reduced if feasible [48,49,51,63] Posaconazole for patients with disease refractory to other agents
Subcutaneous zygomycosis	Infections usually caused by Entomophthorales, *Basidiobolus ranarum*, and *Conidiobolus coronatus;* usually in immunocompetent persons;	*Basidiobolomycosis:* usually has chronic progressive clinical course; hard nodules that spread, often over thighs and buttocks, eventually	*Histology:* Wide sparse septated, thin-walled hyphae with right-angle branching. Splendore-Hoeppli phenomenon present with	No standard treatment defined for entomophthoromycosis (basidiobolomycosis or conidiobolomycosis)

	basidiobolomycosis usually in children, conidiobolomycosis usually in adults [68]	ulcerating overlying skin *Conidiobolomycosis*: begins with swelling of inferior nasal turbinates and extends to facial and subcutaneous tissues and paranasal sinuses; eventually, subcutaneous nodules attach to underlying tissues, causing facial disfigurement [68,77,78]	basidiobolomycosis, sometimes with entomophthoromycosis); culture [68]	Antifungals used to treat entomophthoromycosisinclude potassium iodide, miconazole, ketoconazole, itraconazole, fluconazole, terbinafine, and amphotericin B [68,69,74,76]
Lacaziosis	Men aged 21–40 who live in tropical rain forests and work as farmers, miners, hunters, and rubber workers [3,83]	Very slow evolution over many years; small papules or pustules that evolve into keloid-like lesions, which gradually increase in size; pinna of the ear most commonly affected; original lesion followed by involvement of other areas by subsequent abrasion/autoinoculation; nodule distribution follows lymphatic system [3,29,101]	Direct microscopy of tissue smear from lesion, examination of vinyl adhesive tape preparation; cannot be cultured *Serologic tests*: have high sensitivity but lack specificity because of antigenic cross-reactivity with Paracoccidioides [3,97]	Wide surgical excision, electrodessication in early stage of disease, cryosurgery; clofazimine (300 mg/d until clinical improvement, then 100 mg/d for ≥2 y) Amphotericin B, 5-fluorocytosine, and azoles usually ineffective, but patient with disseminated disease undergoing treatment with itraconazole (200 mg/d) [3,84,86]

bid, Twice daily; CT, computed tomography; d, day; ELISA, enzyme-linked immunosorbent assay; mo, month; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; po, orally; SSKI, saturated solution of potassium iodide; tid, 3 times daily; wk, week; y, years.

decaying material such as sphagnum moss, decaying vegetation, soil, and hay [4,5]. According to recent molecular data, *S. schenckii* is not a single species but constitutes a species complex that includes at least five cryptic species; *S. brasiliensis*, *S. globosa*, *S. mexicana*, *S. albicans* and *S. lurei*. The clinical impact of this genotypic diversity has not been evaluated [6].

Although sporotrichosis has been reported throughout the world, endemic areas are usually considered to be Latin America, South Africa, India, and Japan (Table 3). There is no uniform prevalence of disease by age or sex; sporotrichosis generally occurs sporadically in persons engaged in farming, gardening, mining, or other outdoor activities [1,5,7–9].

The incidence of sporotrichosis varies among Latin American countries, with endemic areas found in Peru, Brazil, Mexico, Uruguay, Costa Rica, Guatemala, and Colombia [5]. The estimated prevalence rates of sporotrichosis range between 0.1% and 0.5% in El Salvador, Uruguay, Colombia, Venezuela, Mexico, and Brazil and between 0.01% and 0.02% in Argentina, Ecuador, and Panama with the disease being extremely rare in Chile [10]. Molecular phylogenetic analyses suggest that *S. schenckii* is developing geographic divergence (e.g, Mexican strains with high virulence and Colombian strains with little thermal tolerance) [11–15].

Sporotrichosis is endemic in a poor, rural region in the south-central Andes Mountains of Peru [16,17]. The mean annual incidence between 1997 and 1999 in this region was 98 cases per 100,000 persons, with a mean incidence of 156 cases in children aged ≤15 years [17]. Higher socioeconomic status in this region was associated with a lower incidence of infection [17]. Patients with AIDS or other causes of immunodeficiencies such as chronic alcoholism or diabetes and those receiving immunosuppressive therapy may be at risk for the development of cutaneous, disseminated, and extracutaneous forms of sporotrichosis (Fig. 1A and B) [18,19].

Since 1998, in Rio de Janeiro and surrounding areas of Brazil, many cases of zoonotically transmitted sporotrichosis have been reported by owners of infected domestic cats, veterinarians, and others whose occupation involves cat care [20–23]. The number of human cases has exploded from 1987–1997 when only 13 cases of human sporotrichosis were reported [21], to 497 cases described from 1998–2003 [22]. Conversely, in the state of Rio Grande do Sul, 304 confirmed cases were identified from 1967 to 2002 (mean of 10.5 cases per year), with the majority diagnosed before 1990, although approximately 75% had occupational hazards as a risk factor [18]. An analysis of 31 cases identified in this area from 1988–1997 suggested that the incidence of sporotrichosis was decreasing among rural residents and increasing among urban dwellers who engaged in fishing and hunting [24].

Table 2 Data supporting potential use of newer antifungals voriconazole, posaconazole, and the echinocandins in the treatment of subcutaneous mycoses.

Drug	Supporting data
Voriconazole	***Chromoblastomycosis:*** potent *in vitro* activity against *Cladophialophora carrionii* (MIC_{90} = 0.125 μg/ml), *Fonsecaea pedrosoi* (G_{mean} MIC = 0.08 μg/ml), and *Phialophora verrucosa* (G_{mean} MIC = 0.12 μg/ml) [100,101]; resolved refractory chromoblastomycosis caused by *F. pedrosoi* in 43-year-old man with diabetes [104] ***Sporotrichosis:*** moderate/low *in vitro* activity against *Sporothrix* spp. (G_{mean} MIC = 1.9–13.2 μg/ml) [105–107] ***Phaeohyphomycosis/eumycetoma:****in vitro* activity against *Exophiala jeanselmei* (G_{mean} MIC = 0.6 μg/ml), *Exophiala dermatitidis* (G_{mean} MIC = 0.22 μg/ml), *Alternaria alternata* (G_{mean} MIC = 0.63 μg/ml) [103], *Scedosporium apiospermum* (MIC_{90} = 0.125 μg/ml) [108], and *Madurella mycetomatis* (G_{mean} MIC = 0.05 μg/ml) [103]; successfully treated cutaneous *S. apiospermum* infections [109,110]
Posaconazole	***Chromoblastomycosis:*** approved to treat refractory chromoblastomycosis in Europe [94]; *in vitro* activity against *Phialophora* spp. (G_{mean} MIC = 0.4 μg/ml) [109]; successfully treated 5 of 6 patients with refractory chromoblastomycosis caused by *F pedrosoi* [112] ***Sporotrichosis:****in vitro* activity against *Sporothrix* spp. greater than that of itraconazole, voriconazole, amphotericin B, caspofungin, and anidulafungin (G_{mean} MIC = 0.7–1.59 μg/ml) [105,111] ***Phaeohyphomycosis:*** successfully treated a patient with chronic disease caused by *Alternaria* spp. that was refractory to voriconazole, amphotericin B, and caspofungin [113]; also effective in a mouse model of disseminated disease caused by *E. dermatitidis* [114]; successfully treated disseminated refractory infections caused by *Ramichloridium mackensiei* [115], and *Espinifera* [116] ***Eumycetoma:*** approved to treat refractory eumycetoma in Europe [94]; potent *in vitro* activity against *E. jeanselmei* and *E. oligosperma* (MIC_{50} = 0.031 μg/ml for both species) [117]; *in vitro* activity against *S. apiospermum* (MIC range = 0.5–2 μg/ml) [118]; successfully treated 5 of 6 patients with refractory eumycetoma caused by *M. grisea*, *M. mycetomatis*, and *S. apiospermum* [112] ***Zygomycosis:****in vitro* activity against clinical species of Zygomycetes greater than that of itraconazole, voriconazole, and fluconazole [119,120]; successfully treated refractory subcutaneous zygomycosis caused by *Rhizopus oryzae* [121,122]; also successful as salvage therapy in disseminated zygomycosis [123]
Echinocandins	***Chromoblastomycosis:*** micafungin has some *in vitro* activity (MIC = 2 μg/ml) [123] and caspofungin has potent *in vitro* activity (G_{mean} MIC = 0.13 μg/ml) [124] against *F. pedrosoi* ***Sporotrichosis:*** moderate *in vitro* activity against *S. schenckii*. (caspofungin and anidulafungin G_{mean} MIC = 5.4 and 3.9 μg/ml, respectively) [111] ***Phaeohyphomycosis:*** caspofungin has potent *in vitro* activity against *Alternaria* spp. (MIC range ≤ 0.12 μg/ml); micafungin has moderate *in vitro* activity against *E. dermatitidis* (MIC range = 1.0–> 8 μg/ml) [118] ***Eumycetoma:****in vitro* activity against *E. jeanselmei* and *E. oligosperma* (caspofungin and anidulafungin MIC_{50} = 4 and 0.5 μg/ml, respectively, for both species [117]; caspofungin G_{mean} MIC = 1.10 μg/ml against *E. jeanselmei*) [124]; micafungin has moderate *in vitro* activity against *Exophiala* spp. (MIC = 0.25–2 μg/ml) [123]; caspofungin has potent *in vitro* activity against *S. apiospermum* (G_{mean} MIC = 0.38 μg/ml) [124]; anidulafungin and caspofungin show moderate activity against *S. apiospermum* (MIC range = 1–4 μg/ml and 0.25–4 μg/ml, respectively), and micafungin shows *in vitro* activity against *S. apiospermum* (MIC range = >8 μg/ml) [119] ***Zygomycosis:*** caspofungin and micafungin showed poor *in vitro* activity against clinical Zygomycetes [120,123,125]

G_{mean}, geometric mean; MIC, minimum inhibitory concentration.

Sporotrichosis has been found in the central region of Mexico, with the highest incidences during the cold and dry seasons. However, its overall incidence has been decreasing, probably because of a general improvement in nutrition and living conditions [10].

Sporotrichosis has also been reported in Uruguay and Venezuela [10]. In Uruguay, 80.5% of cases have been attributed to armadillo hunting, especially around the Easter holidays [10]. In contrast, the first isolation of *S. schenckii* in Venezuela was reported in 2007 and was from an environmental source [25].

Eumycetoma

Mycetoma is a chronic granulomatous infection caused by fungi (eumycetoma) and bacteria (actinomycetoma) [26]. Agents of mycetoma are classified according to their biologic characteristics and grain aspects (color, size, hardness, shape) [27]. There are at least two dozen species of fungi-causing eumycetoma throughout the world, but the most prevalent causative specie (approximately 70% of reported cases) is *Madurella mycetomatis*, which is associated with black-grain mycetomas [27,28]. *Scedosporium apiospermum*, responsible for approximately 10% of reported eumycetoma cases, produces white grains in tissues (Fig. 2) [27]. Other etiologic agents include *Madurella grisea*, *Acremonium falciforme*, *A. kiliense*, *A. recifei*, *Cylindrocarpon cyanescens*, *C. destructans*, *Exophiala jeanselmei*, *Scytalidium dimidiatum*, *Aspergillus nidulans*, *Neotestudina rosatii*, *Leptosphaeria senegalensis*, *Pyrenochaeta romeroi*, and *Phialophora verrucosa* [1,26,27,29]. Eumycetoma generally occurs in a 5:1 ratio of men to women and in adults aged 20–40 years [26,29]. The disease is most commonly seen in herders, farmers, and other field laborers [26].

Worldwide, the prevalence rates of eumycetoma and actinomycetoma are similar, but eumycetomas are more common in Africa and Asia (especially India), whereas actinomycetomas are more common in Latin America [30]. The mycoses generally prevail in the 'mycetoma belt', which

Table 3 Sporotrichosis: demographic and clinical characteristics of patients in selected endemic areas.

Characteristic	Jalisco, Mexico	Costa Rica	Laguna de Ayarza, uatemala	Antioquia, Colombia	Rio Grande do Sul, Brazil	Uruguay	Abancay, Peru	Gauteng, South Africa	Himachal Pradesh, India	Northwest India	Japan
Period	1960–96	1982–92	1972–75	1962–74	1988–97	1963–79	1995–97	NR	1996–97	1988–93	1965–83
Cases	822	100	53	150	31	181	238	154	25	12	200
Age, %											
0–15 y	32	—	NR	37	—	—	60	—	NR	NR	—
0–20 y	—	26	NR	—	13	15	—	26	NR	NR	19
>15 y	68	—	NR	63	—	—	40	—	NR	NR	—
>20 y	—	74	—	—	87	85	—	74	—	—	81
Male, %	58	61	83	63	87	97	56	75	48	42	33
Presentation											
Lymphocutaneous	75	48	87	46	74	83	55	78	68	92	54
Fixed cutaneous	24	48	13	54	26	14	36	20	32	0	46
Disseminated	1	4	0	0	0	3	9	2	0	8	0.5
Lesion location, %[a]											
Upper limbs	49	52	NR	41	74	NR	33	NR	80	58	54
Other	50	47	NR	59	25	NR	91	NR	20	41	47

NR, Not reported.

Adapted with permission from Bustamante and Campos [5].

[a]Percentages may not add up to 100% because of rounding up of values or because of patients having lesions in more than 1 location.

stretches between the latitudes of 15° south and 30° north and includes Sudan, Somalia, Senegal, India, Yemen, Mexico, Venezuela, Colombia, and Argentina [26].

Overall, the prevalence of mycetomas caused by fungi is rising, with *Madurella* spp. and *S. apiospermum* as the major causes of eumycetoma in Latin America [31]. Combined retrospective data from Hospital das Clinicas da Faculdade de Medicina of the Universidade de São Paulo in Brazil, showed that from 1944–2000, 222 mycetoma cases were reported [31,32]. Of the treated cases, the proportion of patients with eumycetoma had increased from 32% (13/41) between 1978 and 1989 [31] to 48% (13/27) between 1990 and 2000 [32]. Of the 47 eumycetoma cases with known causative organisms, the most common agents were *S. apiospermum* ($n = 15$), *M. mycetomatis* ($n = 8$), and *M. grisea* ($n = 8$) [31,32]. Most patients were male field laborers from northeastern Brazil, although the patients in the most recent group represented a broader occupational and geographic range [31,32].

Of the 502 mycetoma cases in patients treated at the Centro Dermatológico Pascua, in Mexico City between 1956 and 1984, 9 (1.8%) were eumycetomas [33]. Similarly, an analysis of 2,105 mycetoma cases in patients treated at Mexican hospitals between 1956 and 1985 found that 47 (2.2%) were eumycetomas [34]. In both series, the most commonly reported causative eumycetoma organism was *Madurella* spp. [33,34]. In the Salta Province (northwest Argentina) from 1972–1982, four of 39 patients (10%) treated for mycetoma had eumycetoma, all caused by *M. grisea* [35]. In Buenos Aires, from 1989–2004, 43 of 76 patients (57%) treated for mycetoma had eumycetoma, most frequently caused by *M. grisea* ($n = 29$) [36].

Chromoblastomycosis

Chromoblastomycosis, or chromomycosis, is a chronic cutaneous and subcutaneous mycotic infection developing at the site of a previous transcutaneous trauma [37–39]. The disease is characterized by the development of verrucose plaques, scaly lesions, and the presence of muriform cells (sclerotic bodies; Fig. 3) [37,38–40]. Several dematiaceous fungi are involved with the disease etiology, most commonly *Fonsecaea pedrosoi* and *Cladophialophora carrionii* [38,39]. More than 70% of cases are indigenous to tropical and subtropical climates [37]. *F. pedrosoi* is found in humid tropical zones or in wet areas within torrid zones, whereas *C. carrionii* is usually the predominant pathogen in dry or semidesert regions [29,37]. Less-frequent causative pathogens include *P. verrucosa*, *Rhinocladiella aquaspersa*, *E. dermatitidis* and *F. monophora* [38,40]. *E. jeanselmei* and *E. spinifera* also have been found forming muriform cells in typical chromoblastomycosis lesions and are therefore also considered etiologic agents of chromoblastomycosis [38,39].

Chromoblastomycosis-causing fungi are found worldwide in soil and decaying plant materials, including wood [7]. Table 4 shows details of transcutaneous traumas leading to cases of chromoblastomycosis in 32 Brazilian patients; most cases of implantation trauma (18/32) were caused by plant material. Chromoblastomycosis is considered an occupational disease, occurring in farm laborers, lumberjacks, or vendors of farm products [37,38,41]. Affected persons are usually poor and lack adequate protective footwear and clothing. Chromoblastomycosis rarely occurs before adolescence with most patients being 30- to

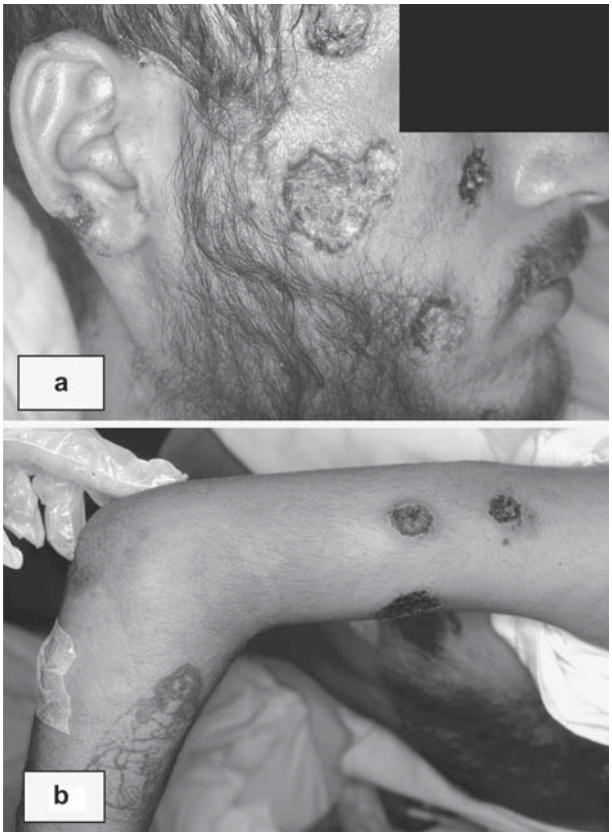

Fig. 1 Disseminated cutaneous sporotrichosis in a patient with AIDS on (a) the face, and (b) the arm.

50-year-old men, with male-to-female ratios of 5:1 and 9:1 reported [37,42].

Although the highest reported prevalence rates of chromoblastomycosis are in Madagascar, South Africa, Brazil, and Costa Rica, the disease has also been reported in other Latin American countries, the United States, Asia, some European countries, and other parts of Africa [37]. In Latin America, the infection also occurs in Mexico, Venezuela, the Dominican Republic, Cuba, Colombia, and Brazil, with a small number of cases being reported in Puerto Rico, Peru, Ecuador, and Argentina [29,43].

In Brazil, the mean annual numbers of cases of chromoblastomycosis reported were 6.4 (71 cases/11 years) for Paraná (South Region), 5.9 (325 cases/55 years) for Pará (North Region), 4.3 (13 cases/3 years) for Maranhão (Northeast Region), and 2.6 (73 cases/28 years) for Rio Grande do Sul (South Region) [1]. Of the 78 caustive agents identified in a retrospective study of 325 cases reported in Pará from 1942–1997, 77 were *F. pedrosoi* [42]. This fungus was also the causative organism in 9 of 13 patients treated in Maranhão between 1988 and 1991 [44]. A potentially important source of infection in the Amazon Region of Maranhão is the harvesting and processing of

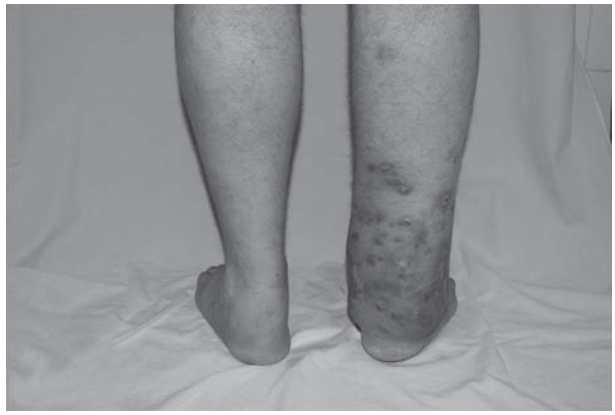

Fig. 2 Leg and foot multifistulous lesions of eumycotic mycetoma caused by *Scedosporium apiospermum*.

the Babassu coconut, whose shells may be colonized by *F. pedrosoi* [45].

After mycetoma and sporotrichosis, chromoblastomycosis is the third most frequent type of cutaneous mycosis in Mexico [7]. It is mostly found in the states of Chiapas, Oaxaca, Veracruz, Guerrero, and Tabasco, all of which have a tropical or subtropical climate [37]. At the General Hospital of Mexico, in Mexico City, of 51 infections treated over 17 years, 48 (90%) were caused by *F. pedrosoi*, and most patients came from warm, humid rural areas along the Gulf of Mexico or the Pacific Ocean [46].

In the semiarid states of Venezuela, the most prevalent causative organism is *C. carrionii,* especially in men who care for goats [29]. From 1992–2004, 22 children and adolescents (aged 2–19 years) living in the semiarid zone of Falcón state were diagnosed with chromoblastomycosis caused by *C. carrionii* [47]. However, in more humid states, including Táchira, Trujillo, Mérida, and Miranda, most cases were caused by *F. pedrosoi* [29].

Fig. 3 Plaque lesion of chromoblastomycoses involving the face.

In Ecuador and especially in rural areas of Colombia, the majority (≥95%) of cases of chromoblastomycosis were caused by *F. pedrosoi* [29]. Similarly, in Cuba, in the Dominican Republic, and throughout Central America, more than 80% of infections were caused by *F. pedrosoi* and occurred in men living in rural areas [29].

Subcutaneous phaeohyphomycosis

Subcutaneous phaeohyphomycosis is included in the spectrum of diseases caused by melanin-pigmented black fungi. The most frequently reported type of subcutaneous phaeohyphomycosis is a chronic localized infection of the deep dermis and subcutaneous tissues [48]. It is usually the result of traumatic implantation of fungi into subcutaneous tissue and has an unknown incubation period [48]. Phaeohyphomycosis is caused by dematiaceous fungi that can be found in decaying wood and plants [49], most commonly by *E. jeanselmei*, *E . moniliae*, *E. spinifera*, *Phialophora* (*Phaeoacremonium*) spp., *Bipolaris* spp., and *Exophiala* (*Wangiella*) *dermatitidis* [46,50–53], and less commonly by *Veronaea botryose* [54], *Exserohilum rostratum* [55], *Colletotrichum crassipes* [56], and *Phoma cava* [57]. Infections occur sporadically, often in older adult men who work as farmers, carpenters, or other occupations that expose them to plant materials [50]. Most phaeohyphomycosis infections occur in immunocompetent persons but with the rising number of iatrogenically immunosuppressed persons, infections have been increasingly reported in immuno hematopoietic stem cell transplant recipients (Fig. 4) [41,48,50,52,54,55].

Table 4 Details of subcutaneous traumas leading to chromoblastomycosis in 32 Brazilian patients.

Type of trauma	Number of cases
Plant	
Wood	9
Straw	2
Grass	2
Thorn	2
Palm tree	1
Bamboo	1
Spiny seed	1
Animal	
Insect sting	2
Buck rear	1
Cock spine	1
Caterpillar	1
Agricultural tool	
Hoe	2
Axe	1
Knife	1
Mill	1
Other	
Fall	2
Brick	1
Shoes	1

Data from Queiroz-Telles F. Mycological, epidemiological, clinical, and therapeutic aspects of chromoblastomycosis. PhD thesis. University of São Paulo, São Paulo, Brazil, 1999.

Phaeohyphomycosis is seen worldwide but is more common in tropical and subtropical climates [48]. By 1995, 19 cases had been reported in Brazil, 10 of which were from Rio Grande do Norte in the northeast [56]. Case reports described infections in immunocompetent persons, but the causative organisms often could not be identified because specimens had been fixed in formalin [58,59]. In other cases, etiologic agents included *E. spinifera* [60], *Cyphellophora pluriseptata* [61], and *B. hawaiiensis* [62]. Case reports of phaeohyphomycosis in Brazil have also involved solid organ transplant recipients and other immunocompromised persons, with infections caused by *E. jeanselmei* [63,64], *Phaeoacremonium parasiticum* [53], *Cladophialophora* spp. [65], *C. crassipes* [56], and *P. cava* [57].

In El Salvador, one case of phaeohyphomycosis was reported in a 6-year-old immunocompetent boy with extensive lesions caused by *E. spinifera* [67]. At a hospital in Medellín, Colombia, infections due to *Exophiala* spp. and unidentified dematiaceous moulds were reported in five renal transplant recipients, representing a prevalence of subcutaneous phaeohyphomycosis in these patients of 0.34% [67].

Subcutaneous zygomycosis

Subcutaneous zygomycosis, or entomophthoromycosis, is usually caused by members of the order Entomophthorales, especially *Basidiobolus ranarum* (formerly *B. haptosporus*) and *Conidiobolus coronatus* [68]. Species of the Entomophthorales are distributed worldwide but are endemic in tropical areas, with most infections occurring in countries situated between 15° north and 15° south latitudes [68,69]. *Basidiobolus* and *Conidiobolus* spp. are most commonly found in tropical climates [68]. *Basidiobolus* spp. are associated with decaying vegetation, insects, wood lice, and the feces of many animals. *Conidiobolus* spp. are found in soils and plant detritus, especially in warm, wet climates [68].

Infections caused by the Entomophthorales usually occur in immunocompetent persons, in contrast to rare cases of subcutaneous infection caused by members of the order Mucorales, which often affect immunosuppressed persons [70]. Conidiobolomycosis usually occurs in men engaged in agricultural and other types of outdoor work, with an 8:1 ratio of infected men to women [70]. Basidiobolomycosis usually occurs in children under age 10 and is more common in boys [70].

Most cases in Latin America have been reported in Brazil, but infections have also been described in Costa Rica, Colombia, and Puerto Rico (Fig. 5) [68,70]. In Brazil, the majority of cases were found in the coastal areas of the Northeast Region [69]. *B. ranarum* infections have been documented in children living in the Northeast Region [71–73] and in a 43-year-old male farmer from the Southeast Region [74]. Case reports of *C. coronatus* infections were reported in adults living in the Northeast and Central-West Regions [69,70,76], whereas an infection due to *Mucor hiemalis* was noted in a 78-year-old male gardener with diabetes (residence unknown) [77] and another case due to *Rhizopus oryzae* was described in a 61-year-old man with diabetes from the South Region [78].

Lacaziosis

Lacaziosis, or lobomycosis, is caused by *Lacazia loboi* (formerly called both *Loboa loboi* and *Paracoccidioides loboi*), a fungal pathogen that affects humans and dolphins [79,80]. This fungus has never been isolated in cultures. In most cases, the agent is probably introduced directly into the dermis through a penetrating entry, such as an insect bite or thorn prick [3]. Although the natural reservoir of *L. loboi* is unknown, its likely habitat is somewhere in the rural environment, with soil and vegetation likely sources of infection [3]. Lacaziosis usually occurs in inhabitants of tropical, humid, or subtropical forests with elevations greater than 200 meters, an average temperature of 24°C, and more than 200 cm of annual rainfall [3].

Nearly all cases of lacaziosis have been reported in Latin America, but isolated cases have also been seen in Europe, the United States, and Canada, usually in persons with a history of travel to Latin America or contact with dolphins [3,81,82]. Lacaziosis generally affects men aged 21–40 who work as farmers, miners, hunters, or as rubber workers [3,83].

Within Latin America, the great majority of cases of lacaziosis have been reported in the Amazon rain forest (Brazil, Ecuador, Colombia, Venezuela, French Guyana, Guyana, and Suriname), but cases have also been described in Peru, Bolivia, Mexico, Costa Rica, and Panama (Fig. 6) [3,84]. In an analysis of 304 reported cases published in 1993, 58% were from Brazil, 13% from Colombia, and 10% from Suriname [83]. In Brazil as reported in 1989, 21% of all known cases worldwide were found in the Cayabi Indians in the state of Mato Grosso (Amazon Region), of which two with long-standing lacaziosis developed squamous cell carcinoma in old scar lesions [85]. Extensively disseminated lacaziosis was reported in an 86-year-old woman with a 55-year disease history, who was a former rubber collector in the state of Acre (Amazon Region) in Brazil [86]. Recurrent lacaziosis lesions have been documented in a patient with human immunodeficiency virus (HIV) infection, suggesting that HIV infection may increase a person's susceptibility to lacaziosis [87]. In

Fig. 4 Cystic lesion of subcutaneous phaeohyphomycosis on the foot of a renal transplant recipient.

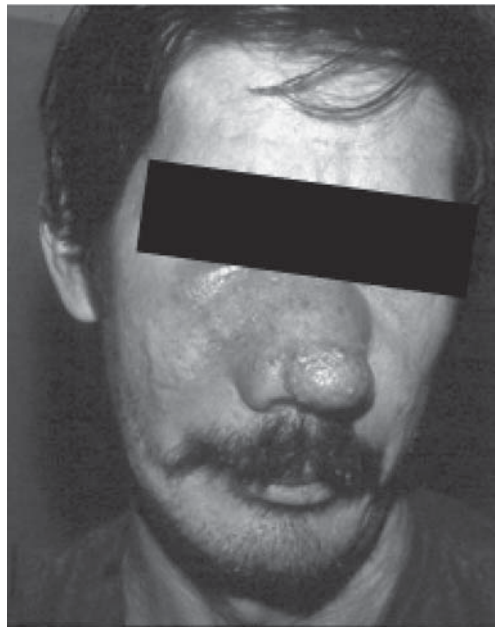

Fig. 5 Subcutaneous zygomycosis.

1992, a high prevalence (8.5%) of lacaziosis was seen among the Amerindians who live near the Colombian-Venezuelan border [88].

Conclusion

Implantation mycoses, also known as subcutaneous mycoses, are a persistent health problem in Latin American countries, yet are often neglected. Because these infections do not require compulsory notification, data related to their incidence and prevalence may be scarce and fragmentary. Although some implantation fungal diseases are found in immunocompromised persons, the immunocompetent population is the principal target in Latin America. The majority of causative organisms are found in soil, vegetation, and decaying matter in tropical, subtropical, and humid environments, and infection is usually the result of penetrating injury, as well as other avenues. Infections especially occur in low socioeconomic groups; in those living in rural areas or involved in farming, hunting, or other outdoor activities; and particularly in adult men. Although subcutaneous mycoses rarely cause disseminated or invasive disease, especially among immunocompetent hosts, their impact on public health is high, and timely diagnosis and appropriate treatment remain important.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

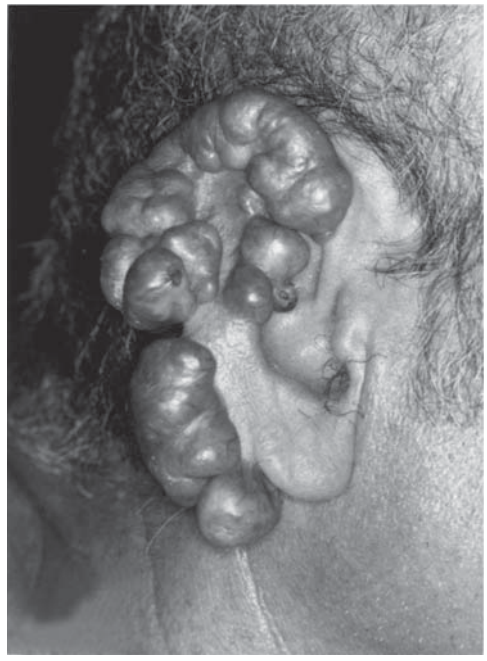

Fig. 6 Auricular lacaziosis. Photograph courtesy of Dr Sinesio Talhari, Brazil.

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