

Epidemiology of Opportunistic Fungal Infections in Latin America

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This review discusses the epidemiology of the most clinically relevant opportunistic fungal infections in Latin America, including candidiasis, cryptococcosis, trichosporonosis, aspergillosis, and fusariosis. The epidemiologic features, including incidence, of some of these mycoses are markedly different in Latin America than they are in other parts of the world. The most consistent epidemiologic data are available for candidemia, with a large prospective study in Brazil reporting an incidence that is 3- to 15-fold higher than that reported in studies from North America and Europe. Species distribution also differs: in Latin America, the most common *Candida* species (other than *Candida albicans*) causing bloodstream infections are *Candida parapsilosis* or *Candida tropicalis*, rather than *Candida glabrata*.

The incidence of invasive opportunistic mycoses has increased because of the expanding population of immunosuppressed patients, including solid-organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) recipients, patients with cancer, patients with AIDS, premature neonates, elderly patients, and patients recovering from major surgery [1, 2]. Despite some effective treatment options, such mycoses are associated with high morbidity and mortality rates.

Opportunistic mycoses show distinct regional incidence patterns throughout the world and may exhibit different epidemiologic features, depending on the geographic region; this may be particularly true for mycoses (such as mold infections) that are acquired from the environment. Most epidemiologic data come from studies conducted in the northern hemisphere. Although some studies from Latin America have been

published, no comprehensive epidemiologic reviews have been performed of invasive opportunistic mycoses occurring in patients from this region. The knowledge of the epidemiologic characteristics in a certain region is important both locally and globally, given the expansion of traveling and migration through different regions of the globe. In this article, we review the epidemiology of the most clinically relevant opportunistic mycoses occurring in Latin America.

METHODS

We identified and reviewed articles on opportunistic invasive mycoses using the complete Scientific Electronic Library Online and Medline databases through June 2008. Articles were reviewed irrespective of the date and language of publication and were retrieved using the following keywords: invasive fungal infection, opportunistic infection, candidiasis, cryptococcosis, trichosporonosis, aspergillosis, fusariosis, and zygomycosis. Each of these terms was combined with the following keywords: Latin America, South America, Central America, Mexico, Brazil, and Argentina. During our analysis, an exhaustive effort was made to collect all available information on geographic distribution of the fungal infections of interest, incidence and prevalence rates, susceptible populations, mortality rates, and sequelae.

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Table 1. Summary of the Epidemiology of Candidemia in Latin America

Study	Description	No. of episodes	Species distribution (% of cases)	Susceptibility pattern/ comments
Colombo et al [4] (March 2003–December 2004)	Prospective, laboratory-based surveillance, 11 tertiary care centers	712 Episodes of candidemia	<i>Candida albicans</i> (41), <i>Candida tropicalis</i> (21), <i>Candida parapsilosis</i> (21)	Fluconazole SDD 4%, resistant 0.8%; linear correlation between fluconazole and voriconazole MICs; prior exposure to fluconazole correlated with higher fluconazole and voriconazole MIC
Nucci et al [5] (March 2003–December 2004 and April 2005–February 2006)	Prospective, laboratory-based surveillance, 12 centers, comparing <i>C. tropicalis</i> with <i>C. albicans</i>	924 Episodes of candidemia	<i>C. albicans</i> (42), <i>C. tropicalis</i> (20)	<i>C. tropicalis</i> : second species in adults (22%) and elderly individuals (23%) and third in neonates (12%) and children (18%); cancer, diabetes, and neutropenia more frequent with <i>C. tropicalis</i>
Brito et al [6] and Colombo et al [7] (March 2002–February 2003)	Prospective, laboratory-based surveillance, 4 centers in São Paulo, Brazil, <i>C. parapsilosis</i> and <i>C. albicans</i>	282 Episodes of candidemia	<i>C. parapsilosis</i> (<i>n</i> = 64), <i>C. albicans</i> (<i>n</i> = 107)	Fluconazole, itraconazole, 5-flucytosine, amphotericin B: no resistance except for 1 isolate with MIC >1 µg/mL to amphotericin B; caspofungin MIC values greater than with <i>C. parapsilosis</i> than <i>C. albicans</i> ; <i>C. parapsilosis</i> candidemia associated with tunneled CVC
Pasqualotto et al [8] (1995–2003)	Retrospective comparison of outpatient and nosocomial candidemia, Porto Alegre, Brazil	Outpatient (<i>n</i> = 19) vs nosocomial (<i>n</i> = 191)	Outpatient: <i>C. parapsilosis</i> (37), <i>C. albicans</i> (26), <i>Candida glabrata</i> (10), <i>C. tropicalis</i> (5), <i>Candida krusei</i> (5)	CRF and HD more common in outpatient group; ileus, GI bleeding, previous bacteremia, use of PPI, ICU stay, receipt of antibiotics, blood transfusions, vasopressors, and invasive medical procedures more common in nosocomial group; similar mortality rates during hospitalization (53% outpatient vs 50% nosocomial)
Ramirez et al [9] (1990–1991)	Retrospective study, Children's Hospital of Mexico	116 Clinical isolates of pathogenic yeasts	<i>C. albicans</i> (60), <i>C. tropicalis</i> (15), <i>Candida guilliermondii</i> (10), <i>C. glabrata</i> (7), <i>C. parapsilosis</i> (1)	

Table 1. (Continued.)

Study	Description	No. of episodes	Species distribution (% of cases)	Susceptibility pattern/ comments
Rodero et al [10] (1993–1995)	Retrospective study, 2 hospitals in Argentina	209 Episodes of candidemia in children	<i>C. albicans</i> (49), <i>C. parapsilosis</i> (28), <i>C. tropicalis</i> (18), <i>C. glabrata</i> and <i>C. krusei</i> (0.4)	Resistance to fluconazole: <i>C. albicans</i> (19%), <i>C. parapsilosis</i> (21%), <i>C. tropicalis</i> (20%); resistance to itraconazole: <i>C. albicans</i> (13%), <i>C. parapsilosis</i> (25%), <i>C. tropicalis</i> (4%)
Mestroni et al [11] (1998–2001)	Retrospective study, 1 center, La Plata, Argentina	35 Preterm neonates and 46 adults	<i>C. parapsilosis</i> (28), <i>C. albicans</i> (26), <i>C. tropicalis</i> (26), <i>Candida pelliculosa</i> (6), <i>C. glabrata</i> (2)	
Giusiano et al [12] (1999–2001)	Retrospective study, 2 hospitals, northeast of Argentina	25 Neonatal ICU patients	<i>C. parapsilosis</i> (36), <i>C. albicans</i> (36), <i>C. tropicalis</i> (16), <i>C. krusei</i> (4)	
Silva et al [13] (January 1998–December 1999)	Retrospective study, antifungal susceptibility, 3 hospitals in Santiago, Chile	50 Clinical isolates from ICU patients	<i>C. albicans</i> (54), <i>C. parapsilosis</i> (24), <i>C. tropicalis</i> (12), <i>C. glabrata</i> (10)	Resistance to itraconazole: 2 <i>C. albicans</i> and 1 <i>C. glabrata</i> isolate; resistance to fluconazole: 1 <i>C. tropicalis</i> and 1 <i>C. glabrata</i> isolate
Silva et al [14] (March 2000–March 2001)	Retrospective study, 13 hospitals	130 Clinical isolates	<i>C. albicans</i> (41), <i>C. parapsilosis</i> (13), <i>C. tropicalis</i> (10), <i>C. glabrata</i> (6), <i>Candida famata</i> (4), <i>C. krusei</i> (1)	
Costa et al [15] (December 1994–December 1996)	Prospective study, fungemia, 1 hospital, São Paulo, Brazil	86 Patients with fungemia	<i>C. albicans</i> (50), <i>C. parapsilosis</i> (17), <i>C. tropicalis</i> (12), <i>C. guilliermondii</i> (10), <i>C. glabrata</i> (2), <i>C. krusei</i> (1)	83% of <i>C. albicans</i> isolates came from burn patients or premature neonates; other underlying conditions: GI disorders (28%); hematologic malignant neoplasm (17%)
Antunes et al [16] (August 2002–August 2003)	Retrospective study, 1 hospital, Porto Alegre, Brazil	120 Episodes of candidemia	<i>C. albicans</i> (48), <i>C. parapsilosis</i> (26), <i>C. tropicalis</i> (13), <i>C. glabrata</i> (3), <i>C. krusei</i> (2)	No resistant isolates were found
Aquino et al [17] (June 1998–July 2004)	Retrospective study, 1 hospital, Porto Alegre, Brazil	131 Episodes of candidemia	<i>C. albicans</i> (45), <i>C. parapsilosis</i> (24), <i>C. tropicalis</i> (15), <i>C. glabrata</i> (7), <i>C. krusei</i> (5)	Resistance to fluconazole: 3% of isolates (all <i>C. krusei</i>); patients with hematologic malignant neoplasms and solid tumors comprised 35% of the candidemia episodes
Rodero et al [18] (April–September 1998)	Retrospective study, 12 centers in Argentina	89 Bloodstream isolates	<i>C. albicans</i> (51), <i>C. tropicalis</i> (22), <i>C. parapsilosis</i> (20), <i>C. krusei</i> (3), <i>C. glabrata</i> (2)	<i>C. krusei</i> : resistance to fluconazole and SDD to itraconazole; resistance to fluconazole and itraconazole: 2 of 2 <i>C. glabrata</i> isolates

Table 1. (Continued.)

Study	Description	No. of episodes	Species distribution (% of cases)	Susceptibility pattern/ comments
Rodero et al [19] (April 1999–April 2000)	Retrospective study, 36 centers in Argentina	265 Bloodstream isolates	<i>C. albicans</i> (41), <i>C. parapsilosis</i> (29), <i>C. tropicalis</i> (16), <i>C. glabrata</i> (3)	Most isolates susceptible to fluconazole and itraconazole
Cuenca-Estrella et al [20] (1996–1999)	Retrospective study, 99 centers, including 44 in Argentina	230 Isolates	<i>C. albicans</i> (41), <i>C. parapsilosis</i> (30), <i>C. tropicalis</i> (20), <i>C. glabrata</i> (3), <i>C. krusei</i> (2)	Decreased susceptibility to fluconazole (9%) and itraconazole (20%)
Avila-Aguero et al [21] (1994–1998)	Retrospective study, 1 hospital, San Jose, Costa Rica	110 Episodes of candidemia in neonates	<i>C. albicans</i> (90), <i>C. tropicalis</i> (10)	

NOTE. CVC, central venous catheter; CRF, chronic renal failure; GI, gastrointestinal; HD, hemodialysis; ICU, intensive care unit; MIC, minimal inhibitory concentration; PPI, proton pump inhibitors; SDD, sensitive dose dependent.

OPPORTUNISTIC YEAST INFECTIONS

Invasive candidiasis. *Candida* remains the most important cause of opportunistic mycoses worldwide and a major cause of nosocomial bloodstream infection [3]. Patients at risk for invasive candidiasis include severely ill patients in intensive care units (ICUs), neutropenic patients with cancer, patients undergoing surgical procedures, and premature neonates [3]. Fungal surveillance programs have provided data regarding the incidence and species distribution of *Candida* bloodstream isolates across the world [3]. However, little has been reported from Latin American countries (Table 1). The Brazilian Network Candidemia Study reported an overall incidence of 2.49 cases per 1000 hospital admissions or 0.37 cases per 1000 patient-days [4]. Although differences in incidence rates are not directly comparable, because they are not risk adjusted, this high incidence is in sharp contrast to the lower incidence of candidemia reported in centers in the Northern Hemisphere, including the United States (0.28–0.96 cases per 1000 hospital admissions) [5–8], Canada (0.45 cases per 1000 hospital admissions) [9], Europe (0.20–0.38 cases per 1000 hospital admissions) [10], France (0.17 cases per 1000 hospital admissions) [11], Norway (0.17 cases per 1000 hospital admissions) [12], Hungary (0.20–0.40 cases per 1000 hospital admissions) [13], Switzerland (0.27 cases per 1000 hospital admissions) [14], Italy (0.38 cases per 1000 hospital admissions) [15], and Spain (0.76–0.81 cases per 1000 hospital admissions) [16, 17]. An even higher incidence (3.9 cases per 1000 hospital admissions) was reported in a single-center study from northeast Brazil [18]. An incidence of 0.38–0.83 cases per 1000 patient-days was reported in a single-center study in an ICU in Brazil [19], and an incidence of 1.09 cases per 1000 ICU admissions was reported for a pediatric ICU in Argentina [20]. The reasons for the high incidence of candidemia in these series are not clear but may be related to a combination of factors, including dif-

ferences in resources available for medical care and training programs, difficulties in the implementation of infection control programs in hospitals in developing countries, a limited number of health care workers available to assist patients in ICUs, and less aggressive practices of prophylaxis and empirical antifungal therapy. More data are needed to address this question.

Several studies characterizing the epidemiology, microbiology, risk factors, and/or patient outcomes associated with candidemia have been published (Table 1) [4, 22–31]. *Candida albicans* is the leading agent, followed by *Candida parapsilosis* and *Candida tropicalis*. This is in sharp contrast to the higher incidence of *Candida glabrata* in the United States [5]. In the Brazilian Network Candidemia Study, *C. albicans* accounted for 40.9% of cases, followed by *C. tropicalis* (20.9%) and *C. parapsilosis* (20.5%); *C. glabrata* accounted for only 4.9% of cases [4]. This species distribution has been consistent across different studies from Brazil [32–34], Argentina [35–37], and Chile [30]. In a study of 2139 clinical isolates from Colombia, Ecuador, and Venezuela, the proportion of *C. albicans* isolates was higher (62%), but *C. parapsilosis* (11%) and *C. tropicalis* (8.5%) were again the most frequent non-*albicans* species, and *C. glabrata* accounted for only 3.5% of isolates [38].

In the northern hemisphere, candidemia due to *C. parapsilosis* is clustered in neonates [39], whereas in Latin America it is distributed through all ages, including (but not limited to) neonates [22, 23]. In a prospective observational study conducted in 4 tertiary care centers in Brazil from 2002 through 2003, *C. parapsilosis* accounted for 23% of cases. Patients with *C. parapsilosis* candidemia were more likely to have a tunneled central venous catheter, which supports the idea that an external source was the main mode of acquisition [23].

Candidemia due to *C. tropicalis* has been associated with cancer, especially in patients with leukemia or neutropenia [40–

43]. In a study of 924 episodes of candidemia, 188 (20%) were caused by *C. tropicalis*; cancer was the most frequent underlying disease, and in adults and elderly patients, diabetes was the second most frequent underlying disease. Of note was the high proportion (12.3%) of candidemia cases due to *C. tropicalis* in neonates [22]. Rates >15% in European and North American general hospitals have only been reported in studies conducted in the 1980s and early 1990s; more recently, rates >15% have been reported in East and Southeast Asia, the Middle East, and Latin America [22].

In the Brazilian Network Candidemia Study, the incidence of candidemia due to *C. glabrata* was 0.12 cases per 1000 hospital admissions [4]. Recent data from 2 of the 11 hospitals involved in that study reported an incidence of 0.08 cases per 1000 admissions (unpublished data). A recent retrospective study from Brazil reported an increase in *C. glabrata* candidemia, from 8 (3.5%) of 228 cases from 1995 through 2003 to 28 (10.6%) of 263 cases from 2005 through 2007 [44]. The study also reported a relationship between fluconazole use and a greater incidence of *C. glabrata* candidemia [44].

Candida guilliermondii and *Candida rugosa* are relatively uncommon agents of candidemia but appear to be increasingly reported [3], including in Latin America [3, 45–48]. A large pseudo-outbreak of *C. guilliermondii* fungemia was reported in a university hospital in Brazil [47]. Both *C. guilliermondii* and *C. rugosa* demonstrate decreased susceptibility to fluconazole and resistance to itraconazole [49, 50]. In a Brazilian study, *C. rugosa* exhibited increased resistance to both fluconazole and itraconazole over time [50].

As indicated in Table 1, antifungal resistance is infrequent in Latin America. In the largest study reporting the susceptibility profile of 1000 *Candida* bloodstream isolates, fluconazole resistance was restricted to 2 of 44 *C. glabrata* isolates, with no

trend to an increase in the proportion of resistance in 2 periods (1995–1999 and 2000–2003) [49].

Cryptococcosis. Cryptococcosis is caused by the *Cryptococcus neoformans* species complex. The geographic distribution of the disease, sources of *C. neoformans* infection, and clinical characteristics associated with the disease are summarized in Table 2 [51–54]. *C. neoformans* is the agent of cryptococcosis that affects immunosuppressed patients, such as patients with AIDS [52], SOT recipients, and patients with sarcoidosis or chronic lymphoproliferative diseases. By contrast, *Cryptococcus gattii* is the agent of the sporadic cryptococcosis that can affect immunocompetent individuals [55]. Although *C. neoformans* has a worldwide distribution [55], *C. gattii* is found in tree detritus (*Eucalyptus* species, *Laurus* species, and *Terminalia catappa*) [53] and is geographically restricted to tropical and subtropical climates, including Australia, Cambodia, Central Africa, Brazil, Mexico, and Paraguay [51]. However, outbreaks of *C. gattii* infection have been recently reported in Vancouver Island and the surrounding area [55].

The incidence of different *Cryptococcus* serotypes was evaluated in the IberoAmerican Cryptococcal Study Group: a total of 340 clinical, veterinary, and environmental isolates from Argentina, Brazil, Chile, Colombia, Mexico, Peru, Venezuela, Guatemala, and Spain were tested [56]. Of 177 clinical isolates obtained from patients with AIDS, 86% were serotype A, 7.4% were serotype AD hybrid, 3.4% were serotype D, and the remaining 2.8% were serotypes B and C [56]. In another study, 178 clinical isolates and 247 environmental isolates obtained from 5 regions of Colombia (1987–2004) demonstrated a clinical isolate profile of serotypes A (91.1% of isolates), B (8.4%), and C (0.5%) and an environmental isolate profile of serotypes A (44.2%), B (42.6%), and C (13.2%); no serotype D or AD isolates were identified [53]. Finally, in another study of 100

Table 2. *Cryptococcus neoformans* Species Complex

Species, varieties, and serotypes [51, 52]	Geographic location [51]	Clinical [52]	Source
<i>Cryptococcus neoformans</i> var. <i>grubii</i> (serotype A), <i>C. neoformans</i> var. <i>neoformans</i> (serotype D), and hybrid serotype AD	Of all 725 clinical isolates studied, 70% were serotype A. All cultures from Austria, Belgium, Denmark, France, Germany, Holland, Italy, Switzerland, and Japan and ~85% of isolates from Argentina, Canada, the United Kingdom, and the United States (except southern California) were <i>C. neoformans</i> serotypes A, D, or AD. Serotype D (9% of the total) was common in Europe but was found infrequently in other regions.	<i>C. neoformans</i> var. <i>grubii</i> (serotype A) causes almost all cases of cryptococcosis in patients with AIDS worldwide.	Soil enriched with pigeon excreta, decaying wood, caged birds, vegetables, and dairy products [54].
<i>Cryptococcus gattii</i> (serotypes B and C)	Prevalent only in tropical and subtropical regions. Serotype B was 4.5 times more prevalent than serotype C, and most type C isolates were from southern California.	Infections can be found in immunocompetent patients.	Tree detritus (eg, <i>Eucalyptus</i> species, <i>Laurus</i> species, and <i>Terminalia catappa</i>) [53].

Table 3. Summary of Latin American Case Histories of Invasive Phaeohyphomycosis

Study	Patient demographic characteristics		Diagnosis	Pathogen	Clinical history and treatment	Antifungal treatment	Outcome
	Sex	Age, years of origin					
Walz et al [96]	Male	33	Cerebral phaeohyphomycosis	<i>Cladophialophora bantiana</i>	Nasal and intravenous cocaine use	Amphotericin B and fluconazole	Fatal; patient died 105 days after first hospital visit
Nobrega et al [97]	Male	28	Cerebral abscess	<i>Fonsecaea pedrosi</i>	Immunocompetent, history of knife wound and abscess in right inguinal area positive for <i>Chromobacterium violaceum</i> 16 years before hospitalization	Amphotericin B (total dose, 1350 mg), surgery, itraconazole	Recovered but patient died of a surgical complication; no residual fungal disease was found at autopsy
Teixeira et al [98]	Male	34	Systemic infection	<i>Chaetomium globosum</i>	HCT recipient	Amphotericin B	Recovered but patient developed chronic graft-versus-host disease and died due to septicemia caused by <i>Enterobacter cloacae</i> , 1 year after transplantation
Negroni et al [99]	Female	41	Disseminated phaeohyphomycosis	<i>Exophiala spinifera</i>	No known immunosuppression; 12-year history of relapsing phaeohyphomycosis not durably treated with standard antifungals; the infection became disseminated and life-threatening during patient's pregnancy	Itraconazole plus fluconazole, amphotericin B; posaconazole salvage therapy initiated after premature delivery and was continued for 13 months, stopped for 7 months, and then continued for >2 years when an <i>Exophiala spinifera</i> nodule was found	Recovered

NOTE. HCT, hematopoietic cell transplantation.

clinical isolates of *C. neoformans* from Brazil, Venezuela, and Chile, of which 60 isolates were from human immunodeficiency virus (HIV)-positive patients, 89 isolates were *C. neoformans* (86 [96.6%] of which were serotype A) and 11 were *C. gattii* (9 [81.8%] of which were serotype B) [57]. All *C. gattii* isolates were from HIV-negative patients, and with the exception of the exclusive localization of *C. neoformans* serotype AD among Chilean isolates, no particular serotype distribution was related to any geographic area [57].

A report on HIV-related opportunistic diseases published by the Joint United Nations Programme on HIV/AIDS in 1998 reported the following prevalence rates for cryptococcosis: Zaire, 19% of cases of HIV-related opportunistic disease; Mexico, 7%–11%; United States, 7%; Brazil, 5%; Ivory Coast, 5%; and Thailand, 2% [58]. In a Colombian national survey that included 931 patients from 76 centers from 1997 through 2005, 78.1% had HIV infection; the mean annual incidence of cryptococcosis was found to be 2.4 cases per 1 million inhabitants in the general population and 3 cases per 1000 patients with AIDS [59].

Of >215,000 patients with AIDS registered in Brazil in 1980–2002, 6% had cryptococcosis at the time of diagnosis [60]. Estimates of the overall mortality due to cryptococcosis in Brazil range from 45% to 65%, and 1 study reported a mortality rate of 79% among patients with AIDS [61].

A Mexican autopsy study of 177 patients with AIDS identified central nervous system involvement by cryptococcosis in 10% of cases before the era of highly active antiretroviral therapy (HAART) [62]. In another Mexican study, among 211 *Cryptococcus* isolates, 183 (86.7% were *C. neoformans* var. *neoformans*, and 10.4% were var. *gattii*. AIDS was the most frequent underlying disease [63].

The adoption of HAART has been associated with a decrease in the incidence of opportunistic infections, including cryptococcosis. A single-center study conducted in Brazil reported a decrease in the incidence of central nervous system cryptococcosis among patients with AIDS from 7.7% in 1995 to 3.1% in 2001 [61]. In a case-control study conducted among HIV-positive Chilean patients, the prevalence of cryptococcosis was reduced by 66% with the use of HAART [64]. In another Chilean study involving 1057 HIV-positive patients, the prevalence of cryptococcal meningitis was reported to be reduced from 3.4% to 0% with the introduction of HAART in treatment-naïve patients [65].

OPPORTUNISTIC MOLD INFECTIONS

Invasive aspergillosis (IA). The incidence of IA is increasing, with estimates ranging from 2.6% to 6.9% [66–69], and it is most commonly caused by *Aspergillus fumigatus* [66, 69]. The main risk factors are prolonged and profound neutropenia and severe T cell-mediated immunodeficiency due to various fac-

tors, including high-dose corticosteroids, graft-versus-host disease, cytomegalovirus reactivation in HSCT recipients, and the use of monoclonal antibodies and nucleoside analogs [70–74]. A wide range of associated mortality rates (42%–77%) have been reported [66, 69, 70].

Data on IA incidence in Latin America are scarce. Preliminary data from a prospective survey involving HSCT recipients and patients with acute myeloid leukemia or myelodysplastic syndromes undergoing induction and consolidation chemotherapy at 8 hematology centers in Brazil (most of whom received fluconazole prophylaxis) reported that IA was the leading invasive mycosis (30 [6.5%] of 460 patients) and that its prevalence was 6 times greater among patients with acute myeloid leukemia [75]. An autopsy study reported 5 deaths due to IA among 925 pediatric patients in Mexico from 1976 through 1990 [76]. In another study, pulmonary IA was identified in 7 (2.2%) of 307 patients with AIDS in a Cuban autopsy study (1986–1997) [77].

Of 64 HSCT recipients who received fluconazole prophylaxis at 2 hospitals in São Paulo, Brazil, during the period 1993–1998, 5 developed invasive mold infections; 2 (5%) had invasive mold infections that were caused by *Aspergillus* [78].

Invasive fusariosis. *Fusarium* is a plant pathogen and a soil saprophyte that can cause a broad spectrum of infections in humans, including disseminated infection (invasive fusariosis) [79]. Risk factors for invasive fusariosis are similar to those for IA (prolonged and profound neutropenia and severe T cell-mediated immunodeficiency). Skin breakdowns, particularly at onychomycosis sites, may serve as portals of entry [79–82]. The mortality rate associated with invasive fusariosis ranges from 50% to ~90% [66, 83–86].

In a retrospective analysis of 84 patients (79 with hematologic malignant neoplasms and 5 with aplastic anemia) with invasive fusariosis who were treated in Brazil (11 centers) and the United States (1 center) [86], fever was the most frequent clinical manifestation (92% of cases), followed by skin lesions (77%). Fusariosis was disseminated in 79% of patients and localized in 10.7%; fungemia without apparent organ involvement was present in 10.7% [86]. The most frequently reported pathogen was *Fusarium solani* (in 18 of 30 patients); only 21% of patients were alive 90 days after diagnosis [86]. A retrospective review of 61 HSCT recipients (54 with allogeneic stem cell transplants and 7 with autologous stem cell transplants) who developed invasive fusariosis (2 centers in the United States and 7 in Brazil) during the period 1985–2001 found that disseminated infection, again with metastatic skin lesions, was the most frequent clinical presentation (75% of cases), followed by fungemia alone (11%) and sinusitis and pneumonia (6.6% each) [85]. Although the overall incidence of fusariosis (5.97 cases per 1000 transplant recipients) varied among the different institutions (range, 5.00–11.33 cases per 1000 transplant recipi-

ents), it did not vary among the countries (6.18 cases per 1000 transplant recipients in Brazil vs 5.89 cases per 1000 transplant recipients in the United States) [85]. Compared with US patients, Brazilian patients were younger, were more likely to have chronic myelogenous leukemia or aplastic anemia, were more likely to have received an human leukocyte antigen-compatible related donor transplant, and were more likely to be neutropenic when fusariosis was diagnosed [85]. The median duration of survival after diagnosis was 13 days; only 13% of patients were alive 90 days after diagnosis.

Other molds. Reports of zygomycosis from individual Latin American countries have been limited to case reports only [87–89]. The incidence of phaeohyphomycosis, an infection caused by dematiaceous fungi, appears to be increasing [90–93]. A 2002 review of 72 published cases of phaeohyphomycosis noted that 75% of cases (and 100% of those that involved *Scedosporium prolificans*) were reported from 1992 through 2001 [92]. Most patients were from Europe (28 patients) and North America (23), whereas there were fewer reports from Australia (9), the Middle East (4), South America (4), and Asia (3) [92]. The greatest number of cases were caused by *S. prolificans* (*Scedosporium inflatum*; 41.7%); other important causative species were *Bipolaris spicifera* (8.3%) and *Wangiella dermatitidis* (*Exophiala dermatitidis*; 6.9%) [92]. Major risk factors for developing phaeohyphomycosis are immunosuppression (especially neutropenia), malignant neoplasm (especially leukemia), SOT, heart valve replacement, diabetes, and asthma [92, 94]. The overall mortality rate in the 2002 case series was 79% (84% among patients with immunodeficiency) [92].

Reports of phaeohyphomycosis from individual Latin American countries have been limited, and there have been no published cases due to *S. prolificans*. From 1996 through 1997, 23 cases of fungemia due to nosocomial *Exophiala jeanselmei* (caused by contaminated hospital water) were diagnosed in Rio de Janeiro, Brazil [95]. Reports of other phaeohyphomycosis cases are summarized in Table 3 [96–99].

CONCLUSION

A number of clinically significant opportunistic infections occur in Latin America, each associated with specific risk factors. The incidence of some opportunistic infections is markedly different in Latin America than in other parts of the world. Still other opportunistic infections have not been studied enough to draw comparative conclusions. The profile of *Candida* species most closely associated with candidemia and other types of invasive candidiasis is different in Latin America than in North America and Europe. Consistent with trends in many other parts of the world, the incidence of invasive infections caused by some opportunistic mycoses in Latin America appears to be increasing.

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