ORIGINAL ARTICLE

Social, environmental and microbiologic aspects of endemic mycoses in Brazil

M. C. Costa[1], **N. Pereira de Sá**[2], **S. Johann**[2] **and D. A. Santos**[1]

1) *Laboratório de Micologia and* 2) *Laboratório de Taxonomia e Biologia de Leveduras, Departamento de Microbiologia, ICB-UFMG, Belo Horizonte, MG, Brazil*

Abstract

Many factors that lead to host immunosuppression are clearly known to predispose the host to fungal diseases, significantly influencing the occurrence of mycoses. However, little or nothing has been discussed regarding social or economic factors that can influence the occurrence of diseases caused by fungi. In this minireview, we discuss several factors that may affect the occurrence of mycoses in Brazil, a continentally extended country that is marked by large climatic variations and severe socioeconomic distortions that may limit access to health services for the population.

Keywords: Brazil, cutaneous, environmental, invasive yeasts, mycoses, opportunistic moulds, social, subcutaneous

Original Submission: 5 October 2018; **Revised Submission:** 14 November 2018; **Accepted:** 14 November 2018

Article published online: 21 February 2019

Corresponding author: D. de Assis Santos, Departamento de Microbiologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Av Antônio Carlos, 6627, PO Box 486, 31270-901, Belo Horizonte, MG, Brazil.

E-mail: das@ufmg.br

Introduction

Mycoses are diseases that occur when fungi colonize and damage a host. Fungi that cause disease in humans and other animals are endogenous (when they are components of the host's normal microbiota) or exogenous (when they are acquired from the environment). In all cases, factors such as immunosuppression and external factors such as access to health services (even preventive or therapeutic) influence the incidence of mycoses. It is also important to consider additional factors, such as occupational conditions and climatic variations. Brazil has both humid and drier regions, ranging from the north (near the Equator), through a centre with low humidity, to the south (which is below the Tropic of Capricorn); and extremes can influence the survival and proliferation of environmental microorganisms, and consequently affect the contact of these microorganisms with hosts [1,2].

The Brazilian territory is marked by deep regional economic inequalities; the distribution of poor cities remains concentrated in the north and northeast [3]. Unfortunately, in 2010, there were 14.6 million people, 10 years of age or older, who did not know how to read, a 9.0% illiteracy rate that reached 29.4% for the elderly. The average monthly income in 2010 was only R$1202 (equivalent to US$707 in that year), with lower incomes in the north and northeast regions, which also suffered from lower access to sanitary sewage and had the highest rates of malnutrition [4,5]. Furthermore, diagnostic and therapeutic equipment of medium and high complexity is concentrated mainly in capitals, metropolitan regions and in a few regional poles, resulting in a large variation in their availability to patients [3]. Considering the impediments to health services access, it is probable that the epidemiologic data currently available do not reflect reality because correct diagnoses may not be performed.

AIDS and organ transplants are classic conditions capable of immunocompromising a host. In Brazil, from 1980 to 2017, 882 810 AIDS cases were identified, with an average of 40 000 new cases in the last 5 years. Interestingly, there was a

https://doi.org/10.1016/j.nmni.2018.11.004

reduction in the detection rate of AIDS in south and southeastern states and an increase in detection in the north and northeastern states [6]. From 2007 to 2017, there were 72 807 solid organ transplantations (heart, liver, lungs, pancreas and kidney) performed [7].

In this minireview we provide details available on endemic mycoses with high occurrence in Brazil, taking into account all the information mentioned above. Table 1 summarizes the data discussed in the text.

Superficial and cutaneous mycosis

Superficial fungal infections affect the skin, hair and nails of 40% of world's population, making these one of the most prevalent forms of infection [8–10]. The main aetiologic agents are the dermatophytes (*Trichophyton, Microsporum* and *Epidermophyton*) and yeasts (*Candida* and *Malassezia*) [11–13].

Dermatophytes affect healthy individuals, but predisposing factors includes dry skin, diabetes, HIV infection, immunosuppressed states, obesity, certain athletic activities and possibly smoking [14,15]. *T. rubrum* (35.6%) is the most frequent species in many studies, most likely representing the profile of urban dermatophyte microbiota, followed by *T. mentagrophytes, T. interdigitale, M. gypseum, T. tonsurans, E. floccosum* and *M. canis* [12,13,15,16]. Onychomycosis is the most common clinical condition in adults; *T. rubrum* is the fungus most frequently isolated and *Candida parapsilosis* ranks second [8,17]. In children aged ≤10 years, the most frequent site of infection was the scalp, mainly caused by *M. canis* (in the south and southeastern regions) and *T. tonsurans* (in the north and northeastern regions) [12,18]. Onychomycoses are frequently associated with nail trauma, excessively sweaty feet, not wearing sandals in public bathrooms and the prolonged use of shoes during the day [19–21]. Onychomycoses affect military, construction, agricultural and forestry workers; and housewives and manual labourers are also at risk as a result of long hours of immersion of hands and feet in water.

Malassezia is member of the human skin microbiota and a health problem in Brazil. This pathogen grows better in moist and humid environments and causes pityriasis versicolor, prevalent in tropical and subtropical countries. In retrospective studies in south and northwest of Brazil, the disease is more prevalent in men than women, and reports show that growth of *Malassezia* tends to increase in summer when temperatures are high and is due to sweat [13,22]. The age group that commonly is affected with pityriasis versicolor is 20 to 40 years [12,13].

Warmer temperatures and altered rainfall patterns are likely to increase the range and burden of dermatomycosis. However, heterogeneous study design has limited the assessment of numerous, potentially confounding factors, and the striking differences that have been observed cannot reliably be

TABLE 1. Summary of aetiologic agents and occurrence of endemic mycosis in Brazil

Site	Mycoses	Aetiologic agent	Local of more incidence	Risk group
Superficial	Malasseziosis [11–13,22]	*Malassezia* spp.	Cosmopolitan disease, with high influence of seasonality of moist and humid climates	Patients undergoing systemic corticotherapy and hosts with intense sweat
Cutaneous	Dermatophytosis [14–16,18–20]	*Trichophyton* spp., *Microsporum* spp. and *Epidermophyton floccosum*	Cosmopolitan disease	People with dry skin, school-age children, rural workers and athletes. People with diabetes, HIV/AIDS infection, immunosuppressed and obese
Subcutaneous	Sporotrichosis [29,31]	*Sporothrix* spp.	Higher incidence occurs in Rio de Janeiro and São Paulo	Children or housewives with frequent contact with domestic and stray cats
	Chromoblastomycosis [23,25–27]	*Fonsecaea, Cladophialophora* and *Rhinocladiella*	Higher incidence occurs in Maranhão and Pará	Rural workers, mainly babassu extractors
Systemic (primary pathogens)	Paracoccidioidomycosis [37–39,41,42,44]	*Paracoccidioides* spp.	Several endemic areas with higher incidence: São Paulo, Paraná, Rio Grande do Sul, Goiás; and also regions with progressive devastation of tropical forests	Working-age men and farmers in contact with soil
	Histoplasmosis [47,48]	*Histoplasma capsulatum*	Higher incidence occurs in regions with caves and/or with progressive devastation of tropical forests	HIV/AIDS patients, rural workers, speleologists, tourists in contact with bat guano and soil
	Coccidioidomycosis [49,50,52,53]	*Coccidioides immitis*	Endemic areas with dry climates, mainly Piauí, Ceará, Bahia and Maranhão; also regions with progressive devastation of tropical forests	Rural workers, armadillo hunters and constructors in contact with soil
Opportunistic yeasts and moulds	Candidiasis [12,13,69–71] (dermatitis, mucocutaneous, bloodstream)	*Candida* spp.	Cosmopolitan disease	Immunocompromised hosts, HIV/AIDS patients, patients with haematologic cancer and stem-cell transplant recipients
	Cryptococcosis [57–59]	*Cryptococcus* spp.	Cosmopolitan disease	Immunocompromised male hosts, HIV/AIDS patients, transplant recipients
	Aspergillosis and fusariosis [72–75]	*Aspergillus* spp., *Fusarium* spp.	Cosmopolitan disease	Hospitalized and immunocompromised hosts, patients with HIV/AIDS, haematologic cancer and stem-cell transplant recipients

attributed to variations in climate. Furthermore, despite the large occurrence of these diseases, the diagnostic methodologies (direct microscopy and culture) remain ineffective to assess actual epidemiology, although there is no demand for more sensitive and rapid methodologies.

Subcutaneous mycosis

With a high occurrence in Brazil, subcutaneous mycoses are caused by dematiaceous fungi and the *Sporothrix schenckii* complex [23,24]. The infection occurs by traumatic inoculation of the pathogen, and the disease may be chronic, leading to fibrotic and granulomatous reactions. Although subcutaneous mycoses are relevant, studies reporting the global burden of neglected diseases rarely mention its occurrence in Brazil. Among patients, rural workers or farmers in regions without access to health services are commonly affected. The Amazon region of Brazil has been considered to be the main endemic area of chromoblastomycosis since the majority of patients are from areas with high pluviometric indexes, with elevated temperatures and dense forestation. Maranhão ranks first in chromoblastomycosis notifications [23], with higher occurrence in babassu (*babaçu*) coconut extractors. Also, there are epidemiologic data from the states of São Paulo, Rio de Janeiro and Rio Grande do Sul [25]. The species *Fonsecaea pedrosoi, F. monophora* and *F. nubica* are the most prevalent agents. *Cladophialophora carrionii* is the only species that is restricted to semiarid areas with *Cactaceae* as the main vegetation [23]. *Rhinocladiella aquaspersa* is an uncommon species found in humid as well as dry climates [26]. The diagnoses, which include diagnoses via tissue biopsy and culture (standard methods of subcutaneous mycosis diagnosis), are not always performed in endemic areas [27], which causes the epidemiologic data to be underestimated.

Obtained from animals and plant debris, sporotrichosis is a neglected zoonotic mycosis caused by pathogenic fungi belonging to the *Sporothrix schenckii* complex, with *S. brasiliensis* as the most prevalent aetiologic agent [24,28]. Classical infection is associated with traumatic subcutaneous inoculation of soil, plants or organic matter contaminated with fungus; but a large number of data also report transmission occurring from infected animals, with cats being the main vehicle of fungi transmission between animal and human [29,30]. In Rio de Janeiro state, this disease reached an epidemic status, with over 4700 domestic felines and around 4000 humans affected since the mid-1990s [31,32]. Many patients are immunocompetent and often are from rural areas, i.e. farmers and gardeners [33]. In urban areas, endemic regions of sporotrichosis in Brazil are characterized by poor sanitation, substandard housing and little or no access to health services. Patients are mainly children or housewives with frequent contact with domestic and stray cats [29,32–34]; indeed, patients report that they need to have cats in their houses as a mode of biological control of rodents. The most severe cases occur in HIV patients, with a higher number of hospitalizations and deaths [33,35].

Systemic mycosis

The main agents of systemic mycosis are the thermodimorphic fungi belonging to the genera *Paracoccidioides, Histoplasma, Coccidioides* and also the yeast *Cryptococcus,* obtained by inhaling infectious propagules. Paracoccidioidomycosis is a granulomatous disease, endemic in South and Latin America, with about 80% of the patients from Brazil (3360 to 5600 cases of paracoccidioidomycosis annually), mainly in the states of São Paulo, Paraná, Rio Grande do Sul, Goiás and Rondônia [36,37]. Paracoccidioidomycosis is caused by *Paracoccidioides brasiliensis* (with a wide distribution in the country) and *P. lutzii* (restricted to the centre-west region) [38–40]. The most frequently affected individuals are working-age men, probably because the transition to parasitic forms of yeast can be inhibited by the action of mammalian oestrogen [41,42]. Epidemiologic data have suggested that in the endemic regions, *Paracoccidioides* spp. exists as a saprophytic fungus in plants and soil. This corroborates the fact that the major risk factor for acquiring infection is any activity related to the management of soil contaminated with the fungus, such as agriculture, earthworks, soil preparation, gardening and transportation of vegetable products [43]. It has been suggested that the fungus resides at a depth of 2 to 20 cm in the soil, that it occurs in places containing natural and/or anthropic disturbed vegetation near water sources and that humidity, precipitation and soil water storage are factors that lead to the growth and sporulation of the fungus [43,44].

Histoplasmosis is caused mainly by *Histoplasma capsulatum,* which is generally found in regions with nitrogen-rich, acid soil and with relative humidity between 60% and 87% and average temperature of 27°C. Frequently it is associated with the presence of bird and bat excreta, but air currents can carry the conidia for longer distances, making it possible for people who have not had direct contact with contaminated sites to contract the infection [45]. In Brazil, there is no compulsory notification (similar to other systemic mycoses), and most of the data are based on cutaneous tests with histoplasmin. Information presented in the surveillance and control proposal of the Ministry of Health in 2010 showed a significant prevalence of histoplasmosis in the south (6.30–89%), southeast (4.60–94.7%), northeast (2.60–61.50), central west (9.60–63.10%) and north (12.8- 50.1%) of the country, according to histoplasmin test results. Nevertheless, in Brazil, there are several endemic areas, and occasionally cases of small outbreaks arise as a result of activities that lead a group of people to have contact with contaminated sites [46–48]. In the state of Ceará, Brilhante et al. [47] estimated that the mortality rate by histoplasmosis among HIV/AIDS patients was 42.3% in a 5-year period.

Aetiologic agents of coccidioidomycosis, *Coccidioides immitis* and *C. posadasii,* are isolated from areas of arid climate with alkaline and sandy soil and very hot summers [49]. In Brazil, the first reports of this disease are from the late 1970s, in the states of Piauí and Ceará [50,51]. Currently endemic areas for coccidioidomycosis are recognized in the states of Piauí, Ceará, Bahia and Maranhão [46,52]. In the state of Piauí, considered the highest density, most of the small outbreaks were associated with armadillo hunting [53].

Cryptococcosis is a systemic mycosis that can occur as both primary and opportunistic infections [54], with meningoencephalitis as the most severe manifestation [55]. This disease is caused by *Cryptococcus neoformans* and *C. gattii,* and is one of the most important opportunistic diseases in HIV/AIDS patients and one of the major contributors to the early mortality of immunocompromised patients, accounting for 13% to 44% of the deaths of HIV-infected individuals in poor countries [56]. It is estimated that in Latin America, *C. neoformans* is widespread and responsible for more than 90% of the cases of cryptococcosis, affecting predominantly patients with HIV [57]. In Brazil, mortality rate ranged from 32% to 60% in HIV-infected population. Meningeal cryptococcosis mostly caused by *C. neoformans* occurs predominantly in these patients despite highly active antiretroviral therapy being widely distributed in Brazil [58–60].

Invasive yeast and opportunistic mould diseases

Several filamentous fungi and yeast are agents of invasive fungal infections in immunocompromised patients. These are mainly patients with haematologic cancer and stem-cell transplant recipients [61,62]. In Brazil, candidaemia is associated with high morbidity and mortality rates [63,64]. In a multicentre surveillance study in Brazil, *C. albicans* (34.3%), *C. parapsilosis* (24.1%), *C. tropicalis* (15.3%) and *C. glabrata* (10.2%) were the most prevalent species in bloodstream infections. Emerging yeast, such as *Saccharomyces cerevisiae,* has also appeared, causing infection in Brazil [65–67]. It is also important to mention the emergence of the yeasts *Trichosporon mycotoxinivorans,* causing invasive infections in Latin America [68], and *C. auris,* a globally emerging yeast pathogen with a high capability of developing multidrug antifungal resistance, which has not been yet reported in the Brazil. This may have occurred because difficulty in identification, since it is not identified by most of the methods used within the hospital laboratories in Brazil. Usually the identification of yeast is made by CHROMagar *Candida* and other tests, such as germ tube or physiological tests. However, these techniques have failed to identify organisms at the species level, which has an impact on the treatment of patients since there are species resistant to certain antifungals [62,69–71].

In Brazil, several moulds have already been isolated that cause opportunistic systemic infection, such as *Aspergillus* section Flavi [72]. Fusariosis was also reported in a haematology ward and was associated with the rise of Brazilian plantations (mainly soybean) and pasture areas where previously there was native vegetation, with a consequent loss of fungal richness and diversity [73,74]. In general little is known about the prevalence of invasive yeast and opportunistic mould diseases because there are few medical centres able to perform accurate identification at the species level [72]. Indeed, this is true for the identification of opportunistic filamentous fungi, such as *Aspergillus,* that has been identified only by colony morphology and microscopic characteristics and may not be reliable for distinguishing between *Aspergillus* species [72,75].

Conclusion

Performing research on these neglected mycosis, as well as knowing endemic areas, how climate influences their occurrence and the population at risk, may improve the ability to combat the high occurrence of these diseases. The attention of public health officials is vital to understanding the real situation of endemic mycoses in Brazil. Furthermore, new public policies and investment are needed to improve the clinical diagnosis, professional training and investment in antifungals for the treatment of fungal infections.

Acknowledgements

DAS is a research fellow of the Brazilian National Council for Scientific and Technological Development (CNPq) (grant 302670/2017-3).

Conflict of interest

None declared.

References

[1] Diniz FA, Ramos AM, Rebello ERG. Brazilian climate normals for 1981–2010. Pesq Agropec Bras 2018;53:131–43.

[2] Pachauri RK, Meyer LA. Contribution of working groups I, II and III to the fifth assessment report of the intergovernmental panel on climate change. In: Climate Change 2014: synthesis report. Geneva: IPCC; 2014. p. 151.

[3] Albuquerque MV, Viana ALD, Lima LD, Ferreira MP, Fusaro ER, Iozzi FL. Regional health inequalities: changes observed in Brazil from 2000–2016. Cien Saude Colet 2017;22:1055–64.

[4] Santos TGD, Silveira JACD, Longo-Silva G, Ramires EKNM, Menezes RCE. Trends and factors associated with food insecurity in Brazil: the national household sample survey, 2004, 2009, and 2013. Cad Saude Publica 2018;34:e00066917.

[5] Instituto Brasileiro de Geografia e Estatística (IBGE). Censo demográfico. 2010. Available at: https://ww2.ibge.gov.br/home/estatistica/populacao/censo2010/default.shtm.

[6] Da Saúde Ministério, de Vigilância Departamento. Prevenção e Controle das IST, do HIV/AIDS e das Hepatites Virais. Boletim epidemiológico HIV/AIDS. 2017. Available at: http://www.aids.gov.br/pt-br/pub/2017/boletim-epidemiologico-hivaids-2017.

[7] Registro Brasileiro de Transplantes (RBT). Dados númericos da doação de órgãos etransplantes realizados por estado e instituição no período: Janeiro/Setembro. 2017. Available at: http://www.abto.org.br/abtov03/upload/file/rbt/2017/rbttrim3-leitura.pdf.

[8] Thomas J, Jacobson GA, Narkowicz CK, Peterson GM, Burnet H, Sharpe C. Toenail onychomycosis: an important global disease burden. J Clin Pharm Ther 2010;35:497–519.

[9] Nweze EI, Eke IE. Dermatophytes and dermatophytosis in the eastern and southern parts of Africa. Med Mycol 2018;56:13–28.

[10] Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses 2008;51(Suppl. 4):2–15.

[11] White TC, Findley K, Dawson TL, Scheynius A, Boekhout T, Cuomo CA, et al. Fungi on the skin: dermatophytes and Malassezia. Cold Spring Harb Perspect Med 2014;4:a019802.

[12] Silva-Rocha WP, de Azevedo MF, Chaves GM. Epidemiology and fungal species distribution of superficial mycoses in northeast Brazil. J Mycol Med 2017;27:57–64.

[13] Di Chiacchio N, Madeira CL, Humaire CR, Silva CS, Fernandes LH, Dos Reis AL. Superficial mycoses at the hospital do servidor público municipal de São Paulo between 2005 and 2011. An Bras Dermatol 2014;89:67–71.

[14] Qadim HH, Golforoushan F, Azimi H, Goldust M. Factors leading to dermatophytosis. Ann Parasitol 2013;59:99–102.

[15] da Silva BC, Paula CR, Auler ME, La Ruiz S, Dos Santos JI, Yoshioka MC, et al. Dermatophytosis and immunovirological status of HIV-infected and AIDS patients from Sao Paulo city, Brazil. Mycoses 2014;57:371–6.

[16] Heidrich D, Garcia MR, Stopiglia CD, Magagnin CM, Daboit TC, Vetoratto G, et al. Dermatophytosis: a 16-year retrospective study in a metropolitan area in southern Brazil. J Infect Dev Ctries 2015;9:865–71.

[17] Heidrich D, Stopiglia CD, Magagnin CM, Daboit TC, Vettorato G, Amaro TG, et al. Sixteen years of dermatomycosis caused by *Candida* spp. in the metropolitan area of Porto Alegre, Southern Brazil. Rev Inst Med Trop Sao Paulo 2016;58:14.

[18] Veasey JV, Miguel BAF, Mayor SAS, Zaitz C, Muramatu LH, Serrano JA. Epidemiological profile of tinea capitis in São Paulo City. An Bras Dermatol 2017;92:283–4.

[19] Leite DP, Amadio JV, Simões SA, de Araújo SM, da Silva NM, Anzai MC, et al. Dermatophytosis in military in the central-west region of Brazil: literature review. Mycopathologia 2014;177:65–74.

[20] Costa-Orlandi CB, Magalhães GM, Oliveira MB, Taylor EL, Marques CR, de Resende-Stoianoff MA. Prevalence of dermatomycosis in a Brazilian tertiary care hospital. Mycopathologia 2012;174:489–97.

[21] Ongsri P, Bunyaratavej S, Leeyaphan C, Pattanaprichakul P, Ongmahutmongkol P, Komoltri C, et al. Prevalence and clinical correlation of superficial fungal foot infection in Thai naval rating cadets. Mil Med 2018. https://doi.org/10.1093/milmed/usx187.

[22] Morais PM, Cunha MG, Frota MZ. Clinical aspects of patients with pityriasis versicolor seen at a referral center for tropical dermatology in Manaus, Amazonas, Brazil. An Bras Dermatol 2010;85:797–803.

[23] Gomes RR, Vicente VA, Azevedo CM, Salgado CG, da Silva MB, Queiroz-Telles F, et al. Molecular epidemiology of agents of human chromoblastomycosis in Brazil with the description of two novel species. PLoS Negl Trop Dis 2016;10:e0005102.

[24] Mora-Montes HM, Dantas AS, Trujillo-Esquivel E, de Souza Baptista AR, Lopes-Bezerra LM. Current progress in the biology of members of the *Sporothrix schenckii* complex following the genomic era. FEMS Yeast Res 2015;15:fov065.

[25] Marques GF, Masuda PY, Sousa JM, Barreto JA, Wachholz PA. Clinical and demographic profile of chromoblastomycosis in a referral service in the midwest of São Paulo state (Brazil). An Bras Dermatol 2015;90:140–2.

[26] González GM, Rojas OC, González JG, Kang Y, de Hoog GS. Chromoblastomycosis caused by *Rhinocladiella aquaspersa*. Med Mycol Case Rep 2013;2:148–51.

[27] Queiroz-Telles F, Esterre P, Perez-Blanco M, Vitale RG, Salgado CG, Bonifaz A. Chromoblastomycosis: an overview of clinical manifestations, diagnosis and treatment. Med Mycol 2009;47:3–15.

[28] Téllez MD, Batista-Duharte A, Portuondo D, Quinello C, Bonne-Hernández R, Carlos IZ. *Sporothrix schenckii* complex biology: environment and fungal pathogenicity. Microbiology 2014;160:2352–65.

[29] Macêdo-Sales PA, Souto SRLS, Destefani CA, Lucena RP, Machado RLD, Pinto MR, et al. Domestic feline contribution in the transmission of *Sporothrix* in Rio de Janeiro state, Brazil: a comparison between infected and non-infected populations. BMC Vet Res 2018;14:19.

[30] Alves SH, Boettcher CS, Oliveira DC, Tronco-Alves GR, Sgaria MA, Thadeu P, et al. *Sporothrix schenckii* associated with armadillo hunting in southern Brazil: epidemiological and antifungal susceptibility profiles. Rev Soc Bras Med Trop 2010;43:523–5.

[31] Pereira SA, Gremião ID, Kitada AA, Boechat JS, Viana PG, Schubach TM. The epidemiological scenario of feline sporotrichosis in Rio de Janeiro, state of Rio de Janeiro, Brazil. Rev Soc Bras Med Trop 2014;47:392–3.

[32] Lopes JO, Alves SH, Mari CR, Brum LM, Westphalen JB, Altermann MJ, et al. Epidemiology of sporotrichosis in the central region of Rio Grande do Sul. Rev Soc Bras Med Trop 1999;32:541–5.

[33] Freitas DF, Valle AC, da Silva MB, Campos DP, Lyra MR, de Souza RV, et al. Sporotrichosis: an emerging neglected opportunistic infection in HIV-infected patients in Rio de Janeiro, Brazil. PLoS Negl Trop Dis 2014;8:e3110.

[34] Almeida-Paes R, de Oliveira MM, Freitas DF, do Valle AC, Zancopé-Oliveira RM, Gutierrez-Galhardo MC. Sporotrichosis in Rio de Janeiro, Brazil: *Sporothrix brasiliensis* is associated with atypical clinical presentations. PLoS Negl Trop Dis 2014;8:e3094.

[35] Ottonelli Stopiglia CD, Magagnin CM, Castrillón MR, Mendes SD, Heidrich D, Valente P, et al. Antifungal susceptibilities and identification of species of the *Sporothrix schenckii* complex isolated in Brazil. Med Mycol 2014;52:56–64.

[36] Prado M, Silva MB, Laurenti R, Travassos LR, Taborda CP. Mortality due to systemic mycoses as a primary cause of death or in association with AIDS in Brazil: a review from 1996 to 2006. Mem Inst Oswaldo Cruz 2009;104:513–21.

[37] Martinez R. New trends in paracoccidioidomycosis epidemiology. J Fungi (Basel) 2017. https://doi.org/10.3390/jof3010001.

[38] Carrero LL, Niño-Vega G, Teixeira MM, Carvalho MJ, Soares CM, Pereira M, et al. New *Paracoccidioides brasiliensis* isolate reveals unexpected genomic variability in this human pathogen. Fungal Genet Biol 2008;45:605–12.
[39] Teixeira MM, Theodoro RC, de Carvalho MJ, Fernandes L, Paes HC, Hahn RC, et al. Phylogenetic analysis reveals a high level of speciation in the *Paracoccidioides* genus. Mol Phylogenet Evol 2009;52:273–83.
[40] Teixeira MM, Theodoro RC, Nino-Vega G, Bagagli E, Felipe MS. *Paracoccidioides* species complex: ecology, phylogeny, sexual reproduction, and virulence. PLoS Pathog 2014;10:e1004397.
[41] San-Blas G, Niño-Vega G, Iturriaga T. *Paracoccidioides brasiliensis* and paracoccidioidomycosis: molecular approaches to morphogenesis, diagnosis, epidemiology, taxonomy and genetics. Med Mycol 2002;40:225–42.
[42] Bocca AL, Amaral AC, Teixeira MM, Sato PK, Sato P, Shikanai-Yasuda MA, et al. Paracoccidioidomycosis: eco-epidemiology, taxonomy and clinical and therapeutic issues. Future Microbiol 2013;8:1177–91.
[43] Shikanai-Yasuda MA, Mendes RP, Colombo AL, Queiroz-Telles F, Kono ASG, Paniago AMM, et al. Brazilian guidelines for the clinical management of paracoccidioidomycosis. Rev Soc Bras Med Trop 2017;50:715–40.
[44] Barrozo LV, Benard G, Silva ME, Bagagli E, Marques SA, Mendes RP. First description of a cluster of acute/subacute paracoccidioidomycosis cases and its association with a climatic anomaly. PLoS Negl Trop Dis 2010;4:e643.
[45] Wheat LJ, Freifeld AG, Kleiman MB, Baddley JW, McKinsey DS, Loyd JE, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. Clin Infect Dis 2007;45:807–25.
[46] Deus Filho A, Deus AC, Meneses AeO, Soares AS, Lira AL. Skin and mucous membrane manifestations of coccidioidomycosis: a study of thirty cases in the Brazilian states of Piauí and Maranhão. An Bras Dermatol 2010;85:45–51.
[47] Brilhante RS, Fechine MA, Mesquita JR, Cordeiro RA, Rocha MF, Monteiro AJ, et al. Histoplasmosis in HIV-positive patients in Ceará, Brazil: clinical-laboratory aspects and *in vitro* antifungal susceptibility of *Histoplasma capsulatum* isolates. Trans R Soc Trop Med Hyg 2012;106:484–8.
[48] Faiolla RC, Coelho MC, Santana RC, Martinez R. Histoplasmosis in immunocompetent individuals living in an endemic area in the Brazilian southeast. Rev Soc Bras Med Trop 2013;46:461–5.
[49] Laniado-Laborin R. Expanding understanding of epidemiology of coccidioidomycosis in the Western Hemisphere. Ann N Y Acad Sci 2007;1111:19–34.
[50] Gomes OM, Serrano RP, Pradel HO, Barros Moraes NL, Varella AL, Fiorelli AI, et al. Coccidioidomicose pulmonar: primeiro caso nacional. AMB Rev Assoc Med Bras 1978;24:167–8.
[51] Vianna H, Passos HV, Sant'ana AV. Coccidioidomicose: relato do primeiro caso ocorrido em nativo do Brasil. Rev Inst Med Trop Sao Paulo 1979;21:51–5.
[52] Cordeiro RA, Brilhante RS, Rocha MF, Bandeira SP, Fechine MA, de Camargo ZP, et al. Twelve years of coccidioidomycosis in Ceará State, northeast Brazil: epidemiologic and diagnostic aspects. Diagn Microbiol Infect Dis 2010;66:65–72.
[53] de Macêdo RC, Rosado AS, da Mota FF, Cavalcante MA, Eulálio KD, Filho AD, et al. Molecular identification of *Coccidioides* spp. in soil samples from Brazil. BMC Microbiol 2011;11:108.
[54] Mitchell TG, Perfect JR. Cryptococcosis in the era of AIDS—100 years after the discovery of *Cryptococcus neoformans*. Clin Microbiol Rev 1995;8:515–48.
[55] Kwon-Chung KJ, Fraser JA, Doering TL, Wang Z, Janbon G, Idnurm A, et al. *Cryptococcus neoformans* and *Cryptococcus gattii*, the etiologic agents of cryptococcosis. Cold Spring Harb Perspect Med 2014;4:a019760.
[56] Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. AIDS 2009;23:525–30.
[57] Firacative C, Lizarazo J, Illnait-Zaragozí MT, Castañeda E, Latin American Cryptococcal Study Group. The status of cryptococcosis in Latin America. Mem Inst Oswaldo Cruz 2018;113:e170554.
[58] de Azambuja AZ, Wissmann Neto G, Watte G, Antoniolli L, Goldani LZ. Cryptococcal meningitis: a retrospective cohort of a Brazilian reference hospital in the post-HAART era of universal access. Can J Infect Dis Med Microbiol 2018;2018:6512468.
[59] Nunes JO, Tsujisaki RAS, Nunes MO, Lima GME, Paniago AMM, Pontes ERJC, et al. Cryptococcal meningitis epidemiology: 17 years of experience in a state of the Brazilian Pantanal. Rev Soc Bras Med Trop 2018;51:485–92.
[60] Aguiar PADF, Pedroso RDS, Borges AS, Moreira TA, Araújo LB, Röder DVDB. The epidemiology of cryptococcosis and the characterization of *Cryptococcus neoformans* isolated in a Brazilian university hospital. Rev Inst Med Trop Sao Paulo 2017;59:e13.
[61] Garcia-Vidal C, Upton A, Kirby KA, Marr KA. Epidemiology of invasive mold infections in allogeneic stem cell transplant recipients: biological risk factors for infection according to time after transplantation. Clin Infect Dis 2008;47:1041–50.
[62] Colombo AL, Júnior JNA, Guinea J. Emerging multidrug-resistant *Candida* species. Curr Opin Infect Dis 2017;30:528–38.
[63] Nucci M, Queiroz-Telles F, Alvarado-Matute T, Tiraboschi IN, Cortes J, Zurita J, et al. Epidemiology of candidemia in Latin America: a laboratory-based survey. PLoS One 2013;8:e59373.
[64] Doi AM, Pignatari AC, Edmond MB, Marra AR, Camargo LF, Siqueira RA, et al. Epidemiology and microbiologic characterization of nosocomial candidemia from a Brazilian national surveillance program. PLoS One 2016;11:e0146909.
[65] de Oliveira RB, Atobe JH, Souza SA, de Castro Lima Santos DW. Epidemiology of invasive fungal infections in patients with acquired immunodeficiency syndrome at a reference hospital for infectious diseases in Brazil. Mycopathologia 2014;178:71–8.
[66] Souza Goebel C, de Mattos Oliveira F, Severo LC. *Saccharomyces cerevisiae* infections. Rev Iberoam Micol 2013;30:205–8.
[67] Guimarães LF, Halpern M, de Lemos AS, de Gouvêa EF, Gonçalves RT, da Rosa Santos MA, et al. Invasive fungal disease in renal transplant recipients at a Brazilian center: local epidemiology matters. Transplant Proc 2016;48:2306–9.
[68] Almeida JN, Francisco EC, Barberino MGMA, Silva LVRF, Brandão OM, Colombo AL, et al. Emergence of *Trichosporon mycotoxinivorans* (*Apiotrichum mycotoxinivorans*) invasive infections in Latin America. Mem Inst Oswaldo Cruz 2017;112:719–22.
[69] Kathuria S, Singh PK, Sharma C, Prakash A, Masih A, Kumar A, et al. Multidrug-resistant *Candida auris* misidentified as *Candida haemulonii:* characterization by matrix-assisted laser desorption ionization–time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by VITEK 2, CLSI broth microdilution, and Etest method. J Clin Microbiol 2015;53:1823–30.
[70] Chowdhary A, Sharma C, Meis JF. *Candida auris:* a rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLoS Pathog 2017;13:e1006290.
[71] Chowdhary A, Voss A, Meis JF. Multidrug-resistant *Candida auris:* 'new kid on the block' in hospital-associated infections? J Hosp Infect 2016;94:209–12.
[72] Negri CE, Gonçalves SS, Xafranski H, Bergamasco MD, Aquino VR, Castro PT, et al. Cryptic and rare *Aspergillus* species in Brazil: prevalence in clinical samples and *in vitro* susceptibility to triazoles. J Clin Microbiol 2014;52:3633–40.

[73] Nucci M, Varon AG, Garnica M, Akiti T, Barreiros G, Trope BM, et al. Increased incidence of invasive fusariosis with cutaneous portal of entry, Brazil. Emerg Infect Dis 2013;19:1567–72.
[74] de Castro AP, Quirino BF, Pappas G, Kurokawa AS, Neto EL, Krüger RH. Diversity of soil fungal communities of Cerrado and its closely surrounding agriculture fields. Arch Microbiol 2008;190:129–39.
[75] Samson RA, Varga J, Witiak SM, Geiser DM. The species concept in *Aspergillus:* recommendations of an international panel. Stud Mycol 2007;59:71–3.