The emerging epidemiology of mould infections in developing countries

Arunaloke Chakrabarti and Rachna Singh

Division of Mycology, Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Correspondence to Dr Arunaloke Chakrabarti, MD, Professor and In-Charge, Division of Mycology, Department of Medical Microbiology, PGIMER, Chandigarh 160012, India
Tel: +91 172 2755156;
e-mail: arunaloke@hotmail.com

Current Opinion in Infectious Diseases 2011, 24:000–000

Purpose of review

The present review describes the emerging trends of mould infections in developing countries, and highlights the major epidemiological differences from the developed countries.

Recent findings

The limited data available from developing countries suggest an alarming increase in invasive mould infections, especially aspergillosis and mucormycosis, and also a difference in risk factors and causative agents between the developed and developing world. Sino-orbital, cerebral and ophthalmic infections due to *Aspergillus flavus* are the major clinical types in aspergillosis, after pulmonary aspergillosis. *Aspergillus* and *Fusarium* spp. are frequent causes of trauma-associated keratitis in agricultural workers. Rhino-orbito-cerebral presentation associated with uncontrolled diabetes is the predominant mucormycosis. Isolated renal mucormycosis has emerged as a new clinical entity. *Apophysomyces elegans* and *Mucor irregularis* are emerging species in these regions and uncommon agents such as *Rhizopus homothallicus* have also been reported. Many pathogens are geographically restricted, with *Pythium insidionum*, *Rhinocladiella mackenziei* and *M. irregularis* being described almost exclusively from Thailand, Middle East and China, respectively.

Summary

Despite limited studies, certain peculiarities have been observed in invasive mould infections in developing countries, including a high incidence of ophthalmic lesions, mucormycosis and aspergillosis; few different clinical presentations; and a varied spectrum of pathogens involved in such lesions.

Keywords

aspergillosis, developing countries, emerging fungal infections, epidemiology, mucormycosis

Curr Opin Infect Dis 24:000–000

0951-7375

Introduction

Mould infections are a significant public health problem worldwide [1,2••,3,4,5•,6,7•,8,9••–11••]. They are being increasingly reported from the developing countries, with invasive mould infections (IMIs) emerging as a major concern owing to the alarming rise in their incidence, and the high morbidity and mortality associated with such infections [1,2••,5•,6,11••,12••,13].

The increasing frequency of IMIs in the developing world has been attributed to the environmental and host factors prevalent in such regions [2••]. The majority of the developing countries are located in the tropical and sub-tropical zones, and provide an optimum environment for survival and growth of moulds [2••]. The population in these countries comprises a large economically deprived section, facing poor hygiene, poor sanitation and below-optimum health-care facilities, and also a limited prosperous section availing the modern medical interventions including transplants and intensive therapy for malignancies [2••]. IMIs occur more frequently in both these population extremes, albeit for different reasons [2••,12••]. A large number of untrained health-care providers, the misuse of steroids, intravenous drug abuse and easy availability of spurious medical-care infusion sets further contribute to the high incidence of IMIs in such countries [2••].

The precise epidemiology of mycotic infections in developing countries is not well known, due to the limited availability of data as a result of sub-optimal awareness, inadequate reporting and diagnostic facilities [2••,4]. However, the available data suggest a considerable variation in the epidemiology of IMIs in the developing and developed world, with differences in the risk factors and

causative agents involved [1,2••,6,7•,8]. The present review describes the emerging trends of mould infections in developing countries, and highlights the major differences in epidemiology from the developed countries, with emphasis on aspergillosis and mucormycosis.

Aspergillosis

Invasive aspergillosis is an important cause of morbidity and mortality amongst hospitalized patients in developing countries [2••]. Several centres from India, China, Taiwan, Thailand, Pakistan, Bangladesh, Sri Lanka, Malaysia, Iran, Iraq, Saudi Arabia, Egypt, Sudan, South Africa, Turkey, Hungary, Brazil, Chile, Colombia, and Argentina have reported series of invasive aspergillosis [2••,5•,14–16]. Such an increased incidence rate of invasive aspergillosis in developing countries has been attributed to the high environmental spore count of *Aspergillus* spp., inadequate air-quality precautions during construction work in the vicinity of neutropenic patients, and poor hospital-care practices [2••].

Apart from the known risk factors such as haematological malignancies, solid tumours, and allogeneic haematopoietic stem cell, liver and lung transplants, invasive aspergillosis can occur in low-risk groups such as renal transplant recipients, with an incidence rate of 2–4% in developing countries [2••,12••]. New risk factors including tuberculosis, diabetes, chronic obstructive pulmonary disease and chronic liver failure have also been associated with invasive aspergillosis in the developing world [2••]. An unusual outbreak of *Aspergillus* meningitis following the administration of spinal anaesthesia for caesarean section was reported in Sri Lanka after the tsunami disaster in 2005, and was linked to the sub-optimal storage of regular supply spinal needles in the warehouse due to huge donations received by the country during that period [17]. Furthermore, although primarily associated with immunocompromised patients, invasive aspergillosis has also been reported to occur in immunocompetent patients [2••]. Nearly 14% 'of the patients suffering from invasive aspergillosis in developing countries do not possess any predisposing risk factor, especially those with isolated cerebral and rhino-orbital-cerebral (ROC) aspergillosis [2••].

In addition to the classical invasive pulmonary aspergillosis, uncommon clinical presentations such as the invasive *Aspergillus* tracheobronchitis have been reported from developing countries [2••,18]. However, sino-orbital and cerebral aspergillosis are distinct clinical types in Asia, Africa and the Middle East [2••]. Amongst the different clinical types of fungal rhinosinusitis (FRS), acute invasive FRS and chronic invasive FRS have been reported from both developed and developing countries,

Key points

- The limited data available from developing countries suggest an alarming increase in invasive mould infections (IMIs), especially in aspergillosis and mucormycosis, and also a considerable difference between the common risk factors and causative agents of IMIs in the developed and the developing world.
- Sino-orbital, cerebral and ocular aspergillosis due to *Aspergillus flavus* are the emerging clinical types of aspergillosis in developing countries, with new risk factors including tuberculosis, diabetes, chronic obstructive pulmonary disease and chronic liver failure also being associated.
- *Aspergillus* and *Fusarium* spp. are frequent causes of mycotic keratitis in the tropics and the sub-tropics, especially trauma-associated lesions in agricultural workers.
- Rhino-orbito-cerebral presentation in patients with uncontrolled diabetes remains the most common manifestation of mucormycosis in developing countries; new clinical entities such as isolated renal mucormycosis and infections due to *Apophysomyces elegans*, *Mucor irregularis* and *Rhizopus homothallicus* are also emerging.
- *Pythium insidionum*, *Rhinocladiella mackenziei* and *M. irregularis* exhibit a geographically restricted distribution, and have been reported almost exclusively from Thailand, the Middle East and China, respectively.

whereas granulomatous invasive FRS is primarily seen in developing countries such as Sudan, India, Pakistan and Saudi Arabia [2••]. Many developing countries with a warm, dry climate such as Saudi Arabia, India and Sudan also record a high number of allergic fungal rhinosinusitis (AFRS) cases due to *A. flavus* [8]. Another common allergic aspergillosis, namely allergic bronchopulmonary aspergillosis (ABPA), is recognized frequently amongst asthmatic patients in India, occurring in nearly 21 and 39% of the patients with bronchial asthma and acute severe asthma, respectively, instead of the commonly believed incidence rate of 1–2% [19]. The contemporaneous occurrence of ABPA and AFRS [sino-bronchial allergic mycosis (SAM) syndrome] or ABPA, AFRS and aspergilloma is also reported occasionally [20,21]. Aspergilloma prior to or consequent to ABPA poses a therapeutic challenge owing to the constant risk of aggravation with corticosteroids [20]. Moreover, cerebral aspergillosis is highly prevalent in the developing world, manifesting either as an extension of invasive (acute or chronic) FRS, or following haematogenous dissemination [2••]. However, the contiguous spread from paranasal sources is the common cause of central nervous system involvement in developing countries, owing to the high incidence of FRS in these regions [2••].

Aspergillus spp. are also a frequent cause of mycotic keratitis, a common ocular fungal infection that accounts for nearly 50–60% cases of microbial keratitis in developing countries [9••]. It usually occurs in the tropical and sub-tropical regions in healthy male agricultural workers following corneal injury due to traumatizing agents of plant or animal origin [9••]. Many environmental factors such as humidity, rainfall and wind influence the occurrence of mycotic keratitis, and perhaps also determine the seasonal variations in the frequency of fungal isolation and types of fungi isolated [9••]. *Aspergillus* endophthalmitis is also an important clinical entity in developing countries, often manifesting as a post-traumatic infection or a postoperative infection in eye surgery camps [2••,22,23]. In an outbreak of endophthalmitis amongst apparently healthy individuals from a rural setting in India, the contaminated dextrose infusion fluid was described as the likely source of infection [23].

Aspergillus fumigatus is considered the leading cause of invasive aspergillosis worldwide [2••]. *A. flavus*, *A. terreus* and *A. nidulans* are also being increasingly reported, based upon regional distinctions [2••,7•]. *A. flavus* causes a disproportionately greater number of paranasal-sinus and eye infections in the developing countries [2••,7•]. Nearly 50 and 80% of AFRS cases in India and the Middle East, respectively, have been attributed to this fungus [8]. These findings are in contrast to the developed world, where dematiaceous fungi are more commonly implicated in AFRS [8]. Such a high frequency of *A. flavus* isolation from developing countries may be due to a greater environmental prevalence of the fungus in these regions [2••]. *A. nidulans* is a common agent in chronic granulomatous disease [7•]. *A. terreus* remains relatively uncommon, but infections caused by this pathogen are often associated with high mortality rates, owing to its resistance to amphotericin B [7•].

Mucormycosis

The emergence of mucormycosis has been reported throughout the world in the past two decades, but the rise in developing countries has been phenomenal [1,5•,6, 11••,13]. Many series of patients with mucormycosis have been reported from several countries including India, China, Taiwan, Kuwait and Latin America [1,6,11••,13].

Although traditionally considered a community-acquired mycosis, mucormycosis is now recognized as a nosocomial infection as well, and has been associated with various procedures or devices used in hospitals, antifungal prophylaxis, bandages or medication patches, intravenous catheters and even tongue depressors [1,13,24,25]. Cheng *et al.* [26] recently reported a nosocomial outbreak of gastrointestinal mucormycosis due to *Rhizomucor microsporus* amongst patients with haematological malignancies in China. On investigation, the cornstarch used for manufacturing of allopurinol tablets and ready-to-eat food items were found to be the likely sources of the contaminating fungus [26].

The risk factors for mucormycosis vary greatly amongst the developed and developing world [6]. A considerable rise in the number of mucormycosis cases has been reported in developing countries, primarily due to a continued increase in the patient population with uncontrolled diabetes [1,6,13,27]. Although other risk factors such as haematological malignancies and transplants have also been implicated, the overwhelming number of mucormycosis cases with uncontrolled diabetes overshadows the role of these risk factors in such countries [1,6]. From only one tertiary-care centre in India, 129 cases over 10 years (1990–1999), 178 cases during the subsequent 5 years (2000–2004) and then 75 cases in an 18 months period during 2006–2007 were reported [1]. Nearly 23% of these patients were found to be ignorant of their underlying diabetic status before presenting with mucormycosis in the hospital [1]. Furthermore, earthquakes and physical disasters such as the tsunami in Thailand and Sri Lanka have also been linked with the increase in the cases of superficial mucormycosis, due to traumatic inoculation of these fungi into wounds [6,13,25].

Rhino-orbital-cerebral is the commonest clinical form of mucormycosis in developing countries, possibly because of its association with diabetes [1,6,27]. Pulmonary, gastrointestinal and cutaneous types occur in patients with haematological malignancies or neutropenia, severe malnutrition, and trauma or burns, respectively [1,6]. Apart from these common clinical types, isolated renal mucormycosis is being reported as a new clinical entity in India and China [1,28–30]. Although the kidney is involved in nearly 22% cases of disseminated mucormycosis, isolated renal mucormycosis has been described rarely in developed countries [1]. Most of the patients (75%) suffering from isolated renal mucormycosis in India are apparently healthy individuals [1], whereas most cases reported from China possess risk factors for developing mucormycosis, except the paediatric population [28–30]. Cases of necrotizing fasciitis due to zygomycetes, occurring via contaminated intramuscular injections, are also a common finding in developing countries [6,31].

Rhizopus, *Mucor* and *Lichtheimia* spp. represent the most frequent causative agents of mucormycosis, accounting for 70–80% of all cases [1,32••]. *Apophysomyces*, *Saksenaea*, *Rhizomucor*, *Cunninghamella*, *Cokeromyces*, *Actinomucor*, and *Syncephalastrum* spp. have also been implicated [1,6,32••]. Although Mucorales are considered opportunistic pathogens, *Apophysomyces elegans* and *Saksenaea vasiformis* can initiate disease in apparently normal hosts following

penetrating trauma during accidents in tropical and subtropical areas [6,32••]. The majority of these patients present with cutaneous mucormycosis only and do not demonstrate any underlying immune system dysfunction [6,32••]; only a few patients manifest rhino-cerebral and pulmonary infections, and have risk factors for developing mucormycosis [6]. Most of the patients (60%) with *A. elegans* infection are from India, where *A. elegans* was first isolated from a mango orchard [6]. However, no correlation between the environmental prevalence of this fungus and clinical cases has been described yet. A few case reports have also described mucormycosis due to other Mucorales such as *Cunninghamella bertholletiae* and *Rhizomucor pusillus* in immunocompetent patients [32••,33].

Several uncommon species such as *Mucor irregularis* (*Rhizomucor variabilis*) and *Rhizopus homothallicus* have been implicated in infections in recent years [34•,35,36]. *Rh. homothallicus* has been reported from patients with cavitary pulmonary mucormycosis in India [34•]. Cutaneous infection due to *M. irregularis* has been described as an emerging endemic mucormycosis in China [36–38], mostly occurring in patients belonging to farming communities, with a history of trauma, bites and surgery but without any underlying illness [36–38]. The lesions are observed on exposed locations of the body, mainly the face [36]. All the cases were reported from three adjacent provinces in central and eastern China, including Jiangsu, Shandong and Hebei provinces [36]. No environmental study has yet been conducted to identify the reasons for geographical restriction of this fungus [36]. Recently, the same agent has also been reported from a case of rhino-facial mucormycosis in India [35].

In contrast to Mucorales, Entomophthorales mostly result in slowly progressive, non angio-invasive infections in immunocompetent hosts [6,13,39]. A few cases of acute, invasive infections due to Entomophthorales have also been described [6,13,40,41]. The disease is endemic to regions of the world with tropical climates, and most of the cases have been reported from India, South America, and Africa [6].

Fusariosis

Fusarium spp. are being increasingly implicated in IMIs in developed countries [3,7•]. The incidence of invasive fusariosis in developing countries is comparatively low, and occasional cases have been reported from Mexico, Brazil, Tunisia, China, Taiwan and India [7•,42–45]. However, keratitis due to *Fusarium* is a common clinical presentation in developing countries, with *F. solani* being the principal species implicated in these infections [9••,46–52]. Like *Aspergillus*, *Fusarium* causes trauma-associated keratitis, mostly in male agricultural workers, and contact-lens wearers [9••]. Invasive manifestations of fusariosis are usually limited to immunocompromised individuals, with the risk factors similar to those for invasive aspergillosis [7•,12••,53].

Scedosporiosis

Scedosporium spp. are also emerging fungi, and have been isolated from respiratory-tract colonization, superficial or locally-invasive and disseminated infections in immunocompromised patients with risk factors similar to invasive aspergillosis [3,7•]. *Scedosporium prolificans* is relatively more common in a few developed countries (Australia and Spain) compared to the developing countries [3,7•]. *S. apiospermum* has global distribution, frequently in association with water, and is often described as a cause of pneumonia and disseminated infection in near-drowning victims [3,7•,53]. Occasional cases of scedosporiosis have been reported from India, Korea, Chile, Brazil and Portugal [5•,54–59].

Pythiosis

Pythium insidiosum, an opportunistic oomycete (pseudofungi), has been reported almost exclusively from Thailand [60–63]. It is frequently isolated from irrigation water and reservoirs in Thailand, and is endemic in its agricultural regions [61,62]. Pythiosis manifests either in a localized form, such as corneal ulcers or chronic cutaneous lesions, or in a systemic or vascular form [61,62] on the extremities in individuals with underlying haemoglobinopathies [61,62].

Infections due to other moulds

Apart from the common IMIs, several other infections due to hyaline and melanized moulds are emerging in the developing countries, as in the Western world. Many dematiaceous fungi including *Alternaria* spp., *Bipolaris* spp., *Cladophialophora bantiana*, *Curvularia* spp., *Exophiala* spp., *Fonsecaea pedrosoi*, *Madurella* spp., *Phialophora* spp., and *Scytalidium dimidiatum* have been implicated in cutaneous, subcutaneous and corneal infections following traumatic implantation in immunocompetent hosts, usually in the tropics and subtropics [10••]. They are also an important cause of invasive sinusitis in both developed and developing countries [8]. Several species, including *C. bantiana*, *Rhinocladiella mackenziei* and *Exophiala dermatitidis*, cause cerebral infections in immunocompetent hosts, without any obvious risk factors [10••]. Although considered as ubiquitous saprophytes, many dematiaceous fungi occupy specific ecological niches [10••]. *R. mackenziei* is almost exclusively reported from the Middle East [10••]. However, the disease may not be strictly restricted geographically, as an autochthonous case has been described recently from India [64].

Infections due to *Colletotrichum* spp., though rare, are also emerging [65]. Although only a limited number of species, including *C. dematium*, *C. coccodes*, *C. gloeosporioides*, *C. graminicola*, *C. crassipes*, and *C. truncatum*, are usually implicated in ophthalmic and subcutaneous infections, a series of five cases of ophthalmic infections due to *C. truncatum* has been recently reported from India [65].

Conclusion

Although the precise epidemiology of mould infections in developing countries is not well studied, the available data suggest an alarming increase in IMIs in such countries, especially in aspergillosis and mucormycosis, and also a considerable difference between the common risk factors and causative agents of IMIs in the developed and the developing world. Sino-orbital, cerebral and ophthalmic infections due to *A. flavus* (in contrast to *A. fumigatus* in the developed world) are the predominant clinical types of aspergillosis in such countries, after pulmonary aspergillosis. Several new risk factors including tuberculosis, diabetes, chronic obstructive pulmonary disease and chronic liver failure have also been associated with these infections. *Aspergillus* and *Fusarium* spp. are frequent causes of mycotic keratitis, especially trauma-associated keratitis in agricultural workers. Mucormycosis in developing countries usually manifests as ROC form in patients with uncontrolled diabetes, compared to haematological malignancies in the developed world. Cutaneous infections due to traumatic implantation of *A. elegans* in immunocompetent individuals are also a common presentation in such regions, especially in India. Isolated renal mucormycosis has emerged as a new clinical entity in India and China. *Rh. homothallicus* and *M. irregularis* have been reported as new causative agents of mucormycosis in these countries. Many pathogens exhibit a geographically restricted distribution. *P. insidiosum*, *R. mackenziei* and *M. irregularis* have been described almost exclusively from Thailand, the Middle East and China, respectively.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

1 Chakrabarti A, Chatterjee SS, Das A, *et al.* Invasive zygomycosis in India: experience in a tertiary care hospital. Postgrad Med J 2009; 85:573–581.

2 •• Chakrabarti A, Chatterjee SS, Das A, Shivaprakash MR. Invasive aspergillosis in developing countries. Med Mycol 2011; 49 (Suppl 1):S35–S47.
This is a comprehensive review on epidemiology and clinical presentations of invasive aspergillosis in the developing countries. It highlights the newly implicated risk factors, and the predominant manifestations of aspergillosis in such countries.

3 Lass-Florl C. The changing face of epidemiology of invasive fungal disease in Europe. Mycoses 2009; 52:197–205.

4 Ameen M. Epidemiology of superficial fungal infections. Clin Dermatol 2010; 28:197–201.

5 • Nucci M, Queiroz-Telles F, Tobon AM, *et al.* Epidemiology of opportunistic fungal infections in Latin America. Clin Infect Dis 2010; 51:561–570.
This review describes the epidemiology of yeast and mould infections in Latin America, with emphasis on aspergillosis, fusariosis, mucormycosis and phaeohyphomycosis.

6 Meis JF, Chakrabarti A. Changing epidemiology of an emerging infection: zygomycosis. Clin Microbiol Infect 2009; 15 (Suppl 5):10–14.

7 • Binder U, Lass-Florl C. Epidemiology of invasive fungal infections in Mediterranean area. Mediterr J Hematol Infect Dis 2011; 3:e20110016.
This review describes the risk factors, causative agents and clinical manifestations of common fungal infections in the Mediterranean region.

8 Chatterjee SS, Chakrabarti A. Epidemiology and medical mycology of fungal rhinosinusitis. Otorhinolaryngol Clin: An Int J 2009; 1:1–13.

9 •• Kalkanci A, Ozdek S. Ocular fungal infections. Curr Eye Res 2011; 36:179–189.
This is an important review on common ocular fungal infections. It describes the risk factors, causative agents, usual clinical presentations, laboratory diagnosis and experimental models of these infections.

10 •• Revankar SG, Sutton DA. Melanized fungi in human disease. Clin Microbiol Rev 2010; 23:884–928.
This is a comprehensive review on melanized fungi. It describes the classification, taxonomy, nomenclature, pathogenesis, clinical manifestations, diagnosis and management of infections caused by these fungi.

11 •• Queiroz-Telles F, Nucci M, Colombo AL, *et al.* Mycoses of implantation in Latin America: an overview of epidemiology, clinical manifestations, diagnosis and treatment. Med Mycol 2011; 49:225–236.
This review describes the epidemiology, disease manifestations and therapy of chromoblastomycosis, phaehyphomycosis and subcutaneous zygomycosis in Latin America.

12 •• Pagano L, Akova M, Dimopoulos G, *et al.* Risk assessment and prognostic factors for mould-related diseases in immunocompromised patients. J Antimicrob Chemother 2011; 66 (Suppl 1):i5–14.
This is an exhaustive review on all major risk factors predisposing the patients to invasive mycoses and affecting the prognosis of such infections.

13 Mantadakis E, Samonis G. Clinical presentation of zygomycosis. Clin Microbiol Infect 2009; 15 (Suppl 5):15–20.

14 Chen CH, Ho C, Liu HC, *et al.* Spontaneous empyema necessitatis caused by *Aspergillus fumigatus* in an immunocompetent patient. JRSM Short Rep 2011; 2:25.

15 Roxo P Jr, de Menezes UP, Condino-Neto A, *et al.* Unusual presentation of brain aspergillosis in chronic granulomatous disease. Pediatr Neurol 2011; 43:442–444.

16 Yilmaz M, Mete B, Ozaras R, *et al.* Aspergillus fumigatus infection as a delayed manifestation of prosthetic knee arthroplasty and a review of the literature. Scand J Infect Dis 2011; 43:573–578.

17 Gunaratne PS, Wijeyaratne CN, Seneviratne HR. Aspergillus meningitis in Sri Lanka: a post-tsunami effect? N Engl J Med 2007; 356:754–756.

18 Wu N, Huang Y, Li Q, *et al.* Isolated invasive Aspergillus tracheobronchitis: a clinical study of 19 cases. Clin Microbiol Infect 2010; 16:689–695.

19 Agarwal R, Nath A, Aggarwal AN, *et al.* Aspergillus hypersensitivity and allergic bronchopulmonary aspergillosis in patients with acute severe asthma in a respiratory intensive care unit in North India. Mycoses 2010; 53:138–143.

20 Shah A. Concurrent allergic bronchopulmonary aspergillosis and aspergilloma: is it a more severe form of the disease? Eur Respir Rev 2010; 19:261–263.

21 Chakrabarti A, Denning DW, Ferguson BJ, *et al.* Fungal rhinosinusitis: a categorization and definitional schema addressing current controversies. Laryngoscope 2009; 119:1809–1818.

22 Chakrabarti A, Shivaprakash MR, Singh R, *et al.* Fungal endophthalmitis: fourteen years' experience from a center in India. Retina 2008; 28:1400–1407.

23 Gupta A, Gupta V, Dogra MR, *et al.* Fungal endophthalmitis after a single intravenous administration of presumably contaminated dextrose infusion fluid. Retina 2000; 20:262–268.

24 Antoniadou A. Outbreaks of zygomycosis in hospitals. Clin Microbiol Infect 2009; 15 (Suppl 5):55–59.

25 Richardson M. The ecology of the Zygomycetes and its impact on environmental exposure. Clin Microbiol Infect 2009; 15 (Suppl 5):2–9.

26 Cheng VC, Chan JF, Ngan AH, *et al.* Outbreak of intestinal infection due to *Rhizopus microsporus*. J Clin Microbiol 2009; 47:2834–2843.

27 Lanternier F, Lortholary O. Zygomycosis and diabetes mellitus. Clin Microbiol Infect 2009; 15 (Suppl 5):21–25.

28 Lin CY, Lee SC, Lin CC, *et al.* Isolated fatal renal mucormycosis in a patient with chronic obstructive pulmonary disease and tuberculosis. Int J Clin Pract 2003; 57:916–918.

29 Yu J, Li RY. Primary renal zygomycosis due to *Rhizopus oryzae*. Med Mycol 2006; 44:461–466.

30 Jianhong L, Xianliang H, Xuewu J. Isolated renal mucormycosis in children. J Urol 2004; 171:387–388.

31 Garg A, Sujatha S, Garg J, *et al.* Fulminant necrotizing fasciitis caused by zygomycetes. J Cutan Pathol 2009; 36:815–816.

32 •• Gomes MZ, Lewis RE, Kontoyiannis DP. Mucormycosis caused by unusual mucormycetes, non-Rhizopus, -Mucor, and -Lichtheimia species. Clin Microbiol Rev 2011; 24:411–445.

This is a comprehensive review on geographical distribution, epidemiology and clinical manifestations of unusual zygomycetes.

33 Kimura M, Udagawa S, Makimura K, *et al.* Isolation and identification of *Rhizomucor pusillus* from pleural zygomycosis in an immunocompetent patient. Med Mycol 2009; 47:869–873.

34 • Chakrabarti A, Marak RS, Shivaprakash MR, *et al.* Cavitary pulmonary zygomycosis caused by *Rhizopus homothallicus*. J Clin Microbiol 2010; 48:1965–1969.

This is the first study of human infection caused by *Rhizopus homothallicus*.

35 Hemashettar BM, Patil RN, O'Donnell K, *et al.* Chronic rhinofacial mucormycosis caused by *Mucor irregularis* (*Rhizomucor variabilis*) in India. J Clin Microbiol 2011; 49:2372–2375.

36 Lu XL, Liu ZH, Shen YN, *et al.* Primary cutaneous zygomycosis caused by *Rhizomucor variabilis*: a new endemic zygomycosis? A case report and review of 6 cases reported from China. Clin Infect Dis 2009; 49:e39–43.

37 Wang SB, Li RY, Yu J. Identification and susceptibility of *Rhizomucor* spp. isolated from patients with cutaneous zygomycosis in China. Med Mycol 2011 [Epub ahead of print].

38 Zhao Y, Zhang Q, Li L, *et al.* Primary cutaneous mucormycosis caused by *Rhizomucor variabilis* in an immunocompetent patient. Mycopathologia 2009; 168:243–247.

39 El-Shabrawi MH, Kamal NM. Gastrointestinal basidiobolomycosis in children: an overlooked emerging infection? J Med Microbiol 2011; 60:871–880.

40 Radhakrishnan N, Sachdeva A, Oberoi J, Yadav SP. Conidiobolomycosis in relapsed acute lymphoblastic leukemia. Pediatr Blood Cancer 2009; 53:1321–1323.

41 Radjou AN, Rajesh NG. Intestinal obstruction due to *Basidiobolus ranarum*: an unusual case. Indian J Med Microbiol 2011; 29:186–188.

42 Chen QX, Li CX, Huang WM, *et al.* Cutaneous hyalohyphomycosis caused by *Fusarium subglutinans*. Eur J Dermatol 2010; 20:526–527.

43 Hsiue HC, Ruan SY, Kuo YL, *et al.* Invasive infections caused by non-Aspergillus moulds identified by sequencing analysis at a tertiary care hospital in Taiwan, 2000–2008. Clin Microbiol Infect 2010; 16:1204–1206.

44 Hu JW, Shu XR, Ren J, *et al. Fusarium solani* infection in a patient after allogeneic hemotopoietic stem cell transplantation: case report and literature review. Zhonghua Jie He He Hu Xi Za Zhi 2010; 33:730–733.

45 Kindo AJ, Rana NS, Rekha A, Kalyani J. Fungal infections in the soft tissue: a study from a tertiary care center. Indian J Med Microbiol 2010; 28:164–166.

46 He D, Hao J, Zhang B, *et al.* Pathogenic spectrum of fungal keratitis and specific identification of *Fusarium solani*. Invest Ophthalmol Vis Sci 2011; 52:2804–2808.

47 Vanzzini Zago V, Manzano-Gayosso P, Hernandez-Hernandez F, *et al.* Mycotic keratitis in an eye care hospital in Mexico City. Rev Iberoam Micol 2010; 27:57–61.

48 Saha S, Banerjee D, Khetan A, Sengupta J. Epidemiological profile of fungal keratitis in urban population of West Bengal, India. Oman J Ophthalmol 2009; 2:114–118.

49 Tilak R, Singh A, Maurya OP, *et al.* Mycotic keratitis in India: a five-year retrospective study. J Infect Dev Ctries 2010; 4:171–174.

50 Wang L, Sun S, Jing Y, *et al.* Spectrum of fungal keratitis in central China. Clin Experiment Ophthalmol 2009; 37:763–771.

51 Choy BN, Tang EW, Lai JS. A case series of contact lens-associated *Fusarium keratitis* in Hong Kong. Cornea 2009; 28:955; author reply 955–956.

52 Anane S, Ben Ayed N, Malek I, *et al.* Keratomycosis in the area of Tunis: epidemiological data, diagnostic and therapeutic modalities. Ann Biol Clin (Paris) 2010; 68:441–447.

53 Quan C, Spellberg B. Mucormycosis, pseudallescheriasis, and other uncommon mold infections. Proc Am Thorac Soc 2010; 7:210–215.

54 Gopinath M, Cherian A, Baheti NN, *et al.* An elusive diagnosis: Scedosporium apiospermum infection after near-drowning. Ann Indian Acad Neurol 2010; 13:213–215.

55 Sireesha P, Manoj Kumar CH, Setty CR. Thyroid abscess due to *Scedosporium apiospermum*. Indian J Med Microbiol 2010; 28:409–411.

56 Jeong JC, Lee H, Lee SW, *et al.* Fungal peritonitis due to *Scedosporium prolificans*. Perit Dial Int 2011; 31:213–215.

57 Soman R, Mahashur AA, Naphade D, *et al.* Pseudallescheria boydii lung infection in an immunocompetent adult, difficulties in diagnosis and management. J Assoc Physicians India 2010; 58:633–634.

58 Marques DS, Pinho Vaz C, Branca R, *et al.* Rhizomucor and Scedosporium infection post hematopoietic stem-cell transplant. Case Report Med 2011; 2011:830769.

59 Nath R, Gogoi RN, Saikia L. Keratomycosis due to *Scedosporium apiospermum*. Indian J Med Microbiol 2010; 28:414–415.

60 Kammarnjesadakul P, Palaga T, Sritunyalucksana K, *et al.* Phylogenetic analysis of *Pythium insidiosum* Thai strains using cytochrome oxidase II (COX II) DNA coding sequences and internal transcribed spacer regions (ITS). Med Mycol 2011; 49:289–295.

61 Jindayok T, Piromsontikorn S, Srimuang S, *et al.* Hemagglutination test for rapid serodiagnosis of human pythiosis. Clin Vaccine Immunol 2009; 16:1047–1051.

62 Laohapensang K, Rutherford RB, Supabandhu J, Vanittanakom N. Vascular pythiosis in a thalassemic patient. Vascular 2009; 17:234–238.

63 Sudjaritruk T, Sirisanthana V. Successful treatment of a child with vascular pythiosis. BMC Infect Dis 2011; 11:33.

64 Badali H, Chander J, Bansal S, *et al.* First autochthonous case of *Rhinocladiella mackenziei* cerebral abscess outside the Middle East. J Clin Microbiol 2010; 48:646–649.

65 Shivaprakash MR, Appannanavar SB, Dhaliwal M, *et al.* Colletotrichum truncatum: an unusual pathogen causing mycotic keratitis and endophthalmitis. J Clin Microbiol 2011 [Epub ahead of print].