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# Emerging issues, challenges, and changing epidemiology of fungal disease outbreaks

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## Abstract

Several high-profile outbreaks have drawn attention to invasive fungal infections (IFIs) as an increasingly important public health problem. IFI outbreaks are caused by many different fungal pathogens and are associated with numerous settings and sources. In the community, IFI outbreaks often occur among people without predisposing medical conditions and are frequently precipitated by environmental disruption. Health-care-associated IFI outbreaks have been linked to suboptimal hospital environmental conditions, transmission via health-care workers' hands, contaminated medical products, and transplantation of infected organs. Outbreak investigations provide important insights into the epidemiology of IFIs, uncover risk factors for infection, and identify opportunities for preventing similar events in the future. Well recognised challenges with IFI outbreak recognition, response, and prevention include the need for improved rapid diagnostic methods, the absence of routine surveillance for most IFIs, adherence to infection control practices, and health-care provider awareness. Additionally, IFI outbreak investigations have revealed several emerging issues, including new populations at risk because of travel or relocation, occupation, or immunosuppression; fungal pathogens appearing in geographical areas in which they have not been previously recognised; and contaminated compounded medications. This report highlights notable IFI outbreaks in the past decade, with an emphasis on these emerging challenges in the USA.

## Introduction

Invasive fungal infections (IFIs) have received increased attention as an emerging public health problem in the past decade, in part because of several high-profile outbreaks.[1] IFIs are often difficult to detect and treat, and can be associated with substantial morbidity and mortality.[2] These issues are becoming increasingly apparent as many IFIs appear to be on

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the rise globally.[3,4] The observed increases in IFIs are multifaceted and include host factors, such as a larger at risk immunosuppressed population, or travel or relocation of immune-naive people to areas in which particular IFIs are geographically restricted; pathogen factors, such as new virulence or resistance mechanisms and expansion to new endemic areas; and environmental factors, including changing land use patterns, agricultural antifungal use, and climate change.[3] Outbreak investigations can provide important insights into the epidemiology and sources of IFIs, including changes in the aforementioned host, pathogen, and environmental factors.

IFI outbreaks usually result from exposure to a common environmental source or a contaminated medical product. Investigations of IFI outbreaks are often challenging but are essential to identify the source and stop the outbreak. Furthermore, outbreak investigations often yield new and important descriptive epidemiological information, uncover risk factors for infection, help identify gaps in awareness and infection control, and identify opportunities for prevention of similar events in the future. This report highlights notable IFI outbreaks and describes new and existing challenges that arise during outbreak investigations. Numerous other outbreaks not described in detail illustrate the diversity of fungal pathogens and their ecological niches (table).

## Community-acquired fungal disease outbreaks

Fungi are abundant in and essential to the natural environment, and only a tiny fraction of all fungi are pathogenic. Fungi have long been known as pathogens of crops and have caused widespread population declines in bats and amphibians, linked to both global movement of people and goods and environmental modification.[18] Fungi pathogenic to human beings exist in many different natural habitats, but the burden of IFIs is generally observed to be highest in tropical and subtropical climates, where fungi capable of growing at human body temperatures can thrive.[19] The emergence of *Cryptococcus gattii*, formerly restricted to tropical and subtropical climates, in a temperate region of North America, provides evidence that fungal pathogens can spread to new geographical areas. Other pathogenic fungi, such as histoplasma, coccidioides, and blastomyces, have existed within specific ecological niches and have been broadly restricted to particular regions of the world. However, climate and other environmental changes could also be altering the distribution of these fungi. IFI outbreaks in the community often occur among people without predisposing medical conditions and are frequently precipitated by environmental disruption, either on a small scale in relation to excavation, construction, or similar activities, or on a larger scale (eg, related to natural disasters).[20]

*C gattii* was believed to be restricted to tropical and subtropical regions, particularly Australia, Papua New Guinea, and South America. In the 1990s, it emerged in the temperate climate of British Columbia, Canada,[21] eventually moving south into the USA Pacific Northwest (PNW), where nearly 100 cases were reported during 2004–11.[22] *C gattii*'s molecular epidemiology has been well studied; most cases related to the PNW epidemic were caused by molecular type VGII, which contrasts with molecular type VGIII, seen in southern California and elsewhere in the USA. Phylogenetic analyses indicate that the VGII type likely originated in South America and underwent multiple dispersal events, but exactly

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how and why *C gattii* arrived in the PNW remains unknown.[23–25] As a result of this outbreak, Oregon and Washington began requiring physicians and laboratories to report *C gattii* cases to public health authorities, and laboratories began to differentiate *C gattii* from *Cryptococcus neoformans*.

Histoplasmosis is generally believed to be the most common endemic mycosis worldwide, although the exact number of new infections annually is unknown. *Histoplasma* spp grow particularly well in soil contaminated with bird or bat droppings, and histoplasmosis outbreaks are often associated with point-source exposures or disturbance of contaminated soil.[26] Outbreaks occur regularly in the USA, with 105 outbreaks reported during 1938–2013, although many more outbreaks are not recognised, investigated, or published.[26] More than 40% of the published histoplasmosis outbreaks in the USA involved workers in an occupational setting, and birds, bats, or their droppings were implicated in 86% of workplace-related outbreaks.[26] The US Centers for Disease Control and Prevention National Institute for Occupational Safety and Health (CDC-NIOSH) has issued guidance for histoplasmosis prevention among workers, as occupational health continues to be an important issue in histoplasmosis outbreaks.[27]

In Central and South America, numerous histoplasmosis outbreaks have been described among people who visited bat-infested caves.[28] In 2015, an unusually severe outbreak occurred in the Dominican Republic, where histoplasmosis outbreaks had not been previously documented. In July, 2015, a group of 35 men cleared several tons of bat guano from tunnels that provided access for inspection and maintenance of a hydroelectric dam. 30 men developed histoplasmosis, of whom 28 were hospitalised and three died, a case-fatality rate approximately ten times higher than is typically described in the USA; the high hospitalisation and mortality rates were probably related to a large inoculum within an enclosed space.[29] Adequate respiratory protection was not used. Low awareness about histoplasmosis risk in this area contributed to the absence of adequate workplace precautions. CDC-NIOSH guidance regarding powered air purifying respirators and other expensive protective equipment would have been difficult to implement in this resource-limited setting.[27] Furthermore, diagnosis of histoplasmosis among ill workers was delayed because of the absence of in-country diagnostic capacity, and involved clinicians were unfamiliar with the treatment and management of histoplasmosis because it had never been previously diagnosed in the Dominican Republic. This outbreak underscores the need for improved diagnostic capacity for histoplasmosis throughout the Americas and the Caribbean.

Although nearly all reported histoplasmosis outbreaks have been associated with environmental disruption, such as disturbance of bird or bat droppings (reported in 40% of outbreaks), soil or plant matter disruption (32%), or demolition or construction (25%), many outbreaks show the possibility for cases to occur in people exposed to aerosolised spores, who were not directly involved in the outbreak-initiating activities.[26] For example, an outbreak of 78 cases among prison inmates in central Illinois was associated with the removal of two trees where many birds had roosted.[30] None of the inmates who participated in the tree removal developed acute histoplasmosis, which might reflect immunity to *Histoplasma* spp acquired during recurrent occupational soil exposures at the prison.[30]

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Furthermore, inmates without evidence of histoplasmosis had a significantly longer median incarceration time than had the patients with histoplasma infection; most inmates previously resided in areas of Illinois where histoplasmosis is not frequently reported, suggesting that reduced immunity to *Histoplasma* spp could have had a role in this outbreak.[30]

Coccidioidomycosis is endemic to southwestern USA and large parts of Latin America. However, coccidioides has also been discovered north of its traditional geographical range, in southcentral Washington.[31] Coccidioides' environmental growth and distribution depends on temperature, precipitation, and other climate factors (and also might be associated with a rodent host); therefore, sporadic coccidioidomycosis cases and outbreaks are likely to be at least partly driven by climate conditions, rodent habitat, and environmental disruption events.[32] Examples of past events leading to coccidioidomycosis outbreaks include an earthquake,[33] a severe dust storm,[34] archaeological excavation,[35] and construction.[36] Similarly, during 2011–14, a large outbreak of 44 coccidioidomycosis cases occurred among workers who were constructing two solar power farms in San Luis Obispo County (CA, USA).[37] Interviews with the affected workers (many of whom came from non-endemic areas and might have lacked immunity to coccidioides) revealed that 58% reported frequently performing soil disruption activities, but of those, only a quarter frequently used respiratory protection.[37] Recommendations to prevent additional cases included improving dust control methods at construction sites and provision of appropriate respiratory protection; however, evidence is limited regarding whether these methods reduce coccidioidomycosis risk.[37] Similar prevention methods have also been attempted in other settings, including prisons in highly endemic areas of California. Despite use of these methods and exclusion of inmates at highest risk for coccidioidomycosis complications from eight prisons in California's Central Valley beginning in 2006,[38] coccidioidomycosis rates remained high in subsequent years. In 2011, rates at two prisons were two orders of magnitude higher than were rates in the surrounding counties in which the prisons were located, probably partly because most inmates in these two prisons resided in geographical are as with lower risk for coccidioidomycosis before incarceration.[39] In January, 2015, a skin test to detect delayed-type hypersensitivity to coccidioides, an indicator of past infection, was administered to nearly 40 000 inmates throughout California. Inmates with a negative skin test result have since been restricted from being housed in the two prisons with the highest coccidioidomycosis rates.[40]

Blastomycosis is much less common than histoplasmosis and coccidioidomycosis, with approximately 15 outbreaks in the USA reported in published literature since the 1950s.[41] Typical features of blastomycosis outbreaks include shared outdoor activities such as camping, hunting, or fishing, or exposure to construction or excavation, often near waterways. By contrast, patients in a large outbreak in Wisconsin during 2009–10 were not more likely than were controls to have these types of exposures.[42] Instead, the outbreak was characterised by a high proportion of cases in Hmong people and unique case clustering within households and neighbourhoods, suggesting that multiple environmental foci were the likely cause.[42]

Community-acquired IFI outbreaks caused by moulds are uncommon because moulds typically affect immunosuppressed people. A noteworthy exception was an outbreak of 13

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cases of soft-tissue mucormycosis caused by *Apophysomyces trapeziformis* in people who were severely injured during a tornado in Joplin (MO, USA) in 2011 (figure 1).[43] Whole-genome sequence typing (WGST) of isolates from patient wounds revealed four distinct but closely related strains of *A trapeziformis*, suggesting that the cases were related to one or more environmental sources rather than a health-care-associated source.[43,44] Other examples of mould infections and outbreaks after natural disasters have been reviewed elsewhere.[45] Although these events are rare, they can result in substantial morbidity and mortality, therefore health-care providers should be aware of the possibility for IFIs after natural disasters. Broader disaster preparedness and response strategies related to health-care services could facilitate faster diagnosis for disaster-associated IFIs and administration of appropriate treatment.[45]

## Health-care-associated outbreaks

Aspergillus, mucormycetes, and other moulds are ubiquitous in the outdoor and indoor environment. Numerous hospital-associated outbreaks of aspergillosis and mucormycosis have occurred; hospital construction, indoor water damage, and improper air filtration have all been associated with these outbreaks. Less commonly, IFI outbreaks in hospitalised patients involve transmission of yeasts via contaminated surfaces and health-care workers' hands. Routine antifungal prophylaxis for some high-risk patient groups and guidelines for environmental infection control aim to prevent IFIs among hospitalised patients;[46] however, outbreaks continue to occur despite these practices. Other health-care-associated IFI outbreaks include those caused by medical products or medications contaminated with fungal pathogens. Contamination of pharmaceuticals with a wide range of fungal species has been increasingly reported over the past decade, and resulting outbreaks are complex and often expose pharmaceutical regulatory gaps. Lastly, a small number of IFI outbreaks in organ transplant recipients have been associated with receipt of infected donor organs.

### In-hospital environment

Outbreaks of hospital-associated invasive mould infections (IMIs) have become increasingly prominent, especially among severely immunocompromised patients, including those with haematological malignancies, haemopoietic stem cell transplants, and solid organ transplant recipients.[47–49] Moulds are ubiquitous in the environment, and opportunities for hospital-associated IMI outbreaks arise when severely immunocompromised patients (eg, patients who have just received a bone marrow transplant and are in the pre-engraftment stage or patients who are persistently neutropenic due to underlying malignancy or chemotherapy) are exposed to building environments with inadequate air filtration, ongoing construction, water damage, and air pressure differentials. Although most hospital-associated IMI outbreaks are caused by *Aspergillus* spp,[47] mucormycosis outbreaks among hospitalised patients in the USA appear to have become more common. The shift from aspergillus to mucormycetes as the causative organism in outbreaks might be due to increasing use of voriconazole prophylaxis in highly immunocompromised patients; voriconazole is active against *Aspergillus* spp but not mucormycetes. Increases in mould outbreaks could also be a result of the increasing number and acuity of patients receiving bone marrow and solid organ transplants and intensive chemotherapy. Three IMI outbreaks in hospitals are described

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below to illustrate the types of problems that can occur in hospitals and lead to such outbreaks.

A mucormycosis cluster occurred among four solid organ transplant recipients in Pennsylvania between May, 2014, and September, 2015.[50] Although the patients did not have a clinical indication for negative-pressure isolation, three of the four received care in the same negative-pressure isolation room. Negative-pressure rooms draw air from the hallway and other parts of the hospital unit into the patient's room and can increase the chance of dust and mould exposure. This investigation led to the important finding that hospitals should avoid placing high-risk patients in negative-pressure rooms unless indicated.[50] In another outbreak, during March–June, 2015, five mucormycosis cases were observed among bone marrow transplant recipients at a hospital in Colorado where construction was ongoing in an adjacent unit. A definitive source could not be identified, but mould that accumulated in the wall due to a slow water leak might have had a role.[51] Mould caused by water leaks is a recurrent theme in hospital outbreaks. Immediately addressing water damage is an important strategy to reduce mould, especially in hospital areas with highly immunocompromised patients.

During July–November, 2014, five patients with haematological malignancies developed rhinocerebral mucormycosis at a hospital in Kansas.[52] The infections, caused by several different mucormycetes, coincided with nearby construction, and the patients were placed in rooms that shared a hallway with construction traffic.[53] Hospital construction is a well recognised risk factor for mould infection, and infection control risk assessments are recommended before beginning construction or other activities that could generate dust or moisture, which might disperse mould spores.[46] Although care was taken to implement control measures within the construction zone in this outbreak, similar precautions were not taken outside the construction zone, with workers using the same hallway as patients on a haematology/oncology ward. This outbreak highlights the importance of ensuring complete separation of patients and construction activities and personnel, even outside construction areas.[52]

Recent mucormycosis outbreaks highlight the need to pay close attention to the hospital environment. Investigating these outbreaks presents several challenges. First, because there is no routine surveillance for mould infections, and cases in an outbreak often occur over several months, it is difficult to determine if and when an outbreak is occurring. Second, numbers of outbreak-associated cases are often small, and case-control studies to determine common exposure might not yield any significant results. Last, more research is needed to understand the optimal indoor environments in hospitals and how to achieve and maintain those standards. In the USA and Europe, no standards exist for airborne mould concentrations, and the value of routine hospital air sampling is unclear,[53] although a study from Spain identified high levels of airborne *Aspergillus fumigatus* associated with aspergillosis cases in patients undergoing heart surgery.[54]

Similar challenges are evident during investigations of other hospital-associated mould infections, such as *Bipolaris* spp surgical site infections in 21 patients undergoing cardiothoracic surgery at ten hospitals in Texas, Arkansas, and Florida, during 2008–13.[55]

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Bipolaris surgical site infections had been rarely reported previously, raising suspicion that a common source might be responsible for this observed temporal and geographical clustering. However, epidemiological investigation did not reveal shared exposures, and the genetic diversity among isolates detected by multilocus sequence typing (MLST) was also consistent with multiple environmental sources.[56] Investigation of another outbreak caused by a different pathogen (*C neoformans*) not known to result in clusters of infection or be transmitted in a health-care setting also did not reveal a common source. This unusual cluster involved six patients at a community hospital in Arkansas, where four patients developed *C neoformans* bloodstream infection and two developed respiratory infections during April–December, 2013. Clinical isolates from the six patients had three separate MLST patterns, suggesting either a point source consisting of multiple cryptococcus strains or an unknown non-point source.[57] The investigation revealed that short-term steroid use was associated with increased risk for cryptococcosis, which had not been previously described for this infection.[57] Thorough investigation of possible outbreaks of hospital-associated IFIs is needed to better understand their sources and to guide prevention measures.

Candida is a common pathogen causing health-care-associated bloodstream infections.[58] However, candidaemia outbreaks are relatively infrequent, probably because many *Candida* species are commensal organisms, and most cases of invasive candidiasis arise from patients' own gastrointestinal or skin flora. Outbreaks with species such as *Candida parapsilosis* and *Candida tropicalis* do occur, typically among patients in neonatal intensive care units, and have been associated with transmission via health-care workers' hands or environmental surfaces.[59–61] Outbreaks of *Candida auris*, a newly emerging, multidrug-resistant yeast, have occurred in the UK and several other countries; early evidence suggests that *C auris* might be transmitted in health-care settings.[62,63]

There has been an overall decline in candidaemia in neonatal intensive care unit populations; these declines could be due to increased use of antifungal prophylaxis, improvements in central venous catheter insertion and maintenance, antibiotic stewardship practices, or under-recognition or under-reporting of small clusters.[64] The observed shift in the distribution of species causing invasive candidiasis towards more non-*Candida albicans* species is concerning given the high rates of antifungal resistance in several of these species, particularly *Candida glabrata*.[65] Multisite population-based candidaemia surveillance in the USA indicates that although fluconazole resistance rates have remained stable or decreased, echinocandin resistance rates have increased.[64] Furthermore, echinocandin non-susceptible *C glabrata* infections appear to be concentrated in a few hospitals, and more than half of these cases occurred in people with no known prior echinocandin exposure, suggesting possible environmental or person-to-person transmission mechanisms.[66]

## Contaminated medical products

Since 2000, several IFI outbreaks in the USA have been linked to contaminated pharmaceuticals produced by compounding pharmacies.[67] Facility inspections revealed deficiencies in production practices, including problems with flow hoods, inadequate training, absence of environmental sampling, and presence of mould in clean areas. These

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outbreaks suggest that clinicians and investigators should remain vigilant for IFIs potentially linked to contaminated medical products.

One of the most remarkable and largest known health-care-associated IFI outbreaks occurred in the USA in 2012–13, and involved 753 cases of *Exserohilum rostratum* infection. Patients who received injections of contaminated preservative-free methylprednisolone from a single compounding pharmacy developed meningitis, localised spinal and paraspinal infections, and peripheral joint infections.[68] Close collaboration between local, state, and federal health agencies and clinicians resulted in rapid public health actions, including recall of the contaminated methylprednisolone, notification of nearly 14 000 people who were potentially exposed to the product, and development and dissemination of diagnostic and treatment guidance for this unfamiliar clinical entity.[69,70] These public health actions were estimated to save more than 100 lives.[69] Although no molecular typing methods for *E rostratum* or knowledge of its population structure existed at the time of the outbreak, WGST analysis of 28 isolates from patients and the contaminated methylprednisolone indicated nearly identical genomes.[70] No more than two single nucleotide polymorphisms (SNPs) separated any of the isolates, whereas substantial genetic diversity (more than 20 000 SNPs) was observed among unrelated control isolates.[70]

Similar fungal contamination of two different compounded products led to an outbreak involving 47 cases of fungal endophthalmitis, including 21 cases linked to Brilliant Blue G intraocular dye (used during retinal surgery) contaminated with *Fusarium incarnatum-equiseti* species complex, and 26 cases linked to intravitreal injection of triamcinolone acetate contaminated with *Bipolaris hawaiiensis*.[71] Both products were produced by a single compounding pharmacy in Florida, which suspended its sterile compounding services and recalled all of its sterile compounded products.[71] Genetic similarity among six of the bipolaris isolates by MLST indicated that these infections were probably linked to contaminated triamcinolone. This finding contrasts with the heterogeneity of bipolaris isolates observed in the outbreak among patients undergoing cardiothoracic surgery.[56]

Contaminated antinausea medication was implicated in an outbreak of *Sarocladium kiliense* bloodstream infections among more than 50 paediatric oncology patients in Colombia and Chile during 2013–14.[72] WGST done on 25 isolates from patients and the contaminated medication confirmed the antinausea medication as the likely outbreak source.[72]

## Donor-derived IFIs in organ-transplant recipients

Cases and small clusters of IFIs transmitted through donation of infected organs are rare but can result in serious complications.[73] Known donor-derived IFIs include histoplasmosis, coccidioidomycosis, cryptococcosis, and various mould infections. Microsporidiosis also appears to be an emerging donor-derived IFI; in the first known donor-derived cluster of this infection, three transplant recipients developed *Encephalitozoon cuniculi* infection after receiving organs from the same donor.[74] Recognition of IFIs transmitted through infected organs remains challenging, since distinguishing these infections from IFI acquired post-transplantation or reactivation of latent IFI can be difficult. Further efforts to improve recognition of these infections, including determining the importance of donor screening practices, are needed.

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## Conclusions

IFI outbreaks are highly diverse, are caused by many different fungal pathogens, affect a wide variety of populations and settings, and are linked to numerous sources. Outbreak-associated IFI cases represent a small proportion of all IFIs, but these cases frequently provide new and important epidemiological information and a better understanding of the environmental niches of the causative fungi. Furthermore, outbreaks often reveal emerging areas of concern that apply to IFIs in general. These topics include IFIs in new populations at risk due to factors such as travel or relocation, occupation, or immunosuppression;[37,39,57] IFIs associated with unusual events and sources such as natural disasters[43,45] and contaminated medications, often with unexpected pathogens;[68,71,72] and fungal pathogens appearing in geographic regions in which they have not been previously recognised.[22,31]

In addition to these emerging issues, IFI outbreaks highlight long-standing clinical and public health challenges. These challenges include the need for more rapid and accurate diagnostic tools for many IFIs and additional methods to determine immunity, which is especially important for endemic mycoses. Other questions pertinent to endemic mycoses include the utility and feasibility of personal protective equipment and environmental remediation methods. In community-acquired and health-care-associated IFI outbreaks, an environmental point source is not always apparent,[42,55] and interpreting environmental sampling (figure 2) results can be challenging, particularly in health-care settings. Health-care infection control, especially as it relates to hand hygiene, construction, and management of indoor air quality and environment, continues to be important in IFI outbreaks. Antifungal stewardship practices also deserve continued attention, particularly given the increases in resistant fungal pathogens and the sometimes very expensive and toxic nature of some antifungal therapies. Last, because primary prevention is challenging for many IFIs, particularly those that are community-acquired, increasing awareness of IFIs among health-care providers and the public remains one of the most important areas for ongoing work in this field. Non-specific signs and symptoms can make IFIs difficult to identify, and improved methodologies are needed for faster and more accurate diagnosis. Advancements in molecular methods to diagnose IFIs and molecular typing methods to assess genetic relatedness will continue to enhance outbreak investigations.

Health-care provider awareness of IFIs is essential for prompt public health responses to outbreaks. In the USA, comprehensive surveillance systems do not exist for most IFIs. Routine surveillance would allow for easier detection of increased numbers of cases over what could usually be expected during a certain timeframe in a specific area. Clinicians should be aware, however, that even two cases of the same type of IFI clustered in time and place can raise suspicion for an outbreak. Given changes afoot in the ranges of the dimorphic fungi, clinicians who practice outside of these historically defined ranges should maintain vigilance for these infections. In most situations, IFI outbreak detection depends on astute clinicians recognising the presence of a possible outbreak and communicating the problem to local public health authorities.

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**Key messages**

- Invasive fungal infection (IFI) outbreaks are caused by many different pathogens and occur both in the community and health-care settings
- Emerging features of IFI outbreaks include new populations at risk, pathogens in geographical areas where they have not previously been recognised, and contaminated compounded medications
- Challenges with IFI outbreak recognition, response, and prevention include the need for improved rapid diagnostic methods, lack of routine IFI surveillance, adherence to health-care infection control practices, and health-care provider and public awareness

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### Search strategy and selection criteria

We searched the US Centers for Disease Control and Prevention Mycotic Diseases Branch archives between May, 2016 and June, 2016 for publications and conference abstracts describing fungal disease outbreaks from the past decade. We also searched PubMed using combinations of the terms “fungal disease”, “mold infection”, “outbreak”, “cluster”, and specific fungal diseases (eg, aspergillosis, mucormycosis, coccidioidomycosis) with no date or language restrictions. Articles were included if they highlighted emerging fungal disease outbreak features or issues, with an emphasis on outbreaks in the USA in the past decade.

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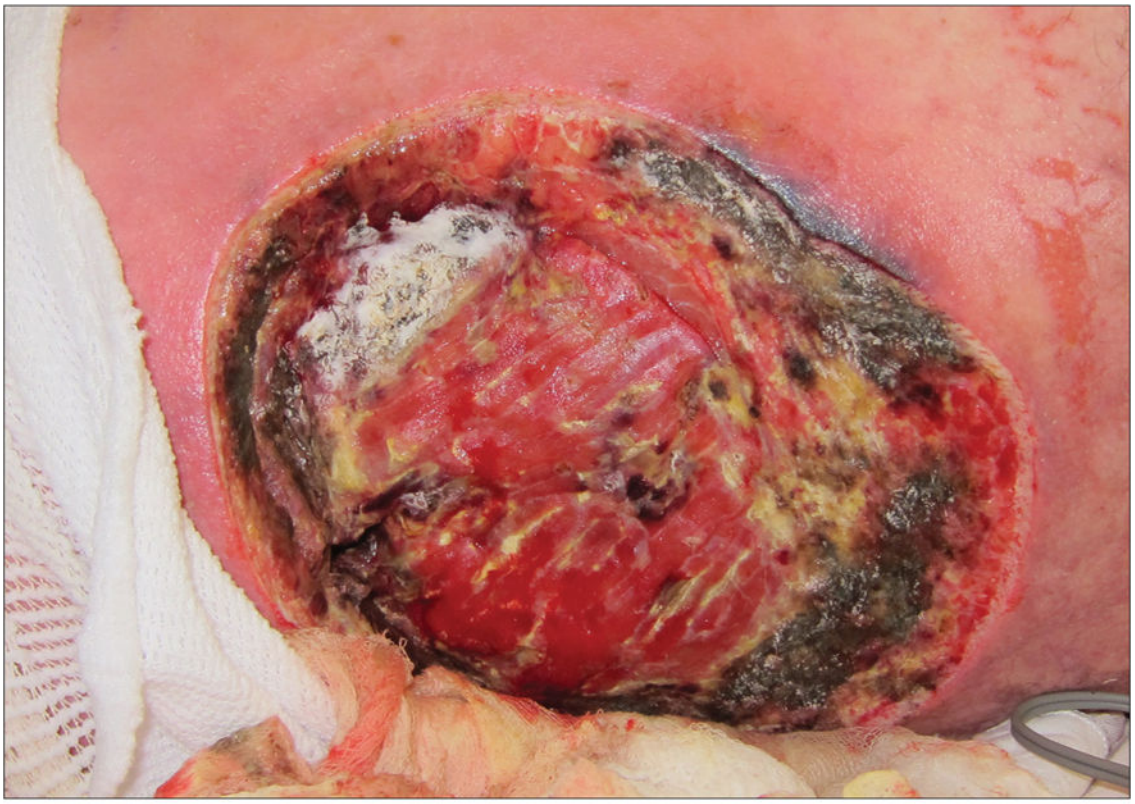

**Figure 1. Soft-tissue mucormycosis caused by Apophysomyces trapeziformis**

Left flank wound in a mucormycosis patient, with macroscopic fungal growth (tissue with white, fluffy appearance) and necrotic borders before repeated surgical debridement.[43,45]

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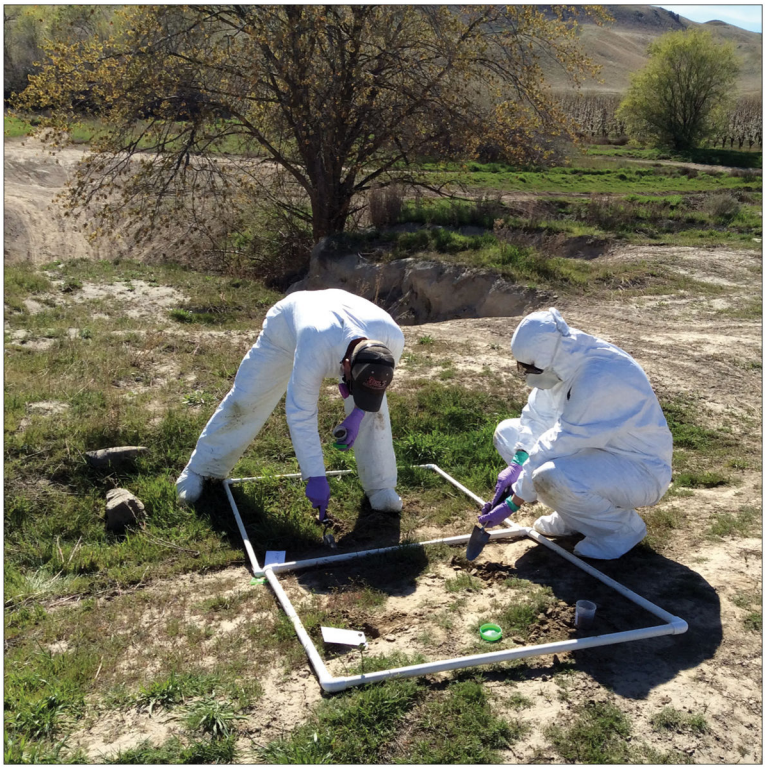

**Figure 2.**
Environmental sampling for *Coccicioides* spp

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*Lancet Infect Dis*. Author manuscript; available in PMC 2018 December 01.

**Table**

Notable fungal disease outbreaks

| | Pathogens | Location | Number of cases and patient population | Outcomes | Suspected source or precipitating factor |
|---|---|---|---|---|---|
| Keratitis[5,6] | *Fusarium* spp | USA, Hong Kong, Singapore | >200 contact lens wearers | Corneal transplantation required in approximately a third of patients | Contamination of contact lens solution bottles or lens cases |
| Endophthalmitis[7] | *Fusarium oxysporum* | Czech Republic | 20 cataract surgery patients | 19 with vision loss, 2 enucleated | Viscoelastic filling solution |
| Fungaemia[8] | *Fusarium verticillioides* | Greece | 7 hospitalised internal medicine patients | 4 deaths | Hospital renovation |
| Mucormycosis[9] | *Rhizomucor* spp | Egypt | 5 paediatric patients with acute leukaemia | 3 deaths | Contaminated air handling units and ventilation ducts |
| Cutaneous mucormycosis[10] | *Rhizopus delemar* | USA | 6 hospitalised paediatric patients | 6 deaths | Contaminated hospital linens |
| Various health-care-associated fungal infections[11] | Various fungi | USA | 50 paediatric patients with cancer | 16 deaths | Excavation adjacent to the hospital |
| Lymphocutaneous sporotrichosis[12] | *Sporothrix schenckii* | South Africa | 17 gold mine workers | Not stated | Contaminated soil and untreated wood used in mines |
| Trichosporonosis[13] | *Trichosporon asahii* | Jamaica | Positive in 63 hospitalised patients | 49 patients had colonisation and 4 had invasive infection, of whom 3 died | Contaminated washbasins |
| Pneumocystis pneumonia[14] | *Pneumocystis jirovecii* | Denmark | 22 renal and liver transplant recipients | 1 death | Hospital transmission |
| Tinea capitis[15] | *Trichophyton violaceum* and *Microsporum audouinii* | Israel | 145 paediatric refugees | Successful treatment with griseofulvin in all patients | Poor living conditions |
| Tinea capitis gladiatorum[16] | *Trichophyton tonsurans* | Turkey | 29 student wrestlers | Successful treatment with terbinafine in >70% of patients | Not stated |
| Tinea corporis[17] | *T tonsurans* | USA | 21 health-care providers, staff, and patients at a paediatric hospital | Not stated | Multiple hospital admissions of the index patient |