

Preventing healthcare-associated *Aspergillus* infections: review of recent CDC/HICPAC recommendations

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Aspergillus spp. are ubiquitous environmental fungi that are increasingly recognized as a cause of severe illness and mortality in immunocompromised patients. More than 60 outbreaks of healthcare-associated invasive aspergillosis have been described in the English literature. Information gained from outbreak investigations, especially control measures, form the basis for current guidelines to prevent healthcare-associated aspergillosis. Guidelines from the Centers for Disease Control and Prevention (CDC) and Healthcare Infection Control Practices Advisory Committee (HICPAC) provide evidence-based recommendations for preventing healthcare-associated aspergillosis and should be adopted by healthcare facilities.

Keywords *Aspergillus*, HICPAC, Guidelines, outbreaks, healthcare-associated

Introduction

Aspergillus spp. are ubiquitous fungi that commonly occur in soil, water, and decaying vegetation. Invasive aspergillosis (IA) has been increasingly recognized as a cause of severe illness and mortality in immunocompromised patients [1–4]. Risk groups for IA include recipients of hematopoietic stem cell transplants (HSCT), solid-organ transplants, patients undergoing chemotherapy, and patients with advanced HIV infection (specifically those with CD4 counts <50/mm³). Other at risk patient populations include those with chronic obstructive lung disease, especially those on corticosteroids [5,6], those with granulomatous disease [7,8], burn injury [9], those receiving prolonged high-dose corticosteroid therapy [10,11], and critically ill patients in an intensive care unit [10–12].

The incidence and mortality of IA depends on the patient population. In the past, incidence figures have been based on reports from individual healthcare facilities. Invasive *Aspergillus* infections have been

reported in 2–26% of HSCT recipients and in 1–15% of solid organ transplant recipients [2]. Historically, the mortality rate has ranged from 74–92% [2]. An estimated 9.3–16.9% of all deaths in transplant recipients in the first year are attributed to IA [13]. More recently, TRANSNET has provided important information on the epidemiology of IA infection among organ transplant recipients at 24 transplant centers in the United States between 2001 and 2006 [14]. The one year cumulative incidence of first episodes of IA was 1.7% in HSCT patients and 0.65% in solid organ recipients. The 90 day all-cause mortality with IA was 58% in HSCT patients and 32% in solid organ transplant recipients. The most common infecting species in HSCT patients were *A. fumigatus* (43%), *A. flavus* (7%), *A. niger* (5%), and *A. terreus* (5%). Among solid organ transplant recipients the most common species were *A. fumigatus* (57%), *A. flavus* (7%), *A. niger* (5%), and *A. terreus* (5%).

This review will succinctly discuss the epidemiology of healthcare-associated aspergillosis and lessons learned from outbreaks of nosocomial aspergillosis. It will then focus on current guidelines for the prevention of healthcare-associated aspergillosis by the Centers for Disease Control and Prevention (CDC) and Healthcare Infection Control Practices Advisory Committee (HICPAC). The diagnosis and therapy for aspergillosis are not discussed.

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Healthcare-associated aspergillosis

Aspergillus spp. have been cultured from numerous hospital sources including unfiltered air, ventilation systems, contaminated dust dislodged during hospital renovation and construction, horizontal surfaces, and food.

Healthcare-associated aspergillosis is most commonly acquired via inhalation of airborne spores resulting in pulmonary aspergillosis. Subsequently, the fungus may disseminate via the bloodstream to involve multiple other deep organs. Post-operative wound infections are felt to result from the deposition of airborne fungal spores into the wounds at the time of operation. Primary cutaneous infection may result from spore deposition on skin damaged or abraded by tape or adhesive devices (e.g., cardiac monitors) or result from contact with contaminated materials such as dressings or arm boards.

Aspergillus spp. and other filamentous fungi have been isolated from hospital water supplies [15,16]. Anaissie and Costa have proposed that patients can develop nosocomial aspergillosis via the airborne route from a hospital water source [17]. However, the strong association of construction and renovation with *Aspergillus* outbreaks suggests that most outbreaks occur as a result of airborne spores from non-water environmental sources [18]. The source for sporadic cases of aspergillosis has not been delineated.

Lessons from healthcare-associated outbreaks

More than 60 outbreaks of aspergillosis in healthcare facilities have been reported in the English literature [19,20]. The epidemiology and mechanisms of these outbreaks, as well as the interventions undertaken to control the outbreaks provides the foundation for the current infection control guidelines. Further, outbreaks of IA continue to be reported despite the development of preventive guidelines (Fig. 1).

Unless otherwise noted, the summary data reported below is derived from the excellent review of nosocomial aspergillosis, 1966–2005, by Vonberg and Gastmeier [20] with the inclusion of additional outbreaks reported between 1966 and 2005 [21] and outbreaks reported from 2005–2007 [22–27]. Other excellent papers have reviewed primary cutaneous aspergillosis [28] and post-operative aspergillosis [29].

Epidemiology

The species of *Aspergillus* associated with outbreaks have included *A. fumigatus*, *A. flavus*, *A. terreus*, *A. niger*, *A. glaucus*, *A. oryzae*, and *A. ustus* (Fig. 2). In many outbreaks multiple species were involved, or the exact outbreak pathogen was not speciated or was unknown.

Vonberg and Gastmeier have summarized the underlying diseases of 458 patients described in 53 outbreaks between 1967 and 2005: hematologic malignancy, 299 patients; solid organ transplant, 44 patients; other immunocompromised patients, 77 patients; and non-immunocompromised patients, 28 [20]. The overall mortality among these patients was 55% and by patient type was as follows: hematologic malignancy 58%, solid organ transplant 56%, other immunocompromised patients 52%, and non-immunocompromised patients 39%.

Hospital sources of *Aspergillus*

Most outbreaks of nosocomial aspergillosis have resulted from contamination of the air due to construction, renovation, or demolition activities (see Fig. 3). Outbreaks in the 1970s and 1980s of filamentous fungal infections (i.e., *Aspergillus* spp., zygomycetes), often resulted from sources outside the hospital with inadequate ventilation systems (e.g., open windows, non-filtered air supply, contamination of ventilation system) [30–35]. Pigeon excreta was suspected to be the source in two outbreaks [30–32].

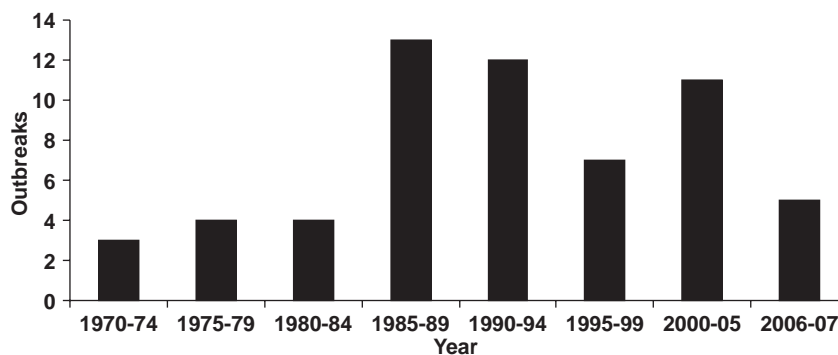
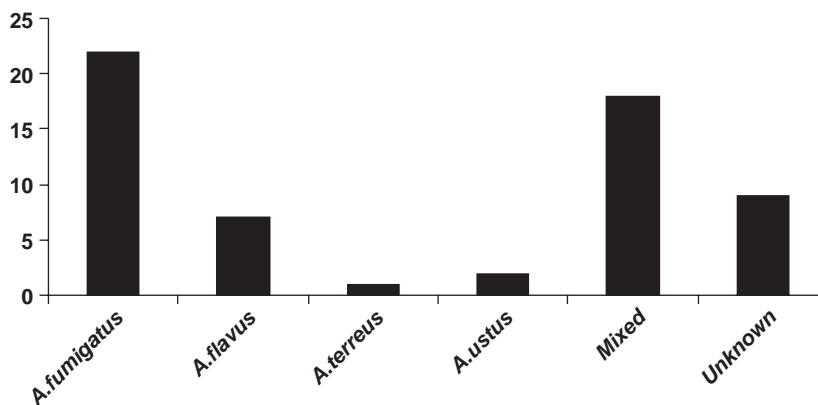


Fig. 1 *Aspergillus* outbreaks reported in the English literature, 1970–2007 based on year of publication.

Fig. 2 Distribution of *Aspergillus* species reported in outbreaks, 1967–2007. If an outbreak included patients with a single species isolated and non-speciated *Aspergillus* strains, it was coded as the species isolated. If an outbreak had included patients with multiple species isolated and non-speciated *Aspergillus* strains, it was coded as a mixed infection.



The source of most outbreaks of nosocomial aspergillosis has been internal construction or renovation with failure to control spread of contaminated dust or debris [25,36–45]. Importantly, outbreaks have resulted from construction or renovations on floors above or below where the infected patients were housed [36,37]. In addition, outbreaks have resulted from construction in hospital locations remote from where the patients were housed but where ancillary procedures were performed such as radiology [38]. Contaminated air vents or filters have often been the source of infection [21,31,32,41,46]. Other environmental sources of infection have included contaminated objects including syringes and spinal needles [22,23], a liquid nitrogen tank near the operating room [27], gauze used to cover venipuncture sites [28], dressing supplies [47], latex finger stalls [48], and electronic equipment in the operating room [49]. In some cases water exposure and damage was determined to be the mechanism of contamination [28]. Dust above acoustical ceiling tiles has been a potential ongoing source for *Aspergillus* spores leading to nosocomial infections when acoustical ceiling tiles have been removed or damaged, allowing airborne dissemination of fungal spores [36,40,50].

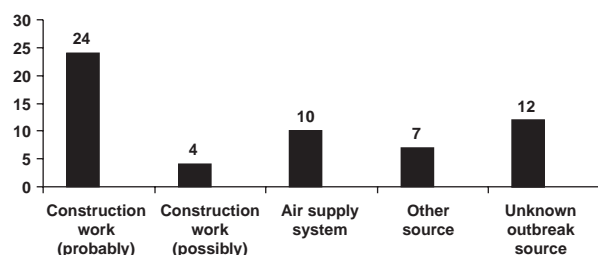


Fig. 3 Distribution of sources of nosocomial *Aspergillus* outbreaks. Modified from reference [20]. Outbreaks were stratified by number and percent of outbreak source.

Infection sites

Most cases of outbreak-related nosocomial aspergillosis were caused by inhalation of airborne fungal spores resulting in pulmonary disease. Dissemination from a pulmonary site is well described. More than 500 cases of post-operative aspergillosis have been described [29]. Most cases are presumed to result from airborne infection during the surgical procedure. The majority of reported cases have been associated with cardiac surgery, ophthalmological surgery, and dental surgery. Cutaneous aspergillosis is also well described often as a result of the use of contaminated dressing materials [28,47,51].

Relationship between airborne *Aspergillus* spore counts and infection risk

Many outbreaks have assessed the relationship of *Aspergillus* spore counts and infection risk [20]. High numbers of spores have often been found in the air during an outbreak, with significant reductions following remediation efforts such as cleaning contaminated filters, improving airflow, and eliminating intake of air from locations with high ambient spore levels (e.g., intake near refuse or internal construction). However, it has been impossible to relate a specific number of airborne spores to a quantifiable infection risk among patients, including highly immunocompromised patients. For this reason, no recommendation has been made by the CDC regarding routine microbiologic air sampling before, during, or after facility construction or renovation, or before or during occupancy of areas housing immunocompromised patients.

Molecular typing

Molecular typing of *Aspergillus* spp. has been extensively reviewed by Birth and colleagues [52]. The

method most commonly used is random amplification of polymorphic DNA (RAPD), though other methods including restriction fragment length polymorphism (RFLP) and polymorphic microsatellite marker (PMM) analyses also have high discriminatory power [53]. Extensive inter-laboratory variability and significant differences in methodologies make it difficult to interpret data obtained from multiple typing methods. In addition, the extreme diversity observed among environmental and patient isolates of *A. fumigatus* contribute to the complexity of defining a molecular strain type [54,55]. Nevertheless, molecular typing of *Aspergillus* strains has proved useful to determine that a common source outbreak existed [26,56] or did not exist [46,57].

Pseudo-outbreaks

Pseudo-outbreaks of aspergillosis have also been reported [58–60]. A pseudo-outbreak is defined as a cluster of ‘infections’ due to contamination of culture materials resulting in patients mistakenly classified as ‘infected’. Weems and colleagues reported a pseudo-outbreak of aspergillosis, which was traced to blood culture bottles that had become contaminated while stored in the same room as *Aspergillus* isolates [58]. Laurel and co-workers reported a pseudo-outbreak that resulted from contamination of culture plates with *A. niger* in a clinical microbiology laboratory due to construction [59]. Finally, Freeman and colleagues reported a pseudo-outbreak of *A. sydowii* keratitis due to contamination of culture media as a result of construction next to an eye clinic [60]. As with true outbreaks, pseudo-outbreaks were usually the consequence of internal hospital construction or renovation.

CDC/HICPAC guidelines for the prevention of healthcare-associated aspergillosis

Four guidelines have been published since 2000 by the CDC and/or HICPAC that provide recommendations relevant to prevention of healthcare-associated aspergillosis: Guidelines for Preventing Opportunistic infections among Hematopoietic Stem Cell Transplant Recipients (2000) [61], Guidelines for Preventing Healthcare-Associated Pneumonia, 2003 [62], Guidelines for Environmental Infection Control in Healthcare Facilities (2003) [63], and Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings, 2007 [64]. The Guideline for Isolation Precautions provides recommendations for protection isolation for HSCT patients, and largely supplants the earlier Guideline on Opportunistic

infections among Hematopoietic Stem Cell Transplant Recipients. The CDC/HICPAC guidelines are evidence-based and recommendations are rated according to the quality of the evidence and whether the recommendation is required by law (Tables 1 and 2).

Additional guidelines of interest include the following: Construction-related Nosocomial Infections in Patients in Health Care Facilities: Decreasing the Risk of *Aspergillus*, *Legionella* and Other Infections (2001) [65], Guidelines for Design and Construction of Health Care Facilities (2006) [66], Treatment of Aspergillosis: Clinical Practice Guidelines of the Infectious Disease Society of America (2008) [67].

Limitations of current guidelines

The current guidelines are largely derived from an assessment of outbreak evaluations and remediation. The guidelines focus on eliminating sources of *Aspergillus* spp. reported in outbreaks and/or preventing transmission from the reported sources to high-risk patients. Unfortunately, there are few controlled trials demonstrating the efficacy or effectiveness of recommended methods for preventing nosocomial aspergillosis.

Several limitations are inherent in the current guidelines because of their reliance on outbreaks. First, the guidelines are focused on preventing outbreaks of aspergillosis rather than the prevention of sporadic infection. Second, the guidelines, in general, do not provide recommendations on preventing aspergillosis in patients once they leave a healthcare facility. Third, since multiple interventions were often instituted to eliminate an outbreak, the efficacy of a single intervention (e.g., copper-8-quinolinolate) is often difficult or impossible to assess. Finally, as with all guideline recommendations (e.g., chemoprophylaxis), they may become outdated as more recent studies become available. Thus the CDC/HICPAC Guidelines for Preventing Healthcare-Associated Pneumonia 2003 state ‘no recommendation can be made for the routine administration of antifungal agents such as itraconazole oral solution or capsules, low-dose parenteral amphotericin B, lipid-based formulations of amphotericin B, or nebulized amphotericin B administered by inhalation as prophylaxis for pulmonary aspergillosis in patients at high risk for this infection’. The Treatment of Aspergillosis: Clinical Practice Guidelines of the Infectious Disease Society of America state ‘antifungal prophylaxis with posaconazole can be recommended in HSCT patients with graft versus host disease who are at high risk for invasive aspergillosis and in patients with acute myelogenous leukemia or myelodysplastic syndrome who are at high risk for invasive aspergillosis

Table 1 Selected recommendations for the prevention and control of healthcare-associated pulmonary aspergillosis

Section	Recommendations (includes all categories IA, IB and IC recommendations, and selected category II recommendations and unresolved issues)	Category
	Surveillance	
I.B.1.	Maintain a high index of suspicion for healthcare-associated pulmonary aspergillosis in severely immunocompromised patients (i.e., ANC <500/mm ³ for 2 weeks or <100/mm ³ for 1 week), most notably HSCT recipients and recipients of solid-organ transplants or patients with hematologic malignancies who are receiving chemotherapy, when they are severely neutropenic and persons receiving prolonged high-dose steroids	IA
I.B.3.a.	Do not perform routine, periodic cultures of the nasopharynx of asymptomatic patients at high risk	IB
I.B.3.b.	Do not perform routine, periodic cultures of equipment or devices used for respiratory therapy, pulmonary function testing, or delivery of inhalation anesthesia in the HSCT unit, nor of dust in rooms of HSCT recipients	IB
I.B.3.c.	<i>No recommendation</i> can be made about routine microbiologic air sampling before, during, or after facility construction or renovation, or before or during occupancy of areas housing immunocompromised patients	UR
I.B.4.	In facilities with PEs, perform surveillance of the ventilation status of these areas either by continuous monitoring or periodic analysis of the following parameters: room air exchanges, pressure relations and filtration efficacy to ensure the appropriate levels are maintained	IB
II.A.1.a.	Prevention of transmission of <i>Aspergillus</i> : Planning new specialized-care units for high-risk patients When constructing new specialized-care units with PE for allogeneic HSCT recipients, ensure that patient rooms have adequate capacity to minimize accumulation of fungal spores via 1) HEPA filtration of incoming air, 2) directed room airflow, 3) positive air pressure in patient's room in relation to the corridor, 4) well-sealed room, and 5) high (≥ 12) air changes per hour.	IB, IC
II.A.1.b.	Do not use LAF routinely in PE	IB
II.A.2.	<i>No recommendation</i> can be made for constructing PE for recipients of autologous HSCTs or solid-organ transplants Prevention of transmission of <i>Aspergillus</i> : In existing facilities with HSCT units and no cases of healthcare-associated aspergillosis	UR
II.B.1.a.	Place an allogeneic HSCT recipient in a PE that meets conditions outlines in section II.A.1.	IB
II.B.1.b.	<i>No recommendations</i> can be made for routinely placing a recipient of autologous HSCT or solid-organ transplant in PE	UR
II.B.2.	Maintain air-handling systems in PE and other high-risk patient-care areas according to published recommendations	IB, IC
II.B.3.	Develop a water-damage response plan for immediate execution when water leaks, spills, and moisture accumulation occur to prevent fungal growth in the involved area	IB
II.B.4.a.	Wet-dust horizontal surfaces daily using a cloth that has been moistened with an EPA-registered hospital disinfectants	IB
II.B.4.b.	Avoid dusting methods that disperse dust (e.g., feather dusting)	IB
II.B.4.c.	Keep vacuums in good repair and equip them with HEPA filters for use in areas with patients at high risk	IB
II.B.5.	Do not use carpeting in hallways and rooms occupied by severely immunocompromised patients	IB
II.B.7.b.	<i>No recommendation</i> can be made about specific types of respiratory-protection device (e.g., surgical mask, N95 respirator) for use by a severely immunocompromised patient who leaves the PE during periods when there is no construction, renovation or other dust-generating activity in progress in or around the healthcare facility	UR
II.B.8.	Systematically review and coordinate infection-control strategies with personnel in charge of the facility's engineering, maintenance, central supply and distribution, and catering services	IB
II.B.9.	When planning construction, demolition, and renovation activities in and around the facility, assess whether patients at high-risk for aspergillosis are likely to be exposed to high ambient-air-spore counts of <i>Aspergillus</i> spp. from construction, demolition, and renovation sites, and if so, develop a plan to prevent such exposures	IA
II.B.10.	During construction, demolition, or renovation activities, construct impermeable barriers between patient-care and construction areas to prevent dust from entering the patient-care areas	IB
II.B.11.	Direct pedestrian traffic that come from construction areas away from patient-care areas to limit the opening and closing of doors or other barriers that might cause dust dispersion, entry of contaminated air, or tracking of dust into patient-care areas.	IB
II.B.12.	Do not allow fresh or dried flowers or potted plants in patient-care areas for severely immunocompromised patients Prevention of transmission of <i>Aspergillus</i> : In existing facilities with HSCT units when a case of aspergillosis occurs	II
II.C.1.b.	Determine if any ventilation deficiency exists in the PEs	IB

Table 1 (Continued)

Section	Recommendations (includes all categories IA, IB and IC recommendations, and selected category II recommendations and unresolved issues)	Category
II.C.2.	If no evidence exists that the patient's aspergillosis is facility-acquired, continue routine maintenance procedures to prevent healthcare-associated aspergillosis (Sections II.B.1 through II.B.12)	IB
II.C.3.	If evidence of possible facility-acquired infection with <i>Aspergillus</i> spp. exists, conduct an epidemiologic investigation and an environmental assessment to determine and eliminate the source of <i>Aspergillus</i> spp.	IB
II.C.4.	Use an antifungal biocide (e.g., copper-8-quinolinolate) that is registered with the Environmental Protection Agency for decontamination of structural materials	IB

Abbreviations: HEPA, high efficiency particulate air; HSCT, hematopoietic stem cell transplantation; LAF, laminar air flow; PE, protective environment, UR, unresolved issue

Evidence-based classification

- Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.
- Category IB. Strongly recommended for implementation and supported by certain experimental, clinical, or epidemiologic studies and a strong theoretical rationale.
- Category IC. Required by state or federal regulation, or representing an established association standard.
- Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies, or a theoretical rationale.
- Unresolved issue: No recommendation is offered. No consensus or insufficient evidence regarding efficacy.

Adapted from Guidelines for Preventing Healthcare-Associated Pneumonia, 2003. Accessed 28 January 2003 from: http://www.cdc.gov/ncidod/dhqp/gl_hcpneumonia.html.

(A-I). Itraconazole may be effective, but tolerability limits its use (B-I)'.

Guidelines for Preventing Healthcare-Associated Pneumonia, 2003

The key CDC/HICPAC recommendations for the prevention of pulmonary aspergillosis are summarized in Table 1. As noted in the Guideline, the recommendations are focused on preventing exposure in HSCT patients housed in a protective environment. Preventing patient exposures to *Aspergillus* spp. outside the hospital is noted to be difficult but healthcare providers are instructed to focus on decreasing the patient's exposure to dusty environments, and by reducing or eliminating obvious sources or reservoirs of *Aspergillus* spp. (e.g., by removing plants or flowers from rooms where high-risk patients reside or receive medical treatment).

The CDC/HICPAC Guideline notes that the cornerstone of prevention of invasive pulmonary aspergillosis is housing severely immunocompromised patients (i.e., HSCT recipients) in a preventive environment. Key provisions of a preventive environment include: (1) use of a central or point-of-use high-efficiency particulate air filtration (HEPA), (2) high rates of room-air changes (± 12 per hour), (3) directed airflow, incoming at one side of the room and outgoing on the opposite side of the room, (4) positive room-air pressure relative to the corridor or anteroom, and (5) well sealed rooms.

The Guideline does not recommend the use of laminar air flow as its value has not been demonstrated. In addition, the Guideline does not recommend routinely placing immunocompromised patients other

than allogeneic HSCT recipients in a protective environment.

Guidelines for Environmental Infection Control in Healthcare Facilities (2003)

The CDC/HICPAC Guideline provides detailed recommendations on preventing nosocomial infections with a water source, environmental source, or transmitted by the airborne route. A key provision of the Guideline is detailed recommendations regarding protecting patients during construction, renovation, or demolition, both inside and outside the hospital (see Table 2). In summary, during construction or renovation, facility planners should (1) intensify efforts to seal off patient care units that house those at high risk for invasive aspergillosis and keep potential spore-bearing air from the construction or renovation site from infiltrating the rooms or areas where severely immunocompromised patients are housed, (2) clean newly constructed or renovated areas before allowing severely immunocompromised patients to enter them, (3) minimize aerosolization of *Aspergillus* spores during unit cleaning by using vacuums with HEPA filters, and cloth wipes and mop heads that have been pre-moistened with an EPA-approved hospital disinfectant, and (4) allow HSCT recipients to leave a protective environment only for essential procedures that cannot be performed in the patient rooms, and when the patients do leave the protective environment, they should be instructed to wear high-efficiency masks in areas near building construction or renovation.

Table 2 Selected recommendations for the environmental infection control in healthcare facilities: construction, renovation, remediation, repair, and demolition

Section	Recommendations (includes all categories IA, IB and IC recommendations)	Category
II.A.	Establish a multidisciplinary team that includes infection-control staff to coordinate demolition, construction, and renovation projects and consider proactive preventive measures at the inception; produce and maintain summary statements of the team's activities	IB, IC
II.B.	Educate both the construction team and the healthcare staff in immunocompromised patient-care areas regarding the airborne infection risks associated with construction projects, dispersal of fungal spores during such activities, and methods to control dissemination of fungal spores	IB
II.C.	Incorporate mandatory adherence agreements for infection control into construction contracts with penalties for noncompliance and mechanisms to ensure timely correction of problems	IC
II.D.	Establish and maintain surveillance for airborne environmental disease (e.g., aspergillosis) as appropriate during construction, renovation, repair, and demolition activities to ensure the health and safety of immunocompromised patients	IB
II.D.1.	Using active surveillance, monitor for airborne fungal infections in immunocompromised patients	IB
II.D.2.	Periodically review the facility's microbiologic, histopathologic, and postmortem data to identify additional cases	IB
II.D.3.	If case of aspergillosis or other healthcare-associated fungal infections occur, aggressively pursue the diagnosis with tissue biopsies and cultures as feasible	IB
II.E.	Implement infection-control measures relevant to construction, renovation, maintenance, demolition, and repair	IB, IC
II.E.1.	Before the project gets underway, perform an ICRA to define the scope of the project and the need for barrier precautions <ul style="list-style-type: none"> a. Determine if immunocompromised patients may be at risk for exposure to fungal spores from dust generated during the project b. Develop a contingency plan to prevent such exposures 	IB, IC
II.E.2.	Implement infection-control measures for external demolition and construction activities <ul style="list-style-type: none"> a. Determine if the facility can operate temporarily on recirculated air; if feasible seal off adjacent areas b. If this is not possible or practical, check the low-efficiency (roughing) filter banks frequently and replace as needed to avoid buildup of particulates c. Seal windows and reduce wherever possible other sources of outside air intrusion (e.g., open doors in stairwells and corridors), especially in PE areas 	IB
II.E.3.	Avoid damaging the underground water distribution system (i.e., buried pipes) to prevent soil and dust contamination of the water	IB, IC
II.E.4.	Implement infection-control measures for internal construction activities <ul style="list-style-type: none"> a. Construct barriers to prevent dust from construction areas from entering patient-care areas; ensure that barriers are impermeable to fungal spores and in compliance with local fire codes b. Block and seal off return air vents if rigid barriers are used for containment c. Implement dust control measures on surfaces and by diverting pedestrian traffic away from work zones d. Relocate patients whose rooms are adjacent to work zones, depending upon their immune status, the scope of the project, the potential for generation of dust or water aerosols, and the methods used to control these aerosols 	IB, IC
II.E.5.	Perform those engineering and work-site related infection control measures as needed for internal construction, repairs, and renovations <ul style="list-style-type: none"> a. Ensure proper operation of the air-handling system in the affected area after erection of barriers and before the room or area is set to negative pressure b. Create and maintain negative air pressure in work zones adjacent to patient-care areas and ensure that required engineering controls are maintained c. Monitor negative air flow inside rigid barriers d. Monitor barriers and ensure the integrity of the construction barriers; repair gaps or breaks in barrier joints e. Seal windows in work zones if practical; use window chutes for disposal of large pieces of debris as needed, but ensure that the negative pressure differential for the area is maintained f. Direct pedestrian traffic that comes from construction zones away from patient-care areas to minimize the dispersion of dust g. Provide construction crews with 1) designated entrances, corridors, and elevators whenever practical; 2) essential services (e.g., toilet facilities), and convenience services (e.g., vending machines); 3) protective clothing (e.g., coveralls, footgear, and headgear) for travel to patient-care areas; and 4) a space or anteroom for changing clothing and storing equipment 	IB, IC

Table 2 (Continued)

Section	Recommendations (includes all categories IA, IB and IC recommendations)	Category
	<p>h. Clean work zones and their entrances daily by 1) wet-wiping tools and tool carts before their removal from the work zone; 2) placing mats with tacky surfaces inside the entrance; and 3) covering debris and securing this covering before removing debris from the work zone</p> <p>i. In patient-care areas, for major repairs that include removal of ceiling tiles and disruption of the space above the false ceiling, use plastic sheets or prefabricated plastic units to contain dust; use a negative pressure system within this enclosure to remove dust; and either pass air through an industrial grade HEPA filter capable of filtration rates ranging from 300-800 ft³/minute, or exhaust air directly to the outside</p> <p>j. Upon completion of the project, clean the work zone according to facility procedures, and install barrier curtains to contain dust and debris before removal of rigid barriers</p> <p>k. Flush the water system to clear sediment from pipes to minimize waterborne microorganism proliferation</p> <p>l. Restore appropriate ACH, humidity and pressure differential; clean or replace air filters; dispose of spent filters</p>	
II.G.	Commission the HVAC system for newly constructed healthcare facilities and renovated spaces before occupancy and use, with emphasis on ensuring proper ventilation for operating rooms, AII rooms, and PE areas	
II.H.	No recommendation is offered on routine microbiologic air sampling before, during, or after construction or before or during occupancy of areas housing immunocompromised patients	UR
II.I.	If a case of healthcare-acquired aspergillosis or other opportunistic environmental airborne fungal disease occurs during or immediately after construction, implement appropriate follow-up measures	IB
II.I.1.	Review pressure differential monitoring documentation to verify that pressure differentials in the construction zone in PE rooms were appropriate for their settings	IB, IC
II.I.2.	Implement corrective engineering measures to restore proper pressure differentials as needed	IB, IC
II.I.3.	Conduct a prospective search for additional cases and intensify retrospective epidemiologic review of the hospital's medical and laboratory records	IB
II.I.4.	If there is no evidence of ongoing transmission, continue routine maintenance in the area to prevent healthcare-acquired fungal disease	IB
II.J.	If there is epidemiologic evidence of ongoing transmission of fungal disease, conduct an environmental assessment to determine and eliminate the source	IB
II.J.1.	Collect environmental samples from potential sources of airborne fungal spores, preferably using a high-volume air sampler rather than settle plates	IB
II.J.2.	If either an environmental source of airborne fungi or an engineering problem with filtration or pressure differentials is identified, promptly perform corrective measures to eliminate the source and route of entry	IB
II.J.3.	Use an EPA-registered anti-fungal biocide (e.g., copper-8-quinolinolate) for decontaminating structural materials	IB
II.J.4.	If an environmental source of airborne fungi is not identified, review infection control measures, including engineering controls, to identify potential areas for correction or improvement	IB
II.J.5.	If possible, perform molecular subtyping of <i>Aspergillus</i> spp., isolated from patients and the environment to establish strain identities	II

Abbreviations: ACH, air changes per hour; All, airborne infection isolation; HEPA, high efficiency particulate air; HVAC, heating, ventilation, air conditioning; ICRA, infection control risk assessment; PE, protective environment, UR, unresolved issue.

Evidence based classification

- Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.
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Adapted from Guidelines for Environmental Infection Control in Healthcare Facilities (2003). Accessed 28 January 2008 from: http://www.cdc.gov/ncidod/dhqp/gl_environmentinfection.html

Evaluation of outbreaks

The CDC/HICPAC guidelines also provide useful information on the measures that should be undertaken if a cluster of *Aspergillus* infections is noted among hospita-

lized patients. A detailed investigation should only be undertaken if the cases are believed to be possibly related to healthcare facility exposure. The first step is to ascertain all possible cases by active surveillance that

would include review of all medical records of patients housed in locations potentially involved in the outbreak or exposed to a potential source of *Aspergillus* and of pertinent microbiology data. Key aspects of an outbreak investigation include (1) construction of an outbreak curve, (2) line listing of all infected patients with review of pertinent clinical data (e.g., degree of immune suppression, admission and discharge dates, date of potential colonization, date of onset of infection, etc.), (3) evaluation of the air handling system including flow rates, pressure differentials, and potentially contaminated filters or ducts, (4) assessment for any water damage of adjacent walls, ceilings or floors, and (5) possible common source exposure (e.g., same operating room, evaluation in the same radiographic suite). Volumetric air sampling and environmental cultures, including water sources, may suggest a possible source, although as noted earlier, the risk of infection cannot be inferred from the presence of any particular number of airborne spores. Molecular typing of patient and environmental isolates may aid in linking a specific environmental source to patient isolates.

Elimination of an outbreak depends on strict adherence to the recommended CDC/HICPAC guidelines and elimination of any potential environmental sources linked to the outbreak. Facilities with a cluster of patients with *Aspergillus* may obtain aid in evaluating the outbreak from their local or state health departments or the CDC.

Conclusions

Invasive *Aspergillus* infections remain an important source of morbidity and mortality in immunocompromised patients. More than 60 outbreaks of healthcare-associated invasive aspergillosis have been described in the English literature. More than 60% of patients involved in these outbreaks have had a hematologic malignancy. Patients with other immunocompromising conditions have also been at risk including: neonates, those with solid organ transplants, high-dose steroid therapy and other malignancies. However, outbreaks have also involved surgical patients (especially those undergoing thoracic surgery) or patients in intensive care units. The overall mortality among patients involved in outbreaks has been in the range of 50–60%.

Most outbreaks of nosocomial aspergillosis have resulted from the circulation of air contaminated with fungal spores. In the 1970s and 1980s, nosocomial aspergillosis often resulted from sources outside the hospital with inadequate ventilation systems. More recent outbreaks have usually been due to internal

construction or renovation with failure to control spread of contaminated dust or debris.

Recent CDC/HICPAC guidelines reviewed in this paper provide detailed recommendations for the prevention of healthcare-associated invasive *Aspergillus* infection. Clinicians, medical specialists, especially physicians specializing in infectious disease, pulmonary medicine, and oncology, and infection control professionals should be familiar with these guidelines. The key interventions include surveillance for nosocomial aspergillosis and engineering controls designed to allow healthcare facilities to safely perform construction and renovations. Unfortunately, the number of ambient *Aspergillus* spores that assures patients will not acquire invasive aspergillosis or predicts an outbreak has not been described.

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