



Review

Prevention of healthcare-associated invasive aspergillosis during hospital construction/renovation works

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SUMMARY

The association between healthcare-associated invasive aspergillosis and hospital construction/building works is well recognized. This infection can cause significant morbidity and mortality and imposes a substantial burden on the healthcare system. The population of patients at risk for this opportunistic infection has expanded and multi-triazole drug resistance has emerged globally. Hence the need for a multi-faceted approach to prevent acquisition of invasive aspergillosis in acute care settings. This article is a summary of the Irish National Guidelines for the prevention of healthcare-associated aspergillosis which is based on published reports, international clinical guidelines, official engineering standards, and technical guidelines. We discuss the key recommendations and strategies for the prevention of invasive aspergillosis from the planning/pre-construction, construction, and post-construction phases. The importance of multi-disciplinary team involvement, education, and communication is emphasized.

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Introduction

Background

Healthcare-associated invasive aspergillosis (HCA-IA) is now well described, and a better understanding of the disease and preventive strategies has resulted in a

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reduction in incidence and mortality rates in high-risk populations where appropriate measures have been taken [1,2]. However, recent data have identified changes in the epidemiology of IA with the recognition of more at-risk patients, including those with severe influenza, chronic obstructive pulmonary disease (COPD), burns, cystic fibrosis, neonates, and some patients not typically regarded as immunocompromised [3]. The association with certain types of construction activity is well recognized, and the need for preventive measures while such activities are taking place has been accepted [4,5]. Similarly, immunocompromised patients are constantly exposed to airborne fungal spores when outside the hospital setting and cases of IA have been linked to *Aspergillus* exposure in patients' homes [6–8]. Therefore, healthcare providers must ensure that all recognized risks are minimized.

This summary is based on the guidelines on the prevention of HCA-IA during hospital construction/renovation works published by the Irish *Aspergillus* Subcommittee of the Scientific Advisory Committee of the Health Protection Surveillance Centre, as well as on international clinical guidelines, official engineering standards and technical guidelines and published literature [9]. Grading of the quality of the evidence was not performed since there are no published randomized controlled trials on the various recommended measures for the prevention of HCA-IA.

The burden of healthcare-associated invasive aspergillosis during hospital construction or renovation

Aspergillus species are ubiquitous fungi that commonly can be recovered from soil, water, dust, organically enriched debris, and decaying vegetation [10]. Many species of *Aspergillus* have been recognized in nature but only a few have been regularly associated with human disease. *Aspergillus fumigatus* belongs to the *Aspergillus* subgenus *Fumigati* section *Fumigati* and is the principal pathogenic *Aspergillus* species [11]. Invasive aspergillosis is primarily an infection of severely immunocompromised patients, notably patients with haematological malignancies undergoing intensive remission–induction chemotherapy, haematopoietic stem cell transplantation or solid organ transplant recipients [1,12–18]. Over the last decade it has been increasingly recognized that patients without known prior immunocompromise who are admitted to critical care, such as patients with severe COPD, influenza or other viral infections are at increased risk of IA [19–27].

Despite advances in our understanding of the interaction between *Aspergillus* species and the human immune response, improved diagnosis of IA, and more effective use of antifungal agents, this disease remains difficult to diagnose and treat early, therefore case fatality rates associated with IA remain high [16,28,29]. This makes prevention a priority in the management of at-risk patients. Recently, antifungal drug resistance in *A. fumigatus* affecting the triazole class has been described, and this threatens to limit future antifungal prophylactic and therapeutic options [30].

In the healthcare setting several environmental risks for IA are recognized although some are better defined than others. One of the major environmental risks continues to be patient exposure to construction work and generation of aspergillus and other mould spores. *Aspergillus* spores are well adapted to airborne dissemination [31,32]. They are passively liberated during construction/renovation activities and can be transported great distances as airborne particles by normal atmospheric conditions such as convection currents and wind. The respiratory tract is the most common portal of entry and the small diameter of the spores (~2.5–3.5 µm) permits them to reach the pulmonary alveolar spaces, where they may germinate to form hyphae [33]. Pulmonary aspergillosis may then develop following inhalation of airborne fungal spores, and high spore counts within patient-care areas represent an extrinsic risk factor for invasive disease [34]. Hospital-acquired outbreaks of IA have become a well-recognized complication of construction, demolition, or renovation work in or near hospital wards in which immunocompromised patients are housed [4,35,36]. In a review of outbreaks reported between 1966 and 2005, there were 53 affecting 458 patients [16]. In all but one outbreak, transmission was airborne and the respiratory tract was primarily affected. The most common (49%) probable or possible source was construction work or renovation activities within or around the hospitals, whereas the source remained unknown in 12 outbreaks. The minimum airborne concentration of aspergillus spores necessary to cause disease remains unknown; however, the authors concluded that airborne mould spores at any concentration may represent a threat for severely immunocompromised patients. A patient's risk of developing IA and its outcome vary according to the level of the individual's exposure to sources of fungal spores and their net state of immunocompromise [37].

Allogeneic haematopoietic stem cell transplant (HSCT) recipients and patients with acute myeloid leukaemia are the population consistently at most risk mainly because of severe prolonged neutropenia. However, not all cases of aspergillus infection that present clinically as IA in the hospital have been nosocomially acquired, as patients may already be colonized with *Aspergillus* spp. prior to their admission and starting immunosuppressive therapy [38]. Over the past decade, a decreased incidence of IA has been seen in this group, due to improved preventive measures of isolation and antifungal prophylaxis [2]. Other conditions have frequently been reported as risk factors for construction-related nosocomial fungal infections: graft-versus-host disease requiring immunosuppressive treatment, prolonged neutropenia following cytotoxic chemotherapy, prolonged use of antibiotics, steroid therapy, and tumour necrosis factor- α antagonists [38]. As the complexity of therapeutics increases and the survival rates from oncologic and haematologic conditions improves, it is likely that more patients will be at risk of IA [3,19,20]. Published incidence rates for IA in at-risk groups are shown in Table 1. At-risk patients may be categorized according to their degree of immunocompromise as enumerated in Box 1. However, this list is not exhaustive, and all patients should be individually risk-assessed.

Table 1
Incidence of invasive aspergillosis (IA) in at-risk groups

Category	Risk group	Incidence of IA (%)	Study design	No. of patients	
Haematopoietic stem cell transplantation	Allogeneic haematopoietic stem cell transplant recipients	2.5	Retrospective single centre [39]	106	
		8.1	Prospective multi-centre [40]	393	
		8.8	Retrospective multi-centre [41]	4213	
		3.5	Retrospective single centre [42]	20	
		15	Prospective single centre [43]	306	
		3.0	Retrospective single centre [44]	61	
		11.4	Retrospective single centre [45]	163	
		2.3–3.9	Prospective multi-centre [46]	8731	
		7.3–10.5	Prospective single centre [47]	327	
		7.66–9.23	Systematic review, 49 articles [48]	16,815	
		0.9	Prospective multi-centre [40]	393	
		1.3	Retrospective multi-centre [41]	4213	
		1.2	Retrospective single centre [42]	20	
		0.5	Prospective multi-centre [46]	8731	
		Solid organ transplantation	Lung transplant recipients	4.1	Retrospective single centre [12]
4.5	Retrospective single centre [49]			242	
13.3	Prospective single centre [50]			60	
6.6	Retrospective single centre [51]			362	
7.0	Retrospective single centre [52]			115	
7.6	Retrospective single centre [53]			251	
6.2 ^a	Review, 40 studies [54]			159	
12.8	Retrospective single centre [55]			2046	
Liver transplant recipients	0.8			Prospective multi-centre [40]	393
	3.4			Retrospective single centre [56]	175
	0.77			Retrospective single centre [57]	3215
Heart transplant recipients	0.7			Retrospective single centre [55]	2046
	4.8			Prospective multi-centre [40]	393
	0.4			Retrospective single centre [55]	2046
Renal transplant recipients	0.3			Prospective multi-centre [40]	393
	0.24	Retrospective single centre [57]	3215		
	1.3	Retrospective single centre [58]	595		
	0.12	Retrospective single centre [59]	2410		
	0.4	Retrospective single centre [56]	175		
Other	Intensive care patients and severe influenza intensive care patients	0.02	Retrospective multi-centre cohort study [25]	412	
		0.52	Prospective single centre [23]	~600	
		19	Retrospective multi-centre [27]	432	
		0.36	Retrospective single centre [21]	239	
		2.6	Retrospective single centre [60]	151	

COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation.

^a Median incidence based on review of literature.

Box 1

Categorization of at-risk groups for invasive aspergillosis

Group 1. No evidence of risk^a

1. Staff members^b, service providers and contractors
2. All patients not listed in Groups 2–4 below

Group 2. Increased risk

1. Patients on prolonged courses of high-dose steroids^c or tumour necrosis factor- α antagonists, particularly those hospitalized for prolonged periods
2. Severely immunosuppressed AIDS patients
3. Patients undergoing mechanical ventilation
4. Non-neutropenic patients on chemotherapy^d
5. Dialysis patients

Group 3. High risk

1. Patients with neutropenia for <14 days following chemotherapy
2. Autologous haematopoietic stem cell transplantation^e, i.e. during the neutropenic period
3. Adult acute lymphoblastic leukaemia patients on high-dose steroid therapy^c
4. Solid organ transplantation
5. Patients with chronic granulomatous disorder
6. Neonates in intensive care units
7. Chronic obstructive pulmonary disease (COPD) patients meeting GOLD stage III and IV criteria^f, patients with severe influenza and in intensive care or high-dependency units
8. Patients with extensive burns

Group 4. Very high risk

1. Allogeneic haematopoietic stem cell transplantation^e
 - a. during the neutropenic period
 - b. with graft-versus-host disease requiring steroid \pm other immunosuppressive therapy
2. Acute myeloid leukaemia
3. Non-myeloablative transplantation
4. Children with severe combined immunodeficiency syndrome
5. Prolonged neutropenia for >14 days following chemotherapy or immunosuppressive therapy
6. Aplastic anaemia patients

Cystic fibrosis patients should also be considered. Each cystic fibrosis patient is assigned to one of the above four categories depending on the stage of his/her illness.

The key measures for prevention of HCA-IA during construction and/or renovation are divided into three phases: planning and pre-construction phase, construction phase, and post-construction phase [4,6,9,35,62–67].

^a Assuming no known immunocompromise.

^b Staff should be informed of pending construction projects, and staff concerned re immunocompromise should be referred to Occupational Health.

^c Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a mean minimum dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks [61].

^d Absolute neutrophil count $>1 \times 10^9/L$.

^e Includes bone marrow transplantation patients.

^f Furthermore, wards with a high occupancy of COPD patients (e.g. respiratory wards) meeting GOLD stage III and IV criteria should be risk-assessed on the basis of the patients' levels of immunosuppression, and the threat posed to the patients by the construction activity. However, the guideline group recognizes that it is not possible to risk assess all COPD patients meeting GOLD stage III and IV criteria who are dispersed throughout the hospital.

Planning and pre-construction phase*Invasive aspergillosis risk assessment*

Prior to commencing any construction/renovation activity, a formal invasive aspergillosis risk assessment (IARA) must be performed [4–6,65,68]. The IARA involves a multidisciplinary team (MDT), the membership of which will be determined by the size and scope of the works and should as a minimum include representation from the following: management of the healthcare facility, project team, technical services, infection prevention and control team (IPCT), healthcare personnel from relevant clinical area(s), and health business services (HBS) estates. There are four steps in the risk assessment process:

- Step 1. Consider patient risk factors and assign to the correct at-risk group, groups 1–4 (Box 1). If more than one risk group is identified within a specific cohort, select the higher-risk group.

- Step 2. Detail the construction activity and assign a type: A1, A2, B, C or D (Supplementary Table I). A combination of factors is taken into account and includes whether the construction activity is major or minor, external or internal, containable or non-containable.
- Step 3. Determine the construction site preventive measures and assign a class, 0–III (Supplementary Box 1). Depending on the class selected, measures include dust control, debris removal and cleaning, patient risk reduction, ventilation systems, and traffic control.
- Step 4. Verify risk assessment by using a matrix as shown in Table II where the type of construction/renovation work is plotted against the patient risk group.

A document outlining the agreed measures required to reduce risk of IA for that specific project should be circulated to relevant stakeholders prior to the commencement of a project and will form the basis for the methods statement produced by the contractor. Implementation of the recommended preventive measures should be assigned to the appropriate groups which extend from ward level to the project manager and hospital management. Compliance with the recommended measures should be monitored by the relevant departments, e.g. technical services, IPCT, and cleaning staff with prior agreement on the monitoring procedures, reporting arrangements using a checklist (Supplementary Table II). Any breaches to the agreed measures should be notified immediately, and, in such instances, if significant risks to patients have been identified, it may be deemed necessary to convene an emergency meeting of the MDT to consider the required action. This could include cessation of the building works until necessary corrective actions have been implemented. The process and procedures for all such cessation of works must be agreed in advance between the stakeholders and specified clearly in the contract tender documents. The instruction to cease must be implemented strictly in accordance with provisions of the contract conditions.

Microbiological air sampling – determining a baseline

Environmental air sampling for aspergillus, although not performed routinely, is recommended where major construction/refurbishment works are to be undertaken, so that

baseline aspergillus levels may be established for both the construction zone and other areas which may be affected either by virtue of their proximity or the risk of airborne spread. Concern for a particularly high-risk patient cohort should prompt further environmental screening. It is recognized that airborne fungal spore counts can vary considerably over a short time span, thus multiple samples will be required weekly for a minimum of four weeks prior to commencement of building works in order to establish a baseline [69].

Currently there are no numerical threshold guidelines available for aspergillus counts; however, counts of <1 cfu/m³ for high-efficiency particulate air (HEPA) filtered rooms with $>99.95\%$ efficiency, and <5 cfu/m³ in ward areas without air filtration, have been suggested [4,5,9,16,65,69]. Microbiological air sampling should be continued while construction is ongoing. High aspergillus air counts when compared to baseline, and/or a higher than expected frequency of isolation of *Aspergillus* spp. from respiratory specimens from patients in the same or adjacent clinical areas, should prompt discussion and/or a meeting with members of the MDT. It is essential to alert clinicians/wards and departments to the potentially increased risk of IA in their at-risk patients. Further investigations should focus on the air-handling units (AHUs) in place and the possibility of ingress of outside air which may be contaminated as a result of ongoing construction/demolition or maintenance works. Preventive measures might include consideration of moving exposed patients to another part of the hospital and initiating or extending mould-active antifungal prophylaxis based on a risk assessment [23,65,70].

Mould-active antifungal prophylaxis

The standard practice of antifungal chemoprophylaxis is supported by several published reviews and meta-analyses of studies conducted in specific high-risk patient populations, especially those receiving treatments for haematological malignancies [71,72]. Current recommendations regarding prophylaxis of IA are summarized in Table III based on guidelines published by the Infectious Diseases Society of America (IDSA), the European Conference on Infections in Leukaemia and the European Society of Clinical Microbiology and Infectious Disease (ESCMID), European Confederation of Medical Mycology (ECMM) and European Respiratory Society (ERS) [73–75]. Some authorities recommend antifungal prophylaxis for selected solid organ transplant recipients [76,77], commenting that studies in these settings have been from non-randomized comparative trials with small patient numbers.

Several authors have published reports on the role of antifungal prophylaxis for the prevention of HCA-IA during construction/renovation work. Chabrol *et al.* in their single-centre experience showed a decreased incidence of IA in acute myeloid leukaemia patients who received prophylaxis during building works near their haematology unit [78]. Prophylaxis with voriconazole formed part of a multi-faceted approach during major hospital construction contributing to the successful control of an HCA-IA outbreak in another centre [79]. Similarly, a retrospective single-centre study showed that when an outbreak in haematology patients was experienced during hospital construction the addition of posaconazole prophylaxis to environmental control measures led to a reduction in further cases of IA [80]. A cost-effectiveness study on interventions for the prevention of IA during hospital

Table II
Matrix of construction project activity type, patient risk group, and class of required infection prevention and control precautions

Patient risk group	Construction activity type				
	Type A1	Type A2	Type B	Type C	Type D
Group 1. No evidence of risk	0	I	I	III	III
Group 2. Increased risk	0	I	II	III	III
Group 3. High risk	I	I	II	III	III
Group 4. Very high risk	I	I	II	III	III

This matrix was adapted from Haiduven [4].

Engagement with the infection prevention and control team is required irrespective of type of construction activity.

This is a guide, and, if specific risk issues are identified, an individual risk assessment of that issue may be required.

Table III

Consensus guidelines on antifungal prophylaxis against invasive aspergillosis (grading of evidence is shown in parentheses)^a

Type of patient	European Conference on Infections in Leukaemia [73]	Infectious Diseases Society of America [74]	European Society of Clinical Microbiology and Infectious Disease/ European Confederation of Medical Mycology/European Respiratory Society [75]
Induction chemotherapy in acute myeloid leukaemia	Posaconazole (AI) Itraconazole (BI) Aerosolized liposomal amphotericin B with fluconazole (BI) Voriconazole BII	Posaconazole (strong recommendation; high quality evidence) Voriconazole (strong recommendation; moderate quality evidence)	Posaconazole (AI) Aerosolized liposomal amphotericin B with fluconazole (BI) Voriconazole (CII) Liposomal amphotericin B (BII)
Induction chemotherapy in acute lymphoblastic leukaemia	No recommendations	No recommendations	Liposomal amphotericin B (BII)
Allogeneic haematopoietic stem cell transplant (HSCT) recipients, neutropenic phase	Voriconazole (BI) Itraconazole (BI) Posaconazole (BII) Aerosolized liposomal amphotericin B with fluconazole (BII) Micafungin (CI) Intravenous polyene (CII)	No recommendations	Posaconazole oral (BII) Aerosolized liposomal amphotericin B with fluconazole (BII) Micafungin (CI) Voriconazole (CI) Itraconazole (DI)
Allogeneic HSCT recipients with graft versus host disease (GVHD)	Posaconazole (AI) Itraconazole (BI) Voriconazole (BI) Micafungin (CII) Liposomal amphotericin B (CII)	Posaconazole (strong recommendation; high-quality evidence) Itraconazole (strong recommendation; high-quality evidence) Voriconazole (strong recommendation; moderate-quality evidence)	Posaconazole oral (AI) Voriconazole (CII) Itraconazole (CII) Micafungin (CIII)
Patients with prolonged neutropenia (haematologic disorders with poorly functioning neutrophils (e.g. aplastic anaemia and variants thereof, myelodysplastic syndromes), acute leukaemia with repeated and/or prolonged neutropenia, or a history of IA prior to transplantation)	Posaconazole (AI) Itraconazole (BI) Aerosolized liposomal amphotericin B with fluconazole (BI) Voriconazole BII	Posaconazole (strong recommendation; high-quality evidence) Voriconazole (strong recommendation; moderate-quality evidence) Micafungin (weak recommendation; low-quality evidence)	Posaconazole oral (AI) Aerosolized liposomal amphotericin B with fluconazole (BI) ABLC (CII) Micafungin (CII) Liposomal amphotericin B (CII) Voriconazole (CII) Itraconazole (DII)
Lung transplant recipients	No recommendations	Voriconazole, itraconazole or inhaled amphotericin B for 3–4 months after transplant (strong recommendation; moderate-quality evidence)	No recommendations

For the most up-to-date guidelines, please refer to the relevant websites of the Infectious Diseases Society of America, the European Conference on Infections in Leukaemia, the European Society of Clinical Microbiology and Infectious Diseases, the European Confederation of Medical Mycology, and the European Respiratory Society.

^a Not all the recommendations in these guidelines are licensed indications/approvals for use.

Box 2

Key recommendations for the prevention of healthcare-associated invasive aspergillosis (IA) during construction/renovation in acute care settings

Planning and pre-construction phase

- Measures should be taken to protect patients at risk of acquiring *Aspergillus* sp. infection as a consequence of hospital renovation, construction, or demolition work in or near to clinical areas.
- Hospital management must give sufficient notice (appropriate to the complexity of the project) to all interested parties including the infection prevention and control team (IPCT) of any planned activities before they start so that a comprehensive IA risk assessment is performed and appropriate preventive measures can be put in place to protect vulnerable patients.
- The hospital IPCT should take the lead in informing management of the risks involved by drafting local policies based on national and international guidelines.
- Contractors must agree to, and sign, a construction permit and be compliant with the local infection prevention and control policy.
- Surveillance of fungal spore burden by microbiological air sampling should be performed prior to the build to establish baseline levels and throughout the duration of the construction/renovation activity.
- Education and communication to hospital staff on the measures to prevent nosocomial IA.

Construction phase

- Major internal or external works may require transfer of at-risk patients to another part of the hospital if the environment cannot be protected from ingress of airborne fungal spores.
- Affected clinical areas should be monitored for ingress of dust in spite of preventive measures, and in the highest-risk groups air sampling should be used to monitor fungal counts.
- High-efficiency particulate air-filtered positive pressure facilities are preferred for the protection of high- and very high-risk patients during major internal, and non-containable external activities.
- In consultation with the clinical team(s) involved, consideration should be given to prescribing antifungal drug prophylaxis in selected patients based on a risk assessment.
- Microbiological air sampling should continue throughout this phase.
- Patients should be monitored throughout the project for clinical, radiological and mycological evidence that would suggest a diagnosis of invasive pulmonary aspergillosis.
- The microbiology laboratory should inform the IPCT of any increase in isolation of *Aspergillus* spp. from respiratory and air-sampling specimens that are above baseline/expected rates.

Post-construction phase

- Commissioning and validation should be performed by a competent third party and meet international standards.

construction revealed that the addition of antifungal prophylaxis to environmental control measures led to higher costs. However, it was shown to be more effective than environmental measures alone [81].

Patients receiving triazole prophylaxis should have therapeutic drug monitoring to ensure adequate serum concentrations are achieved and to allow for individualized optimized dosing [74,76,82]. Given its global emergence, ongoing surveillance of triazole resistance in *A. fumigatus* is important [83]. A recent report on surveillance of *A. fumigatus* in a single centre during hospital demolition demonstrated that 15% (30/200) and 4% (6/152) of environmental and clinical isolates, respectively, were triazole-resistant [84]. Genotyping of the triazole-resistant isolates showed a polyclonal distribution [84].

Management of existing ventilation systems

Many areas of the hospital may have mechanical ventilation systems already in use. The specification of these units will have been determined at the time of their original design and subsequent installation. Upgrading may be required on existing installations depending on the patient type to be housed in these units, construction activity classification, and overall risk assessment. It is important that all such units are reviewed at

the time of planning, that a risk assessment is undertaken, and that their appropriateness for the current situation is assessed. Temporary or permanent corrective measures may need to be in place due to the planned construction activity. These corrective measures should comply with local regulations and legislation such as the UK Health Technical Memorandum (HTM) 03 guidelines [85,86]. For healthcare facilities, relevant local engineering standards and technical guidelines must be referred to before designing the permanent correct solution. Where a room's environmental control system is made up of multiple components such as room-air, HEPA filter units, radiators, cooling units, and toilet extract fans, indoor environmental conditions should be in accordance with relevant current indoor environmental control and building standards (e.g. HTMs/Health Building Notes (HBNs)) [85–88].

Education and communication

Healthcare workers, cleaning staff, project managers, contractors and health-and-safety supervisors should be educated on the risk of invasive aspergillosis prior to construction taking place and during construction work whereby the infection control measures required to decrease its occurrence are explained. Clear communication through an

institution-wide information campaign should also be provided. Patients and relatives should be supplied with information leaflets.

Construction phase

Measures to reduce dust emission from the construction site

It is essential to use measures to minimize dust generation from construction or renovation sites which will ultimately depend on the type of construction activity (Supplementary Table I). An impermeable dust barrier from floor to slab/floor must be constructed and air-tightness ensured, particularly if the works are proximal to clinical areas until the project is complete. Windows and doors should be sealed and a separate entrance away from patient traffic should be created for use by construction workers. Construction workers should wear protective clothing which should be removed when leaving the construction site. The direction of airflow between the construction zone and the existing hospital should be maintained in a clean to less-clean direction by using a portable extract fan and to ensure that this less-clean air from the construction zone is exhausted directly to the outside where feasible and away from intake vents or filtered through a minimum of an F9 filter. Debris should be contained in covered containers and removed at the end of the work day. The work area should be cleaned and vacuumed with HEPA-filtered vacuums daily or more frequently if required [5,9,65,89].

Creating a protective environment

Because inhalation is the major route of acquisition of infection, an efficient and controlled ventilation system is essential in the prevention of nosocomial aspergillosis. The method by which patients are protected will depend on the IARA performed during the planning stage. If at all possible, patients should ideally be moved away from the construction area prior to commencing, and throughout the duration, of the construction works in order to decrease the risk of exposure to dust. It has been shown that the burden of airborne fungal spores is higher during the demolition stage when compared to the building work [90,91]. The IPCT and the patients' clinical team should assess the risk posed to the patients as detailed in the IARA. Patients at high and very high risk, i.e. groups 3 and 4 (Box 1), should preferably be treated in HEPA-filtered specialized ventilation isolation rooms (Supplementary Table III). Based on published literature, positive pressure ventilated (PPV) rooms are currently recommended [4,63,65,92].

Positive pressure ventilated rooms are designed to protect an immunocompromised patient from infectious diseases, particularly those spread by the airborne route. PPV rooms have been shown to protect vulnerable HSCT and acute leukaemia patients from fungal infections acquired by the airborne route [5,65,93,94].

Neutral pressure rooms have only been introduced into the healthcare setting over the last decade; consequently long-term 'in-use validation' of these rooms for all patient categories has not been established. The neutral pressure isolation room (i.e. a room with a positive pressure ventilated

lobby, PPVL) has been designed to provide both protective and source isolation. The basic elements of the design are a positive pressure lobby with extensive air changes per hour, which helps prevent corridor air from entering the room. The patient room is at neutral pressure to the corridor and there is a negative extract, typically via the bathroom. To date, there has been no published report specifically investigating its effectiveness for protecting patients at risk for IA. Recently, Ryan *et al.* compared the relative efficacy of PPVL and PPV rooms in reducing exposure to airborne mould elements in two hospitals in Ireland while in use. They showed the median *Aspergillus* spp. and total mould concentrations were similar in both room types, which suggests that PPVL rooms provide protective isolation comparable to that of PPV rooms [95]. We note, however, that one of the PPVL rooms included did not have a properly designed positive pressure lobby. Clearly further studies are required to confirm their findings and for clinical validation of PPVL to provide protection against IA. Until then, the local IPCT is best placed to give advice regarding use of PPVL rooms following individual patient assessments. Clear and good communication is required between HBS Estates and the local IPCT such that building and engineering controls are captured and agreed at project briefing stage for new capital works projects.

It is equally important to ensure that the essential elements of specialized ventilation rooms should be as per relevant technical guidelines such as the UK HTM 03-01 [85,86] and the HBN 04-01 supplements requirements (Supplementary Table III) [87,88]. Monitoring and documentation of compliance with these guidelines during construction work and contingencies should be in place in case of failure to meet the standards set.

Other measures to minimize exposure to airborne spores such as wearing surgical masks and limiting patient movements either for therapeutic or diagnostic reasons are also recommended [5,6,63,65,93].

Surveillance of nosocomial aspergillosis

It is imperative to maintain a high index of suspicion for the diagnosis of IA in the at-risk patients (Groups 2–4, Box 1). This surveillance may be achieved through a diagnostic-driven system using the European Organisation for Research and Treatment of Cancer and Mycoses Study Group (EORTC/MSG) revised definitions as a model for defining infections in high-risk patients [61]. Of note, these definitions were published 10 years ago. With the expansion of the type of patients at risk for IA, there clearly is a need for diagnostic criteria for other patient cohorts such as those with severe influenza requiring critical care and advanced COPD. Blot *et al.* have validated a clinical diagnostic algorithm which may be useful for detection of IA in critical care patients [96]. Similarly, Bulpa *et al.* have published diagnostic criteria for patients with COPD [97]. Bi-weekly serum galactomannan in high-risk groups is suggested as a useful adjunct for detection of cases [81,91,98]. Nevertheless, cases should be reviewed at ward level and relevant microbiological, histological and post-mortem data should be checked regularly. Once a case of probable/proven IA has been identified, it is imperative to assess whether the infection was healthcare- or community-acquired. When confirmed to be nosocomial aspergillosis, a complete epidemiological investigation should be carried out immediately by a multi-disciplinary team. The occurrence of two or more cases that are temporally related to

each other or an incidence above the normal surveillance levels should prompt an investigation into the possibility of an environmental source. Genotypic analysis of *Aspergillus* spp. isolated from clinical and environmental samples should be considered to assist in identifying the possible source of the outbreak [99,100]. Such an approach has led to the detection of cases of suspected nosocomial IA [18,101].

Post-construction phase

The process for testing, commissioning, and validation should be clearly set out in the contract documents, having been agreed in advance with the relevant IPCT advisors and the hospital management hospital maintenance manager along with HBS Estates representatives. The objective shall be to ensure that the Contractor achieves a satisfactory standard of construction and completion of all elements prior to issuing the Certificate for Substantial Completion by the design team. The ventilation systems should be commissioned in accordance with relevant national guidance along with HTM 03-01 requirements and HBN 04-01 supplements where they apply [85–88]. The AHU should be commissioned in accordance with relevant local technical guidelines such as the HTM 03-01 and the European standard EN 1886:2007 and EN 13053:2006+A1:2011 and witnessed by a competent independent third party [102,103].

Conclusion

Box 2 summarizes the key measures recommended to prevent HCA-IA during construction/renovation work. Hospital construction works and the list of at-risk groups will continue to increase, therefore it is important to ensure adherence to measures to prevent nosocomial IA at all times. It is important to emphasize that exposure to *Aspergillus* spp. and other moulds is not confined to the acute hospital setting. Continuing education and communication to the hospital staff and the patient are crucial for the prevention of invasive aspergillosis and/or other invasive mould infections. Further research on the role of PPVL isolation rooms and the critical minimum levels of airborne fungal spores to prevent IA are required.

Conflict of interest statement

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Appendix A. Supplementary data

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