INTERNAL MEDICINE JOURNAL

*Internal Medicine Journal* **44** (2014)

# Consensus guidelines for implementation of quality processes to prevent invasive fungal disease and enhanced surveillance measures during hospital building works, 2014

C. C. Chang,[1,2,3] M. Ananda-Rajah,[1,4] A. Belcastro,[5] B. McMullan,[6,7] A. Reid,[8,9] K. Dempsey,[10] E. Athan,[11,12,13] A. C. Cheng[1,14,15] and M. A. Slavin[12,16,17]

[1]Department of Infectious Diseases, Alfred Health and Monash University, Prahran, Victoria, [2]Centre for Biomedical Research, Burnet Institute, Victoria, [3]Lewin-Cameron Laboratory, The Doherty Institute for Infection and Immunity, Parkville, Victoria, [4]Department of General Medicine, Alfred Health, Prahran, Victoria, [5]Johnstaff, Sydney, New South Wales, [6]Department of Immunology and Infectious Diseases, Sydney Children's Hospital, Randwick, New South Wales, [7]School of Women's and Children's Health, The University of NSW, Kensington, New South Wales, [8]Departments of Infectious Diseases and General Medicine, Wollongong Hospital, Wollongong, New South Wales, [9]School of Medicine, University of Wollongong, Wollongong, New South Wales, [10]Infection Prevention and Control Unit, Westmead Hospital, Westmead, New South Wales, [11]Department of Infectious Diseases and Infection Prevention, Barwon Health, Geelong, Victoria, [12]School of Medicine, The University of Melbourne, Melbourne, Victoria, [13]School of Medicine, Deakin University, Melbourne, Victoria, [14]Infection Prevention and Healthcare Epidemiology Unit, Alfred Health, Prahran, Victoria, [15]Infectious Diseases Epidemiology Unit, Monash University, Melbourne, Victoria, [16]Department of Infectious Diseases and Infection Control, Peter MacCallum Cancer Centre, East Melbourne, Victoria, [17]Victorian Infectious Diseases Service, The Doherty Institute for Infection and Immunity, Parkville, Victoria

**Key words**
invasive fungal disease, hospital building work, HEPA filtration, environmental sampling, antifungal stewardship.

**Correspondence**
Monica Slavin, Department of Infectious Diseases, Peter MacCallum Cancer Centre, Locked Bag Number 1 A'Beckett Street, East Melbourne, Vic. 8006, Australia.
Email: monica.slavin@petermac.org

doi:10.1111/imj.12601

## Abstract

Healthcare-associated fungal outbreaks impose a substantial economic burden on the health system and typically result in high patient morbidity and mortality, particularly in the immunocompromised host. As the population at risk of invasive fungal infection continues to grow due to the increased burden of cancer and related factors, the need for hospitals to employ preventative measures has become increasingly important. These guidelines outline the standard quality processes hospitals need to accommodate into everyday practice and at times of healthcare-associated outbreak, including the role of antifungal stewardship programmes and best practice environmental sampling. Specific recommendations are also provided to help guide the planning and implementation of quality processes and enhanced surveillance before, during and after high-risk activities, such as hospital building works. Areas in which information is still lacking and further research is required are also highlighted.

## Introduction

The population of patients susceptible to invasive fungal disease (IFD) continues to grow due to advances in chemotherapeutic regimens, transplantation medicine and immune-modulating agents. The related economic burden is substantial,[1–3] regardless of the method used for cost determination, with pharmacy expenditure the overwhelming cost driver. In 2011, the median hospitalisation cost attributable to IFD in a cohort of high-risk haematology–oncology patients at a major Victorian hospital was conservatively estimated to be AU$30,957 (95% confidence interval (CI) AU$2368–59 546).[4]

An improved and growing appreciation of this economic burden has led to improved IFD preventative strategies and more (and refined) clinical care pathways to aid early diagnosis and therapy. Accordingly, the scope of the current guidelines has expanded beyond our 2008 recommendations,[5] which primarily focused on the prevention of IFD in the setting of hospital building works. Here, we also include a review of institution-wide quality processes that contribute to the prevention of IFD, including antifungal stewardship programmes and environmental sampling.

Funding: None.
Conflict of interest: The following working group members are consultants or advisory committee members; or receive honoraria, fees for service or travel assistance from; or have research or other associations with the organisations listed: Michelle Ananda-Rajah, Gilead, Merck Sharp & Dohme, Schering Plough; Monica Slavin, Gilead, Merck Sharp & Dohme, Pfizer, Schering Plough. Alexandra Belcastro is an employee of Johnstaff, a national management and delivery practice, serving as commercial advisors, project managers and construction managers for public and private clients. The views expressed here are her own and may not necessarily reflect those of Johnstaff.

**Table 1** Summary of key recommendations for the prevention of IFD in healthcare institutions

| |
|---|
| Standard quality processes |
| Employ an institution-wide antimicrobial stewardship programme that encompasses antifungal agents. |
| Manage highly immunosuppressed patients in a HEPA-filtered ward. |
| Install and maintain HEPA and other filtration systems. |
| Employ targeted air sampling prior to the commissioning of a new ward or air-handling systems. |
| Educate high-risk patients about infection prevention measures. |
| Hospital building works |
| Involve multiple disciplines and stakeholders in pre-emptive planning. |
| Include a thorough infection control risk assessment and conduct a thorough review of the mechanical air filtration and supply to high-risk areas prior to starting works. |
| Employ best practice measures to reduce patients' exposure to dust, stagnant water and damp areas. |
| Consider using targeted environmental sampling as a measure of enhanced surveillance during any hospital building works. |
| Ensure implementation of infection control and infection prevention measures through ongoing and coordinated supervision, including a monitoring checklist. |
| Outbreak management |
| Commence active (and enhanced) surveillance for IFD cases |
| Conduct a thorough review of infection control measures, including sealing of clinical areas and air filtration. |
| Consider using targeted environmental sampling to facilitate outbreak investigations. |
| Store fungal isolates from suspected outbreaks for future analysis. |

HEPA, high-efficiency particulate air; IFD, invasive fungal disease.

It should be noted that the quality processes discussed here are not easily assessed through randomised controlled studies. National Health and Medical Research Council levels of evidence are difficult to apply, and thus, our recommendations predominantly represent expert opinion. However, the principles that underpin our recommendations are deeply embedded in a large number of international guidelines[6–13] and we believe readily applicable to the Australian and New Zealand context. Key recommendations are summarised in Table 1.

## Methodology

### Questions asked

In preparing this update, we aimed to address the following questions:

**1** What new or updated strategies and hospital processes are there to improve the quality of prevention and care of patients at risk of IFD?

**2** Is there any new information on infection prevention practices and likely risk of IFD in the setting of hospital building works?

### Search strategy

A literature review was performed using PubMed to identify papers published since 2007 that pertained to antifungal stewardship programmes, environmental sampling, high-efficiency particulate air (HEPA) filtration, fungal outbreaks and hospital building works. Search terms included 'antifungal stewardship', 'environmental sampling', 'air sampling', 'water sampling', 'HEPA filtration', 'building works', 'hospital construction', 'fungal outbreaks', 'nosocomial fungal infection', 'healthcare-associated fungal infection' and 'guidelines'. International and national antifungal and infection prevention guidelines and associated papers were also reviewed.

## Quality processes for the prevention of IFD

### Antifungal stewardship programmes

In this era, all hospitals should employ an antimicrobial stewardship programme that encompasses antifungal agents. The essential elements of an antifungal stewardship programme are not dissimilar to an antimicrobial stewardship programme, albeit with a focus on quality use of drugs, avoidance of toxicity and cost management rather than the reduction of antifungal resistance.[14] Hospital-wide antifungal stewardship programmes should be based on best available evidence and adapted to the local context. Initial goals should be modest and achievable to help demonstrate success of the programme in the short term (e.g. targeting a few high-cost antifungal drugs or measuring antifungal agent consumption at the unit or ward level). Programme guidelines should specifically address empiric antifungal therapy as it

**Table 2** Process measures in establishing and maintaining antifungal stewardship programmes

| |
|---|
| Process measures in antifungal stewardship |
| Antifungal drug consumption |
| Minimum standards of prescribing |
| Documentation of treatment rationale |
| Dose optimisation using therapeutic drug monitoring (TDM) |
| Therapeutic streamlining |
| De-escalation of empiric antifungal therapy |
| De-escalation from broad to narrower spectrum drugs |
| Intravenous to oral switch therapy |
| Timeliness and completeness of diagnostic investigations when IFD suspected |
| Concordance of prescribing with institutional guidelines using an indication-driven approach |
| Outcome measures |
| IFD incidence in targeted groups |
| Antifungal drug expenditure |
| Structural measures |
| Antifungal policy/guideline |

Adapted from Ananda-Rajah *et al*.[14]

accounts for approximately two-thirds of in-patient antifungal agent prescriptions.[15,16]

There are various models of stewardship: pre-prescription, point of prescription and post-prescription. Restrictive interventions, such as pre-prescription approval and formulary restriction, are valuable and superior to academic detailing or targeted educational activities.[17] However, pre-prescription approval or expert review should not delay the timely initiation of antifungal agents, where indicated. Post-prescription review and feedback by the antifungal stewardship team are a core activity.[18,19] It provides an opportunity to identify deficiencies in prescribing, educate prescribers, build trust and promote the benefits of antifungal stewardship. Periodic monitoring of processes, outcomes and structural measures is important (see Table 2). Quantitative data collection needs to be balanced against qualitative measures, such as appropriateness and timeliness of prescribing. Quantitative data should also be evaluated against clinical outcomes, such as IFD incidence rates and drug-related adverse events.

## HEPA filters

Guidelines and standards, both within Australia and internationally, support the use of adequately managed isolation to prevent transmission of pathogens from the outside environment to profoundly immunocompromised patients.[6–13] There are two main classes of isolation rooms: negative pressure rooms for isolating patients who are capable of transmitting infection by airborne droplet (Class N) and positive pressure rooms for protecting immunocompromised patients susceptible to infection (Class P).[20]

It is now widely accepted that HEPA filters (among other types of filters, such as ultra-low penetration air filters and medium efficiency particulate air filters) assist in protecting immunocompromised patients. Most guidelines, as well as the Centers for Disease Control and Prevention (CDC), recommend that patients at high-risk for IFD, including recipients of haemopoietic stem cell transplants (HSCT), be nursed in HEPA-filtered rooms.[6,7,10,12,13] HEPA filters with 99.97% efficiency for removing particles ≥0.3 μm in diameter at ≥12 air exchanges per hour are recommended for severely immunocompromised patients, particularly during hospital construction works.[6,7,10,12,13] While a meta-analysis of HEPA-filtered rooms demonstrated no significant reduction in deaths (pooled RR, 0.86 (95% CI 0.65–1.14)) or fungal infection (pooled RR, 0.57 (95% CI 0.13–2.53)), the analysis was based on relatively small studies with short follow-up periods.[21]

Retrofitting of HEPA filters can be complex. Health facilities are required to ensure adequate maintenance of HEPA filtration systems and other appropriate types of filters with medium- to high-efficiency filtration.[6,7,10,12,13] Annual reports should include pressurisation, air exchanges per hour, maintenance schedules and replacement of filters. Improper or poor maintenance of sophisticated ventilation systems can lead to outbreaks of invasive aspergillosis in units equipped with HEPA facilities.[6,22] General advice on mechanical services design, including ventilation air flow rates and air exchanges, can be found in *Technical Series TS11 – Engineering Services & Sustainable Development Guidelines*, written by New South Wales (NSW) Health.[20]

In general, all air handling units and filters within air conditioning systems in hospitals or health facilities need to be intended, designed and maintained to suit the infection risk specific to the areas in which they are to be used. The type of filter and level of filtration required will depend upon the size of particles and spores that pose an increased risk to the patient profile concerned. It should also be noted that humidity and environmental factors can affect the size of particles and spores; however, the implications for filter selection are not yet clear.

## Environmental sampling

The fungi responsible for invasive disease in immunocompromised hosts are ubiquitous and have been isolated from air, water and surfaces within hospitals.[23] Disease attribution (i.e. healthcare-associated vs community-acquired) is further complicated by the

fact that the incubation period for opportunistic moulds, including invasive aspergillosis, is unknown. Thus, while methods for environmental sampling exist, the significance of fungi found in hospital environments remains uncertain, and a direct linkage to healthcare-associated IFD remains arguable.

## Air sampling

A written, defined, standardised, multidisciplinary protocol for sample collection and culturing is required in institutions where targeted air sampling is performed. Analysis and interpretation of results should use scientifically determined or anticipatory baseline values for comparison. Expected actions, based on the results obtained, should also be defined.[6] Unfortunately, the sensitivity, specificity and threshold values are unclear, and there are no uniform air quality standards.

## Water sampling

While environmental water sampling has largely focused on legionellae and other bacterial organisms,[24] water distribution systems (WDS) may also be a source of invasive moulds, such as *Aspergillus* spp., *Fusarium* spp. and Mucor.[25–27] Indeed, hospital WDS may serve as an indoor reservoir for moulds leading to potential patient exposure through aerosolisation of spores.[25] In some settings, it is recommended that high-risk patients avoid drinking tap water and showering.[24] Targeted water sampling should be considered in comprehensive investigations of healthcare-associated outbreaks of IFD,[28] again with the necessary caveats on standardised methodology.

## Timing of sampling

Environmental sampling may be performed pro-actively for surveillance or reactively in response to a fungal outbreak. It may also be performed longitudinally in well-designed research studies to monitor a potentially hazardous environmental condition, to evaluate a change in infection control practice as part of a quality-assurance programme or to ensure equipment and systems perform to specification.[6] Sudden changes in longitudinal sampling, particularly in the setting of enhanced surveillance during hospital building works, may signal an increased risk of IFD. In this case, it may be prudent to enhance control efforts, such as increased cleaning, maintenance of air filters and intensified microbiological vigilance. Results from a single environmental sample are difficult to interpret.

## Variation in sampling techniques

Microbiological sampling of air, water and inanimate surfaces is not only expensive and time-consuming but is also hampered by the variability in collection protocols, analysis and interpretation. There are numerous commercial air sampling machines, which employ a variety of sampling methods. The lack of standardised protocols to guide both the application of these machines (e.g. collection time, airflow rate) and the analysis of data impedes comparisons between studies.[6,29]

Selection of an instrument for air sampling will depend on whether a particular organism or all organisms are being targeted; on the concentration and size of the viable particle/s or organism/s; on qualitative versus quantitative results; and on ambient conditions. Briefly, liquid impinger and solid impactor samplers are the most practical as they sample large volumes of air in relatively short time periods.[6] Settle plates (sedimentation or depositional methods) are not recommended for sampling fungal spores as spores can remain suspended in the air indefinitely.[6,30]

The practical considerations of air sampling and a suggested method for sampling of *Aspergillus* spp. have been summarised elsewhere.[30] General principles and recommendations on environmental sampling are also provided by the CDC.[6]

## Laboratory processing, interpretation and storage

Microbiologic air sampling should be limited to thermotolerant moulds (organisms capable of growing at 35–37°C) as these are the primary pathogens of interest in immunocompromised hosts.[6] Microbiological analysis should be performed in accredited laboratories. Initial identification is generally morphological; use of selective media (e.g. Sabaroud dextrose agar or inhibitory mould agar) may help with the initial identification of recovered organisms.[6]

There are no universally accepted standards or guidelines for the interpretation of fungal spore or colony counts collected in response to an outbreak. Fungal spore levels vary over time and with other factors, such as ambient light and humidity.[30] An exposure level of <5 CFU/$m^3$ of *Aspergillus* spp. in protective isolation areas and <0.1 CFU/$m^3$ in HEPA-filtered environments, with limits of 15 CFU/$m^3$ for gross colony counts of all fungal organisms, is recommended.[6,30,31]

Molecular identification of strains may be particularly helpful in investigating for healthcare-associated transmission of a point source outbreak. There is no unifying molecular method to genotype all fungal species. Many methods exist including polymerase chain reaction (PCR)

fingerprinting, probe-based typing and specific locus-based typing. In one investigation of a suspected *Aspergillus fumigatus* outbreak, multi-locus microsatellite typing was found to be more discriminatory than PCR fingerprinting or cell surface protein typing.[32] Fungal strains may also fluctuate rapidly; therefore, an environmental outbreak may be associated with more than one strain type. Investigators should consult the literature on the species of concern for the optimal genotyping methodology.

Storage of environmental and infecting isolates is important for future analysis. Storage methods may include sterile water or mineral oil, but cryopreservation in liquid nitrogen appears to be the most reliable method of long-term storage.[33]

### Patient education

Severely immunocompromised patients should be informed and educated about their reduced immunity and susceptibility to infections. Activities in and out of hospitals and consumption of foodstuff associated with an increased risk of IFD should be discussed.[12,28,34] A long list of food to be avoided may be found in Marr *et al*.[28]

## Prevention of IFD during hospital building works

Hospital building works is an established risk factor for IFD with numerous reports of healthcare-associated fungal outbreaks.[4,35] The overall mortality of these outbreaks was 50–60%.[4] Capital works, refurbishment, maintenance and repairs have become *sine qua non* in modern-day healthcare. Moulds are ubiquitous in soil, water, decaying vegetation, and in walls and ceilings of old buildings. Spores may be dispersed or aerosolised, not only during excavation and demolition but also during lower-risk dust-generating activity, such as recarpeting or installation of new fit-outs. Further, capital works may lead to intermittent bursts of fungal spore aerosolisation, which has the potential to lead to polyclonal outbreaks.[36,37]

While hospital building works now constitute an established risk factor for IFD, quantification of the rate of IFD caused by building works is imprecise as the incubation period for IFD is difficult to define and remains unknown. Infection rates of 7.9% have been reported at the height of construction in at-risk patients.[37] *Aspergillus* species remain the most notorious construction-related pathogen; with spores measuring 1.9–3.2 μm, *A. fumigatus* may remain aerosolised for extended periods and travel long distances in the air.[38] However, other fungi, including *Scedosporium* species and the Zygomycetes, have also been linked to building works.[35–37,39]

### Pre-emptive planning and enhanced surveillance

Given that hospital building works increase the risk of IFD, particularly in immunosuppressed patient populations, a pre-emptive approach to planned building works is paramount.[40] Multiple authorities provide guidelines to facilitate early and sustained coordinated planning between infection control teams, building and engineering teams, and other relevant ancillary teams and strongly encourage hospitals to keep up to date with current best practices (see Table 3).[6–11,41,42]

Prior to starting works, a thorough infection control risk assessment should be performed. A risk assessment matrix utilising the classifications of the type of construction activity type and patient group may be useful for defining risk.[43] In this approach, the type of construction activity is first risk-stratified into types A to D, where type A includes low-risk inspection activities and type D includes demolition and construction work.[43] Risk groups are then classified into low, medium, medium–high and high risk, depending on patient group or ward type.[43]

A formal list detailing the various infection prevention and infection control measures to be implemented during the period of works should be developed and regularly revised and updated in line with best practice. At a minimum, this list should include the relocation of high-risk patients, preferred ventilation system types and their potential impact, induction of all construction workers to dust reduction measures, regular inspections by infection control practitioners, minimisation of movement in and out of the site, intensification of efforts to seal off patient care units that house high-risk patients and keep spore-bearing air from infiltrating these areas, cleaning of newly constructed areas, and minimisation of aerosolisation of fungal spores during cleaning.[5,6,8,10]

Any medical unit that handles immunosuppressed patients must have a code of practice on air quality that clearly states the responsibility of each of the supporting services, including engineering, cleaning and ancillary staff.[22] Where building works are being undertaken adjacent to infection risk areas, a detailed and thorough review of the mechanical air filtration and supply to such areas by an appropriately qualified engineer is recommended. The retrofitting of pre-filters to any air intakes adjacent to construction sites is also recommended. A monitoring checklist should be regularly completed to ensure compliance with barrier measures, traffic control, personal protective equipment, and the handling of air, trash and debris. The additional costs associated with

**Table 3** Recommendations from international guidelines for infection control and prevention measures during building works and specific recommendations for healthcare facilities managing HSCT recipients in the setting of building works

| Intervention | Generic health facility building guidelines | | | Guidelines targeted to reducing infection risk in high-risk patients | | | | |
|---|---|---|---|---|---|---|---|---|
| | Australia 2012[8] | United Kingdom 2013[11] | Canada 2010[9] | CDC 2003[6] | HICPAC 2007[7] | Ireland 2002[10] | Tomblyn 2009[12] | Yokoe 2009[13] |
| Keep at-risk patient areas positively pressurised compared with outside/maintain negative pressure in the construction area | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Install and maintain filters properly | | | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Seal clinical areas from outside air effectively | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Carry out surveillance for active cases | | | | ✓ | ✓ | ✓ | ✓ | ✓ |
| N95 masks for high-risk patients when outside of their protective environment | | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| HEPA filter the air of high-risk patient rooms during construction | | | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Minimum air exchanges for high-risk patient rooms >12 per hour | | | | ✓ | ✓ | ✓ | ✓ | ✓ |

CDC, Centers for Disease Control and Prevention; HEPA, high-efficiency particulate air; HICPAC, Healthcare Infection Control Practices Advisory Committee; HSCT, haemopoietic stem cell transplants.

environmental sealing and maintenance of air quality throughout the building period should be forecast and budgeted for.[44]

Reducing patient exposure to dust, stagnant water and damp areas is a key imperative. Where possible, HSCT recipients, healthcare workers and visitors should avoid construction and renovation sites, and clinical areas should be effectively sealed from outside air and the building site quarantined.[6–13] Typical quarantine measures include establishing barriers to prevent dust dispersal; reducing dust production by watering excavation sites and modifying demolition/excavation techniques; and using suitable barriers, including geographic separation, masks and filtered air supply, to quarantine at-risk patients.[5,6,8,10,41] In a series of 113 cases of healthcare-associated IFD in a single centre undergoing construction over a 6-year period, the use of high-efficiency masks by high-risk patients when outside of protected areas reduced the rate of IFD from 0.73 to 0.24 per 1000 hospital days ($P < 0.001$).[45] Allogeneic HSCT recipients should avoid construction areas and may benefit from wearing N95 respirators while outside HEPA-filtered areas.[6,7,9,10,12,13]

There are no controlled studies of antifungal prophylaxis use specific to the setting of building works. The use of routine antifungal prophylaxis during works varies from unit to unit, based on patient case mix and local epidemiology. Institutions may consider lowering their usual threshold for antifungal prophylaxis in the setting of imminent building works.[46] There is, however, no evidence to support provision of antifungal prophylaxis outside of the immunocompromised population, regardless of the extent of building works.

## Outbreak management

During construction activities, prospective surveillance of IFD is recommended to ensure the timely identification of outbreaks. The general approach to an outbreak includes confirmation of the outbreak, an audit of case records in order to identify common factors, a review of those factors implicated in previous outbreaks and implementation of measures to mitigate ongoing risk.

Measures for control of healthcare-associated IFD include relocation of high-risk patients to a distant location, masking, wet-cleaning, reduction in unnecessary thoroughfare and sealing of patient care areas with impermeable barriers,[6,41,42] as well as consideration of antifungal prophylaxis. Transparency of care is vital, as are accountability and the maintenance of open channels of communication between all clinical units, infection control, engineering, cleaning and ancillary staff.

In the midst of an outbreak, reactive air sampling without prior baseline data is difficult to interpret.[47] Air sampling initiated after the recognition of an outbreak may not record previous spikes in IFD incidence associated with high-risk activities or specific alteration in the environmental. In 24 outbreaks of invasive aspergillosis with reported volumetric air samples, the concentration of airborne fungi in patient care areas during outbreak investigations ranged from 0 to 100 spores/$m^3$.[39] While many healthcare-associated outbreak investigations report a benefit from installing HEPA filters as a control measure,[48–50] hospitals typically employ a range of environmental control measures during an outbreak; as such, it is not possible to attribute these benefits solely to HEPA filters.

It is important to conduct a clinical investigation of any suspected outbreak in parallel to environmental sampling. Potential and actual cases of IFD should be identified, and the patients' location, movement and exposures fully documented. The finding of unrelated clinical fungal strains does not negate the possibility of a healthcare-associated outbreak.[39] Storage of isolates for future analysis is recommended.

## Implications for future research

The research needs highlighted in the 2008 guidelines[5] remain broadly unanswered. We see a particular need for prospective sampling to be performed before, during and after hospital construction works and for these samples to be analysed relative to both clinical and microbiological data. A national surveillance database of fungal isolates and IFD rates, along with monitoring of hospital-based antifungal practices during building works, would facilitate the success of fungal infection prevention strategies and antimicrobial stewardship programmes. Improved clarity on the level of protection and air filtration required for different risk groups is also needed.

## Conclusion

Immunosuppression is increasingly prevalent in our hospital systems due to advances in chemotherapeutic regimens, transplantation medicine and immune-modulating agents. The concomitant rise in the number of patients at increased risk of IFD, and the related economic and clinical burden, has placed an increased focus on the importance of institution-wide preventative strategies. The planning and implementation of best practice quality processes and enhanced surveillance, particularly during activities that increase the risk of spore dispersal, such as hospital building works, are paramount. The guidelines presented here will need continued revision as these quality processes are further refined, and advances in research and technology enable new preventative strategies and improved control measures.

## Acknowledgements

The authors would like to thank members of ALLG, ASID and ANZCHOG for their review of the draft document and Dr Candice O'Sullivan from Wellmark Pty Ltd for her assistance in preparing the manuscript for submission.

## References

1 Menzin J, Meyers JL, Friedman M, Perfect JR, Langston AA, Danna RP *et al.* Mortality, length of hospitalization, and costs associated with invasive fungal infections in high-risk patients. *Am J Health Syst Pharm* 2009; **66**: 1711–17.

2 Slavin M, Fastenau J, Sukarom I, Mavros P, Crowley S, Gerth WC. Burden of hospitalization of patients with Candida and Aspergillus infections in Australia. *Int J Infect Dis* 2004; **8**: 111–20.

3 Wilson LS, Reyes CM, Stolpman M, Speckman J, Allen K, Beney J. The direct cost and incidence of systemic fungal infections. *Value Health* 2002; **5**: 26–34.

4 Ananda-Rajah MR, Cheng A, Morrissey CO, Spelman T, Dooley M, Neville AM *et al.* Attributable hospital cost and antifungal treatment of invasive fungal diseases in high-risk hematology patients: an economic modeling approach. *Antimicrob Agents Chemother* 2011; **55**: 1953–60.

5 Chang CC, Athan E, Morrissey CO, Slavin MA. Preventing invasive fungal infection during hospital building works. *Intern Med J* 2008; **38**: 538–41.

6 Sehulster L, Chinn RYW, Arduino MJ, Carpenter J, Donlan R, Ashford D *et al.* *Guidelines for Environmental Infection Control in Health-Care Facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC)*. Chicago, IL: American Society for Healthcare Engineering/American Hospital Association; 2003.

7 Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. doi: 10.1016/j.ajic.2007.10.007. S0196-6553(07)00740-7 [pii]. 2007 [updated 12/2007]. [cited 2014 Sep 30]. Available from URL: http://www.cdc.gov/hicpac/pdf/isolation/isolation2007.pdf

8 Australasian Health Infrastructure Alliance. Australian health facility guidelines – part D: infection prevention and control: AHIA; 2012.

9 Facility Guidelines Institute (Canada). *Guidelines for Design and Construction of Health Care Facilities*. Canada: FGI; 2010.

10 National Disease Surveillance Centre (Ireland). *National Guidelines for the Prevention of Nosocomial Invasive Aspergillosis During Construction/Renovation Activities*. Dublin: NDSC; 2002.

11 Department of Health Estates and Facilities (UK). *Health Building Note 00–09: Infection Control in the Built Environment UK*. quarry hill, London: Department of Health; 2013.

12 Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek J *et al.* Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant* 2009; **15**: 1143–238.

13 Yokoe D, Casper C, Dubberke E, Lee G, Munoz P, Palmore T *et al.* Infection prevention and control in health-care facilities in which hematopoietic cell transplant recipients are treated. *Bone Marrow Transplant* 2009; **44**: 495–507.

14 Ananda-Rajah MR, Slavin MA, Thursky KT. The case for antifungal stewardship. *Curr Opin Infect Dis* 2012; **25**: 107–15.

15 Pagano L, Caira M, Candoni A, Offidani M, Martino B, Specchia G *et al.* Invasive aspergillosis in patients with acute myeloid leukemia: a SEIFEM-2008 registry study. *Haematologica* 2010; **95**: 644–50.

16 des Champs-Bro B, Leroy-Cotteau A, Mazingue F, Pasquier F, Francois N,

Corm S *et al.* Invasive fungal infections: epidemiology and analysis of antifungal prescriptions in onco-haematology. *J Clin Pharm Ther* 2011; **36**: 152–60.
17 Davey P, Brown E, Charani E, Fenelon L, Gould IM, Holmes A *et al.* Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2013; (4): CD003543.
18 Australian Commission on Safety and Quality in Healthcare. *Antimicrobial Stewardship in Australian Hospitals 2011*. Duguid M, Cruickshank M, eds. Sydney: ACSQH; 2012.
19 Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP *et al.* Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; **44**: 159–77.
20 Health N. *Technical Series TS11 – Engineering Services and Sustainable Development Guidelines. Version 2*. Sydney: NSW Department of Health; 2007.
21 Eckmanns T, Ruden H, Gastmeier P. The influence of high-efficiency particulate air filtration on mortality and fungal infection among highly immunocompromised patients: a systemic review. *J Inf Dis* 2006; **193**: 1408–18.
22 Anderson K, Morris G, Kennedy H, Croall J, Michie J, Richardson MD *et al.* Aspergillosis in immunocompromised paediatric patients: associations with building hygiene, design, and indoor air. *Thorax* 1996; **51**: 256–61.
23 Lee LD, Hachem RY, Berkheiser M, Hackett B, Jiang Y, Raad II. Hospital environment and invasive aspergillosis in patients with hematologic malignancy. *Am J Infect Control* 2012; **40**: 247–9.
24 Anaissie EJ, Penzak SR, Dignani MC. The hospital water supply as a source of nosocomial infections: a plea for action. *Arch Intern Med* 2002; **162**: 1483–92.
25 Anaissie EJ, Stratton SL, Dignani MC, Summerbell RC, Rex JH, Monson TP *et al.* Pathogenic Aspergillus species recovered from a hospital water system: a 3-year prospective study. *Clin Infect Dis* 2002; **34**: 780–9.
26 Hayette MP, Christiaens G, Mutsers J, Barbier C, Huynen P, Melin P *et al.* Filamentous fungi recovered from the water distribution system of a Belgian university hospital. *Med Mycol* 2010; **48**: 969–74.
27 Arvanitidou M, Kanellou K, Constantinides TC, Katsouyannopoulos V. The occurrence of fungi in hospital and community potable waters. *Lett Appl Microbiol* 1999; **29**: 81–4.
28 Marr KA, Bow E, Chiller T, Maschmeyer G, Ribaud P, Segal B *et al.* Fungal infection prevention after hematopoietic cell transplantation. *Bone Marrow Transplant* 2009; **44**: 483–7.
29 Buttner MP, Willeke K, Grinshpun SA. Sampling and analysis of airborne microorganisms. In: Hurst CJ, Knudsen GR, McInerney MJ, Stetzenbach LD, Walter MV, eds. *Manual of Environmental Microbiology*. Washington, DC: ASM Press; 1997; 629–40.
30 Morris G, Kokki MH, Anderson K, Richardson MD. Sampling of Aspergillus spores in air. *J Hosp Infect* 2000; **44**: 81–92.
31 Munoz P, Burillo A, Bouza E. Environmental surveillance and other control measures in the prevention of nosocomial fungal infections. *Clin Microbiol Infect* 2001; **7**: 38–45.
32 Kidd SE, Ling LM, Meyer W, Orla MC, Chen SC, Slavin MA. Molecular epidemiology of invasive aspergillosis: lessons learned from an outbreak investigation in an Australian hematology unit. *Infect Control Hosp Epidemiol* 2009; **30**: 1223–6.
33 Homolka L. Methods of cryopreservation in Fungi. In: Gupta VK, Tuohy MG, Ayyachamy M, Turner KM, O'Donovan A, eds. *Laboratory Protocols in Fungal Biology – Current methods in fungal biology*. New York: Springer; 2013; 9–16.
34 Yokoe D, Casper C, Dubberke E, Lee G, Munoz P, Palmore T *et al.* Safe living after hematopoietic cell transplantation. *Bone Marrow Transplant* 2009; **44**: 509–19.
35 Alvarez M, Ponga BL, Rayon C, Gala JG, Porto MCR, Gonzalez M *et al.* Nosocomial Outbreak caused by Scedopsorium prolificans (inflatum): four fatal cases in leukemic patients. *J Clin Micro* 1995; **33**: 3290–5.
36 McCann S, Byrne JL, Rovira M, Shaw P, Ribaud P, Sica S *et al.* Outbreaks of infectious diseases in stem cell transplant units: a silent cause of death for patients and transplant programmes. *Bone Marrow Transplant* 2004; **33**: 519–29.
37 Antoniadou A. Outbreaks of zygomycosis in hospitals. *Clin Microbiol Infect* 2009; **15**: 55–9.
38 Streifel AJ, Lauer JL, Vesley D, Juni B, Rhame FS. Aspergillus fumigatus and other thermotolerant fungi generated by hospital building demolition. *Appl Environ Microbiol* 1983; **46**: 375–8.
39 Vonberg RP, Gastmeier P. Nosocomial aspergillosis in outbreak settings. *J Hosp Infect* 2006; **63**: 246–54.
40 Streifel AJ. In with the good air. *Infect Control Hosp Epidemiol* 2002; **23**: 488–90.
41 Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. Recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. *MMWR* 2000; **49**: 1–128.
42 Centers for Disease Control and Prevention. Guidelines for environmental infection control in health-care facilities: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR* 2003; **52**: 1–48.
43 *Infection Control Risk Assessment Matrix of Precautions for Construction & Renovation*. Charlotte, NC: Premier Inc; 2014. https://legacy.premierinc.com/quality-safety/tools-services/safety/topics/construction/icra.jsp
44 Fitzpatrick F, Prout S, Gileece A, Fenelon LE, Murphy OM. Nosocomial aspergillosis during building work – a multidisciplinary approach. *J Hosp Infect* 1999; **42**: 170–1.
45 Raad I, Hanna H, Osting C, Hachem R, Umphrey J, Tarrand J *et al.* Masking of neutropenic patients on transport from hospital rooms is associated with a decrease in nosocomial aspergillosis during construction. *Infect Control Hosp Epidemiol* 2002; **23**: 41–3.
46 Yonemari K, Takezako N, Nishimura K, Onose T, Yamanishi F, Kawahata H *et al.* Fungal infection in neutropenic patients in a hospital during construction. *Jpn J Infect Dis* 2002; **55**: 126–7.
47 Hajjeh RA, Warnock DW. Counterpoint: invasive Aspergillosis and the environment -rethinking our approach to prevention. *Clin Infect Dis* 2001; **33**: 1549–52.
48 Hahn T, Cummings KM, Michalek AM, Lipman BJ, Segal BH, McCarthy PL. Efficacy of high-efficiency particulate air filtration in preventing aspergillosis in immunocompromised patients with

haematologic malignancies. *Infect Control Hosp Epidemiol* 2002; **23**: 525–31.
49 Loo VG, Bertrand C, Dixon C, Vitye D, Eng B, DeSalis B *et al.* Control of construction-associated nosocomial Aspergillosis in an antiquated haematological unit. *Infect Control Hosp Epidemiol* 1996; **17**: 360–4.
50 Opal SM, Asp AA, Cannady PB, Morse PL, Burton LJ, Hammer PG. Efficacy of infection control measures during a nosocomial outbreak of disseminated aspergillosis associated with hospital construction. *J Inf Dis* 1986; **153**: 634–7.