REVIEW

Positive-pressure isolation and the prevention of invasive aspergillosis. What is the evidence?

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Summary
Positive-pressure ventilation implies a sealed room, usually with an anteroom to facilitate the donning of protective clothing, airflows of at least 12 air changes per hour and high-efficiency particulate air (HEPA) to prevent infection in susceptible patients. Laminar airflow (LAF) involves much greater air changes, expense and inconvenience to the patient due to noise and draughts. There are few, if any, truly controlled trials on the impact of positive-pressure ventilation and the prevention of invasive aspergillosis (IA); most are observational studies conducted during an outbreak or retrospective analyses of the incidence of IA over periods of time when a variety of preventative interventions were introduced. Therefore, it is often difficult to determine the specific impact of positive-pressure ventilation with HEPA in leading to a reduction in IA. During periods of hospital demolition or construction, HEPA significantly reduces the aspergillus spore counts and in many studies, the incidence of IA, but other measures such as enhanced cleaning, the sealing of windows and the use of prophylactic anti-fungal agents are also important. On balance, the additional expense and inconvenience of LAF does not appear to be justified. Where positive-pressure ventilation is installed, it is imperative that the system be monitored to ensure that the pressure differentials and air changes are appropriate. Whist there is a role for positive-pressure ventilation in reducing the incidence of IA, we need a better definition of the importance of hospital-acquired IA compared with community-acquired infection and of the relationship between strains of Aspergillus species isolated from the environment and those strains causing infection.

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**Introduction**

As the number of patients undergoing chemotherapy for neoplastic disease increases, accompanied by a rise in the number of patients with neutropenia, infection control teams are often asked about the requirement for positive-pressure isolation facilities, either within an existing unit, or during the planning stages for a new haematology/oncology unit. Many believe that the scientific evidence is convincing in favour of positive-pressure isolation, specifically in preventing invasive aspergillosis (IA). However, the requirement to balance the needs of patients, the expense of both constructing and maintaining a positive-pressure isolation facility, and the need for other infection preventative measures, make the assessment complicated in the absence of well-conducted trials. Some knowledge of the principles and design of positive-pressure isolation facilities and what they offer is also required to make such a decision.

What follows is a combination of a literature search (MedLine), a review of various guidelines and official documents published in English in the area, and the author’s own experience and perspectives. In the absence of controlled trials, as discussed below, the conclusions and recommendations are not graded or ranked in terms of priority and are personal opinions only.

**Positive-pressure ventilation**

Positive-pressure isolation, sometimes referred to as ‘protective environment’ or ‘positive-pressure rooms,’ is where a patient is placed in a separate environment because the patient is more susceptible to infection, and therefore, needs protection from both other patients and from the hospital environment. Air pressures within such a facility are higher than in the surrounding areas to prevent the ingress of potentially contaminated air, and there is also an anteroom with a handwash basin. Categories of patients for which this usually applies are those with significant immunodeficiency, e.g. neutropenia, or patients with extensive burns. Whilst these patients are at risk from infection acquired from an external source, such as the hands and clothes of a member of staff, the purpose of protective isolation is to prevent acquisition from other patients or from the environment. Endogenous infection is still possible and common.

Bishop Joscelin of Bath and Wells in 1219 was perhaps the first to describe protective isolation, but this was in the context of preventing patients with infectious diseases from being admitted to hospital in the first place and spreading infection. Throughout the early and mid decades of the 20th century, there were various recommendations from the USA and the UK which identified the need for private rooms to prevent infection, in some instances mechanically ventilated to provide clean air. Protective isolation facilities, especially those that consist of high efficiency particulate air (HEPA) and laminar airflow (LAF) have been advocated for the prevention of IA in immunocompromised patients or for patients with extensive burns, who are non-infected. However, it could be argued that for burns patients who are already infected, negative-pressure ventilation is required to prevent the organisms causing infection spreading to other parts of the unit.

The protected environment of a room or unit commissioned for the prevention of infection in susceptible patients (Table I) usually consists of HEPA filters (99.97% efficient at 0.3 μm particles), at least 12 air changes per hour, sealed rooms, air direction from the patient to the exhaust systems, with re-circulation of air. When LAF is provided, the air is usually swept across the room parallel to the floor driving contaminants out through the ducts. This usually involves 400 air changes per hour or more and is expensive, uncomfortable due to draughts and noise, and may not appreciably add to the degree of protection, as discussed later. Apart from regional or referral units where burns patients are usually cared for, most of the issues pertaining to protective isolation relate to patients with malignancy, patients on chemotherapy, or patients after bone marrow or solid organ transplantation. In this group of patients, the purpose of protective isolation is to reduce or remove, in particular, the risk of fungal infection caused by moulds such as *Aspergillus* species, *Mucorales/Rhizopus* species, *Scedosporium* species, *Acremonium* species and *Penicillum* species. Most commonly it is the risk of IA that motivates the requirement for positive-pressure isolation.

**Epidemiology and pathogenesis of IA**

Aspergillus spores are ubiquitous, and in most normal healthy individuals are removed by the innate defences of the upper respiratory system, e.g. nasal hairs and ciliated respiratory epithelium. Probably only a minority of spores that enter the lower respiratory tract actually remain there and only some of these will germinate. Deposition and germination are probably pre-requisites for IA,
which is only likely to occur in patients with severe or prolonged neutropenia.

*Aspergillus fumigatus* is ubiquitous and found in every region of the world, including the Antartica. It is believed that the primary ecological niche is decomposing vegetable material, and therefore, rural areas are a major source of this organism. Possible domestic sources of *A. fumigatus* and other species include potted plants, flower arrangements and carpets, but the ambient air spore count does vary. In the USA, air counts in some areas are highest in the spring, but in the UK they appear to be higher in the winter. Whilst aspergillus spores are likely to be found in the hospital environment, as well as outside the hospital environment, it is not always clear whether aspergillus diagnosed in hospital is hospital-acquired or community-acquired and endogenous, i.e. organisms present as part of the normal flora such as in the nose translocating to the lower respiratory tract, causing invasive infection. Manuel and Kibbler have reviewed the epidemiology and prevention of IA, and amongst their conclusions are that half or more of cases are acquired in the community, that indistinguishable strains often appear first in patients before being detectable in the environment when molecular typing methods are used, and that often when a cluster of cases occurs, each patient is infected with an individual single strain that differs from those strains acquired by other patients.

When considering the need for positive-pressure ventilation in the prevention of aspergillosis, it is worth reviewing the risk factors for IA and assessing whether the patient mix includes some in the high-risk categories. There is universal agreement that because monocyte-derived and resident macrophages contribute to spore ingestion during killing neutropenia and dysfunctional neutrophils are important risk factors. Profound neutropenia (granulocytes less than $0.1 \times 10^9 \text{ L}^{-1}$) such as follows chemotherapy or conditioning for bone marrow transplantation, is the major factor, but patients who develop graft failure and/or who receive corticosteroid therapy after bone marrow transplantation, are also at increased risk. The incidence varies amongst patients after solid organ transplantation, but is probably highest in those with a lung or a combined lung and heart transplant.

Various efforts have been made to correlate environmental spore counts with the risk of IA. In a study that included 3100 air and 9800 surface samples, a significant positive link between the incidence of nosocomial IA and the degree of fungal contamination was suggested. Nonetheless, there is no agreed level at which the risk can be numerically defined for IA. However, although some guidance has been provided for air sampling and assessing the results of air counts, some degree of interpretation is required in the light of the ‘at-risk’ population, the season, the degree of ventilation in the area sampled and other factors. Rather than trying to interpret the result from one single sample, it is probably best to conduct a series of samples over a period of time to detect a trend. If the total fungal count exceeds 1.0 cfu/m³ on several occasions, then it has been recommended that the ventilation system or the environment requires evaluation.

Recent guidelines produced in Ireland to help reduce nosocomial IA have suggested categorizing patients into one of four risk groups depending on the likelihood of infection. Although these are not scientifically validated, they do offer a mechanism of identifying those patients most at risk and thus requiring specific interventions such as HEPA.

### The impact of positive-pressure ventilation

There are many trials, descriptions of outbreaks and observational studies on positive-pressure ventilation, but most have deficiencies in one aspect or another (Table II). In particular, many of the studies record interventions at a particular point in time with a benefit subsequently occurring. Few, if any, could be considered randomized, controlled trials. It is also not clear whether the beneficial outcome from some of the studies is as a

**Table I** Specifications of a positive-pressure ventilated isolation room

<table>
<thead>
<tr>
<th>Specification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room</td>
<td>Adequate size to care for patient with ensuite facilities</td>
</tr>
<tr>
<td>Anteroom</td>
<td>Anteroom off corridor with handwash basin</td>
</tr>
<tr>
<td>Air changes</td>
<td>$&gt;12$/h; laminar airflow, optional but not essential</td>
</tr>
<tr>
<td>Filtration</td>
<td>99.7% efficient at 0.3μ particles, high-efficiency particulate air</td>
</tr>
<tr>
<td>Sealed room</td>
<td>Essential</td>
</tr>
<tr>
<td>Air direction</td>
<td>Patients to exhaust vents</td>
</tr>
<tr>
<td>Re-circulation</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Positive-pressure ventilation and aspergillosis 95*
result of the specific intervention or would have occurred as a result of the natural history of the outbreak or incident. Furthermore, in many studies, multiple interventions and not just positive-pressure ventilation, result in a beneficial effect.

One of the first reports from the early 1970s studied patients who were randomly allocated to protective isolation with oral non-absorbable antibiotics, routine hospital ward care with oral antibiotics or ward care alone without positive-pressure ventilation or oral non-absorbable antibiotics. Sixty-four patients in total with non-lymphocytic leukaemia were allocated to one of these three groups and the positive-pressure ventilated rooms had consistently low levels of microbial contamination. Patients who were in protective isolation with oral antibiotics and patients on the ward who were receiving oral antibiotics had a lower infection rate, including a lower rate of severe infection and bacteremia, than those on the ward without either. However, most of the infections recorded were bacterial, but there was a significant decrease in the number of infections caused by *Candida* spp. Fewer patients on oral antibiotics and in positive-pressure ventilated facilities died. Whilst there was some benefit gained from positive-pressure ventilation in this particular study, monitoring the incidence of IA was not a particular feature of this study and it is difficult to separate the effect of ventilation from oral non-absorbable antibiotics that included an anti-fungal agent, nystatin.

Thirty-seven patients experiencing 43 episodes of granulocytopenia were randomized to positive-pressure ventilation or standard care and this was accompanied by microbiological surveillance in a later study. There was no statistical difference between the incidence of infection overall between the two groups but the number of patients studied was small and the incidence of bacteremia or bloodstream infection was, however, significantly

### Table II  Studies of positive-pressure ventilation and infection

<table>
<thead>
<tr>
<th>Year (Ref)</th>
<th>Study (no. of patients)</th>
<th>Patient groups</th>
<th>Results</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970–1973</td>
<td>Open, randomized (64)</td>
<td>Acute leukaemia</td>
<td>LAF and oral antibiotics reduced incidence of infection and mortality</td>
<td>Difficult to separate effect of ventilation and antibiotics</td>
</tr>
<tr>
<td>1977–1978</td>
<td>Open, randomized (37)</td>
<td>Acute leukaemia</td>
<td>No difference in overall infection rate</td>
<td>Isolation may have had adverse consequences on patient care</td>
</tr>
<tr>
<td>1973–1977</td>
<td>Open, randomized (89)</td>
<td>Acute leukaemia</td>
<td>Fewer infections, better survival in LAF facilities</td>
<td>LAF room not always available; few fungal infections in either group</td>
</tr>
<tr>
<td>1981–1985</td>
<td>Prospective, intervention (113)</td>
<td>Bone marrow transplant recipients</td>
<td>Reduced aspergillus air counts with HEPA; fewer infections</td>
<td>HEPA not contributory to reduced risk on multivariate analysis</td>
</tr>
<tr>
<td>1985–1986</td>
<td>Prospective, intervention (38)</td>
<td>Bone marrow transplant recipients</td>
<td>No aspergillus infection after LAF installed</td>
<td>Suggestive of benefit</td>
</tr>
<tr>
<td>1988–1993</td>
<td>Retrospective and prospective after intervention (141)</td>
<td>Leukaemia/bone marrow transplant recipient</td>
<td>Reduced incidence of aspergillosis</td>
<td>Other measures, apart from HEPA likely to have contributed</td>
</tr>
<tr>
<td>1996–1997</td>
<td>Prospective, with observational study of air counts (No patients)</td>
<td>Haematology patients</td>
<td>HEPA reduced air counts compared with normal rooms; need LAF during construction</td>
<td>No increase in incidence of infection observed during construction</td>
</tr>
<tr>
<td>1990–1998</td>
<td>Retrospective (555)</td>
<td>Solid organ and bone marrow transplant recipient, ICUs</td>
<td>&gt;60% of aspergillosis community-acquired. Removal of carpeting and false ceilings may have led to a decrease in aspergillosis</td>
<td>Lots of variables impact on risk of aspergillosis</td>
</tr>
<tr>
<td>1992</td>
<td>Retrospective (91)</td>
<td>Haematology/oncology patients</td>
<td>Installation of HEPA filters ended outbreak</td>
<td>Small number of cases</td>
</tr>
<tr>
<td>1997–1994</td>
<td>Retrospective (291)</td>
<td>Chemotherapy patients with neutropenia</td>
<td>Nebulized amphotericin B with HEPA reduced incidence of aspergillosis</td>
<td>Many changes in practice occurred over 18 years</td>
</tr>
</tbody>
</table>

LAF, laminar airflow; HEPA, high-efficiency particulate air; ICU, intensive care unit.
higher in the isolated patients. Not surprisingly, infection caused by *Staphylococcus aureus* and *Pseudomonas aeruginosa* was similar in both groups. The incidence of candida infection was also similar in both groups (two cases) and there were two cases of aspergillosis in the group of patients receiving standard care and none in the group of patients in isolation. Survival rates for the two groups of patients were similar. The authors acknowledged that the reason for the increased incidence of bloodstream infection amongst isolated patients could have been that these patients were given less care and attention particularly in the context of intravenous cannulae and that the low numbers in the study may have precluded seeing an overall benefit in terms of reduced infection.

The advent of bone marrow transplantation represents a significant advance in the treatment of many causes of haematological malignancy. However, such patients undergo more profound immunosuppression and are therefore at increased risk of IA. Ninety transplanted patients were randomly allocated to care in a LAF room compared with controls in a room without artificial ventilation. There were fewer episodes of infection, including bloodstream infection, in patients randomized to the LAF group, but the microbiological surveillance of patients did not appear to be of value in the diagnosis. Most of the infections recorded were bacterial, with *Candida* spp. being the main fungus implicated. There were more cases of candidaemia (sixteen) in the control group compared with those in LAF (three) but this difference does not appear to have been statistically significant. The incidence of IA is not specifically mentioned in this study, but there were similar numbers of patients with interstitial pneumonitis in both groups. Interestingly, patients in the LAF rooms required fewer granulocyte transfusions as in general they had a less complicated inpatient stay.

In response to the increasing diagnosis of nosocomial IA accompanied by positive air culture results, LAF and HEPA systems were installed in a bone marrow transplant unit in Florida together with restrictions on what the patients ate and prophylactic anti-bacterial agents were also used as a preventative measure. Although the authors recorded both community-and-hospital acquired IA, HEPA with LAF significantly reduced the air counts of aspergillus and there were no cases of IA amongst patients cared for under these conditions. In contrast there were 14 cases of hospital-acquired IA amongst 74 bone marrow transplant patients who were cared for elsewhere. The number of infections, age, and severe graft-versus-host disease were significantly associated with nosocomial aspergillus infection, but neither the duration of neutropenia or the use of HEPA filtration made a contribution, according to multivariate analysis. However, the authors did not consider the exclusion of HEPA, as a significant protective factor, reasonable. This is a detailed and complex study as a number of different patient groups were studied over a four-year period with extensive clinical and environmental surveillance. Overall positive, protective ventilation with HEPA does appear to have had an impact in reducing the incidence of IA.

Barnes and Rogers described an outbreak of hospital-acquired IA during the construction of a new LAF unit built adjacent to their bone marrow transplant ward. Air sampling revealed high fungal spore counts that declined as did the incidence of nosocomial IA once the LAF unit was installed and open. This suggests the efficacy of the intervention, i.e. the installation of LAF, but there are no air spore counts available before the construction of the LAF unit. Nonetheless, this is strong circumstantial evidence for the benefit of positive, protective isolation, especially during construction.

As part of a hospital expansion programme in Canada, a new addition to a hospital was constructed, which involved demolition of adjacent buildings. Air sampling was conducted on three occasions during this period and a number of environmental measures were taken to prevent IA, including the use of portable HEPA units, the application of copper-8-quinolinolate formulations applied to walls, doors, etc., the sealing of windows, replacement of perforated ceiling tiles, the replacement of horizontal dust-accumulating blinds, enhanced maintenance of the ventilation systems and the transfer of patients to non-affected areas of the hospital when possible. The incidence of nosocomial IA during the pre-construction period, the period when the construction was taking place, and the period when the construction was taking place but the infection control measures were in place were, 3.18/1000 neutropenic days, 9.88/1000 neutropenic days and 2.91/1000 neutropenic days, respectively. Not surprisingly, there was a reduction in the air counts of aspergillus after the introduction of these infection control measures. This report highlights the importance of a multifaceted approach to the prevention of IA during building work, including simple measures such as enhanced cleaning and adequate ceilings in rooms. It is not clear from this study, however, the exact contribution that HEPA filtration made although it is likely to have been contributory.

In another study of air counts during a period of...
construction, 1047 air samples and 1178 surface samples were taken during a two-week period, when construction was taking place. Although HEPA filtration significantly reduced the air counts for aspergillus during periods when no construction was taking place, only HEPA filtration plus LAF had a significant impact during periods of construction. The authors concluded that although HEPA filtration is effective during normal conditions in reducing the ambient aspergillus spore counts, it may be overwhelmed during building renovation and consequently LAF may be required during such a period.

In many studies the distinction between hospital-and-community-acquired IA is not clearly stated or determined at diagnosis. In a retrospective study from California, invasive pulmonary aspergillosis was classified as hospital-acquired if the patient had a respiratory culture or histopathological report consistent with aspergillosis that was obtained seven or more days after admission with at least one prior negative respiratory culture before the positive sample. Over a nine-year period, 505 patients were identified as having Aspergillus species according to microbiological records; 72 patients with definite aspergillus infection and 433 who were colonized only. Acquisition of IA was deemed to be hospital-acquired in 25% of cases, community-acquired in 62.5% of cases and in the remainder of indeterminate origin. Although the incidence of IA remained relatively stable throughout the period, the removal of carpets from the post-transplant ICU and the replacement of ceiling tiles were associated with a significant decrease in the incidence of IA amongst transplant patients. This study emphasizes the importance of minimizing the environmental reservoir of aspergillosis in clinical areas and often simple measures can have a beneficial effect. Even the occurrence of an earthquake in the Los Angeles area in 1994 and the subsequent demolition and construction activity did not result in an increase in the incidence of IA.

A retrospective cohort study was undertaken to investigate the cause of an outbreak of 10 cases of nosocomial IA from a patient population of 91 admitted for four or more days on a haematology oncology unit in New York. It was believed that this outbreak was due to high counts of aspergillus spores in air from non-bone marrow transplant areas, and after the installation of HEPA filters, the incidence decreased. Again the authors acknowledge the contribution of a number of different infection control measures, despite the circumstantial evidence that installation of HEPA filters brought the outbreak to an end.

The installation of HEPA filtrations is often accompanied by changes in practice and other additional infection control measures such as routine anti-fungal prophylaxis. In a review of 291 patient records over an 18 year period between 1977 and 1994 in New Zealand during which there was a number of changes in the physical design of the unit, the incidence of proven IA declined from 24.4% during the first seven years of the review to 7.1% during the remainder of the period. In particular, the authors recorded no proven or probable cases of IA after the movement of their patient cohort to a HEPA filtered unit between 1992-1994. This was also associated with a decline in the use of intravenous amphotericin B. Whilst the installation of HEPA filtration is likely to have contributed to the lowering of the incidence of IA, it is likely that a range of measures contributed to this over quite a long period, i.e. 18 years.

Other issues in prevention

The provision of positive, protective isolation requires regular maintenance, monitoring and the surveillance of air pressures. However, it is often assumed that an appropriately constructed facility will deliver what it was designed to, but this requires monitoring and sometimes additional maintenance. Pressure readings were taken three times per week to obtain representation of room pressures in three categories of room, i.e. a standard room, a negative-pressure ventilated room and a positive or protective isolation facility. Whilst there were small fluctuations in pressure in most of the standard rooms, most of the negative-pressure ventilated rooms had an overall negative pressure differential as intended. The pressure differential in the positive, protective rooms, however, was greatest, but on some occasions the air pressure dropped to very low levels possibly because the air change rates were lower than intended in the original design. This report emphasizes the need to monitor pressure levels and to take rapid action when the differential is insufficient to maintain positive-pressure ventilation. A small-scale model permitting the cost-effective and unobtrusive study of relevant indices of performance of positive, protective isolation rooms revealed that ventilation efficacy was close to 50% and that there are areas of rooms with poor ventilation. Eventhough there may be positive-pressure ventilation, the air pressures, and therefore the degree of clean air, will vary throughout a room and consequently, the patient should be placed in the best ventilated areas of the room.
Streifel\textsuperscript{23} has reviewed the implications of the installation of HEPA filtration and in particular the need to increase the fan size to drive the increased air volume to provide the facilities likely to provide clean air. Building air pressure requirements usually means that 12 air changes or more are required to provide this but often these critical ventilation parameters are not met because of the minimum maintenance of mechanical healthcare systems. He argues that although air sampling to detect aspergillosis can be of assistance, there needs to be greater emphasis on mechanical parameters and defined particle analysis with optical or condensation particle counters that can provide real time measurements, with the possibility of immediate intervention, especially during construction activity.\textsuperscript{23}

This was well illustrated in a study of the impact of a building implosion on fungal spore counts and IA.\textsuperscript{24} A series of measures to minimize the incidence of IA was taken, including ensuring that windows remained sealed and reducing pedestrian traffic through clinical areas. However, particle counting, including those within the diameter range of fungal spores, gave results almost immediately, enabling rapid action to be taken, if required, compared with the time taken to obtain the results of fungal cultures.\textsuperscript{24}

Although patients may be adequately protected if housed in a HEPA filtered facility, patients often require transfer to other areas of the hospital either for diagnostic or therapeutic intervention such as in the operation theatre, X-ray department or elsewhere, during which time they may be at risk of acquiring aspergillosis. Consequently, it cannot be expected that a HEPA filtered facility will completely remove the risk of infection. During a period of construction in 1993 patients wore high-efficiency filtration masks (filtering to a particle of 0.1 \textmu g) at any time they left their rooms. This resulted in a significant decrease in IA compared with when masks were not worn both for patients with leukaemia and patients after bone marrow transplantation.\textsuperscript{25}

There has been some suggestion recently that water may be a significant source of nosocomial IA as \textit{Aspergillus} species can be isolated from hospital water and that after the decontamination of surfaces and shower heads, the number of aspergillus spores is significantly reduced.\textsuperscript{26,27} However, this is disputed on the basis that many hospital water sources are negative for aspergillus and that measures to reduce air contamination as a possible source should take priority on the basis of the published evidence.\textsuperscript{28,29} It makes sense to review the quality of both drinking and domestic water in clinical areas with severely immunocompromised patients to minimize the occurrence of well-known waterborne infections such as legionellosis and this may have some benefit in reducing the incidence of IA.

The literature on the efficacy of antimicrobial prophylaxis in preventing IA is incomplete. Whilst the use of amphotericin B or itraconazole may be indicated in some groups of patients, there is a need for more accurate definition of at-risk groups and further studies to definitely answer this.\textsuperscript{30} The widespread prescription of antifungal agents to all patients with risk will result in considerable expense and some side effects, and therefore a clear definition of which categories of patient will benefit is required.

Much of the emphasis in the prevention of IA focuses on air quality, but there are many simple issues that need to be addressed in the construction or renovation of a new facility based on practical and basic infection control principles. These include the number of isolation beds, handwashing facilities, waste disposal, the type of flooring, and appropriate ceilings, in particular the absence of perforated flat-pan ceiling tiles.\textsuperscript{31,32}

\section*{Conclusions}

Whilst the evidence suggesting a benefit for positive, protective isolation in preventing IA is not beyond argument, retrospective, observational studies and descriptions of outbreaks during construction, do suggest that in those patients at highest risk of developing IA, positive-pressure ventilation will contribute to reducing infection in addition to other routine infection control measures. All these measures apply especially during periods of building demolition or construction when the need for HEPA filtration is greatest. However, the evidence would not appear to justify, routinely, the addition of LAF facilities, which significantly add to the expense of construction and maintenance. However, basic infection control measures remain of paramount importance. This is confirmed by a very recent report, where, although the ventilation specifications of clinical areas are not described, there was no increase in the incidence of IA or in the air counts of \textit{Aspergillus} spp. during a period of major construction after simple measures such as vacuum cleaning surfaces, ensuring the safe transport of debris, and the sealing of construction areas, were implemented all of which were agreed in advance by the hospital and the construction company.\textsuperscript{33,34}
Whilst prospective randomized studies of at-risk patients cared for in positive pressure and routine isolation rooms seem unlikely to be undertaken for ethical and logistical reasons, we need better definition of the at-risk groups of patients, studies determining the true impact of enhanced cleaning regimens on environmental contamination and IA and trials of prophylactic agents in high-risk groups. We also need better epidemiological data on the proportion of cases of IA that are truly hospital acquired, studies on the importance of environmental monitoring and finally, a greater understanding of the relationship between aspergillus strains isolated from patients and their surroundings.

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