Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Hospital Infection (2007) **65**(S2) 43–49

Available online at www.sciencedirect.com

SCIENCE DIRECT®

www.elsevierhealth.com/journals/jhin

Hospital and community acquired infection and the built environment – design and testing of infection control rooms

J.T. Walker[a,]*, P. Hoffman[b], A.M. Bennett[a], M.C. Vos[c], M. Thomas[d], N. Tomlinson[e]

[a]*Health Protection Agency, Centre for Emergency Response and Preparedness, Porton Down, Salisbury, SP4 0JG, UK*
[b]*HPA, Centre for Infection, Colindale, London, UK*
[c]*Erasmus University Medical Center Rotterdam, Dept of Medical Microbiology and Infectious Diseases, Rotterdam, the Netherlands*
[d]*Consulting Engineer, Leeds, UK*
[e]*Estates and Facilities Directorate, Department of Health, London, UK*

KEYWORDS
Isolation rooms;
HCAI;
Infection control;
Airborne infection;
Built environment;
Multi-drug resistant tuberculosis;
Tracer gas test;
Potassium iodide

Summary Negative-pressure isolation rooms are required to house patients infected with agents transmissible by the aerosol route in order to minimise exposure of healthcare workers and other patients. Housing patients in a separate room provides a barrier which minimises any physical contact with other patients. An isolation room held at negative pressure to reduce aerosol escape and a high air-change rate to allow rapid removal of aerosols can eliminate transmission of infectious aerosols to those outside the room. However, badly designed and/or incorrectly operating isolation rooms have been shown to place healthcare workers and other patients at risk from airborne diseases such as tuberculosis. Few standards are available for the design of isolation rooms and no pressure differential or air-change rates are specified. Techniques such as aerosol particle tracer sampling and computational fluid dynamics can be applied to study the performance of negative-pressure rooms and to assess how design variables can affect their performance. This should allow cost-effective designs for isolation rooms to be developed. Healthcare staff should be trained to understand how these rooms operate and there should be systems in place to ensure they are functioning correctly.

*Corresponding author. Tel: +44 (01980) 612643. E-mail: jimmy.walker@hpa.org.uk (J.T. Walker).

Introduction

Effective interventions to interrupt transmission of infection in hospitals should be based on knowledge of the relevant transmission mechanisms involved. Unfortunately there is a lack of evidence-based knowledge of such transmission mechanisms, with much "fact" established by retrospective observation and anecdote. Most infections will have multiple routes of potential transmission and some will have an airborne route as one of those routes of transmission. A true airborne route (i.e. solely transmission by a particle so small that it has neutral buoyant density and will remain airborne for long periods) is currently thought to be rare. *Aspergillus* spp. constitute one group of pathogens thought to be transmitted primarily by aerosols and are present in the hospital environment.[1] However, most pathogens will be transferred by direct or indirect contact, or by larger temporarily airborne particles (>10 μm "droplets") that will fall to the ground within 2 metres of their point of generation.[2]

The acute hospital environment

Infection control teams (ICTs) should be consulted for their input on any building project in a hospital [www.pef.scot.nhs.uk/guest/SHFN30/SHFN30V2.pdf]. When building isolation rooms, the ICT's input should be to provide specifications of isolation rooms together with the estimated number of rooms required by defining indications of use, and infection hazards, such as the aspergillus risk to highly immunocompromised patients, from the building work itself.[3-6] In construction projects, experience shows it is important for the ICTs to work together with both the project team (e.g. an independent commercial contractor) and the management of each individual unit.

The revised guidance for acute in-patient accommodation for adults in general wards in the UK is in draft stage at the time of writing and it is likely that there will be infection control benefits [www.hefma.org.uk/news/hbn4consult.pdf]. For example, these include increased distances between beds due to the requirements for patient hoists, an increase in the proportion of beds in single rooms as well as the proportion of single rooms with en suite toilets and showers, and a decrease in the numbers of beds in bays. All these improvements are due to the requirements for patient safety, such as nosocomial infections, and patient comfort and privacy during their hospital stay.

Patient or source isolation

The isolation of patients is not an abrupt jump from no isolation to full isolation. There is an incremental process from a basic set of infection control measures (general or standard precautions) meant to prevent dispersion or acquisition of unknown infectious agents, through to increased precautions on the ward as infection or colonisation becomes known or suspected (particularly if there are no single rooms available). In addition there is cohorting on wards or in bays, to the use of non-specialist single rooms (preferably with their own toilet and bathing facilities) and finally the use of specially-engineered isolation rooms if there is an airborne element to transmission.[7]

Interest in the use of airborne isolation rooms has increased due to the occurrence of new emerging diseases such as severe acute respiratory syndrome (SARS),[8] avian influenza[9] and multi-drug resistant tuberculosis (MDR-TB).[10] The recognition of the possibility of pandemic outbreaks of influenza has required authorities to put in place "emergency planning" for dealing with infected patients that may require isolation,[10,11] although with influenza, airborne isolation is not thought to be an issue unless specific "aerosol-generating procedures" are occurring such as bronchoscopy or sputum induction. Isolation rooms can be used to constrain the spread of small-particle aerosols, which some evidence suggests may play a role in all these diseases.[12] In order to maximise the use of such specialist facilities there can be financial issues for these rooms to be multifunctional, i.e. to be used as non-specific pressure (low risk – normal use), negative pressure (protection of healthcare workers and visitors in the room, and healthcare workers and patients outside the room) or positive pressure (highly immuno-compromised patient protection from inhalation of fungal spores if the incoming air is filtered by a "High Efficiency Particulate Air" filter [HEPA-filtered]). Isolation rooms which can be switched from one functional type to another such as changing a positive-pressure room into a negative-pressure room are highly hazardous and should be avoided due to the possibility of use at the incorrect pressure regime. If multifunctional facilities are to be used staff must be trained correctly, rooms must have written operating and auditing procedures, and in addition electronic warning systems and alerts must be in place.

Airborne infection in hospitals caused by inappropriate use or design of facilities

Schwartzman *et al.* in 1996[13] carried out a study of tuberculosis infection in healthcare workers in

two hospitals in Montreal in which they found a high incidence (over 2% annual risk) in tuberculin reactions and conversions. Major deficiencies in the ventilation systems of both hospitals were noted. There was no negative pressure in the bronchoscopy and sputum induction rooms in all but the most recently built isolation suites. Very low air-change rates were found in many areas of both hospitals. The hospital with the higher incidence of tuberculosis infection had the least effective isolation ventilation system.

An outbreak of MDR-TB occurred in London in the 1990s when a patient with MDR-TB was inadvertently placed in an isolation room at positive pressure on a ward where a high proportion of patients were immuno-compromised by HIV infection and thus highly susceptible to TB infection.[14] This demonstrates the operational problems when the two types of room occur close together. In the USA 17 healthcare workers were infected with MDR-TB due to exposure to infectious patients, with five fatalities resulting.[15,16]

Design considerations for isolation rooms

The majority of patients who need extra precautions in specialised rooms need not have specialist ventilation as most transmission will occur by direct or indirect transmission and droplet spread. For these situations, all those who use isolation rooms should facilitate good infection control practices.

Only where there is thought to be a significant airborne component to the infection transmission should isolation rooms be operated at negative pressure to their adjacent areas or PPVL be used. Any microbial aerosols generated inside the room will be diluted by ingress of air from the hospital and will be extracted through a duct (HEPA-filtered) to the outside environment. The door to the room should be kept closed as much as possible and patient contact with other patients and visitors should be minimised.

No information on isolation rooms is given in Health Technical Memorandum (HTM) 2025,[17] but an outline of negative-pressure room requirements is given in the UK guidance on MDR-TB and TB in the context of HIV.[18] However, in the USA there are many documents recommending design criteria for negative-pressure isolation rooms, including those written by the CDC,[19] ASHRAE,[20] American Institute of Architects (AIA) [www.aia.org/SiteObjects/files/04_Review_and_Anal_Literature.pdf], and the Department of the Army.[21]

Isolation rooms should have minimum air-change rates of 6 air changes an hour (ach) for the protection of staff and visitors in the room.[19,22] If possible, this should be increased to the 12 ach recommended as a minimum by the AIA.[23] The room airflow pattern should be designed to provide healthcare workers or visitors with clean air.

The level of negative pressure in isolation rooms is often in question. The CDC[19] recommend a minimum negative pressure of 0.001 inch of water (0.25 Pa) and an exhaust flow of 50 cubic feet per minute (CFM) (1.8 m^3/min) or 10% greater than supply. The US Department of the Army[21] specifies an exhaust flow of 20% greater than supply for their isolation rooms. Both CDC and the UK recommend the use of alarmed pressure devices to provide continuous monitoring of the negative pressure.[18] However, infection control considerations only require that the air flows inwards through gaps in the room's fabric (hence "negative pressure"). The value of this pressure, given a robust difference between extract and supply rates, is irrelevant. However, the number of air changes per hour should be calculated as this allows the time in which the air is "cleaned" from a pathogen to be calculated.

Methods to measure the effect of design variables on the performance of isolation rooms

Routine monitoring of negative-pressure isolation rooms

Rooms where airflow is meant to be in a particular direction should be monitored continuously by the pressure differential between the room and its neutral-pressure surround. The value of such pressure is relatively unimportant as long as the direction of airflow it signifies is clearly indicated. This should be monitored in such a way that the users of the ward are instantly aware of any failure. However, remote building management systems (BMS) may cause a considerable delay in ward staff becoming aware of a system failure. Any system must measure the desired parameter (negative pressure) directly or it is prone to failure. Hoffman *et al.* in 2004[24] reported an unnoticed failure where the fans in an air-handling unit were monitored and working but an inadvertently closed ductwork damper prevented any actual extract airflow, resulting in a "negative-pressure" room being at positive pressure although the BMS did not indicate the failure. This demonstrates that dampers and pressure stabilisers have a role in generating flow stability and also provide a visual indication (as the damper moves in a particular direction) that air is flowing in the intended direction.

Visible-smoke tests

A regular (monthly) test that can be undertaken is the use of visible smoke around the perimeter of doors to each patient room and, where appropriate, at both the anteroom–corridor and anteroom–patient room doors; this can form the basis of a regular (monthly) test to confirm the integrity of the negative-pressure system.[25,26] Directional airflow is determined by observing the movement of smoke under the door and through spaces between the door and frame. In a US hospital study the percentage of rooms that did not meet the directional airflow criterion using this technique fluctuated between 12% in 1994 and 60% in 1993. In other studies 45% of 115 designated negative-pressure rooms actually had positive airflow to the corridor.[27] The main factors that were identified to be associated with outward directional airflow at the time of the authors' study included ventilation systems not balanced (14%), turbulent airflow patterns (11%), and automated control system inaccuracies (10%).

In one facility with its own computer-controlled and monitored heating, ventilation and air-conditioning (HVAC) system, infection control staff chose to continue their policy of monitoring respiratory isolation rooms on a daily basis using visible smoke despite claims from the manufacturer that this practice would be unnecessary. However, five months after installation, smoke testing by the staff of an isolation unit housing a patient known to have MDR-TB showed air to be flowing out of the patient room through the anteroom and into the corridor. The airflow contradicted the display screen data and the selected operational setting, indicating the usefulness of simple approaches such as the visible-smoke test in addition to continuous monitoring devices.[25] In practice, however, smoke tests can prove problematic, not least in activating smoke alarms.

Methods for assessment of design parameters

There are a number of techniques available to measure the efficiency of isolation rooms and to identify problems with their design. This section outlines techniques used experimentally to assess design criteria.

Tracer gas tests – sulphur hexafluoride (SF_6)

Tracer methods can be used as research tools to assess the adequate functionality of isolation rooms.[28] This technique involves releasing the tracer gas within the isolation facility and then measuring its presence in parts per trillion in the anterooms outside the patient rooms and corridor outside the isolation room suites 5–25 min later. By using such research methods, Rydock and Eian[29] demonstrated that one room was poorly functioning in comparison to another, as a negative pressure with respect to the corridor could not be maintained. Problems were identified with both the flow rates and the design of one particular isolation unit, where the inlet ducts were in the patient room and the exhaust ducts were in the bathroom and anteroom. In a study of four "state of the art" isolation rooms, this methodology exhibited easily reproducible measurable tracer concentrations in the anteroom outside each suite.[29] Such tests provide evidence that will help determine what level of tracer is acceptable and will also assist in determining policy for the specification of minimum acceptable pressure differentials and the optimisation of ventilation system design.

Potassium iodide tracer test

Other studies have investigated methods to quantify the effectiveness of containment laboratories that operate under negative pressure to prevent the egress of airborne microorganisms.[30] A technology using potassium iodide (KI) was initially developed to study movement of particulate contaminants between rooms in a hospital burns unit.[31–33] This technique has been used to assess the effectiveness of containment laboratories and is measured in terms of the laboratory protection factor (LPF), which is the ratio of KI particles generated within the laboratory to those detected outside the laboratory. The same technique has been used to measure the performance and operator protection factor (OPF) of microbiological safety cabinets where a protection factor of 10^5 is regarded as being adequate.[17] BL-3 laboratories without an anteroom were found to provide an LPF of approximately 10^4 whilst the provision of an anteroom increased the LPF approximately tenfold. There was no direct relationship between the magnitude of negative pressure and LPF. However, the authors did find a direct relationship between the in-flow velocity and LPF. In terms of flow, a volumetric in-flow of 10 m^3/min into a laboratory through an anteroom gave an LPF of greater than 10^5. The significant findings of the study are that the LPF, a measure of containment, is dependent on the laboratory in-flow and of the magnitude of the pressure differential.[30] Since

negative-pressure rooms are normally designed only on the basis of the pressure-differential magnitude, this finding has major implications for the design of containment laboratories and isolation rooms.

Computational flow dynamics

Engineering simulations employing computational fluid dynamics (CFD) provide a convenient means of investigating airflow behaviour, temperature distribution and contaminant dispersion in isolation rooms for various ventilation arrangements.[34] In other studies[35] a cough model was constructed to permit the numerical simulation of virus diffusion inside an isolation room for different configurations of the ventilation system. An analysis of the region of droplet fallout and the dilution time of virus diffusion of coughed gas in the isolation room was also performed for each ventilation arrangement. The results indicated that the parallel-directional airflow pattern is the most effective means of controlling airflows containing virus droplets. Additionally, staggering the positions of the supply vents at the door end of the room relative to the exhaust vents on the wall behind the bed head provides effective infection control and containment. These results suggest that this particular ventilation arrangement enhances the safety of staff when performing medical treatments within isolation rooms.

A number of other different ventilation strategies were investigated using CFD in a "negative-pressure" isolation room.[36] The authors demonstrated that a low-level extraction technique was very effective in removing pollutants at the human breathing zone as compared to extraction at ceiling level. In addition, the ventilation strategies and furniture layout were found to have an influence on the airflow and pollutant distribution patterns in the isolation room.

Protective isolation

The other category of isolation is the protection of particularly vulnerable patients, known as "protective isolation".[37] Whilst the majority of hospital patients are at some increased vulnerability to infection, due to infirmity, wounds, age etc., infection transmission to them is by direct and indirect contact, and protection is only assured by staff adherence to good infection control behaviour. In such circumstances single rooms may add an element of quality assurance to staff behaviour.[38,39] However, there are patients with profound or prolonged neutropenia, typically bone marrow transplant (BMT) patients, to whom inhalation of fungal spores presents a risk of infection.[40,41] Fungal spores generally originate outside the hospital and will be part of the hospital air, as this air is not filtered. In particular, their aerosolisation may be associated with demolition or renovation/construction work.[42,43] They can also originate inside the hospital but this requires prolonged damp conditions in the patient's proximity or renovation/construction work.[44] In addition to the prevention of infection by direct and indirect contact, it has to be ensured that all the air available for these patients to breath has had the fungal spores filtered from it. This is done by supplying air filtered by HEPA filters that can remove fungal spores with very high efficiency to the patient's environment and ensuring that this is the only air available for them to breath.[1,45] As there will inevitably be gaps in the patient's room, for example via cable and pipe entry points and around the door, if the room is at positive pressure, the clean air leaking outwards will prevent unfiltered air from leaking inwards. These areas cannot have opening windows. This type of isolation is generally known as "positive pressure", but the filtration of the air is more important; positive pressure by itself will not achieve safety. Air change rates would be irrelevant to infection control and should be determined by patient comfort criteria.

HEPA-filtered positive-pressure rooms are indicated for allogenic BMT patients. The need for these rooms in autologous BMT patients is not established, but should be evaluated for those recipients if they experience prolonged neutropenia, a substantial risk factor for nosocomial aspergillosis, and is indicated in BMT centres with ongoing construction and renovation.[46] Some BMT units supply centrally HEPA-filtered air to the whole unit, which itself is at positive pressure to its surroundings. This enables patients to use common ward facilities when they are able to do so, thus giving a degree of release from a long confinement in one room.

Conclusions

Housing infectious patients in single rooms allows a barrier to be placed between the patient and the other hospital patients and staff not tending to the patient. In most cases of infectious disease this will be enough to prevent further spread of the disease if infection control measures are enforced. However, for a small number of infectious diseases, the chance of aerosol spread will require that the patient is housed in a

room in which ventilation controls are used to ensure no leakage of infectious aerosols into the hospital environment. This can easily be undertaken by ensuring the room is held at a small negative pressure with an adequate air-change rate (12 ach). It is essential that if isolation rooms are to be used effectively, all staff are fully trained in their operation and the rooms are regularly tested, e.g. using smoke pencils.

Acknowledgement

This manuscript was presented at the HIS Meeting 2006 and the authors gratefully acknowledge the invitation from Nigel Tomlinson to speak at the meeting and the generosity of the HIS society for contributing towards travel expenses and accommodation for the meeting. The authors also acknowledge Prof. Phil Marsh for his critical evaluation of the manuscript.

References

1. Humphreys H. Positive-pressure isolation and the prevention of invasive aspergillosis. What is the evidence? *J Hosp Infect* 2004;**56**:93–100.
2. Tang JW, Li Y, Eames I, Chan PK, Ridgway GL. Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises. *J Hosp Infect* 2006;**64**:100–114.
3. Skladny H, Buchheidt D, Baust C, *et al*. Specific detection of *Aspergillus* species in blood and bronchoalveolar lavage samples of immunocompromised patients by two-step PCR. *J Clin Microbiol* 1999;**37**: 3865–3871.
4. Anonymous. Construction related nosocomial infections in patients in health care facilities – decreasing the risk of *Aspergillus*, *Legionella* and other infections. *Can Communicable Dis Rep* 2001;**2752**:1–55.
5. Hahn T, Cummings KM, Michalek AM, *et al*. Efficacy of high-efficiency particulate air filtration in preventing aspergillosis in immunocompromised patients with hematologic malignancies. *Infect Control Hosp Epidemiol* 2002;**23**:525–531.
6. Maertens J, Boogaerts M. The place for itraconazole in treatment. *J Antimicrob Chemother* 2005;**56**:33–38.
7. Phillips DA, Sinclair R, Schuyler G. *Isolation Room Ventilation Design Case Studies: American Society of Heating, Refrigeration and Air-Conditioning Engineers*. IAQ: 2004, pp. 1–16.
8. Fung CP, Hsieh TL, Tan KH, *et al*. Rapid creation of a temporary isolation ward for patients with severe acute respiratory syndrome in Taiwan. *Infect Control Hosp Epidemiol* 2004;**25**:1026–1032.
9. Fica CA, Cifuentes DM, Ajenjo HM, *et al*. Precautions in attending avian influenza H5N1 inpatients. *Rev Chilena Infectol* 2006;**23**:290–296.
10. Fennelly KP, Martyny JW, Fulton KE, *et al*. Cough-generated aerosols of *Mycobacterium tuberculosis*: a new method to study infectiousness. *Am J Respir Crit Care Med* 2004;**169**:604–609.
11. Dull PM, Wilson KE, Kournikakis B, *et al*. *Bacillus anthracis* aerosolization associated with a contaminated mail sorting machine. *Emerg Infect Dis* 2002;**8**: 1044–1047.
12. Tellier R. Review of aerosol transmission of influenza A virus. *Emerg Infect Dis* 2006;**12**:1657–1662.
13. Schwartzman K, Loo V, Pasztor J, Menzies D. Tuberculosis infection among health care workers in Montreal. *Am J Respir Crit Care Med* 1996;**154**:1006–1012.
14. Breathnach AS, de Ruiter A, Holdsworth GM, *et al*. An outbreak of multi-drug-resistant tuberculosis in a London teaching hospital. *J Hosp Infect* 1998;**39**: 111–117.
15. Menzies D, Fanning A, Yuan L, FitzGerald JM. Tuberculosis in health care workers: a multicentre Canadian prevalence survey: preliminary results. Canadian Collaborative Group in Nosocomial Transmission of Tuberculosis. *Int J Tuberc Lung Dis* 1998;**2**:S98–S102.
16. Menzies D, Fanning A, Yuan L, Fitzgerald M. Tuberculosis among health care workers. *N Engl J Med* 1995;**332**: 92–98.
17. Anonymous. Advisory Committee on Dangerous Pathogens. *Categorisation of Biological Agents according to Hazard and Categories of Containment*. Sudbury: HSE Books; 1995.
18. Anonymous. *The Prevention and Control of Tuberculosis in the United Kingdom*: UK guidance on the Prevention and Control of Transmission of 1) HIV-related Tuberculosis 2) Drug-resistant, Including Multiple Drug-resistant, Tuberculosis. London: Department of Health; 1998, pp. 1–94.
19. Anonymous. *Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Facilities, 1994,* Atlanta: Centers for Disease Control and Prevention. *NRR-13* 1994;**43**:41–94.
20. Hitchings DT. Laboratory space pressurization control systems. *ASHRAE J* 1994;**36**:336–340.
21. Anonymous. *Heating, Ventilation and Air Conditioning of Hardened Buildings*. Washington: US Department of the Army; 1996. TM 5–835–4.
22. Menzies D, Fanning A, Yuan L, FitzGerald JM. Hospital ventilation and risk for tuberculous infection in Canadian health care workers. Canadian Collaborative Group in Nosocomial Transmission of TB. *Ann Intern Med* 2000; **133**:779–789.
23. Anonymous. *Guidelines for Design and Construction of Hospital and Health Care*. Washington: American Institute of Architects; 1996, pp. 1–33.
24. Hoffman PN, Weinbren MJ, Stuart SA. A practical lesson in negative-pressure isolation ventilation. *J Hosp Infect* 2004;**57**:345–346.
25. Pavelchak N, Cummings K, Stricof R, *et al*. Negative-pressure monitoring of tuberculosis isolation rooms within New York State hospitals. *Infect Control Hosp Epidemiol* 2001;**22**:518–519.
26. Pavelchak N, DePersis RP, London M, *et al*. Identification of factors that disrupt negative air pressurization of respiratory isolation rooms. *Infect Control Hosp Epidemiol* 2000;**21**:191–195.
27. Fraser VJ, Johnson K, Primack J, *et al*. Evaluation of rooms with negative pressure ventilation used for respiratory isolation in seven midwestern hospitals. *Infect Control Hosp Epidemiol* 1993;**14**:623–628.
28. Rydock JP. A simple method for tracer containment testing of hospital isolation rooms. *Appl Occup Environ Hyg* 2002;**17**:486–490.
29. Rydock JP, Eian PK. Containment testing of isolation rooms. *J Hosp Infect* 2004;**57**:228–232.

30. Bennett AM, Parks SR, Benbough JE. Development of particle tracer techniques to measure the effectiveness of high containment laboratories. *Appl Biosafety* 2005; **10**:139–150.
31. Foord N, Lidwell OM. Airborne infection in a fully air-conditioned hospital. I. Air transfer between rooms. *J Hyg London* 1975;**75**:15–30.
32. Foord N, Lidwell OM. Airborne infection in a fully air-conditioned hospital. II. Transfer of airborne particles between rooms resulting from the movement of air from one room to another. *J Hyg London* 1975;**75**:31–44.
33. Foord N, Lidwell OM. The control by ventilation of airborne bacterial transfer between hospital patients, and its assessment by means of a particle tracer. I. An airborne-particle tracer for cross-infection studies. *J Hyg London* 1972;**70**:279–286.
34. Chow TT, Yang XY. Ventilation performance in the operating theatre against airborne infection: numerical study on an ultra-clean system. *J Hosp Infect* 2005;**59**: 138–147.
35. Kao PH, Yang RJ. Virus diffusion in isolation rooms. *J Hosp Infect* 2006;**62**:338–345.
36. Cheong KWD, Phua SY. Development of ventilation design strategy for effective removal of pollutant in the isolation room of a hospital. *Building and Environment* 2006;**41**:1161–1170.
37. Nagao T. Experience with protective isolation for infection prevention in the compromised host. *Tokai J Exp Clin Med* 1986;**11**(Suppl):23–28.
38. Gould D, Wilson-Barnett J, Ream E. Nurses' infection-control practice: hand decontamination, the use of gloves and sharp instruments. *Int J Nurs Stud* 1996;**33**: 143–160.
39. Kuzu N, Ozer F, Aydemir S, Yalcin AN, Zencir M. Compliance with hand hygiene and glove use in a university-affiliated hospital. *Infect Control Hosp Epidemiol* 2005;**26**:312–315.
40. Moller J, Skinhoj P, Hoiby N. Microbial colonization and infectious complications in bone marrow transplant recipients treated in strict protective isolation. *Scand J Infect Dis* 1984;**16**:43–50.
41. Russell JA, Poon MC, Jones AR, Woodman RC, Ruether BA. Allogenic bone-marrow transplantation without protective isolation in adults with malignant disease. *Lancet* 1992;**339**:38–40.
42. Iwen PC, Davis JC, Reed EC, Winfield BA, Hinrichs SH. Airborne fungal spore monitoring in a protective environment during hospital construction, and correlation with an outbreak of invasive aspergillosis. *Infect Control Hosp Epidemiol* 1994;**15**:303–306.
43. 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**:375–378.
44. Bartley JM. APIC state-of-the-Art report: the role of infection control during construction in health care facilities. *Am J Infect Control* 2000;**28**:156–169.
45. Eckmanns T, Ruden H, Gastmeier P. The influence of high-efficiency particulate air filtration on mortality and fungal infection among highly immunosuppressed patients: a systematic review. *J Infect Dis* 2006;**193**: 1408–1418.
46. Anonymous. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America. *Morb Mortal Wkly Rep* 2000;**49**:491–128.