

Review

Isolation in the allogeneic transplant environment: how protective is it?

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Summary:

Aggressive infection control measures that include isolating patients within protective hospital environments have become a standard practice during allogeneic stem cell transplantation. A wide range of interventions includes the management of ventilation systems, BMT unit construction and cleaning, isolation and barrier precautions, interactions with health-care workers and visitors, skin and oral care, infection surveillance, and the prevention of specific nosocomial and seasonal infections. However, many of these practices have not been definitively proven to provide patients the intended benefit of decreased infection rates or improved survival. Furthermore, each intervention comes with a financial and social cost. With institutional cost containment efforts and recent trials suggesting that patients may be safely cared for in the outpatient environment after allogeneic transplantation, many widely held practices in managing the transplant environment are being reconsidered. With changing practices, transplant teams are encouraged to review local patterns of infections and associated complications and communicate regularly with infection control committees for guidance on the evolution of isolation needs for the immunosuppressed patient.

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Time spent on an allogeneic transplant service raises questions about the nature and benefit of the isolation precautions used to prevent infectious complications, the associated costs with each measure, and the institutional variability that is apparent across the country. Recent examples from our own institution range from determining the needs for and planning the construction of a new clinical facility, to halting the spread of vancomycin-resistant *Enterococcus* (VRE) and to analyzing the potential for delays in response time to acute emergencies while putting on contact isolation materials (gowns, masks,

gloves, etc). Standards for isolation may be subject to change when managing infection outbreaks or with new construction, and may be influenced by the changing financial pressures of the institution.

In an era of ongoing cost-containment, the clinical value of each isolation intervention and the associated expenditures are due to be examined. With changes in the number of patients undergoing allogeneic transplantation, the financial constraints of care, and advances in supportive care, there has been a trend to relax the degree of patient isolation in the absence of definitive data to support its use (Figure 1). Even the use of protected hospital environments is being questioned, with recent trials assessing the safety and efficacy of outpatient care during the pre-engraftment phase after allogeneic transplants. Guidelines for infection control were published in 2000 by the Centers for Disease Control (CDC) with the Infectious Disease Society of America (IDSA) and the American Society of Blood and Marrow Transplantation (ASBMT), but most recommendations were based on uncontrolled studies or expert opinion rather than randomized controlled trials.¹ The Foundation for the Accreditation of Cellular Therapy (FACT) calls for a designated in-patient unit that minimizes airborne microbial contamination and a designated area for outpatient care that reasonably protects the patient from transmission of infectious agents and can provide, as necessary, appropriate patient isolation. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standards call for incorporation of an infection control program with ongoing assessments to identify risks for the acquisition and transmission of infectious agents using an epidemiological approach of surveillance, data collection, and trend identification. The purpose of this Mini review is to consider various interventions used to control patient environments, examine the evidence behind many common interventions, and discuss some of the associated costs. In doing so, we hope to provide some guidance for managing transplant environments and encourage appropriately controlled trials to assess appropriate infection control interventions.

Reasons for patient isolation

Caring for patients after an allogeneic stem cell transplant within a protective hospital environment has been considered standard of care based upon the spectrum and severity of infections to which this immune-compromised population is susceptible. The risks of infection after

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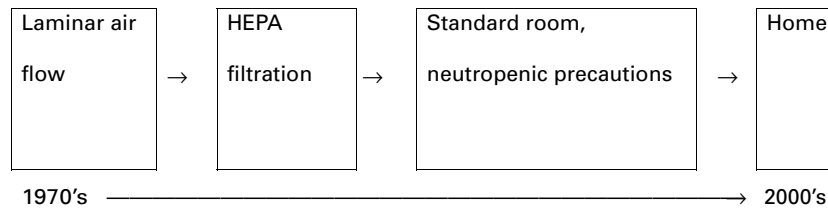


Figure 1 Trends in the intensity of isolation practices for patients after allogeneic transplantation. Influences: (a) Increased number of patients undergoing transplantation. (b) Increased financial constraints: patient, payer, and institution. (c) Advances in supportive care: hematopoietic growth factors and antibiotics. (d) Lack of evidence supporting aggressive isolation.

Table 1 High incident (>10%) opportunistic infections by phases after myeloablative allogeneic hematopoietic stem cell transplantation (adapted from CDC guidelines)

<i>Pre-engraftment (<30 days)</i>	<i>Post-engraftment (30–100 days)</i>	<i>Late phase (>100 days)</i>
Herpes simplex virus ^a	Cytomegalovirus ^a	Cytomegalovirus ^a
Gram-negative bacilli	<i>Staphylococcus epidermidis</i>	Varicella zoster virus
<i>Staphylococcus epidermidis</i>	<i>Candida</i> species	Encapsulated bacteria (eg pneumococcus)
Streptococci species	<i>Aspergillus</i> species	<i>Aspergillus</i> species
<i>Candida</i> species	<i>Pneumocystis pneumonia</i>	<i>Pneumocystis pneumonia</i> (PCP) ^a
<i>Aspergillus</i> species	(PCP) ^a	

^aWithout standard prophylaxis.

allogeneic transplant are highlighted by reports of infection outbreaks from conventional and opportunistic pathogens. Early studies of patients receiving chemotherapy for acute leukemia or undergoing bone marrow transplantation for aplastic anemia suggested clinical benefit to aggressive infection control measures.

Scope of infectious complications

Opportunistic infections from bacterial, viral, and fungal organisms are common after allogeneic hematopoietic stem cell transplantation. Infections of varying severity occur in >90% of patients after allogeneic transplantation, and are considered the most common single cause of mortality. The scope and timing of infectious complications after transplant have been reviewed.¹ Periods of varied risk after myeloablative allogeneic transplant have been defined as pre-engraftment, post-engraftment (through day +100), and late phase (Table 1).

The epidemiology of these infections continues to evolve based on the degree, type, and duration of immune suppression, the use of prophylactic antibiotics, surveillance for organisms associated with nosocomial infections, the emergence of drug-resistant organisms, and the use of isolation precautions.

The advent of reduced-intensity allogeneic transplants has also significantly changed the timing and duration of the phases of infection risk. Even with reduced-intensity conditioning, substantial risks for infectious complications have been reported.² Despite a shorter duration of neutropenia and less mucosal damage, quantitative and qualitative T-cell defects over the first 12 months are similar to those after myeloablative transplants.³ In matched controlled studies of patients after nonmyeloablative and myeloablative transplants in Seattle, there were fewer episodes of bacteremia during the first 30 days after

reduced-intensity conditioning (9 vs 27%, $P=0.01$), but the difference was less pronounced by day +100 (27 vs 41%, $P=0.07$).⁴ There was no decrease observed in the rate of invasive aspergillosis during the first year (15 vs 9%). The overall risk of CMV disease was also similar between these groups, but was delayed in onset among recipients of reduced-intensity transplants (median day +130 vs day +52).⁵

The epidemiology of invasive fungal infections has also changed, reflecting the use of antifungal prophylaxis as well as changes in conditioning regimens. There has been a reduction in the incidence of *Candida* infections, but a relative increase in non-*Albicans* species, often resistant to fluconazole.^{6–8} There has also been an increased incidence of *Aspergillus* infections, including nonfumigatus species.⁹ Temporally related to the increased use of *Aspergillus*-active antifungal drugs for prophylaxis, there have been recent reports of an increasing incidence of non-*Aspergillus* molds.⁹

Infection outbreaks

In addition to understanding the spectrum of routinely acquired pathogens among immunocompromised hosts, infectious outbreaks in stem cell transplant units have highlighted the potential importance and need for controlled environments.

Infection outbreaks occurring on stem cell transplant units include reports involving bacterial, viral, and fungal pathogens. A recent survey from the EBMT reported 23 outbreaks among 13 centers involving 231 patients, including 56 attributable deaths.¹⁰ In this series of 10 bacterial, eight viral, and five fungal outbreaks, all were reported to be hospital acquired and 12 centers reported a partial or total unit closure prior to resolution. Notably, all viral, four of 10 bacterial and three of five fungal outbreaks

occurred in high-efficiency particulate air (HEPA)-filtered wards.

Aspergillus is a common airborne infection and outbreaks have been widely reported not only in association with construction activity but also with contamination of water supplies.^{11–14} Outbreaks of infection with other fungi have also been reported, including a series of infections with *Paecilomyces lilacinus* associated with contaminated skin ointment.¹⁵ Bacterial outbreaks have included waterborne pathogens such *Legionella* and *Pseudomonas* species.^{16,17} The risk of *Clostridia difficile*-associated diarrhea is substantial in a population heavily exposed to antibiotics, and recommendations highlight outbreaks reported in association with nondisposable rectal thermometers or infected gastrointestinal endoscopes.¹ Respiratory viral outbreaks, including seasonal pathogens such as respiratory syncytial virus (RSV) and influenza, are not prevented by HEPA filtration and require increased attention to recognizing individuals with symptoms and removing them from the vicinity of vulnerable patients.^{18–20}

Outbreaks of RSV in transplantation units illustrate the potential for the rapid spread of lethal pathogens. One such outbreak occurred among 30 patients in a 13-week period and included an additional 35 family members and health-care workers.²¹ Of the 18 patients with lower respiratory infections from RSV, the mortality was 78%. Another center reported an outbreak in which 45% of hospitalized BMT patients with acute respiratory illness in a 2-month period had RSV disease, and two-thirds were considered hospital acquired.²² Mortality for those untreated or those treated requiring mechanical ventilation was 100%. In another outbreak, genotyping showed eight of nine isolates from a BMT unit were the same RSV strain.²³

VRE is an emerging bacterial pathogen reported in transplant unit outbreaks that is associated with the widespread use of vancomycin.^{24–26} A recent description of an outbreak of VRE illustrates the importance of hospital infection surveillance and control programs.¹⁰ After noting a marked increase in colonization with VRE as well as the emergence of VRE infections, initial control measures included strict hand-washing protocols, isolation of patients, attention to ward cleaning, and the restriction of vancomycin use. However, after detecting continued VRE infections with a molecular typing confirming a shared predominant strain of *Enterococcus faecalis*, the unit was closed for 6 months. Patients colonized or infected with VRE were cohorted in units where all staff were required to wear gowns and gloves. A computer flagging system was implemented to alert for VRE-carriers on readmissions. Since reopening the transplant unit, only one new case of VRE was observed in 3 years.

In our own institution, VRE has also become problematic. The organism did not arrive at OHSU until 1996, but by the year 2000, 30 new cases were identified among immune-compromised adults. In 2002, a cluster of 16 patients in the adult oncology unit was found to have VRE infection (14) and colonization (2). This led to the creation of a VRE Management Team and the implementation of enhanced contact precautions, environmental cultures, compliance monitoring, and education programs for patients and families, nursing, housekeeping, transporta-

tion, imaging, and associated medical staff. Specific interventions included the regular use of gloves for each patient encounter and contact precautions with gloves and gown for patients with VRE. Patients were screened for VRE with rectal swabs upon hospital admission, and colonized patients were flagged in our hospital computer system for care in dedicated VRE outpatient clinic rooms. By February 2003, after a period of identifying no new cases in 4 weeks, enhanced isolation was relaxed, but active surveillance in oncology units continued. Sporadic cases were reported until 1 week in October 2004 when nine new cases of VRE colonization were found among 80 patients screened. Isolates including those nine and an additional four from preceding weeks were sent for DNA analysis, which revealed that six isolates were genetically identical and an additional three were closely related, suggesting a shared source. Since that time, enhanced isolation was reinstated with ongoing monitoring for the transplant ward as well as the intensive care unit.

Benefits of isolated environments: early studies

Early studies among patients undergoing chemotherapy for leukemia suggested that environmental infection control measures might have a positive impact on patient outcomes. These included the use of laminar air flow (LAF) units, patient isolation units, prophylactic antibiotics, sterile and low-microbial diets, and antimicrobial decontamination.^{27–36} A randomized trial among patients with acute leukemia performed in 1978 showed a decrease in fatal infections, an increase in complete remission rates, and an improved survival among patients treated in a protected environment with prophylactic antibiotics.³⁷ However, even in these early studies, there was recognition of emerging antibiotic-resistant strains of bacteria when using antibiotics for patient protection.³¹

Early prospective, randomized studies of protective environments among bone marrow transplant recipients suggested that laminar air flow isolation and decontamination procedures resulted in a significant reduction in infections, but no difference in survival, with most deaths due to interstitial pneumonia or recurrent disease.³⁸ After 5 years, the same group published retrospective data, suggesting that these protective environments reduced mortality associated with a reduction in and delayed onset of acute GVHD after allogeneic transplantation for the treatment of aplastic anemia.³⁹ Further studies of intestinal bacterial decontamination, including suppression of anaerobic bacteria, decreased the severity of acute GVHD.⁴⁰ Finally, retrospective studies of the use of HEPA filtration units showed a reduction in the number of *Aspergillus* organisms in the air and a decrease in the risk of nosocomial *Aspergillus* infections.^{11,13,41}

Specific interventions

Recommendations for infection control have focused on issues of ventilation, construction, room cleaning, isolation and barrier precautions, interactions with health-care workers and visitors, skin and oral care, infection

Table 2 Evidence-based rating system

<i>(A) Strength of recommendation</i>	
A	Strongly recommended. Strong evidence for efficacy and substantial clinical benefit
B	Generally recommended. Moderate evidence for efficacy or only limited clinical benefit
C	Optional. Insufficient evidence for efficacy or benefit may not outweigh the risk or cost
D	Generally not recommended. Moderate evidence against efficacy or of adverse outcome
E	Never recommended. Strong evidence against efficacy or of adverse outcome
<i>(B) Quality of evidence</i>	
I	Evidence from at least one well-executed randomized controlled trial
II	Evidence from at least one well-designed non-randomized trial, cohort or case-control studies, multiple time-series studies, or dramatic results from uncontrolled experiments
III	Evidence from expert opinions based on experience, descriptive studies, or committees

surveillance, and prevention of specific nosocomial and seasonal infections.¹ The strength of the recommendation and the quality of supporting evidence is graded (Table 2).

CDC level I evidence

While the CDC/IDSA/ASBMT guidelines contain over 200 recommendations for infection control among hematopoietic stem cell recipients, only seven are supported by level I (randomized trial) evidence (Table 3). Six recommendations hold clinical benefit and one is associated with harm. These level I recommendations do not include the use of patient isolation units, ventilation systems, construction or cleaning guidelines, skin or oral care, or the prevention of catheter-associated infections.

The first AI recommendation (strongly recommended with randomized trial support) involves the long-held infection control practice of hand washing. Guidelines for hand hygiene have been published, which specifically address issues of the indications for hand washing and antiseptics, the hand-washing technique, surgical hand antiseptics, the selection of hand-hygiene agents, and even health-care worker educational and motivational programs.⁴² However, a cross-sectional survey of university hospital physicians showed a dismal 57% average adherence.⁴³

CDC level II or III evidence

A recent systematic review of randomized controlled trials on the use of parachutes to prevent major trauma from fall identified a complete absence of such trials in the medical literature.⁴⁴ This review serves as a captious reminder that many effective interventions can be accepted on the basis of observational study alone.

The CDC/IDSA/ASBMT guidelines address an additional 12 recommendations graded AII (strongly recommended with well-designed nonrandomized trial support) (Table 4). While the utility of specific isolation and barrier precautions have not been studied, a level AIII recommen-

Table 3 Level I infection control recommendations, based on at least one properly randomized trial

AI recommendations

1. All persons should wash their hands before entering and after leaving the rooms of HSCT recipients and candidates undergoing conditioning therapy, or before any direct contact with patients regardless of whether they were soiled from the patient, environment, or objects.
2. All health-care workers with diseases transmissible by air, droplet, and direct contact (eg varicella zoster virus, infectious gastroenteritis, herpes simplex lesions of lips, or fingers and upper respiratory tract infections) should be restricted from patient contact and temporarily reassigned to other duties.
3. When a case of laboratory confirmed legionellosis is identified in a person who was in the in-patient HSCT center during all or part of the 2–10 days before illness onset, or if two or more cases of laboratory-confirmed Legionnaire's disease occur among patients who had visited an outpatient HSCT center, hospital personnel in consultation with the hospital infection control team should perform a thorough epidemiologic and environmental investigation or determine the likely environmental source(s) of *Legionella* species (eg showers, tap water faucets, cooling towers, and hot water tanks).
4. To control VRE exposure, strict adherence to standard infection control measures is necessary, as outlined in the text.
5. All HCWs who anticipate contact with a *Clostridium difficile*-infected patient or the patient's environment or possessions should put on gloves before entering the patient's room and before handling the patient's secretions and excretions.
6. HSCT candidates with a recently positive tuberculin skin test or a history of a positive skin test and no prior preventive therapy should be administered a chest radiograph and evaluated for active TB.

DI Recommendation

1. HSCT centers should not use large-volume room air humidifiers that create aerosols (eg by Venturi principle, ultrasound, or spinning disk) and, thus, are actually nebulizers.

dation (strongly recommended with expert opinion support) is given to follow other published guidelines for hospital isolation and the prevention of nosocomial infections such as pneumonia or surgical site infections.^{45–47} Additional infection control recommendations can be considered for epidemiologic factors such as the host, human-to-human interactions, fomites, air, food, water, soil, and construction and cleaning.

Host. The use of routine bacterial or fungal surveillance cultures among asymptomatic patients is discouraged (DII, generally not recommended with well-designed nonrandomized trial support). Recommendations are also aimed at reducing infections from host-derived organisms that reside on the skin, oral or gastrointestinal surfaces. CDC recommendations for skin care are limited to daily showers or baths using mild soap with attention to the hygiene and skin integrity of the perineal area (BIII, generally recommended with expert opinion support). AIII recommendations are listed for dental care before and after transplant. Oral hygiene is recommended by performing rinses four to six times daily using sterile water, normal saline, or sodium bicarbonate solutions (AIII).

Recent studies of preventing mucosal injury after transplantation further address the loss of mucosal integrity as a portal of entry for host-derived Gram-negative and

Table 4 Level AII infection control recommendations

1. HSCT centers should prevent birds from gaining access to hospital air-intake ducts.
2. Appropriate gloves should be used by all persons when handling potentially contaminated biological materials.
3. Work exclusion policies should be designed to encourage HCWs to report their illnesses or exposures.
4. Visitors who might have communicable infectious diseases should not be allowed in the HSCT center or have direct contact with HSCT recipients or candidates undergoing conditioning therapy.
5. If *Legionella* species are detected in the water supplying an HSCT center, the water supply should be decontaminated, and eradication of *Legionella* should be verified.
6. HSCT centers should follow basic infection control practices for control of MRSA infection and colonization, including hand washing between patients and use of barrier precautions, including wearing gloves whenever entering the MRSA-infected or MRSA-colonized patient's room.
7. HSCT personnel should institute prudent use of all antibiotics, particularly vancomycin, to prevent the emergence of staphylococci with reduced susceptibility to vancomycin.
8. Use of intravenous vancomycin is associated with the emergence of VRE; vancomycin and all other antibiotics, particularly antianaerobic agents, should be used judiciously.
9. All patients with *Clostridium difficile* disease should be placed under contact precautions for the duration of the illness.
10. When caring for an HSCT recipient or candidate undergoing conditioning therapy with upper or lower respiratory tract infection, HCWs and visitors should change gloves and wash hands in circumstances outlined in the text.
11. Visitors and HCWs with infectious conjunctivitis should be restricted from direct patient contact until the drainage resolves and the ophthalmology consultant concurs that the infection and inflammation have resolved to avoid possible transmission of adenovirus to HSCT recipients.
12. For patients with suspected or proven pulmonary or laryngeal TB, HSCT personnel should follow guidelines regarding the control of TB in health-care facilities.

anaerobic bacterial organisms. A phase III randomized trial of iseganan, a peptide with broad-spectrum microbicidal activity, did not lead to a reduction in mucositis or its clinical sequelae after autologous or allogeneic transplantation.⁴⁸ However, a randomized phase III trial of a recombinant human keratinocyte growth factor, palifermin, showed not only a decrease in the duration of advanced grade mucositis but also a decrease in the incidence of febrile neutropenia and a trend towards fewer episodes of blood-borne infections after autologous transplantation.⁴⁹ Trials of palifermin in the allogeneic setting have recently been completed, but it is not yet clear from preliminary reports that the severity of mucositis or the incidence of infections was significantly improved.⁵⁰

Human to human. While hand washing before entering and after leaving patient rooms and before and after direct patient contact carries an AI recommendation, the use of antimicrobial soap and water vs hygienic hand rubs is not mandated (AIII). Gloves should be changed between patients and prior to touching a clean area when they are soiled (AIII). Items that may serve as a nidus such as rings, artificial nails, or bandages should be avoided (BII, generally recommended with well-designed nonrandomized trial support). Visitors should be screened for potentially infectious conditions prior to patient contact (BII).

Fomites. Established guidelines exist for the sterilization or disinfection and maintenance of hospital equipment and devices (AIII). Owing to reports of *Aspergillus* isolated from their soil or surfaces, exposure to plants and flowers is discouraged (BIII). Recommendations are given for the use of disposable toys (BIII), and the regular cleaning or hot water washing of toys (BIII), the avoidance of water-retaining toys (DII), and the cleaning and disinfecting of occupational and physical therapy items (BIII).

Air. Air flow systems capable of least 12 exchanges per hour and point-of-use HEPA filters (0.3 μm) are recommended based largely on expert opinion (AIII). The use of LAF systems for patients with aplastic anemia remain controversial based on conflicting results from retrospective studies (CII, optional with well-designed nonrandomized trial support). The use of fit-tested N95 respirators near construction can be considered (CIII, optional with expert opinion support), but little protection is offered from standard surgical masks near construction (DIII, generally not recommended with expert opinion support).

Food and water. A low microbial diet is recommended for recipients of allogeneic stem cell transplantation until all immunosuppressive drugs are discontinued (BIII). Patients are discouraged from drinking well water from private wells or public wells in small communities where bacterial contamination is tested less than twice daily (DIII). Naturopathic medications that may contain molds are discouraged (DIII).

Soil, construction, and cleaning. During construction activities, several recommendations have been made including intensification of the BIII recommendations for *Aspergillus*-control (AIII), avoidance of construction areas for recipients, health-care workers, and visitors (AIII), cleaning newly constructed areas using BIII guidelines prior to their use (AIII), and avoiding carpets or vacuuming (AIII). Cleaning of transplant units should be performed at least once daily, with attention to exhaust vents, window sills, and all horizontal surfaces using cloths or mop heads premoistened with a registered hospital disinfectant (BIII).

These evidence-based infection control recommendations are aimed at the control of selected pathogens of fungal, bacterial, and viral origin based largely on the epidemiology of infections observed in the hospital setting. The burden and spectrum of exposure and associated risk of infection may differ in alternative settings, including the outpatient environment.

Costs of isolation

Finances

The financial costs of hospital protective environments are substantial and often difficult to calculate. Direct costs of patient care include isolation supplies (gloves, gowns, hand cleansers, etc), cleaning and maintaining isolation units, and materials and personnel for infection surveillance. In our institution's nine-room HEPA-filtered BMT unit, the

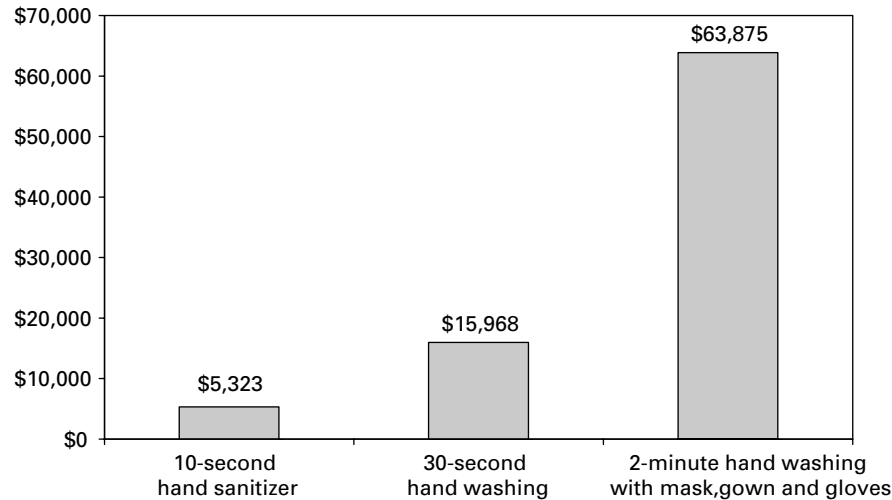


Figure 2 Theoretical annual costs of nursing time in preparation to enter patient rooms in a nine-bed BMT unit, based on assumptions of three nurses earning \$35 per hour and entering the room 25 times in a 12-h shift.

expenditures for ‘medical materials’ last year alone (including gloves, gowns, soaps, hand rubs, and masks as well as nursing items such as tubing and syringes) was \$390 940. Other costs include the need to engineer, construct, and maintain an adequate number of patient units with single rooms and unique air and water supplies, and the need to providing staffing for adequate nurse-to-patient ratios. Seemingly simple interventions such as a 10-s hand sanitization or a 1-min scrub with gown-and-glove can be costly when scaled annually for routine clinical practice (Figure 2).

Given high costs and the lack of formal proof of efficacy, institutions have begun to study alternatives to the use of sterile units with positive air pressure and HEPA filtration during the care of patients undergoing intensive chemotherapy. A study of 59 consecutive and nonselected patients undergoing autologous transplantation found comparable toxicities and treatment-related death rate when treated in conventional hospital rooms.⁵¹ In another retrospective analysis, one institution compared outcomes after first abandoning LAF units, and then changing from routine to targeted IVIG replacement among patients receiving allogeneic transplantation.⁵² There were fewer episodes of septicemia per hospital day but not per day with neutropenia in the combined LAF room and routine IVIG cohort. No other differences in outcome, including 100-day treatment-related mortality, were observed.

To further reduce the costs of in-patient care, several institutions are reporting outcomes after outpatient care for hematologic malignancies and autologous transplantation. Outpatient high-dose chemotherapy and autologous transplantation has been reported among patients with multiple myeloma with a trend towards fewer infections compared to historic controls (25 vs 35%).⁵³ A retrospective analysis of bacteremia incidence after 623 cycles of chemotherapy for acute myeloid leukemia suggested a decrease in Gram-negative bacteremia among outpatients, with no infection-related deaths in the outpatient group.⁵⁴

Patient interactions

Beyond the direct and indirect financial costs of treating patients within a protective environment, additional social costs should be considered. Emotional disturbance is common, with one series reporting DSM-IV psychiatric diagnoses among 41% after transplantation.⁵⁵ Physical isolation can lead to emotional isolation after transplantation.⁵⁶ Major themes in the experience of transplant patients include maintaining control in a seemingly out of control situation, intellectualizing the need for isolation, and staying in contact with family and staff.⁵⁷ When abandoning protective isolation for patients with prolonged neutropenia, patient satisfaction improved, costs were reduced, and no increases in infection risk were observed.⁵⁸

Outpatient care for allogeneic transplantation

Despite rigorous attempts to maintain a safe in-hospital microbiological environment for recipients of allogeneic stem cell transplantation, it should be recognized that hospitals are also sources for exposure to resistant opportunistic organisms. Outpatient care, whether in contiguous hospital-affiliated settings or the patient’s home, has been considered as a possible alternative to avoid many of these nosocomial risks.

In 1992, a report was published describing 50 consecutive patients receiving an allogeneic transplant from either a sibling or an unrelated donor who were treated in standard single hospital rooms.⁵⁹ In all, 20 patients who lived locally were allowed to go home a median of 8 days prior to engraftment. The reported incidence of infection (24%), acute GVHD (34%), and 100-day treatment-related mortality (6%) were favorable. An update was published in 2000, after 288 patients were treated in standard single hospital rooms with the ability to leave the room and the hospital, although remaining hospitalized until at least the

second week after transplant.⁶⁰ Avoidance of crowds was encouraged but no changes were made to the home environment, except to advise against renovations. Approximately one-quarter of 'in-patient' days were spent outside of the hospital including 80% during the neutropenic phase. In all, 57% of patients developed fever, with a positive culture or focal infection in 35%. Four patients (1%) died of *Aspergillus* infection. The overall 100-day treatment-related mortality was 13%.

In another series examining home care after allogeneic transplantation, 36 patients who chose home care were compared to 18 who chose hospital care and to 36 matched controls who were not offered home care.⁶¹ The home care cohort was allowed home after the graft had been infused, and were visited once or twice daily by a nurse experienced in stem cell transplantation. In a multivariate analysis, home care patients were discharged earlier, had fewer days of total parenteral nutrition, fewer episodes of grade II–IV acute GVHD, and lower transplant-related mortality. Costs were also lower, with a median cost from day 0 to day +76 of \$25 340 in the home care group vs \$36 437 for those choosing hospital care and \$33 620 for those not offered home care.

Recently, a review examined the six published studies, including four comparative but nonrandomized analyses, describing the experience of home care for patients with cytopenias after high-dose therapy and stem cell transplantation.⁶² The pooled statistics suggest that protective environments provided no benefit in decreasing mortality for the transplant patient.

Our algorithm

In our institution, patients undergoing allogeneic transplantation are managed in a BMT unit with HEPA filtration and controlled visitor entry with keypad door locks and face-to-face instructions of the ward-specific infection control guidelines (mandatory hand washing, no live plants, and screening visitors for respiratory illnesses). Those patients undergoing autologous transplantation or leukemic induction are routinely managed in standard single-patient hospital rooms and confined to those quarters during the period of absolute neutropenia. Health-care workers and family members with respiratory illness are restricted from patient contact. Although difficult to implement, a culture of avoiding contact with respiratory illness has been established, such that peers contribute to monitoring and enforcement. Strict hand-washing practices with alcohol-based hand rubs are maintained. One of us (JFL) sits on the institution's infection control committee where trends in infectious isolates are monitored. Owing to nearby construction, portable HEPA filters have been added to our outpatient clinic and adjacent hallways. Air quality monitoring has evolved from volumetric mold sampling to weekly dust monitoring in areas of the hospital that house transplant patients or that are undergoing construction, as well as the outpatient clinic. Dust monitoring is compared with outside ambient air to assess the adequacy of dust removal, and the hospital infection control committee makes

determinations on initiation of additional dust or mold testing based on these results. As opposed to a general 45-min hospital room discharge cleaning, our 90-min 'discharge BMT clean' procedure includes removing and disinfecting the showerhead and curtain, cleaning the shower drain, washing the walls and ceiling, and cleaning all exposed surfaces including blinds. With a recent outbreak of both colonization and infection with VRE, additional infection control measures have been added (as described above).

Conclusions

Infectious complications are a major source of morbidity and mortality after allogeneic stem cell transplantation. Only a few infection control and protective environment interventions have been proven useful in randomized trials. In an era of increasing financial pressures, specific interventions such as the use of special transplant unit rooms are being questioned. It is important to remember that expert experience and observational studies are sufficient proof for some infection control measures, ranging from formal infection control programs with interdisciplinary communication and surveillance for infection outbreaks to interventions as fundamental as strict and regular hand washing. Given the lack of proof for the necessity of isolated transplant units and encouraging preliminary studies of the safety of outpatient care, randomized trials would be the best mechanism to establish the safety of caring for recipients of allogeneic transplants outside of a protected in-hospital unit. However, this goal may be logistically difficult due to multiple factors of scale and finance influencing transplant practices (Figure 1). Continued monitoring for trends in infectious complications and communication with a multidisciplinary infection control committee are recommended in any setting.

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