Assessment of Bioaerosol Reduction Methods in Stem Cell Transplant Units at a University Hospital

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Abstract

Severely immunocompromised patients, such as those who have undergone stem cell transplantation, must be housed in a protective environment to reduce the risk of acquiring health care-associated fungal infections. This 11-month study was conducted at Duke University Hospital to evaluate the efficacy of the existing engineering controls (EC) for two such protective units: the pediatric stem cell transplant unit (PTU) and the adult stem cell transplant unit (ATU). In addition, a standard intensive care unit (ICU) was included as a “control” nursing unit. The engineering controls evaluated during the study included high efficiency particulate air (HEPA) filtration of supply air, supplemental HEPA refiltration, air change rates, directional airflow in patient rooms, positive pressure gradient (directional air flows) throughout the unit, and an interlocked airlock. Significant performance differences were identified when the bioaerosol sampling data from the three units were compared. These differences were related to the presence and performance of the evaluated EC. The concentration of airborne fungal spores in the PTU, which was equipped with all the evaluated EC performing at design specification, was less than both the ATU \( (p = 0.0007) \) and the ICU \( (p = 0.001) \). This suggests that utilizing an appropriate combination of engineering control measures is an effective means of controlling airborne bioburden. This study also provides evidence of the importance of supplemental HEPA refiltration and the establishment and maintenance of a strong positive pressure gradient \( (>2.5 \text{ Pascals}) \).

Introduction

That exposure to clinically significant fungal spores can lead to opportunistic infections in immunocompromised patients has been well documented. This is particularly true among hematopoietic stem cell transplant (HSCT) recipients (Baddley et al., 2001; Rainer et al., 2001; Sheretz et al., 1987; Wald et al., 2000; Weems et al., 1987). The term HSCT is preferable to “bone marrow transplant (BMT) recipients” since it more accurately describes the current use of the technology (Dykewicz, 2001). Donor cells for transplant today may come from a number of sources including peripheral blood, umbilical cord blood, and bone marrow.

Because fungal spores are ubiquitous in nature, prevention of exposure is the primary means of controlling opportunistic infections in immunosuppressed patients (Weems et al., 1987). Invasive fungal infections in this “high-risk” patient population are often caused by environmental molds, such as Aspergillus species (Baddley et al, 2001). Aspergil-
*lus fumigatus* and *A. flavus* are the most common causative agents of filamentous fungal infections in immunocompromised patients; however, *A. niger*, *A. terreus*, and *A. glaucus* have been reported as well (de Pauw & Meunier, 1999). Other filamentous fungi considered potentially pathogenic to this patient population include *Fusarium sp.*, *Mucor sp.*, *Paecilomyces sp.*, and *Penicillium sp.*, among others. It is important to note that yeasts cause the majority of fungal infections in this immune-suppressed population; however, because these fungi (i.e., *Candida sp.*) are normal inhabitants of human mucosal surfaces, the prevention of “exposure” is usually not possible (Marr & Bowden, 1999).

The housing of immune-suppressed patients in a protective environment to prevent exposure to airborne pathogens has decreased the incidence of invasive infections (Rainer et al., 2001). Establishing this protective environment involves utilization of various engineering controls such as high efficiency particulate air (HEPA) filtration, positive pressure rooms in relation to corridors, and a relatively high number of air changes per hour (i.e., ≥12). Several studies have shown that the utilization of HEPA filtration can reduce the risk of nosocomial infections such as those caused by *Aspergillus* organisms (Buckner et al., 1978; Cornet et al., 1999; Oren et al., 2001; Thomann et al., 1986). In fact, one 3-year study showed a 0% incidence of invasive pulmonary aspergillosis in patients housed in a HEPA-filtered ward, whereas 29% of those housed on a ward with standard hospital ventilation did contract aspergillosis (Oren et al., 2001).

Despite intensive infection control efforts, nosocomial infections still can and do occur. When this happens, it is important to assess the environment accurately to determine the source of the outbreak and check the performance of existing control measures, and if deemed necessary, to institute additional controls (Thio et al., 2000).

The generation of fungal spores primarily occurs outdoors where molds play an important role in the breakdown of organic debris, such as wood and leaves. Spores can be introduced into the hospital environment by both exogenous and endogenous sources. Airborne infiltration through doors, windows, and breeches in the building’s envelope are the most common routes of entry. Potential endogenous sources of fungal spores in the patient care environment are supplies, packaging, personnel, visitors, fresh fruit, dried or fresh flowers, shoes, and even soil of potted plants (Dykewicz, 2001). Although rare, mold growth can occur inside the hospital, especially if water intrusion is not adequately addressed. Additionally, the heating, ventilation, and air conditioning (HVAC) system of the hospital can become contaminated and can serve as a means of introducing these agents throughout the patient care environment (Schaal, 1991).

The objective of our research was to evaluate and compare the airborne bioburden of three different nursing units at Duke University Hospital. Because both the engineering and administrative controls in each area were quite different, it was hypothesized that the collected air samples would yield varying concentrations of fungal spores. The study was designed to evaluate the existing engineering control measures to further assess their relative effectiveness for reducing the airborne bioburden in a controlled environment. The conclusions from this study were intended to support recommendations for engineering controls for future construction or renovation of HSCT units. Additionally, the study was intended to address the requirements of the Joint Commission on the Accreditation of Healthcare Organizations’ Environment of Care; Utilities Management Standards, which require hospitals to develop a plan for reducing the potential for hospital-acquired illness (JCAHO, 2003).

**Setting**

Duke University Hospital, a 1,019-bed, full-service tertiary care center, is located in Durham, North Carolina. An integral part of the comprehensive patient care provided at Duke is its internationally recognized Stem Cell Transplantation Program. The program provides transplant as a treatment option for a variety of acquired and congenital disorders of adults and children including hematopoietic malignancies and solid tumors, inherited immune deficiency syndromes, bone marrow failure syndromes, and inherited metabolic diseases. By the beginning of 2002, more than 2,600 patients (adults...
and children) had received stem cell transplants at Duke.

**Patient Care Units of Study**

Duke University Hospital presently has two units that are dedicated to the care and treatment of HSCT recipients, the adult stem cell transplant unit (ATU) and the pediatric stem cell transplant unit (PTU). These units are located on the ninth and fifth floors of the hospital, respectively, each having 16 private patient rooms.

The ATU, which was last renovated in 1987, is served by the main air handling unit (dual duct) for the southwest tower of the hospital. Although essential engineering features that maintain a protective environment were designed into the ATU, it lacks some of the engineering components found on the PTU. The PTU, which was last renovated in 1996, has a dedicated air handling unit, several advanced engineering controls, and is continuously monitored by the Hospital's Building Automated System.

A third unit was included in this study to provide a comparison of the “protective environments” to standard hospital ventilation and engineering controls. This standard intensive care unit (ICU) is located on the third floor of the hospital, within the same building tower as the other two units involved in the study. The ICU, which is supported by the same air handling unit as the ATU, was also chosen because heart and lung transplant patients, whose immune systems are suppressed, are frequently housed on this unit. One study suggests that heart transplant recipients develop fungal infections in up to 21% of cases (Paya, 1993).

Table 1 shows the comparison of engineering control measures for each of the units of study.

**Methods**

**Sample Collection and Assessment of Engineering Controls**

Bioaerosol samples for this study were collected over an 11-month period, from October 30, 2000 to September 28, 2001. Two types of impaction sam-

<table>
<thead>
<tr>
<th>Control Measures</th>
<th>ICU</th>
<th>ATU</th>
<th>PTU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air handling unit (95% efficient filtration)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Air changes per hour in patient rooms (designed)</td>
<td>6</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Point-of-use supply HEPA-filtration in patient rooms</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Point-of-use supply HEPA-filtration throughout unit</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Recirculation HEPA-filtration in each patient room</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recirculation HEPA units in unit hall</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Pressure gradient established throughout unit</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Continuous electronic monitoring of HVAC system</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Airflow monitor at doorway of each patient room</td>
<td>-</td>
<td>-</td>
<td>* +</td>
</tr>
<tr>
<td>Enter unit through airlock</td>
<td>-</td>
<td>+</td>
<td>+ *</td>
</tr>
</tbody>
</table>

* Indicates that the control measure is available
* Static pressure indicator installed within the patient room
# Indicates an interlocked airlock
Assessment of Bioaerosol Reduction Methods in Stem Cell Transplant Units at a University Hospital

Samplers were used to assess viable airborne fungal spore concentrations: Thermo Andersen two-stage viable impactor samplers (Thermo Andersen, Inc., Atlanta, GA), and Mattson Garvin Slit-to-Agar (STA) samplers, model 200 (Barramundi Corporation, Homosassa Springs, FL). For the purposes of this study, we were interested only in the collection of viable spores because of their infectious risk.

STA samplers were used for patient room samples, where the majority of a patient’s stay is spent, and Thermo Andersen samplers were used throughout the other areas of the unit. Past experience has shown that airborne fungal concentrations in patient rooms are lower than other areas of “protective” units; therefore, samples collected over longer periods would allow us to better assess changes in airborne bioburden. We chose to use STA samplers which were equipped with 60-minute motors. The use of STA samplers in previous investigations at the hospital had allowed us to successfully demonstrate that certain activities (i.e., opening the stairwell door next to a protective environment) result in increased airborne fungal spore concentrations.

Sampling was conducted in and immediately outside 40 patient care rooms: 16 on both the PTU and the ATU, and 8 on the ICU. Samplers were positioned over the patient bed (patient breathing zone), at the room entry (just inside the patient room doorway), and in the unit hallway (just outside the patient room). The only variation to this was on the ICU, where patient room doors remained open at all times. Samples on this unit were taken at the patient bed and just outside the patient room. Samples were also collected at the entrance areas of each unit. On the ATU and the PTU, samples were collected just outside the entrance airlock (main hospital hall), inside the airlock, and in the unit hallway near the airlock entrance. Entrance samples for the ICU were collected just outside the unit entry door in the main hospital hallway and in the unit hallway near the main entrance. Finally, samples were also collected inside the southwest tower stairwell, which serves each of the study units.

Outdoor samples were collected for comparison with indoor samples. These samples were collected on the roof of the hospital near the ventilation air intakes of the air-handling unit supplying the patient care units. The intake of outside air represents the greatest exogenous contaminant challenge to the HVAC system.

All samplers were calibrated to sample 1 cubic foot of air per minute. A total of 15 cubic feet of air were collected per sample. Each sample was collected on malt extract agar (MEA) and allowed to incubate for 96 hours at room temperature. MEA is a preferred medium with a long history of use in conducting indoor fungal studies. Colony forming units (cfu) were noted for each plate, allowing the calculation of cfu per volume of air, or cfu/m³. Fungi were identified to a genus level using standard procedures based on macroscopic and microscopic morphology. Wet mounts, stained with cotton-blue, were prepared and then viewed under 400X magnification. Those colonies identified as Aspergillus sp. were sent to a certified mycologist for speciation.

During the study several parameters were noted for each area where bioaerosol samples were collected. These included smoke trail tests to demonstrate direction of airflow at doorways, pressure differentials taken across doorways, airflows to allow air change rate calculations, time of day, temperature, humidity, and whether the room was occupied during sampling. Air current tubes (Draeger Safety, Inc., Pittsburgh, PA) were used to perform smoke trail tests on all patient care doors, hallway entries, and unit entrances to check for the desired direction of airflow. Pressure change readings were collected by utilizing a TSI Velocicalc Plus, model 8386A (TSI, Inc., St. Paul, MN). These readings were used to compare the quantitative check versus smoke trail testing (qualitative). Air changes and refiltrations per hour were calculated by using data collected either by an Alnor Electronic Balometer, Model 150 (Alnor Instrument Company, Skokie, IL) or provided by the hospital’s building automated system (BAS). We use the term “refiltration” to describe the recirculation of room air through an independent HEPA unit. A TSI Velocicalc Plus was also used to document all temperature and humidity readings.

Data Analysis

Data were analyzed using SAS/STAT® software (SAS Institute, Cary, NC). P-values < .05 were con-
sidered significant. Mean spore concentrations at different positions were first tested for statistical differences using Satterthwaite t-tests. Patient room data (collected at the bedside, at the room entry, or in the unit hall directly outside each patient care room) were then fit using a Poisson model for repeated measures. This model required estimation using Generalized Estimating Equations (GEE) which is a method of accounting for the fact that multiple samples were collected in or at each room (Zeger & Liang, 1986). Data collected at other unit locations were analyzed using simple arithmetic methods.

**Results**

**Respirable Fungal Bioburden**

Nine genera of fungi were isolated from the patient unit sample plates: *Alternaria* sp., *Aspergillus* sp., *Cladosporium* sp., *Epicoccum* sp., *Fusarium* sp., *Moniliella* sp., *Paecilomyces* sp., *Penicillium* sp., and *Rhizopus* sp. Six species of *Aspergillus* were identified, which included *A. fumigatus*, *A. flavus*, *A. nidulellus*, *A. niger*, *A. ochraceus*, and *A. versicolor*.

As noted in the introduction, fungal spores of the genus *Aspergillus* are of greatest concern when found in the air of an HSCT unit. Table 2 shows the concentrations of *Aspergillus* sp. collected inside each unit and within the stairwell which served each of the units of study. No *Aspergillus* sp. were isolated from samples collected inside patient care rooms (bedside and room entry sample locations) on either stem cell transplant unit, whereas 7 of 51 (13.7%) bedside samples collected on the ICU yielded these “high-risk” fungi. Fifteen of 44 (34%) unit hallway samples collected on the ICU, 7 of 61 (11%) on the ATU, and 2 of 47 (4.3%) on the PTU yielded *Aspergillus* sp. One of 18 (5.6%) samples collected in the ATU airlock and 1 of 31 (3.2%) of those collected in the PTU airlock yielded *Aspergillus* sp. Samples collected in the stairwell yielded the greatest concentration of *Aspergillus* sp. Seventeen of the 30 (57%) samples were positive for this fungus.

Shown in Table 3 are the mean airborne fungal spore concentrations for each of the three patient room sampling locations, separated by unit. Samples collected in patient care rooms yielded significantly lower counts than those outside the rooms. When

<table>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Concentrations of <em>Aspergillus</em> sp. and Total Viable Spores</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Positive for <em>Aspergillus</em></th>
<th>Percent Positive</th>
<th><em>Aspergillus</em> Conc. (cfu/m³)</th>
<th>SD</th>
<th>Total Viable Spore Conc. (cfu/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unit Hall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ICU</td>
<td>44</td>
<td>15</td>
<td>34.0</td>
<td>0.8</td>
<td>1.15</td>
<td>14.42</td>
</tr>
<tr>
<td>ATU</td>
<td>61</td>
<td>7</td>
<td>11.0</td>
<td>0.3</td>
<td>0.92</td>
<td>9.67</td>
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<tr>
<td>PTU</td>
<td>47</td>
<td>2</td>
<td>4.3</td>
<td>0.1</td>
<td>0.49</td>
<td>2.94</td>
</tr>
<tr>
<td><strong>Room Entry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATU</td>
<td>59</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.00</td>
<td>4.34</td>
</tr>
<tr>
<td>PTU</td>
<td>84</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.00</td>
<td>1.59</td>
</tr>
<tr>
<td><strong>Bedside</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>51</td>
<td>7</td>
<td>13.7</td>
<td>0.3</td>
<td>0.83</td>
<td>6.41</td>
</tr>
<tr>
<td>ATU</td>
<td>68</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.00</td>
<td>2.61</td>
</tr>
<tr>
<td>PTU</td>
<td>84</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.00</td>
<td>1.31</td>
</tr>
<tr>
<td><strong>Airlock</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATU</td>
<td>18</td>
<td>1</td>
<td>5.6</td>
<td>0.2</td>
<td>0.82</td>
<td>16.5</td>
</tr>
<tr>
<td>PTU</td>
<td>31</td>
<td>1</td>
<td>3.2</td>
<td>0.1</td>
<td>0.43</td>
<td>19.5</td>
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<tr>
<td><strong>Stairwell</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*</td>
<td>30</td>
<td>17</td>
<td>57.0</td>
<td>2.8</td>
<td>3.2</td>
<td>60.8</td>
</tr>
</tbody>
</table>

* Serves each of the three nursing units
comparing the mean airborne fungal spore concentrations for each sampling location for each unit (i.e., Bedside to Room Entry, Bedside to Outside Patient Room, and Room Entry to Outside Patient Room), all but one were found to be statistically different. The one exception was the comparison of the bedside and room entry concentrations on the PTU (p = 0.49).

Figure 1 compares data collected in rooms that were occupied versus those that were not. The statistical model, while considering combined data from each unit of study, indicated that room occupancy was not a significant predictor of airborne spore concentrations. However, a z-test performed on the PTU room data only indicated that spore concentrations in occupied rooms were significantly higher than in those that were not occupied (p = 0.49).

Table 3
Comparisons of Mean Spore Concentrations for Patient Room Sample Locations

<table>
<thead>
<tr>
<th></th>
<th>Mean (cfu/m³)</th>
<th>SD</th>
<th>Satterthwaite t-value (df)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICU</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedside vs.</td>
<td>6.41</td>
<td>5.29</td>
<td>3.86 (55.4)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Outside Room</td>
<td>14.42</td>
<td>12.88</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATU</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedside vs.</td>
<td>2.61</td>
<td>3.57</td>
<td>2.50 (115)</td>
<td>0.014</td>
</tr>
<tr>
<td>Room Entry</td>
<td>4.34</td>
<td>4.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedside vs.</td>
<td>2.61</td>
<td>3.57</td>
<td>4.86 (71.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Outside Room</td>
<td>9.67</td>
<td>10.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rm. Entry vs.</td>
<td>4.34</td>
<td>4.15</td>
<td>-3.58 (77.7)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Outside Room</td>
<td>9.67</td>
<td>10.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PTU</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedside vs.</td>
<td>1.31</td>
<td>2.47</td>
<td>0.7 (177)</td>
<td>0.49</td>
</tr>
<tr>
<td>Room Entry</td>
<td>1.59</td>
<td>2.86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedside vs.</td>
<td>1.31</td>
<td>2.47</td>
<td>2.88 (76.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Outside Room</td>
<td>2.94</td>
<td>3.59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rm. Entry vs.</td>
<td>1.59</td>
<td>2.86</td>
<td>-2.31 (85.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Outside Room</td>
<td>2.94</td>
<td>3.59</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean outdoor airborne spore concentration detected during the study was 619 cfu/m³ (Range: 155-1349 cfu/m³, SD = 306). Outdoor concentrations were added to the model as a possible explanatory variable, but were not found to be significant.

There were 30 samples collected inside the stairwell, which intersects each of the units of interest. The mean spore concentration was 60.8 cfu/m³ (Range: 2.4-196.3 cfu/m³, SD = 41). Of these samples, 17 of 30 (57%) were positive for Aspergillus sp. The mean concentration of Aspergillus sp. in all 30 samples was 2.8 cfu/m³ (Table 2).

The statistical model was used to test the hypothesis that the PTU samples would yield lower airborne fungal spore concentrations than the ICU and the ATU, and that the ATU samples would yield lower spore concentrations than the ICU. The data showed that the airborne fungal concentrations on the PTU were significantly lower than both the ICU (p = 0.0010) and the ATU (p = 0.0007). The ATU was found to yield significantly lower counts than the ICU (p = 0.0334). One interesting exception was the comparison of data collected outside patient rooms on the ICU and the ATU. There was no significant difference in the two, although the ATU is considered a protective environment.

As shown in Figure 2, only the PTU entrance samples yielded a lower mean airborne spore concentration just inside the nursing unit when compared
**Figure 1**
Mean spore concentrations in occupied vs. unoccupied rooms (includes bedside and room entry data for each unit)

**Figure 2**
Viable spore concentrations at unit entrances
to the main hospital hallway. The average concentration collected in the main hospital hallway outside the PTU was 17.9 cfu/m$^3$ and 2.4 cfu/m$^3$ just inside the unit near the airlock. The average airborne spore concentration just inside each of the other two study units (ICU and ATU) was actually higher than that in the main hospital hallway.

**Quantification of Engineering Controls**

Figure 3 details pressure differentials across doorways throughout the HSCT units. Each of the doorways tested on the PTU exceeded the CDC’s recommendation for maintenance of pressures at >2.5 Pascals. The pressure changes monitored on the ATU were less than 2.5 Pascals, with the one exception being that across the stairwell door.

Air change and filtration rates, for individual rooms, were calculated for both HSCT units. Data collected on the PTU yielded average air change rates of 12.7 per hour (Range: 8.9 - 14.4), and average refiltration rates of 11.6 per hour. The average air changes per hour on the ATU were calculated to be 9.9 (Range: 8.7 - 11.7) and average refiltration rates were 23.6. The average air changes per hour for the ICU were calculated to be 5.8 (Range: 5.2 - 6.4).

Maintenance records for each HEPA filter documented that performance testing had been conducted on each unit within the past year. Such testing included a scan of the filter for leaks and airflow checks. Temperature and humidity readings were always within acceptable ranges. As was expected, these parameters were found to be nonsignificant predictors of airborne spore concentrations when added to our statistical model.
Discussion

Benefits of Specialized Ventilation Controls

The results of this study document the efficacies of specialized ventilation controls at reducing the airborne bioburden in patient care environments. Airborne bioburden can be managed through the interaction of five primary controls: room air change rates of >12 per hour, assuming high-quality filtration of supply-air as prescribed by AIA guidelines (2001); strong pressure differentials between rooms and hallways, and between unit hallways and outer corridors (>2.5 Pascals); refiltration throughout the protective isolation unit for removing endogenous and exogenous sources of fungal spores; point-of-use HEPA filtration; and directional airflows so that air enters the room near the patient’s breathing zone and moves to the opposite side of the room, preferably towards the room entrance. The PTU was the only one of the three patient units included in this study that combined the use of all these engineering control measures, and it had significantly less airborne bioburden than the other two study units.

The pressure differential data (Figure 3) show that pressure change gradients on the PTU are significantly higher than those on the ATU, exceeding 2.5 Pascals at all locations. This finding, coupled with overall mean spore concentrations (Table 3), strongly supports the CDC recommendation that pressure differentials should be maintained at >2.5 Pascals (CDC, 2003). Although all smoke trail tests performed on the PTU and the ATU showed air movement in the desired direction, it was observed that some flows were stronger than others. It was demonstrated during the study that weak pressure gradients (slow, waffling smoke trails), such as those found on the ATU (Figure 3), were easily disrupted or even reversed by cross drafts created by activities such as hallway traffic or opening and closing doors. It should be noted that the use of smoke tubes to test directional airflow is not a substitute for quantitative testing.

Although our study did not prove statistically that room occupancy could be used as a predictor of airborne spore concentration, we believe that it most likely influences the airborne bioburden. Our conclusion is supported by the data collected in patient care rooms on the PTU (Figure 1), where samples collected in occupied rooms yielded significantly higher airborne concentrations than in the unoccupied spaces (p < 0.0001). In addition to family and friends visiting the patient, daily physician and nursing rounds are conducted through each unit. As a teaching hospital, the number of individuals participating in rounds is usually no less than three and many times significantly more. During the study, observations appeared to indicate that there was a correlation between human activity and the number of airborne fungal spores. Unfortunately, it was not possible to control the movement of traffic throughout the sampling areas; therefore, no statistical correlation was attempted. Additionally, there are other continuous contributors to traffic on the units, including dietary services, maintenance staff, and housekeepers. A future study designed to test the significance of this observation would be useful.

The mean spore concentration data in Table 3 show the comparisons of patient room samples within each unit. It was demonstrated that the airborne bioburden in patient rooms is significantly less than that in the unit hallways. The bedside (patient breathing zone) data for each unit indicate that air in this location is less contaminated with fungal spores than any other area on the unit. This is important since the majority of a patient’s hospital stay is spent lying in the bed. Optimally, the airborne bioburden at the bedside would be less than the room entry, and the room entry less than the unit hallway. This was the case on each unit with one exception, the bedside versus room entry on the PTU (p = 0.49). This exception is considered insignificant and is attributed to the overall low airborne concentrations at both sampling positions.

Unit Entrances, Stairwell, and the Importance of Pressure Gradients

Of the three unit entrances evaluated, only the airlock on the PTU effectively separated the unit from airborne bioburden in the main hospital hallway (Figure 2). Mean airborne fungal spore concentrations in the main hallway outside the PTU were 17.9 cfu/m³, as compared to 2.4 cfu/m³ just inside the unit. Conversely, concentrations outside the other two units of study were actually less than those
inside the unit. These findings suggest that inter-
locked airlocks and pressure differentials >2.5 Pas-
cals play an important role in effectively protecting
the unit from infiltra-
tion of airborne contaminants.

No direct correlation was found between out-
door or stairwell samples and the samples collected
on the PTU. This may be attributed to the advanced
engineering controls (Table 1) and the locked stair-
well door. There may have been some infiltration of
contaminants into both the ATU and the ICU from
the stairwell, although not found statistically signifi-
cant. During the time of the study, the stairway en-
try, leading to each of these two units, was not
locked and was frequently used by staff, thus defeat-
ing the protective pressure gradient. It was demon-
strated by smoke trail tests that “stairwell air” was
able to infiltrate these two units, when the respective
stairwell door was opened.

Samples collected in the stairwell demonstrated
that an elevated bioburden existed in the immediate
vicinity of the patient care area, separated only by a
single door. Although the samples collected in the
patient care areas did not prove statistically that this
contributes to the bioburden on each unit, it is logi-
cal to surmise that allowing access to units through
stairwells increases the risk of infiltration of fungal
spores. Furthermore, finding 17 of 30 (57%) samples
in the stairwell positive for Aspergillus sp. is signifi-
cant in itself considering the proximity of this “high-
risk” contaminant to the protective environment.

This study demonstrates the potential impor-
tance and effectiveness of the establishment and
maintenance of pressure gradients. The protection
of the nursing units from the stairwell air is one ex-
ample of this. The pressure differential across the
stairwell door for the PTU and the ATU averaged
about 5.0 Pascals, or 0.02 inches water gauge (Figure
3). This is twice the minimal recommended pressure
change (CDC, 2003). When stairwell doors are kept
closed, as was the case on the PTU, this pressure
gradient adequately protects the unit. When the
door is frequently used, as was the case on the ATU
and the ICU, this protective factor seems to be easily
violated.

Another example of the importance of pressure
gradients is the mean spore concentrations at the
bedside on the ATU. Although the unit hallway con-
centrations were elevated, the bedside concentra-
tions were relatively low, with no viable Aspergillus sp.
collected.

**Recirculating HEPA Filtration**

It is worth noting the difference in unit hallway
mean spore concentrations on the PTU (2.94
cfu/m³) and the ATU (9.67 cfu/m³). These data sug-
gest that the utilization of recirculating HEPA filter
units is an efficient means of removing airborne con-
taminants released into the patient care area from
endogenous sources, even when not in an environ-
ment supported by HEPA-filtered supply air. This
suggestion is further supported by Thomann et al.
(1986). The patient room data from the ATU
yielded relatively low spore concentrations and no
Aspergillus sp., while the unit hallway samples yielded
spore concentrations comparable to those collected
in the unit hallway of the ICU, the “less-protective”
unit of study. Furthermore, 11% of the 61 samples
collected in the unit hallway were positive for Asper-
gillus sp., as compared to none in the patient care
rooms. On the PTU, refiltration HEPA units were
located throughout the unit, including the hallway,
whereas such filtration units were available only in
the patient rooms on the ATU. The utilization of
recirculating HEPA units is further supported by the
data from samples collected just inside each nursing
unit (Figure 2). The area of the nursing unit nearest
the airlock likely receives a significant insult of en-
dogenous contaminants from the continuous traffic
in and out of the unit. The airborne concentration
at this location on the PTU was considerably less
than the other nursing units. A future study to fur-
ther assess the efficacy of utilizing recirculating
HEPA units, as a supplement to other engineering
control measures, would be useful.

**Aspergillus sp.**

As documented in the literature, air must be
nearly free from Aspergillus sp. spores in order to
minimize the risk of infections in this severely immu-
nosuppressed population (Rhame et al., 1985;
Sheretz et al., 1987). Rhame (1991) suggested that
providing protective environments with concentra-
tions of <0.1 cfu/m³ of Aspergillus sp. is required to
minimize the risk of opportunistic infections in
high-risk patients. However, in another publication, Rhame (1984) concluded that to prevent nosocomial aspergillosis in a high-risk patient population, “Hospital air should be free of Aspergillus spores.” Considering this statement, the data presented in Table 2 may be particularly important with regard to the unit hallway data for the ATU. An average airborne concentration of Aspergillus sp. of 0.3 cfu/m$^3$ may pose an increased risk to ambulatory HSCT patients walking the hallway of this unit. Seven of the 61 (11%) samples collected in the hallway were positive for this “high-risk” fungi.

Another potentially significant finding is the airborne concentrations of Aspergillus sp. from samples collected at the bedside (0.3 cfu/m$^3$) and unit hall (0.8 cfu/m$^3$) on the ICU.

**Future Renovations**

The data from this study supported recommendations for a planned renovation of the ATU. The data suggest that a significantly lower bioburden can be achieved if the following engineering controls are provided:

1. A main entrance airlock configured similarly to that of the PTU in that simultaneous door openings are not permitted.
2. Strategically placed HEPA refiltration units to “clean-up” contamination introduced by endogenous sources.
3. Patient rooms that have directed airflow, from patient breathing zone, towards the room entrance.
4. Rooms with positive pressure to unit hallway, the unit hallway positive to airlock, and airlock positive to the main hospital hallway, (>2.5 Pascals pressure differential across each doorway).

In addition, the following other controls seem to be supported by past experiences:

1. Point-of-use supply air filters (99.97% efficient) should be installed.
2. The HVAC system should provide ≥ 12 air changes per hour.
3. The HVAC system should be continuously monitored by an electronic system with automatic alarms for contacting maintenance staff in case of failure.
4. Airflow monitoring devices should be installed at each room entry to allow nursing staff to easily check (qualitatively) for appropriate room pressure.
5. No carpet should be allowed on the unit.
6. Horizontal surfaces should be reduced as much as possible to minimize dust collection.

Each of the listed recommendations was made as a result of this and past studies and by personal experiences of the “design team,” which included members of Duke’s Occupational and Environmental Safety Office, Hospital Infection Control and Epidemiology, and Medical Center Engineering and Operations.

**References**


