

# Levels of Total Fungus and *Aspergillus* on a Pediatric Hematopoietic Stem Cell Transplant Unit

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*The purpose of this descriptive study was to determine the levels of total fungus (TF) and *Aspergillus* in a pediatric hematopoietic stem cell transplant (HSCT) unit. One hundred twenty air samples and 120 floor samples were collected from the same locations in 10 patient rooms and bathrooms for 4 consecutive days. The count in colony-forming units of TF and *Aspergillus* from each of the samples was measured by the institution's mycology laboratory. Means, standard deviations, minimum values, and maximum values were determined for levels of TF and *Aspergillus* from different locations and on different days in the air and on the floor. Determination of a mean value of TF and *Aspergillus* for each room allowed for analysis of mean values of TF and *Aspergillus* for sample category, room side, room type, and room status. After visual examination of the mean values for the air samples collected, it was determined that the TF and *Aspergillus* in the air were less than the institution's acceptable air baseline standard. *t* tests and analysis of variance were used to verify the findings.*

**Key words:** fungus, *Aspergillus*, HSCT, pediatrics

Some of the most vulnerable and immunocompromised patients are those that undergo hematopoietic stem cell transplantation (HSCT). Many complications are due to opportunistic infections that affect these patients

when they are most vulnerable. Despite aggressive treatment measures, invasive aspergillosis (IA) is difficult to eradicate and oftentimes fatal. Even when treatment is deemed successful, IA has the propensity to reactivate, especially in the setting of prolonged immunosuppression (Kontoyiannis & Bodey, 2002). Some believe there is a dormant, quiescent *Aspergillus* that is activated to a pathogenic status in the setting of immunosuppression (Paterson & Singh, 1999; Richardson et al., 2000; Warnock, 1991). Little is known of the time lapse between fungal contamination and the occurrence of IA in neutropenic patients (Alberti et al., 2001).

Treatment of fungal infection is suboptimal, and therefore prevention is of utmost importance. The most important prophylactic measure against IA involves decreasing the quantity and variety of fungi that enter into contact with patients. Prevention must be aimed at elimination of fungi from the environment.

To ascertain if preventive measures are effective, surveillance measures including periodic, random sample collection for total fungus and *Aspergillus* must be done. Measurement of fungal presence in the hospital environment evaluates the efficiency of the preventive measures adopted as institutional environmental safeguards.

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## Purpose

The purpose of this study was to obtain air and floor samples to detect the environmental presence and level of total fungus and *Aspergillus* on a pediatric hematopoietic stem cell transplant unit. Fungal infection has been documented as a resilient, opportunistic infection in immunocompromised patients (Centers for Disease Control and Prevention, 2000). *Aspergillus* is a major cause of morbidity and death in patients with hematological malignancies or HSCT (Kullberg & Lashof, 2002; Martino & Subira, 2002).

The environment has been implicated in playing a pivotal role in the epidemiology of IA. Preventive measures are based on the elimination of *Aspergillus* from the environment, thereby decreasing exposure to this pathogen in the hospital setting. According to Martino and Subira (2002), the most important currently available prophylactic measures against invasive fungal infection involve reducing the quantity and variety of fungi that enter into contact with patients during their most vulnerable periods. According to the Centers for Disease Control and Prevention (2000), prevention of these fungal infections is preferable to the insufficient treatment that is presently available. Therefore, surveillance of the hospital environment should include periodic, random sample collections for the determination of total fungus and *Aspergillus* levels on the HSCT unit.

## Research Questions

*Research Question 1:* What are the levels of total fungus and *Aspergillus* of air and floor samples obtained from patient rooms and bathrooms on a pediatric HSCT?

*Research Question 2:* Are the levels of total fungus and *Aspergillus* obtained from the air samples less than or equal to the accepted institutional air baseline standard?

*Research Question 3:* Are there differences in total fungus and *Aspergillus* levels among sample category (air or floor), location (patient room and bathroom; see Tables 1 and 2 for specific locations), day of week, room side (west, north, east), room status (occupied or unoccupied), and room type (isolation or non-isolation)?

## Background and Significance

The suspicion of infection with *Aspergillus* invokes a dismal and pessimistic outcome for those patients who are immunocompromised and vulnerable to life-threatening infections. Adult studies underscore the grim findings for the patient with fungal infection. According to Hajjeh and Warnock (2001), invasive aspergillosis affects 28% of patients who have undergone allogeneic stem cell transplantation. Perfect et al. (2001) found that management of IA remains incomplete: Only 38% of allogeneic transplant patients are alive 3 months after the diagnosis of IA. Furthermore, only 40% of patients who received amphotericin-B for treatment of IA were alive at 3 months. The overall case fatality rate (CFR) reported by Lin, Schranz, and Teutsch (2001) was 58%. The CFR was highest for bone marrow transplant recipients (86.7%) and for patients with central nervous system or disseminated aspergillosis (88.1%). The crude mortality rate as reported by Kontoyannis and Bodey (2002) remains high. Ten percent of all deaths in patients who undergo allogeneic transplant are attributed to IA, which has a mortality rate of 90% in this setting. Failure of antifungal therapy was seen in 85% of the patients who had IA, the majority of whom died within 6 weeks. Furthermore, according to Dasbach (2000), the financial burden of IA-associated hospitalization is enormous: U.S. data from 1996 estimated the total cost of IA treatment to be \$633 million, with an average cost per case of \$65,000.

Institutional data from 1997 to 2002 were reviewed to determine the most current experiences with *Aspergillus* infection. There was a hospital-wide total of 57 aspergillosis cases documented. Of these 57 patients, 32 (56%) involved allogeneic transplant recipients. Of all the *Aspergillus* cases reported, 23% were considered nosocomial and 77% were considered community acquired. From 1997 to 2001, there were 51 nosocomial infections attributed to fungi. Infections reported included *Candida tropicalis*, *Aspergillus fumigatus*, *Malessezia furfur*, and *Cunninghamella* species.

## The HSCT Patient

Hematopoietic stem cell transplant recipients are at greatest risk for the acquisition of fungal infection and invasive aspergillosis. HSCT treats diseases caused by hematologic malignancies, blood dyscrasias, solid

**Table 1. Total Fungus and *Aspergillus* at Different Locations in the Air**

Fungus Type	Location	<i>M</i>	<i>SD</i>	Minimum	Maximum	<i>p</i> Value
Total fungus	1	2.599	1.999	0.835	8.375	.0335
	2	2.178	1.601	0.5	5.875	
	3	4.325	2.158	1.625	9.000	
<i>Aspergillus</i>	1	0.011	0.038	0	0.125	.0824
	2	0.034	0.058	0	0.125	
	3	0.106	0.157	0	0.500	

NOTE: Location 1 = first complete floor tile, facing room; location 2 = left side of bed, midline, and facing the head; location 3 = bathroom midline.

**Table 2. Total Fungus and *Aspergillus* at Different Locations on the Floor**

Fungus Type	Location	<i>M</i>	<i>SD</i>	Minimum	Maximum	<i>p</i> Value
Total fungus	1	4.553	3.945	1	12.5	.0197
	2	4.765	4.049	1	14.0	
	3	1.045	0.384	0.5	1.5	
<i>Aspergillus</i>	1	0	0	0	0	.1574
	2	0.295	0.669	0	2.25	
	3	0.023	0.075	0	0.25	

NOTE: Location 1 = threshold, first complete floor tile; location 2 = below left corner of window seal; location 3 = bathroom, left of commode.

tumors, bone diseases, immunologic disorders, and congenital enzyme deficiencies (Centers for Disease Control and Prevention, 2000). Oftentimes, due to the very nature of the underlying disease requiring treatment with stem cell transplantation, the patient is already experiencing immune dysfunction. Complicating and exacerbating this process is the ablative conditioning regimens given prior to transplantation.

The risk of acquiring a life-threatening invasive fungal infection is related to the intensity of the cytotoxic regimen and the duration of the resultant neutropenia (Bow et al., 2002; Fridkin & Jarvis, 1996; Kontoyianis & Bodey, 2002; Marr, Carter, Crippa, Wald, & Corey, 2002; Martino & Subira, 2002; Warnock, 1991). These risk factors are reflected in a bimodal time distribution for the development of IA (Marr et al., 2002; Martino & Subira, 2002; Paterson & Singh, 1999). Approximately 40% of patients develop IA around 2 weeks after transplant while neutropenic, before engraftment. A second peak of infection occurs approximately 100 days posttransplant while receiving graft versus host disease prophylaxis and treatment. Auner, Sill, Mula-becirovic, Linkesch, and Krause (2002) reported that patients with total body irradiation (TBI) as part of their conditioning regimen had more infections due to longer

duration of neutropenia in the early posttransplant period than patients without TBI.

The average duration of neutropenia for autologous and allogeneic transplants in this pediatric HSCT unit is 7 days and 22 days, respectively. The duration of this neutropenia determines length of stay. This extended time frame increases the exposure of the pediatric HSCT recipient to the hospital environment.

These conditioning regimens destroy normal hematopoiesis for neutrophils, monocytes, and macrophages. Damage to mucosal progenitor cells causes a temporary loss of mucosal barrier integrity. Virtually all HSCT recipients rapidly lose all T and B lymphocytes after conditioning. Even with successful engraftment, the recipient will not regain normal immunologic function for 6 to 12 months.

The use of immunosuppressive agents such as cyclosporine and mycophenolate to prevent and treat graft versus host disease inhibits T-cell and B-cell growth and function. Corticosteroids decrease the number of circulating T cells and B cells and has harmful effects on macrophage and neutrophil function that suppress the inflammatory response (Baddley, Stroud, Salzman, & Pappas, 2001; Kullberg & Lashof, 2002; Martino & Subira, 2002; Warnock, 1991). Suppression

of cell-mediated and humoral responses contributes to the predisposition of pediatric HSCT recipients to fungal infections (Marr et al., 2002; Martino & Subira, 2002; Warnock, 1991).

General risk factors for fungal infection common to HSCT recipients are the use of central venous catheters, total parenteral nutrition, broad spectrum antibiotics, and prolonged hospitalization (Ellis, 2001; Fridkin & Jarvis, 1996; Soubani & Chandrasekar, 2002). The use of these supportive measures is required throughout the transplantation process until engraftment and discharge occurs. Return admissions to the hospital are common after the initial discharge until the patient's immune status becomes more stable.

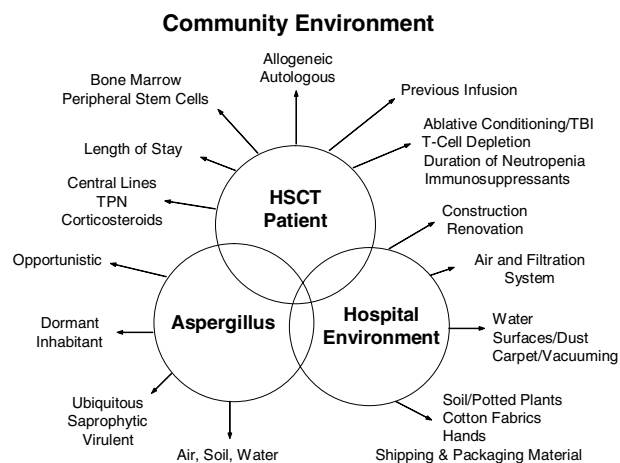
In conclusion, patient immune characteristics should be recognized so that relationships to predisposition and acquisition of fungal infection can be made. The manipulation of the immune system and the supportive treatment required predisposes the pediatric HSCT patient to life-threatening opportunistic infections. Until the hematopoietic system recovers, the patient is very vulnerable to invasive disease after exposure to pathogenic fungi in the environment.

### Conceptual Framework

The interplay of the HSCT patient, the organism, and the hospital environment is depicted within the wider community environment. Characteristics of each of these entities contribute to the predisposition of HSCT patients to invasive aspergillosis. The traits and the evasive abilities of the organism, the risk factors inherent to HSCT treatment, and the potential sources of *Aspergillus* in the hospital affect the potential for infection (see Figure 1).

Incomplete knowledge of the etiology of *Aspergillus* infection is apparent. It is difficult to determine if an *Aspergillus* infection is nosocomial or community acquired. Prevention of community-acquired infection poses even greater challenges. The incubation period of *Aspergillus* is uncertain. Some suggest that there is a dormant colonization with *Aspergillus* that becomes invasive and pathogenic in the vulnerable host.

Hospital environmental measures are present to decrease the likelihood of *Aspergillus* transmission to the immunocompromised HSCT patient (see Figure 2). Pharmacological and supportive measures are used to provide prophylaxis and treatment against fungal



**Figure 1. The Interplay of the Hematopoietic Stem Cell Transplant (HSCT) Patient, the Organism, and the Hospital Within the Community Environment**

NOTE: TBI = total body irradiation. TPN = total parenteral nutrition

infection and to decrease the period of neutropenia after transplant.

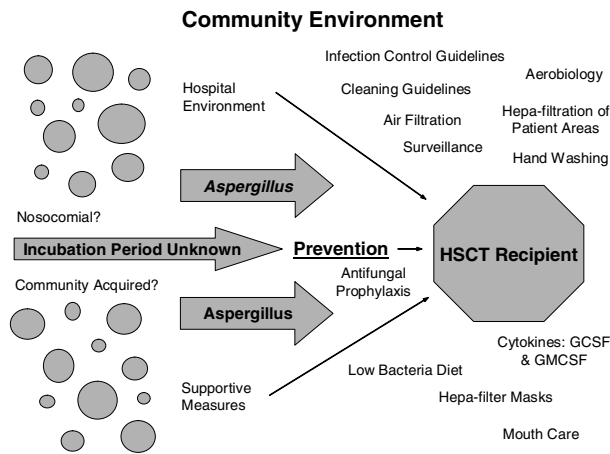
Despite these environmental precautions, supportive measures, and antifungal agents, *Aspergillus* continues to infect patients and remains a difficult disease to detect, diagnose, and treat. Because treatment of disease with existing antifungal agents is suboptimal, it is imperative that efforts be aimed at prevention. Until diagnostic methods and pharmacological agents are more effective, prevention must be aimed at elimination of fungi from the environment.

### Design

A descriptive study design was used to assess and provide an accurate portrayal of the levels of total fungus and *Aspergillus* of 120 air samples and 120 floor samples collected from a pediatric HSCT unit. These samples were obtained from the same locations in 10 patient rooms and bathrooms over 4 consecutive days. The level of total fungus and *Aspergillus* from each air sample and each floor sample was determined and reported in colony-forming units (CFUs) by the Mycology Laboratory of the Clinical Microbiology section of the Department of Pathology.

### Setting

The investigation took place within a pediatric hematopoietic stem cell transplantation unit located



**Figure 2. Conceptual Framework: *Aspergillus* Transmission to the Hematopoietic Stem Cell Transplant (HSCT) Patient**

on the fourth floor of a major pediatric research hospital. The unit specializes in autologous and allogeneic stem cell transplantations. Average patient length of stay varies according to treatment protocol and type of transplant. Allogeneic transplantation is associated with a greater length of stay than is autologous transplantation.

The number of organisms to which the susceptible patient is exposed is a factor in the establishment of infection. The infection control guidelines as outlined in the institution's *Procedure Manual for Infection Control* for the HSCT unit are strictly taught to personnel and families and are followed by all who enter the unit. There is an attitude of infection awareness on this HSCT unit, and deviations from infection control policies are not tolerated or ignored.

### Sample

The sample consisted of 120 air samples and 120 floor samples collected from the same locations in 10 patient rooms and bathrooms over 4 consecutive days. The selection of patient rooms and bathrooms was based on patient census and room status. All occupied rooms were included in the sample collection. Seven rooms were occupied, and three rooms were unoccupied during collection of the air and floor samples. The determination of total fungus levels and *Aspergillus* levels in CFUs was then made by the Mycology Laboratory of the institution's Clinical Microbiology Section of the Department of Pathology.

The air samples and floor samples were collected from the same locations each day. The three floor sam-

ples from each room each day were obtained from the threshold, below left corner of window, and from bathroom to the left of the commode. The locations for the three air samples collected from each room each day were obtained from the threshold facing into room; beside patient bed, midline, and facing the head; and from the midline of the patient bathroom.

### Instruments

#### Brain Heart Infusion Plates With Gentamicin

Brain heart infusion 150 mm diameter plates with gentamicin were used as the medium for fungal growth of the air samples and floor samples collected.

This growth medium has always been used by the institution to measure levels of total fungus and *Aspergillus*. The use of these plates allowed more reliable comparisons to historical total fungus and *Aspergillus* level findings obtained by the institution.

#### Instruments for Floor Samples

A plastic template measuring 10 inches by 10 inches was used for the collection of the floor samples. The template was placed on the floor for each of the three locations to ensure that the same area (10 × 10 inches) was swabbed for each floor sample obtained.

Cotton-tipped applicator swabs were moistened with normal saline and used for collection of the floor samples. Test tubes measuring 16 × 25 mm containing 1 cc of normal saline were used for the transport medium.

#### Instruments for Air Samples

Collection of the air samples was done using the Staplex Company air-sampling device using 1-micron felt filters. Passing air through a filter causes particles to be trapped on the filter medium. A gauge on the device to measure the pressure against the filter was used, and a time chart was consulted to determine how long the device must be on to run 2 m<sup>3</sup> of air through the filter with each sample collected. A stopwatch was used to time each air sample collected. This is important to ensure that each air sample collected consistently represents the presence of total fungus and *Aspergillus* from 2 m<sup>3</sup> of air each time.

## Procedure

Sample collection occurred for 4 consecutive days in April 2002. Two floor samples and two air samples were obtained in 10 patient rooms from the same location each day. One floor sample and one air sample were obtained in the 10 patient bathrooms from the same location each day. Because fungal conidia can be transported on fabrics, the investigator changed protective gowns, gloves, and masks for each room sampled to decrease the likelihood of unintentional contamination (Mitka, 2001; Neely & Orloff, 2001; Obendorf, 2001).

### Floor Sample Collection

All floor samples were obtained early in the morning between 5 a.m. and 7 a.m. before the activity for the unit had started for the day. The last room cleaning had occurred by 10 p.m. the night before. The investigator purposefully chose this time assuming there would be minimal disruption of any settled conidia.

The floor samples were taken from the same two locations in each patient room for 4 days. The locations were the first complete floor tile at threshold and below left corner of window. In each bathroom, the location selected was to the left of the commode.

### Air Sample Collection

Due to the noise created by the air-sampling device, air samples were obtained each day from 9 a.m. to 5 p.m. according to patient schedules and family convenience. The locations for the air samples in the patient room were the first complete floor tile at threshold of the room facing into the room and beside the midline of the bed facing the head. One air sample was taken from the bathroom, midline, and facing inward.

### Statistical Analysis

Analysis was accomplished with Statistical Analysis Software (SAS) and Microsoft Excel designed for Microsoft Windows environment desktop computing. The criterion for statistical significance was set at  $\alpha = .05$ .

The categories for statistical analysis were the following: sample category being air sample or floor sample; room side being the west, north, or east location

of the patient room; room type described as a nonisolation or an isolation room; and room status being unoccupied or occupied during the 4 days of sample collection.

Before the statistical analysis, the air sample values were converted from CFU per 2 m<sup>3</sup> of air to CFU per 1 m<sup>3</sup> of air. This allowed for the comparison of the air sample results to the acceptable institutional air baseline standard that was established a few years ago. The satisfactory baseline established for the air is 8.1 cfu/m<sup>3</sup> of total fungus and 0.4 cfu/m<sup>3</sup> of *Aspergillus*. This baseline represents the average value of fungal conidia in the air at all locations in the patient care building from past air samples collected since 1995. These samples were random and collected from patient rooms, corridors, nursing stations, elevators, and stairwells (Dr. Jon McCullers, personal communication, October 8, 2002).

There has never been an acceptable institutional baseline level established for total fungus and *Aspergillus* for samples collected from the floor or from any other surfaces. Thus, no comparisons can be made between floor sample values of total fungus and *Aspergillus* and a floor standard baseline level for total fungus and *Aspergillus*.

## Results

### Research Question 1

What are the levels of total fungus and the levels of *Aspergillus* of air samples and floor samples obtained from patient rooms and bathrooms on a pediatric HSCT unit?

Sample sizes, sample means, sample standard deviations, minimum values, and maximum values of total fungus and *Aspergillus* for the air and the floor were determined for location and type of room (see Tables 1-4). Then the mean values were determined for sample category, room side, room type, and room status. After visual inspection of the results of the mean values in the air for location, day, sample category, room side, room type, and room status, it was determined that none of the mean values were above the acceptable, institutional baseline standard. This was further verified by *t* tests.

**Table 3. Total Fungus and *Aspergillus* at Different Type of Rooms in the Air**

Fungus Type	Room Type	<i>M</i>	<i>SD</i>	Minimum	Maximum	<i>p</i> Value
Total fungus	Noncontagious	2.486	0.699	1.555	3.833	.0029
	Contagious	5.500	2.062	4.042	6.958	
<i>Aspergillus</i>	Noncontagious	0.086	0.102	0	0.333	.3496
	Contagious	0.167	0.118	0.083	0.25	

**Table 4. Total Fungus and *Aspergillus* at Different Type of Rooms on the Floor**

Fungus Type	Room Type	<i>M</i>	<i>SD</i>	Minimum	Maximum	<i>p</i> Value
Total fungus	Noncontagious	1.949	0.859	0.667	3.167	.0870
	Contagious	0.729	0.206	0.583	0.875	
<i>Aspergillus</i>	Noncontagious	0.130	0.270	0	0.833	.5317
	Contagious	0	0	0	0	

### Research Question 2

Are the levels of total fungus and *Aspergillus* obtained from the air samples less than or equal to the accepted institutional air baseline standard?

The *t* test for total fungus and *Aspergillus* in the air showed no statistically significant differences,  $t = -11.07$ ,  $p > .99$  for total fungus, and  $t = -9.54$ ,  $p > .99$  for *Aspergillus*, between the measured value and the standard air baseline value (see Table 5).

The *t* test for total fungus and *Aspergillus* in different room types in the air showed no statistically significant differences for nonisolation rooms,  $t = -24.09$ ,  $p > .99$  for total fungus and  $t = -9.20$ ,  $p > .99$  for *Aspergillus*, or for isolation rooms,  $t = -1.78$ ,  $p = .837$  for total fungus and  $t = -2.8$ ,  $p = .891$  for *Aspergillus*, between the measured value and the standard air baseline standard (see Table 6).

The *t* test for total fungus and *Aspergillus* for different room status in the air showed no statistically significant differences for unoccupied rooms,  $t = -8.02$ ,  $p > .99$  for total fungus and  $t = -2.61$ ,  $p = .94$  for *Aspergillus*, or for occupied rooms,  $t = -8.41$ ,  $p > .99$  for total fungus and  $t = -11.41$ ,  $p > .99$  for *Aspergillus* (see Table 7).

### Research Question 3

Are there differences in total fungus and *Aspergillus* among sample category, location, day, room side, room type, and room status?

There was a significant difference in total fungus in the air for room type,  $p = .0029$  (see Table 8). When referring to the mean values of total fungus for room type in the air, it is found that the total fungus levels are higher in the isolation rooms than in the nonisolation rooms. The mean total fungus level for the nonisolation rooms was 2.486. The mean level of total fungus for the isolation rooms was 5.500 (see Table 3). Therefore, the level of total fungus was higher in the isolation rooms than the nonisolation rooms.

There also was a significant difference in total fungus for location in the air,  $p = .0335$  (see Table 8). When referring to the mean values of total fungus for location, it is found that the bathroom location air samples for total fungus were higher than the other two air sample locations in the patient room (see Table 1).

Last, there was a significant difference in total fungus on the floor among locations,  $p = .0197$  (see Table 9). When referring to the mean values obtained for location (see Table 2), it is found that the floor location in the bathroom had smaller values than those of total fungus in the other two locations in the patient room.

### Conclusions

Despite the stringent environmental controls adopted by the institution to protect the HSCT patient, environmental fungus and *Aspergillus* were detected. The prevalence and levels of total fungus and *Aspergillus*

**Table 5. *t* Test for Total Fungus and *Aspergillus* in the Air Compared With Baseline Values**

Fungus Type	Baseline Level	<i>M</i>	<i>t</i>	<i>p</i> Value
Total fungus	8.1	3.034	-11.07	>.99
<i>Aspergillus</i>	0.4	0.101	-9.54	>.99

**Table 6. *t* Test for Total Fungus and *Aspergillus* in Different Room Types in the Air**

Room Type	Fungus Type	<i>df</i>	<i>t</i>	<i>p</i> Value
Noncontagious	Total fungus	8	-24.09	>.99
Noncontagious	<i>Aspergillus</i>	8	-9.20	>.99
Contagious	Total fungus	1	-1.78	.837
Contagious	<i>Aspergillus</i>	1	-2.8	.891

**Table 7. *t* Test for Total Fungus and *Aspergillus* in Different Room Status in the Air**

Room Type	Fungus Type	<i>df</i>	<i>t</i>	<i>p</i> Value
Unoccupied	Total fungus	2	-8.02	>.99
Unoccupied	<i>Aspergillus</i>	2	-2.61	.94
Occupied	Total fungus	7	-8.41	>.99
Occupied	<i>Aspergillus</i>	7	-11.41	>.99

on a pediatric HSCT were determined. The results of the study indicated three areas of significant findings.

First, the levels of total fungus among room type in the air of the isolation rooms were higher than the total fungus found in the nonisolation rooms. It may be necessary for a maintenance inspection to be performed to ensure that the use of negative pressure, glass doors, and an anteroom has not interfered with the air flow efficiency in the isolation rooms. The air in the isolation rooms should be surveyed randomly, over a longer period of time, to see if the total fungus levels are consistently higher in the isolation rooms than in the nonisolation rooms. Also, longer periods of sample collection at random times may be more beneficial for detecting relationships among sample category, locations, days, room side, and room status. It may be useful to determine a standard baseline for the isolation

**Table 8. Results of Analysis of Variance for Samples in the Air**

Classification	Fungus Type	<i>p</i> Value
Side (west, north, east)	Total fungus	.6058
Side (west, north, east)	<i>Aspergillus</i>	.7977
Room type (noncontagious, contagious)	Total fungus	.0029*
Room type (noncontagious, contagious)	<i>Aspergillus</i>	.3496
Room status (unoccupied, occupied)	Total fungus	.4519
Room status (unoccupied, occupied)	<i>Aspergillus</i>	.4884
Location (1, 2, 3)	Total fungus	.0335*
Location (1, 2, 3)	<i>Aspergillus</i>	.0824
Date (16, 17, 18, 19)	Total fungus	.4208
Date (16, 17, 18, 19)	<i>Aspergillus</i>	.3423

\**p* < .05.

**Table 9. Results of Analysis of Variance for Samples on the Floor**

Classification	Fungus Type	<i>p</i> Value
Side (west, north, east)	Total fungus	.8420
Side (west, north, east)	<i>Aspergillus</i>	.4987
Room type (noncontagious, contagious)	Total fungus	.0870
Room type (noncontagious, contagious)	<i>Aspergillus</i>	.5317
Room status (unoccupied, occupied)	Total fungus	.4770
Room status (unoccupied, occupied)	<i>Aspergillus</i>	.1030
Location (1, 2, 3)	Total fungus	.0197*
Location (1, 2, 3)	<i>Aspergillus</i>	.1574
Date (16, 17, 18, 19)	Total fungus	.1683
Date (16, 17, 18, 19)	<i>Aspergillus</i>	.5063

\**p* < .05.

rooms and the nonisolation rooms. It seems that because isolation rooms are used for patients who are carriers of a contagion that further complicates their immune status, the acceptable levels of total fungus and *Aspergillus* should at least be the same as in the nonisolation rooms if not deserving of an even lower standard air baseline.

Second, surveillance of the total fungus levels from the air in patient bathrooms should occur over a longer period of time because it was found that the total fungus levels among locations in the air were higher in the patient bathroom than in the air of the other two locations in the patient room. It may be beneficial to establish a standard baseline for the total fungus of air samples from patient bathrooms. The bathroom air supply is not hepafiltered a second time at point of entry (as it is in the patient room). Lack of a second hepafil-

tration at point of entry in the bathroom may contribute to the increased levels of total fungus in the air of the patient bathroom. The water fixtures in the bathroom may contribute to the growth and aerosolization of fungal conidia (Anaissie et al., 2002; Graybill, 2001; Kullberg & Lashof, 2002; VandenBergh, Verweij, & Voss, 1999). It may not be effective or economically practical to provide this second hepa filtration in the patient bathroom. Therefore, to establish the need to provide point-of-entry hepa filtration in the patient bathroom, additional samples over time should be collected to show that consistently high total fungus levels are present. It seemed better that the levels of total fungus in the other two locations in the patient room were lower because the patient spends more time in the patient room than in the bathroom.

The last finding involved a significant difference between locations on the floor and amount of fungus. The bathroom floor sample location had less total fungus than the floor samples from the other two locations in the patient room. The attitude of the bathroom being a "dirty" place may promote a more thorough cleaning procedure to be applied in the bathroom by environmental services personnel. The threshold floor location may have higher total fungus counts than what is shown. The door to the patient room opens inward. The air current produced may have caused some aerosolization of settled conidia to occur prior to the collection of the sample from the threshold in the patient room. It may be beneficial for surveillance efforts to include the establishment of standard surface or floor baselines for locations in the patient room and bathroom. Floor sample and surface sample results can detect minor contamination and can serve as a good marker for lack of cleaning or filtration (Faure et al., 2002).

There are few standards for surveillance of nosocomial fungal presence in hospitals. It is difficult not only to compare findings institutionally but also to compare findings across studies because of the lack of a universal definition of IA, a lack of agreement on extent of disease, and the lack of widely recognized surveillance protocols. The lack of unstandardized methodology implies that the frequency of fungal isolation depends on a great number of factors. These include type of sampling (surfaces and/or air), frequency, location, and sampling size. Other factors such as culture medium, condition of incubation (time and temperature), and method of processing are also important. "The lack of

standardized protocols and reference values for fungal environmental surveillance impairs comparison between studies" (Faure et al., 2002, p. 5).

These reference values should be standard baseline levels established for air, floor, and surface samples to ascertain the optimal acceptable levels for total fungus and *Aspergillus* on the HSCT unit. There are often no data on the baseline concentrations of total fungus and *Aspergillus*, and this makes it difficult to determine if an infection is associated with higher levels of total fungus in the hospital setting (Hajjeh & Warnock, 2001).

The results showed there were no levels of total fungus and *Aspergillus* in the air that was greater than the institution's standard baseline for acceptable air levels. These acceptable standard baseline levels were determined from air samples taken from patient rooms, bathrooms, and common areas such as hallways and nurses' stations. It would seem that comparison findings would be more reliable if weighed against institutional criteria established from the mean values of samples collected only from the HSCT unit. It has not been determined if the acceptable standard baseline levels of total fungus and *Aspergillus* on the HSCT unit should be made more strict and therefore lower than the other areas of the hospital because of the profound immunosuppression induced by HSCT.

It is expected that the air and floor values for total fungus and *Aspergillus* should be lower in the patient rooms than in the common areas of the hospital. The air to the patient room is hepa filtered twice, whereas the air to the common areas is hepa filtered once. There is less activity and fewer people in the room, thereby decreasing the disruption and subsequent aerosolization of settled conidia. It needs to be determined if the single hepa filtration in the patient bathroom and common areas of the hospital contribute to the higher total fungus and *Aspergillus* levels in the air, thereby increasing exposure to environmental contaminants.

For meaningful comparisons to be made, standard baseline levels should be established for air, floor, and surface samples collected from the HSCT unit alone. These standard baselines should provide acceptable levels for the locations of patient room, bathroom, and common areas. Then, evaluation of the HSCT environment can be based on consistent collection procedures and sampling routines.

In summary, the possibility of complete eradication of total fungus and *Aspergillus* from the hospital environment is questionable, and this expectation may be

unrealistic. The most effective and extant control measures for prevention of fungal exposure and transmission have been implemented on this HSCT unit. Routine standard collection methodology should be established for random air, floor, and surface sampling for total fungus and *Aspergillus* on the HSCT unit. The levels obtained should then be used to establish standard institutional baselines for acceptable levels of total fungus and *Aspergillus* on the HSCT unit. Deviation from these baselines can alert to increased levels of total fungus and *Aspergillus*, and initiation of appropriate corrective measures can be determined. Certainly, protective measures and surveillance of the hospital setting have an important role to play in the prevention of exposure to fungi and *Aspergillus*.

Increasing incidence of IA is evident after recovery of neutropenia and discharge from the protection of the hospital environment. Control of the outside environment obviously presents obstacles to effective control of environmental sources of fungus. Exploration into other areas that show potential efficacy in the diagnosis and treatment of fungal infection should be investigated.

### Limitations

The 4-day sample collection was brief. This sample size was determined by capacity of the mycology laboratory to analyze the number of samples that were needed. Furthermore, the biostatisticians indicated that the number of samples collected over this 4-day period would suffice to represent the levels of total fungus and *Aspergillus* on the unit.

The reaction of the institution's Environmental Services Department to the obvious sample collection on the unit could have been to apply more stringent cleaning to the patient rooms and bathrooms over this 4-day period. The department may have been concerned that the findings from this study could be used to evaluate cleaning practices on the unit.

### Future Direction

Most cases of IA are infrequent and occur sporadically. It is unknown whether some cases of IA are hospital or community acquired. The minimal acceptable level of conidial density exposure has not been estab-

lished; therefore, it is unknown how much exposure causes disease. Varying degrees of immunosuppression among patients affects the incubation period of *Aspergillus* as well as the time of exposure to initial symptoms. There is evidence that shows that *Aspergillus* has the propensity to reactivate in the setting of prolonged or recurring immunosuppression (Kontoyiannis & Bodey, 2002).

Treatment for IA is suboptimal without optimistic, convincing assurances for positive outcomes. The overall CFR reported by Lin et al. (2001) was 58%, and the CFR was highest for HSCT recipients (86.7%). Oftentimes, signs of infection do not occur until dissemination of disease is present. In a hospital-based survey of aspergillosis, Perfect et al. (2001) reported that despite receiving treatment with amphotericin B, more than half of the patients with IA do not survive more than 3 months.

It seems that the treatment of existing infection is a late intervention. It would be better to initiate measures before evidence of fulminating infection, when the chances of survival are greatest. The development of the new tests for the detection of circulating fungal cell wall antigens such as galactomannan and (13)-beta-D-glucan and the detection of fungal DNA by polymerase chain reaction (PCR) assay should be perfected. According to Ellis (2001), "Sensitivities and specificities for *Aspergillus* diagnosis are among the highest when a combination of galactomannan sandwich ELISA [enzyme-linked immunosorbent assay] and PCR is used" (p. 950). The significance of galactomannan and PCR at different stages of fungal burden and infection and their usefulness for guiding therapy should be examined.

Prophylaxis with antifungal agents may be warranted in the HSCT setting due to the increased risk of infection and poor outcomes following treatment. Studies should be done to investigate the maximum tolerated doses to be used for prophylaxis and for treatment so that toxicities can be minimized. The use of combination drug therapy should be investigated for the use of antifungal agents as synergists in their attack against fungal infection. Drug-resistant fungal organisms are being identified, and this has increased concern about the inadequacy of the present treatment available. *Aspergillus* infection is associated with a high mortality rate, but infection with a drug-resistant organism is almost always fatal.

Further investigation into the use of cytokines such as colony-stimulating factors and interferon to decrease the duration and effects of immune deficiencies should be continued (Ellis, 2001). If reconstitution of the hematopoietic system occurs with subsequent immunorestitution, the chances of acquisition of opportunistic fungal infection will be decreased.

### Implications for Nursing Practice

It seems that diagnosis with invasive fungal disease evokes the same feelings of pessimism in nurses as it did 20 years ago. Treatment outcomes and prognosis remain poor. Nurses who care for pediatric HSCT patients with fungal infections are witnesses to the suffering that accompanies this illness. Also, the nurses' workload increases due to fungal infections and care of these high acuity patients. Nurses must understand that immunosuppression, opportunistic pathogens, and the hospital environment are contributory factors to the acquisition of invasive fungal infection. Nursing responsibilities in the care of the HSCT patient include delivery of physical care, provision of education regarding infection, enforcement of infection control guidelines and policies, recognition of the clinical signs of fungal infection, and contribution to the research regarding prevention of fungal infection.

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