Fungal Infections

81. Enhanced Surveillance for Hospital-associated Invasive Aspergillosis During a Period of Extensive Hospital Renovation

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Background: Construction dust is a well known risk factor for Aspergillosis, but surveillance for hospital-associated invasive Aspergillosis (HIA) is hampered by the lack of an accepted case definition and unknown incubation period. NYU Medical Center (NYUMC) recently embarked on a multiyear construction project, and in December 2006 routine surveillance of microbiology data revealed a relative increase in clinical cultures yielding Aspergillus species. In January 2007, an enhanced surveillance system was established to identify potential HIA cases retrospectively from January 1, 2006 and prospectively. Infection prevention education for construction personnel was assessed and revised.

Objective: Increase sensitivity of HIA surveillance during extended period of hospital construction.

Methods: The enhanced HIA surveillance identified patients admitted to NYUMC after January 1, 2006 with the following microbiology, radiology and/or pathology test results obtained 7 or more days after admit date:

- Microbiology test results yielding Aspergillus species
- Chest computed tomography scan (CT) reports containing the key words: aspergilloma, aspergillosis, aspergillus, fungal, fungus, or mold.
- Pathology reports consistent with invasive fungal/mold infection

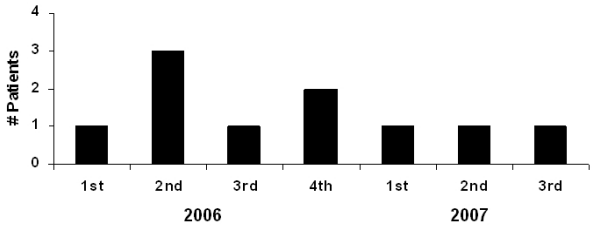
A standardized HIA case definition based on accepted clinical factors, host characteristics and test results classified each patient as: possible HIA, probable HIA, proven HIA or not a case. Patients with possible HIA required attending physician documentation that invasive fungal/mold infection was likely. Prevention of HIA was enhanced by mandatory infection control training of construction personnel and daily worksite assessment using a standardized checklist.

Results: During the period January 1, 2006 - October 1, 2007, 49 patients were identified by surveillance; 10 of 49 (20%) patients met case definition for HIA infection (5 possible HIA, 2 probable HIA and 3 proven HIA), 36 of 49 (73%) were not a case and records for 3 patients were unavailable. HIA cases declined after implementation of enhanced infection prevention at construction sites (figure 1). HIA cases were identified by CT in 6 of 10 (60%) cases, microbiology in 4 of 10 (40%) cases and pathology in 1 of 10 (10%) cases. One HIA case was identified by CT and microbiology culture, both tests were obtained within 3 days of each other.

Conclusions: The addition of radiology and pathology test results to standard microbiology surveillance increased the sensitivity of HIA detection. Education and daily assessment of infection prevention at worksites was associated with decreased

HIA. Hospitals undergoing construction should consider enhanced HIA surveillance.

Figure 1: Patients Meeting HIA Case Definition by Quarter, NYUMC, 1st Qtr 2006 - 3rd Qtr 2007



82. Trends of Candidemia In 4 Community Hospitals in North East Ohio between 2000 and 2004: *Candida glabrata* as the most common pathogen

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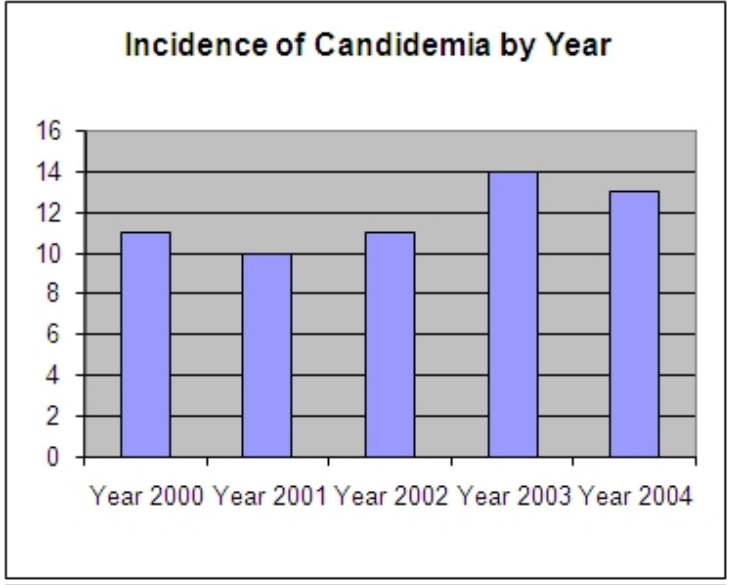
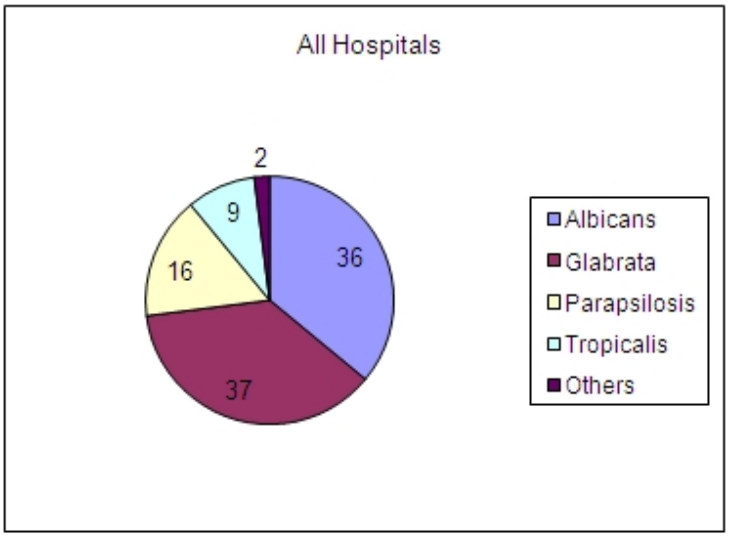
Background: Candida species are the 4th commonest cause of bloodstream infections in the U.S. and are associated with significant morbidity and mortality. Recent data indicates a shift from albicans to non-albicans species. This development could impact choice of antibiotics since some non-albicans species such as glabrata are intrinsically resistant to Fluconazole, the most commonly used antifungal agent.

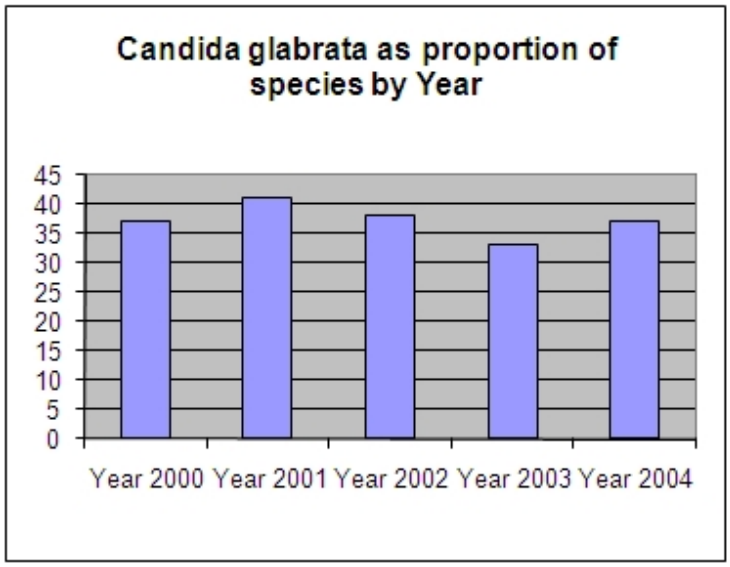
Objective: To evaluate trends of Candida bloodstream infections in 4 community hospitals to determine overall incidence, and proportion of various species. Susceptibility of Candida glabrata isolates to Fluconazole in 2003 and 2004 was also analyzed.

Methods: All adult patients in 4 community hospitals in North East Ohio with candidemia between January 1st 2000 and December 31st 2004 were included in the study.
Patients were identified from microbiology records.
Incidence was calculated as number of episodes per 10,000 admissions.
A retrospective descriptive analysis was performed.

Patients: Results: Candida was isolated in 410 blood cultures representing 214 episodes of candidemia during the study period. The overall incidence was 12.1 per 10,000 admissions. The incidence varied from 10.4- 14.3 per 10,000 admissions during the study period. There was no statistically significant difference in incidence between 2000 and 2004 (11 vs. 13 episodes per 10,000 admissions). The most frequently isolated species overall was Candida glabrata, which was marginally higher than Candida albicans (38 vs. 37 % $p > 0.05$). There was no difference between the proportion of Candida glabrata species between 2000 and 2004 (37% in both years). The percentage of Candida glabrata isolates resistant to Fluconazole in 2003 and 2004 were 26 and 42% respectively ($p < 0.05$).







Conclusions: During the study period, the incidence of candidemia was higher than previously published studies, with no statistically significant annual variation. Candida glabrata was the most frequently isolated species and its proportion remained stable during the study period. *Candida glabrata*'s resistance to Fluconazole increased significantly between 2003 and 2004.

83. Outbreak of Invasive Fusariosis in a Bone Marrow Transplant (BMT) Unit: Host, Environment or Bug?

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Background: Invasive fusariosis is a major fungal infection in severely immunocompromised patients. The most likely portal of entry is the airways, and outbreaks of nosocomial infection have been described in BMT units, associated with hospital environmental sources. On the other hand, an increased incidence of superficial mycoses caused by Fusarium spp. occurring in immunocompetent outpatients has been recently reported. We observed 7 cases of invasive fusariosis in our BMT unit in an 8-month period in 2007. All patients were severely immunosuppressed (neutropenia and/or graft versus host disease) and had a portal of entry in the skin and/or nails of the feet.

Objective: To identify the source of the outbreak

Methods: We calculated incidence rates of invasive fusariosis in the past 3 years, and reviewed all results of positive cultures for Fusarium spp. from the Mycology Laboratory since 1996. In addition, we performed an environmental investigation in the unit. Air (Andersen 6-stage bioaerosol sampler) was collected from the patients' rooms and bathrooms before (dry) and after (wet) allowing the shower to run for 10-20 minutes. Water was collected from showers and sinks from patients' bathrooms, and swabs of lavatory drains, sink faucet aerators, shower heads, toilet bowls and shower wall surfaces were collected.

Results: The incidence of invasive fusariosis increased from 0.2 in 2005 to 0.4 in 2006 and 1.84/1,000 patient-days in 2007 ($p=0.01$). Preliminary results of environmental cultures showed growth of Fusarium spp. from 7 water samples (shower and douche of 3 bathrooms), 33 swabs from water-related structures of the 12 patients' rooms, and from 2 air samples from one room. However, the frequency of superficial infections caused by Fusarium in immunocompetent outpatients increased from <1% until 2006 to 2.37% in 2007 ($p<0.001$). This fact brings the possibility that infection was acquired in the community, and the patients were colonized or had superficial infections by Fusarium on admission, and developed invasive infection after becoming immunosuppressed.

Conclusions: These preliminary results underscore how complex is the definition of the origin of mould infections in immunocompromised patients (community versus nosocomially-acquired). Molecular studies are underway and may help to define the source of invasive fusariosis in this outbreak. Likewise, epidemiologic studies in the population of immunocompetent outpatients with superficial fusariosis are needed.

84. Predictors of Candiduria in Hospitalized Patients with Indwelling Urinary Catheters: A Multivariate Analysis

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Background: Candiduria is common among hospitalized patients with indwelling urinary catheters. However, data on the predictors of candiduria is limited.

Objective: We undertook a prospective study to determine independent predictors of candiduria in hospitalized patients with indwelling catheters.

Methods: We undertook secondary analysis of a dataset consisting of two randomized controlled trials. Patients participating in 2 randomized trials of 2 novel urinary catheters one a nitrofurazone-impregnated silicone catheter, and the other, a silver-polyurethane hydrogel catheter formed the study population. Participants in both trials were hospitalized patients scheduled to receive an indwelling urethral (Foley) catheter who were expected to be catheterized for more than 24 hours; patients were excluded if they were younger than 18 years, pregnant, or had a known allergy to silicone, nitrofurazone, or silver. Both studies were approved by the institutional Human Subjects Committee. In those trials, paired quantitative urine

cultures were obtained daily, from the catheter specimen port and from the collection bag, using a technique that could detect 1 colony-forming unit/mL. Candiduria was defined as any detectable growth of a candida species. Univariate analysis comparing patients with and without candiduria was undertaken using Chi-square (or Fishers exact) test for categorical variables and Students t-test for continuous variables. For multivariate analysis, logistic regression was performed.

Results: Of 1516 patients, 74 had candiduria. The median colony count for cases was 336,000 CFU/ml (range 1000-180,000,000 CFU/ml). Candida albicans accounted for 60% of the candiduria cases and Candida glabrata accounted for 20% of the candiduria cases. The remainder were not speciated. In univariate analysis, increasing age, female gender, antibiotic use and ICU stay were more frequent in patients with candiduria than in patients without candiduria. In multivariate analysis, independent predictors of candiduria included age > 60 years (OR 2.4, 05% CI 1.2-4.6) and antibiotic use prior to development of candiduria (OR 254, 95% CI 74.5-868.6).

Conclusion: Antibiotic use in patients with indwelling urinary catheters represents a major modifiable risk factor for the development of candiduria. Judicious antimicrobial usage is essential to lower the risk of candiduria.

85. The Epidemiology of Aspergillosis among Human Immunodeficiency Virus Infected Patients at the Owen Clinic, 1994-2004

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Background: Invasive aspergillosis (IA) is a rare disease among HIV infected patients as the prevalence and incidence ranges from 2-4% and 2-35 cases per 100 person years, respectively. IA, however, remains a serious disease among HIV infected patients because of the high morbidity and mortality and the significant toxicities associated with therapy.

Objective: To characterize and calculate rates of invasive (IA) and non invasive aspergillosis (NIA) in HIV infection before and after the introduction of potent antiretroviral therapy (ART), and explore risk factors for IA.

Methods: Inclusion into the study required documented HIV infection, a positive Aspergillus culture (A+) and at least one clinic visit at the University of California, San Diego (UCSD) Owen clinic 2-4 months before A+. IA was defined adapting criteria published in the international consensus statement for defining opportunistic invasive fungal infections in cancer and hematopoietic stem cell transplants. Rates of IA and NIA were the number of cases per 100 HIV patients followed at the Owen clinic. Independent variables of interest included clinical symptoms, laboratory and radiographic data, medications, HIV risk. Univariate and logistic regression analyses were performed to identify independent variables significantly associated with IA.

Results: From 1994 to 2004, 130 HIV Owen patients with A+ were identified. Most were middle-aged men having sex with men. Median CD4 counts were 50 cells/mm3 and HIV RNA was 11.6 log10 copies/ml. 21 (16%) had IA. While rates of IA were

constant at 0.2/100, rates of NIA decreased abruptly from 1.8/100 to 0.6/100 in 1997 and then to 0.3/100 over the remaining study period. Although in univariate analysis, race, HIV exposure mode, and CD4 counts were significantly associated with IA, in a logistic regression model, CD4 counts below 50 cells/mm3 was the only significant predictor of IA (OR: 8.6; 95% CI: 2.4-31.6).

Conclusions: These data suggest that Aspergillus remains a significant pathogen in patients with advanced HIV. Unlike risk factors identified in other susceptible populations, ART induced improvement of T-cell mediated immunity, measured by CD4 counts, appears to be the single most significant factor in preventing invasive disease in HIV-infection.

86. Epidemiologic Characterization Of Candidemia In A Large Tertiary Medical Center

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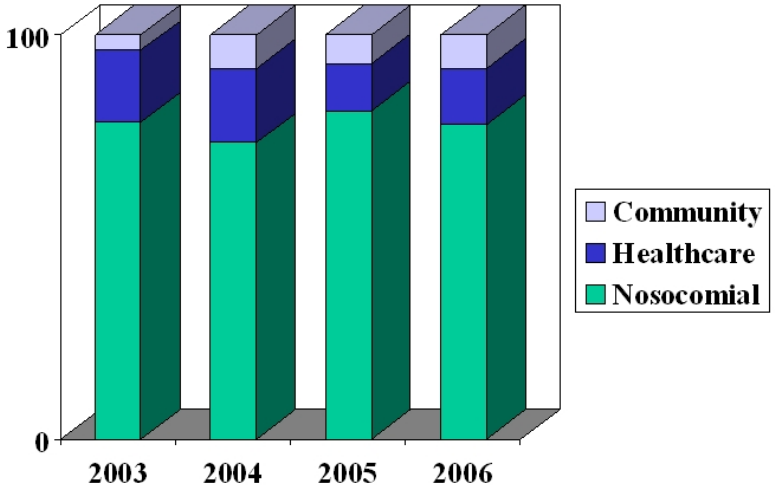
Background: There are limited contemporary data that profile the setting of acquisition of candidemia. With advances in medical and surgical therapies, candidemia is no longer restricted to nosocomial acquisition. Currently, cases also occur in both the health care-associated and community setting.

Objective: To determine the setting of acquisition of candidemia and to describe the species identification of blood culture isolates. In addition, to characterize associated bloodstream infections (BSI) that occurred prior to or within 30 days if ambulatory (sequential) or simultaneous to candidemia onset and multiple-species candidemia.

Methods: Medical records of all patients (ambulatory and inpatient) who had a first episode of candidemia at Mayo Clinic-affiliated hospitals between January 1, 2003 and December 31, 2006 were reviewed. A chi-square or Fisher's exact probability test was used to compare frequencies of candidemia and associated BSI among the three settings of acquisition.

Results: The distribution of candidemia cases by setting of acquisition are shown in Figure 1. Overall, 19-27% of cases developed candidemia in the community or health care-associated setting.



The frequencies of Candida species causing candidemia per setting of acquisition are shown in Table 1. Overall, the group of non-albicans species (58%) was more common than *C. albicans* (42%). *C. glabrata* (32%) was the second most

common isolated species.

Table 1			
Candida species (N°)	Community (n=19)	Health care (n=40)	Nosocomial (n=203)
albicans	8	12	90
glabrata	7	13	65
parapsilosis	0	6	14
tropicalis	0	1	14
krusei	1	1	9
Other	3	7	11

As shown in Table 2, there was a significant association between simultaneous or sequential BSI, which were due to bacteria in all cases, and nosocomial-acquisition setting (§ p=0.01).

Table 2. Associated bloodstream infections in patients with candidemia			
Associated BSI § (N° of patients)	Community (n=18)	Health care (n=38)	Nosocomial (n=196)
Yes	3	8	88
No	15	30	108

Simultaneous BSI and multiple-species candidemia were present in 12 and 3% of nosocomial, 18 and 5% of health care-associated, and 17 and 6% of community-acquired candidemia, respectively. Multiple-species candidemia was not associated with the acquisition setting (p= 0.44).
Conclusions: Health care-associated and community-acquired settings are important venues for the acquisition of candidemia. C. albicans remains the most common species causing candidemia in all three settings of infection acquisition. Associated BSI more often characterized patients with nosocomially-acquired candidemia. Multiple-species candidemia was uncommon in all three settings of infection acquisition.