**Objectives:** To evaluate the utility of BGL monitoring in neutropenic cancer pts at high risk of IA and IC.
**Methods:** Prospective study of consecutive episodes of neutropenia (median duration 22 d) in pts with acute leukemia. IA and IC were defined according to EORTC-MSG criteria. Blood was collected 2 times weekly before onset of fever and daily thereafter. BGL was measured by turbidimetric or colorimetric assays (Wako, Japan). Positive tests defined by 2 consecutive BGL values >6 and >5 pg/ml, or >11 pg/ml for both tests (2 cut-off values).
**Results:** 23 episodes of invasive mycoses occurred during 130 neutropenic episodes: 12 IC (1 proven, 11 probable) and 11 IA (3 proven, 8 probable). 16 samples/episode (3–35) were analyzed over 35 days (17–122). Diagnostic performance of BGL (turbidimetric test): sensitivity, specificity, PPV, NPV, negative likelihood ratio were 43/100/100/86/0.57% and 24/100/100/82/0.76% for 2 consecutive values >6 and >11, respectively. Diagnostic performance of BGL (colorimetric test): sensitivity, specificity, PPV, NPV, negative likelihood ratio were 86/91/72/96/0.15% and 43/100/100/86/0.57% for 2 consecutive values >5 and >11, respectively. Colorimetric BGL with cut-off of 2 consecutives values >5 provided the best performance for diagnosis of IA and IC. Median time (0 d) between fever onset (as first sign of IFI) and BGL positivity was significantly shorter than that between fever onset and conventional diagnosis of IFI (13 d) ($p < 0.0001$).
**Conclusions:** Serial screening of blood beta-1,3-D-glucan is a promising non-invasive tool, in combination with other diagnostic methods, to identify persistently febrile neutropenic pts in whom empirical therapy may be unnecessary.

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## Invasive Fungal Infections among Pediatric Patients with Hematologic Malignancies at KFSH&RC/KFCCC&R

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**Objectives:** To define the magnitude of the problem, study factors associated with increased risk of invasive fungal infections (IFI) and outcome.
**Methods:** From June 1998 to March 2003, all radiological studies of patients with hematologic/oncologic disorders were evaluated for inclusion. All cases of invasive fungal infection were reviewed. The criteria for inclusion were obvious lesion suggestive of fungal infection shown on radiological studies, and fungal infections were classified as "proven", "probable", "possible" or "insufficient evidence" according to a prior definitions.
**Results:** A total of 1615 patient charts were reviewed. The underlying diagnoses include ALL 410, SCT 293, AML 133, non-malignant hematology 288, NHL/solid tumors 491. 152 (9%) had evidence of fungal infection (55 [36%] 'definite = proven/probable', 97 [64%] 'possible'). Biopsy was performed in 94 cases and the findings included budding yeast in 10 patients, septated hyphae in 19, and hyphae with no specifications in 12 patients. Delays in performing diagnostic procedures possibly resulted in the lower incidence of 'definite' IFI (36% vs 64% 'possible"). The overall incidence of fungal infection was 9%, being highest for AML (39%), followed by ALL (17%). The majority of IFI developed during or immediately after induction (42% of IFI in AML and 53% of IFI in ALL), which can be a target for intervention. The infections included disseminated fungal infection (36%), CDC (11%), pulmonary fungal infection (43%) and *aspergillosis* (9.5%) including pulmonary, Para nasal sinuses, skin and disseminated. IFI was radiologically diagnosed during neutropenia in 123 patients (81%). Ten patients died due to fungal infection (7%), 75 (49%) were cured, 26 (17%) were alive with fungal infection, and 39 patients (26%) died due to primary disease seemingly unrelated to fungal infection. Mortality due to IFI in this study is less than what is reported in the literature and could be a result of our practice of early intervention. The average LOS for IFI was 56 days compared with the usual 12 days, which can add to the increased cost.
**Conclusions:** Invasive fungal infection is becoming a serious problem. Furthermore, acute invasive fungal infection is associated with a much higher mortality. Early diagnosis with prompt antifungal therapy, or even with surgical intervention, might be warranted to save patients' lives.

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## Daptomycin Therapy of Gram-Positive Infections (GPI) in Pediatric Cancer Patients

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**Background:** Daptomycin is a novel lipopeptide recently approved for treatment of complicated skin and skin structure infections (SSTIs)

caused by susceptible Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). Clinical data in pediatric patients is limited.

**Methods:** A retrospective chart review of pediatric patients (<18 y) who received >2 doses of daptomycin between 8/2003 and 11/2006 was performed.

**Results:** Eleven infections [9 Gram-positive bacteremias (GPB) and 2 SSTIs] in 10 patients (7 male, 3 female) were treated with daptomycin (eight received 6 mg/kg/day and three – 4 mg/kg/day). Seven patients had hematological malignancies (5 ALL, 1 AML, 1 CML) and all were allogeneic transplant recipients. Two patients had solid tumors (neuroblastoma-1 and lung cancer-1). Median age was 11 years (range, 2–18). Eight infections occurred during neutropenia and four during corticosteroid therapy. Of the nine bacteremias, all were catheter related (6 CVC, 3 implanted port). Organisms isolated were coagulase-negative *Staphylococcus* (CoNS): 5; *Enterococcus faecalis*: 2, and 2 polymicrobial infection – CoNS + *E. mundii*, CoNS + Lactobacillus. Two infections were SSTIs including leg abscess: 1, cellulitis: 1. Eleven infections had failed standard antimicrobial therapy (vancomycin for >4 days in 8 episodes; linezolid for >3 days in 2 episodes; and quinupristin–dalfopristin – 21 days in 1 episode) and had persistently positive blood cultures (8 episodes) and/or fever (7 episodes) prior to initiation of daptomycin. Although susceptible, 4 CoNS had vancomycin MICs of 2.0 μg/ml and 3 had MICs of 3.0 μg/ml. The linezolid MIC of one *E. faecalis* rose from 1.5 to 4.0 μg/ml while on daptomycin therapy. Median duration of daptomycin therapy was 10 days (range, 4–15). Outcomes included clearance of blood cultures and defervescence within 72 h in 7 episodes, 1 – grew *E. faecalis* on daptomycin, 1 – persistently febrile and resolution of both SSTIs. No drug related adverse events were documented.

**Conclusion:** Daptomycin appears to be a promising antimicrobial agent for the treatment of GPI in pediatric cancer patients and merits further clinical evaluation.

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## Mortality Rates for Breakthrough Invasive Fungal Infections in a Multicenter Trial of Posaconazole vs Standard Azole Prophylaxis

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**Background:** Patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) undergoing induction chemotherapy are at high risk for invasive fungal infections (IFIs). In a multicenter, randomized study of AML/MDS patients, posaconazole (POS) prophylaxis prevented significantly more breakthrough IFIs than standard azole (fluconazole [FLU] or itraconazole [ITZ]) prophylaxis.

**Objectives:** We evaluated mortality rates and causes of death in patients from this study who developed a breakthrough IFI during POS or standard azole prophylaxis.

**Methods:** Patients with AML or MDS and chemotherapy-induced neutropenia ($\leqslant$500 cells/mm$^3$) were randomly assigned to POS oral suspension 200 mg tid or oral standard azole prophylaxis (FLU suspension 400 mg qd or ITZ solution 200 mg bid) with each chemotherapy cycle for $\leqslant$12 weeks. All patients were closely monitored for IFIs by current culture, serological, and radiographic methods. Primary endpoint was the incidence of proven/probable IFIs during the treatment phase (from randomization to 7 days after last dose), as determined by a blinded expert panel using EORTC/MSG criteria. Survival information was collected at 30 days after last dose of study drug or 100 days after randomization, whichever occurred later. Cause of death was investigator-determined.

**Results:** 602 patients were enrolled (304 POS; 298 standard azole [240 FLU, 58 ITZ]). Significantly fewer IFIs occurred among POS patients (POS, 7 [2%] vs standard azoles, 25 [8%]; P = 0.0009). Aspergillosis was the most common IFI in both groups, but significantly fewer cases occurred in the POS group (POS, 2 [1%] vs standard azoles, 20 [7%]; P = 0.0001). Overall mortality was n = 49 (16%) and n = 67 (22%) for patients in the POS and standard azole groups, respectively (P = 0.048). Of patients who developed a breakthrough IFI, 1 of 7 (14%) POS patients and 11 of 25 (44%) standard azole patients died during the study (table). The mortality rates for patients without proven/probable IFIs were 48/297 (16%) and 56/273 (21%) for POS and FLU/ITZ, respectively.