Methods: This retrospective cohort study evaluated patients who underwent CBT at the Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, WA between 2006 and 2009. Data were collected from patient medical records and the center's clinical databases. All IFI were classified as early (≤ 40 days post-transplant), late (41-180 days) or very late (181-365 days), and pretransplant infections were not included. Only proven or probable IFIs as defined by standard criteria were analyzed. Incidence rates were determined and *a priori* risk factors for IFI were assessed using chi squared or Wilcoxon rank-sum analyses where applicable.

Results: A total of 103 CBT recipients were eligible for inclusion in this study. Median age at time of transplant for the cohort was 30.4 years (interquartile range [IQR] 14, 48), and most patients underwent myeloablative conditioning (71/103 [69%]) and received a double cord transplant (88/103[85%]). Overall, 16 patients (15.5%) developed 19 total IFIs (5 proven, 14 probable) within the first year posttransplant. Following their primary episode 3 patients developed a second IFI due to a different fungal pathogen, and 6 patients had a known pretransplant IFI which were excluded from analyses. The median onset of first IFI was 65.5 days posttransplant (IQR 28, 126). The cohort specific incidence rate of IFI during the first year was 0.92 cases per 1000 patient days (95% CI 0.56, 1.49). The majority of IFIs occurred during the high risk early and late periods (both 9/19 [47%]). Invasive *Aspergillus* was the most common IFI (12/19 [63%]) during the period of observation, but others included Zygomycetes (3), *Scopulariopsis* (1), *Fusarium* (1) and candidal species (2). Of the 16 patients that developed at least one IFI, 4/16 (25%) died as a direct result of their fungal infection. Comparing CBT recipients who did and did not develop IFI, graft-versus-host disease, time to engraftment, age, conditioning regimen, and CMV serostatus were not associated with the development of IFI.

Conclusions: Cord blood transplant recipients appear to be at high risk for developing postransplant IFIs. As most IFIs occurred prior to day 180 in this cohort, early prevention strategies and the use of extended-spectrum azole prophylaxis may be needed in this population.

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EVALUATION OF A NOVEL VIRAL LOAD BASED SURVEILLANCE STRATEGY FOR PREVENTION OF CYTOMEGALOVIRUS (CMV) DISEASE IN HEMATOPOIETIC CELL TRANSPLANTATION

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Introduction: Surveillance and preemptive therapy for CMV reactivation is the most commonly used strategy to prevent CMV disease in hematopoietic cell transplant (HCT) recipients. In 2007, our center switched from a strategy using pp65 antigenemia testing with treatment for any level of antigen, to one using quantitative PCR tests (*J. Clin. Microbiol.* 42:p1142, 2004), with treatment thresholds determined by each patient's disease risk. We hypothesized that this both sensitive and specific testing strategy would lead to earlier diagnosis, thereby decreasing the incidence of CMV disease.

Methods: We retrospectively examined two cohorts of patients receiving their first allogeneic HCT who were either CMV seropositive (R+) or had a seropositive donor (D+/R-). Patients in the first cohort (2002-2005, n = 703) received weekly antigen testing and antiviral therapy was initiated for any positive test. Patients in the second cohort (2007-2009, n = 385) were tested by PCR weekly and received therapy at a DNA level of > 500 copies/ml, unless receiving ≥ 1mg/kg of prednisone or anti-T cell therapies in whom therapy was initiated at a level > 100 copies/ml. Cord blood recipients were excluded from analyses. Results were analyzed using multivariable Cox regression and competing risk regression models including several pretransplant risk factors.

Results: In a multivariate model, PCR based testing resulted in a similar overall 1 year mortality (adjusted HR 0.91, 95% CI 0.7-1.1, p = 0.38) to antigenemia testing. The cumulative incidence of CMV disease by day 100 was also similar between the two groups (aHR 1.25, 95% CI 0.7-2.3, p = 0.48). Patients who were CMV R+ pretransplant were more likely to develop CMV disease than D+/R- patients (aHR 3.3, 95% CI 1.0-10.6, p = 0.05). While the overall rates of CMV disease were similar, PCR surveillance was associated with more gastrointestinal disease and less pneumonia (RR 0.36, 95% CI 0.08-0.86, p = 0.02).

Conclusions: We have demonstrated that a preemptive treatment strategy based on viral load and host risk factors resulted in similar rates of CMV disease and overall survival compared to an antigenemia based strategy. The PCR based strategy was associated with a decreased incidence of CMV pneumonia. Future studies are needed to further examine the characteristics of gastrointestinal CMV disease in seropositive patients that is not detected by blood based PCR surveillance.

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SURVEY RESULTS OF IMMUNIZATION PRACTICES FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANT AMONG CENTERS IN THE UNITED STATES

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Vaccine immunity declines in recipients following hematopoietic stem cell transplant (HSCT) placing patients at risk for significant complications from vaccine-preventable diseases. An international, collaborative group recently published recommendations to standardize revaccination of HSCT recipients. The purpose of this study was to survey HSCT centers within the United States to characterize current vaccination practices.

Methods: A 25-question web-based survey was distributed six months after the publication of updated guidelines to administrators of HSCT centers throughout the United States registered with the National Marrow Donor Program. All submitted survey responses were included in the analysis.

Results: Forty-seven of the 124 eligible HSCT centers (38%) completed the survey. All survey responses were included in the analysis although only 29 centers (62%) completed the full survey. Thirty-one centers of 40 responding (78%) developed a standard operating procedure which addressed revaccination and 38 programs (95%) followed a standardized vaccination schedule. Approximately half of the centers reimmunized autologous and allogeneic HSCT recipients on the same schedule and a majority of centers (90%) altered the vaccination schedule for patients receiving immunosuppression. Nineteen of 37 responding centers (51%) routinely monitored immunologic markers prior to revaccination and thirteen of 29 centers (45%) utilized the results to modify therapy. Following vaccine administration, 8 of 37 responding centers (22%) obtained antibody titers. The updated guideline included changes to administration of the pneumococcal, diphtheria, tetanus, and acellular pertussis vaccines and these practices were less consistent with the newly published recommendations. Immunization practices that closely followed the updated recommendations included vaccination with the *Haemophilus influenzae* type b conjugate vaccine, inactivated polio and hepatitis B vaccines.

Conclusions: Vaccination practices following HSCT vary considerably among programs within the United States despite the recent publication of updated guidelines. Overall, the international recommendations may help to standardize practice and improve patient outcomes following HSCT. These findings highlight future educational opportunities for health care providers and the need for additional research.

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PREVENTION OF INVASIVE MOLD INFECTION POST ALLOGENEIC STEM CELL TRANSPLANTATION (AlloSCT) IN PEDIATRIC RECIPIENTS USING THE SEQUENTIAL COMBINATION OF LIPOSOMAL AMPHOTERICIN B (Ambisome®) FOLLOWED BY MICAFUNGIN (Mycamine®)

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Invasive mold infections (IMI) have been associated with significant infectious related mortality post AlloSCT (Mehta et al ASBMT, 2010). We have previously demonstrated the safety and efficacy of prophylactic liposomal amphotericin B (AMB) for 100 days post AlloSCT in pediatric recipients (Roman/Cairo et al PBC, 2008). Although AMB is effective for prophylaxis against IMI post AlloSCT, its association with nephrotoxicity and infusion related reactions results in its discontinuation in > 10% of patients. Micafungin, an echinocandin has been shown to be efficacious against both Candida spp and Aspergillus spp with minimum toxicity and is now approved for use as prophylaxis against invasive fungal infections in patients undergoing AlloSCT. (Pappas et al, 2009).

Methods: We conducted a prospective trial of administering prophylactic AMB (3mg/kg/day) IV from d 0-44 then transitioning to Micafungin (1mg/kg/day) IV at d 45 until d 100 if < grade II AGVHD at d +45. AGVHD prophylaxis were tacrolimus and mycophenolate mofetil (n = 34) as we have previously described (Bhatia/Cairo et al BBMT, 2009). Those who received CD-34 selected PBSC (T-depleted) received tacrolimus only (n = 15). Treatment success was defined as prevention of IMI prior to day +100 post AlloSCT.

Result: Median age: 8 yrs (2mo-23yr) Sex:14F, 35M Diagnoses:7ALL, 9AML, 6NHL, 1NBL, 6SAA, 1beta-Thal, 1MDS, 9SCD, 1FA, 1ALD, 2SCID, 1PNH, 1Atypical Wolmans, 3HLH. There were 17CB donors (15-unrelated, 2-related), 16PBSC (15-unrelated, 1-related), 13RBM and 3URBM. The probability of developing ≥ grade II acute GVHD and extensive chronic GVHD was 12.2% and 6%, respectively. There were no documented IMI within 100 days post transplantation. There were 7 documented invasive candida infections (ICI). 4 ICI occurred while on AMB prior to switching to Micafungin, (mean of 21 days post AlloSCT), all infections resolved in this cohort, the other 2 ICI occurred after switching to Micafungin (mean of 30 days after switching) with one death due to ICI. There were no reported side effects attributable to Micafungin or discontinuation due to toxicity.

Conclusion: AlloSCT recipients are at high risk for both ICI and IMI. Our preliminary data suggests that prophylaxis of AMB (D 0-44) and Micafungin (D 45-100) during the first 100 days post AlloSCT is both safe and efficacious in preventing IMI. Larger randomized studies are still needed to compare this combination to other standard antifungal prophylaxis regimens.

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THE USE OF INTRAVENOUS ANTIBIOTICS AT THE ONSET OF NEUTROPENIA IN PATIENTS RECEIVING HEMATOPOIETIC STEM CELL TRANSPLANTS: A "PRE-EMPTIVE" STRATEGY

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Background: Hematopoietic Stem Cell Transplant (HSCT) recipients are at risk for fatal bacterial infections during the engraftment period. Empirical antibiotic(s) at the onset of febrile neutropenia remain the standard of care. HSCT recipients began receiving intravenous once daily ceftriaxone at the onset of neutropenia (neutrophils < 1.0) regardless of fever as part of The Ottawa Hospital Blood and Marrow Outpatient Programme policy from Jan 2009; "pre-emptive" approach. We examined the impact of this policy on HSCT recipient outcomes.

Methods: A retrospective "before-after" study was conducted to compare 2 cohorts [Jan 2008 - Dec 2008 (Empiric strategy) vs. Jan 2009 - Dec 2009 (Pre-emptive strategy)] of patients receiving HSCT. Baseline characteristics between the groups were compared with 2 sample tests. Categorical variables and continuous variables were compared using Chi-squared and Wilcoxan rank-sum tests respectively.

Results: There were 238 HSCTs performed between Jan 2008 and Dec 2009 with 127 and 111 in the earlier and later cohorts respectively. Baseline characteristics between the cohorts were similar. Infection related mortality at 100 days after HSCT and during the engraftment period were similar with a pre-emptive strategy compared to an empiric strategy (7.2% vs 10.2%; p = 0.41 and 3.6% vs 7.1%; p = 0.24) respectively. Further, there were no differences in ICU admissions or length of hospital stay. Both microbiologically (MDI) and clinically documented infections (CDI) were reduced (11.7% vs 29.1%;p = 0.001 and 18.2% vs33.9%;p = 0.007) with the pre-emptive strategy compared with an empiric strategy. Importantly, recipients of autologous HSCT appear to have a lower infection related mortality and reduced infection related ICU admissions during the engraftment period with the pre-emptive strategy compared to an empiric strategy (0% vs 6.8%; p = 0.03 and 2.9% vs 12.2% p = 0.04). The need for escalation of antimicrobial treatments, resistance pattern of MDIs and cost of antimicrobial treatment were not different between the two groups.

Conclusions: The use of once daily intravenous ceftriaxone at the onset of neutropenia in patients receiving HSCT is safe and effective particularly in patients receiving autologous HSCT. Further studies are warranted to study the impact of this "pre-emptive" strategy.

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THE USE OF PSYCHOTROPIC MEDICATIONS IN PEDIATRIC STEM CELL TRANSPLANT PATIENTS

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The use of psychotropic medications during and following pediatric hematopoietic stem cell transplant (HSCT) is not well described. We performed a retrospective review of the prescription of psychotropic medications during a two year period at our institution. We report the use of the following medications from admission to one year post-HSCT: fluoxetine, sertraline, fluvoxamine, citalopram, trazodone, clonazepam, methylphenidate, ziprazodone, apiprazole, risperidone, mirtazepine, bupropion, escitalopram, olanzepine, and paroxetine. During this period 130 patients had a total of 152 transplants. Seventeen patients (13.1%) were prescribed at least one of the medications investigated. The majority of patients (55.6%) were prescribed more than one medication. The medications used included: citalopram (55.6%), risperidone (27.8%), methylphenidate (27.8%), clonazepam (27.8%), trazodone (22.2%), mirtazepine (11.1%), escitalopram (5.6%), and bupropion (5.6%). The timing of the initial prescription of a psychotropic medication was prior to admission (47.1%), during the initial transplant admission (29.4%), and 3-6 months post-HSCT (23.5%). Anxiety was the most common indication for starting a medication (30.3%) followed by depression (18.2%), sleep disturbance (15.2%), mood stabilization (12.1%), fatigue (9%), and other indication (15.2%). The median duration of medication use was 116.4 days (range 3-374 days). Medications were discontinued prior to one year post-HSCT due to symptom improvement (38.5%), toxicity (7.7%), or patient refusal (11.5%). 34.6% were still on drug at one year post-HSCT and 7.7% died prior to one year while receiving psychotropic medication. The median age of patients who received psychotropic medications was 13.5 years (4-19.6 years) compared to 7.4 years (0.5-22 years) (p < 0.0001) in patient who did not receive medications. There was no significant difference in the sex, type of transplant, underlying diagnosis, or presence of graft-versus-host disease between the groups. Psychotropic medications are commonly prescribed in this group of pediatric HSCT patients particularly in adolescents and young adults. Further investigation is needed into the psychiatric needs of this high-risk population.

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USE OF PROCALCITONIN MEASUREMENTS TO DIAGNOSE INFECTION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS WITH FEVER

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Background: Increase of CRP, WBC, and inflammatory cytokines suggest the presence of inflammation but do not necessarily indicate