when compared to pts with normal NS (19.3±7.8 days, P = <.0001) and mildly compromised NS (19.5±8.8 days, P = <.0001).
Conclusions: Pts with a normal NS prior to transplantation, as defined by the VA-NSCS, have a superior survival rate than pts with compromised NS prior to APBSCT. Additional studies will be necessary to corroborate the value of the VA-NSCS in determining toxicity and outcome after APBSCT.

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BK VIRUS-ASSOCIATED HEMORRHAGIC CYSTITIS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS

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Background: BK Virus-associated hemorrhagic cystitis (BKHC) has emerged as a serious infection after HSCT, however data in children are limited.

Objective: To describe the clinical characteristics, treatment, and outcomes of BKHC in children after HSCT.
Patients and Methods: Retrospective review of medical records of children who underwent HSCT at Children's Medical Center Dallas from Jan 1, 2006 – July 31, 2011 with evidence of BKHC. Demographic, clinical, microbiologic, management, and outcome data was collected.
Results: 20 children (incidence 13%), 9 males, median age 11 y [range 5-18], developed BKHC a median of 15 days [-2 to 57] post autologous (1) and allogeneic (19) HSCT: MRD (6), MUD (6), MMUD (6), syngeneic (1) for ALL (7), AML (4), aplastic anemia (4), and other conditions (5). Conditioning included busulfan/cyclophosphamide/ATG (10), TBI/thiotepa/cyclophosphamide (9), & carboplatin, etoposide, melphalan (1). Only 8 (40%) patients had engrafted and 7 (35%) were receiving systemic corticosteroids at BKHC onset. 7 (35%) patients complained of dysuria; 15 (75%) had moderate to large blood on initial urinalysis, all had BK viruria, 14 (70%) had ≥ 10^6 BK copies/mL urine. 6 (30%) had BK viremia at HC onset, 16 (80%) developed viremia with median peak BK of 10, 850 copies/mL blood [439-1.5 million] on D+42 (7-91), resolving in 11/16 by D+76 [22-134]. There was no correlation between viruria and viremia at onset (Spearman R 0.41, p = 0.07). 8 (40%) had abnormal initial ultrasounds (5 echogenic debris/clot, 4 bladder wall thickening). Patients had grade 1 (4), 2 (6), 3 (4), and 4 (6) HC. 14 (70%) patients were already receiving fluoroquinolone prophylaxis at BKHC onset; 17 (85%) patients received Cidofovir at 1 mg/kg 3x/wk (11), 3mg/kg qwk (1), or 5mg/kg qwk (5) for a median of 62 days [1-119]. 6 (30%) patients developed renal insufficiency requiring CVVH, one patient developed Fanconi's syndrome; 2 (10%) had urological interventions for obstruction and bleeding. 7 children died from other causes. Concomitant infections included: bacteremia (5), candidemia (3), peritonitis (2), UTI (2), detectable CMV (5), EBV (2), and adenovirus (4) viremia.
Conclusions: Incidence of BKHC was high in our HSCT population, with most children presenting pre-engraftment. Though many had clinical and virological resolution, morbidity was not negligible. Additional data in pediatric BKHC after HSCT is needed to guide optimal treatment guidelines.

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SAFETY OF PROBIOTIC USAGE IN CHILDREN UNDERGOING HEMATOPOIETIC CELL TRANSPLANTATION (HCT): A PRELIMINARY REPORT

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Myeloablative chemotherapy is associated with prolonged periods of cachexia/anorexia, nausea/vomiting, mucositis, and compromised gut integrity (CGI). The toxicities associated with HCT often lead to prolonged periods of poor oral intake and may result in overt malnutrition. CGI decreases oral tolerance to foods, reduces QOL and functional status, delays the transition from the hospital to home setting, and increases the risk of the development of gut-derived infections. CGI may increase the risk of acute graft versus host disease. Probiotics have emerged as a possible therapeutic agent in preserving gut integrity. Probiotics can improve the gut dysbiosis, promote cell survival, improve barrier function, prevent adherence of pathogenic bacteria, and suppress proinflammatory cytokines. Clinical trials in adults receiving organ transplants have found that probiotics decrease the incidence of infection, decrease the duration of antibiotic use, and decrease the incidence of multiorgan failure and systemic inflammation. However, the safety and feasibility of probiotics has not been investigated among children and adolescents undergoing HCT. Our ongoing 30-patient trial aims to evaluate/investigate:

-Safety of orally administered *Lactobacillus plantarum* in children undergoing myeloablative HCT
-Feasibility of administering the probiotic
-Overall incidence of probiotic bacteremia
-Overall incidence of acute GVHD in patients who received probiotic

Lactobacillus plantarum (strains 299 and 299v; 1 x108 CFU/kg/day) was given orally or via enteral tube daily from Day -7 through Day + 14 to 7 children. No patients had probiotic bacteremia, 2/7 had non-lactobacillus bacteremia, 3/7 had C. diff in their stool and all patients survived through Day + 100. Compliance was excellent. There were no SAE's. One unexpected adverse event(AE), acute appendicitis, occurred on Day + 21; pathology showed a mixed, mostly gram-negative flora and the patient had *C.diff*. This AE was not considered to be attributable to lactobacillus administration. These preliminary results suggest that it is feasible to administer this probiotic and lactobacillus bacteremia has not been identified. There are no SAE's to date and no Grade 2-4 GVH by Day 28.

Table 1. Preliminary Findings

	Age in Years	Donor	Compliance	SAE	Non-lactobacillus bacteremia	C.diff by Day 28	GVH by Day 28
PT 1	2.11	UCB	91%	No	Yes	Yes	0
PT 2	3.7	MUD	100%	No	No	No	0
PT 3	17	MRD	100%	No	No	Yes	0
PT 4	8.5	MRD	100%	No	No	No	0
PT 5	4	MRD	100%	No	No	Yes	0
PT 6	8.5	UCB	100%	No	Yes	No	II
PT 7	3.1	MUD	91%	No	No	No	0

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LOWER BIOAVAILABILITY AND SHORTER HALF-LIFE OF VORICONAZOLE IN PEDIATRIC BMT PATIENTS

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Introduction: Voriconazole, a triazole antifungal agent with excellent oral bioavailability has been used for mold prophylaxis in transplant recipients. Lack of detailed pharmacokinetic information in the pediatric BMT setting has been an impediment to optimal dosing regimen of this agent in children.
Materials & Methods: Voriconazole pharmacokinetics (PK) profiles were evaluated in 20 allogeneic BMT patients. Mean age at transplant was 9.4 y (0.4-22 y); 12 females, 8 males; all whites. All patients received initial dose of 7 mg/kg twice daily; doses were adjusted to achieve C_{trough} ≥1 mcg/ml. For each patient, eight timed blood samples were collected on three occasions at steady-state: the first while on an oral dosing (d-10 to d+2), the second while on intravenous dosing (d+6 to d+26), and the third after switching to an oral dosing (d+19 to d+110). Voriconazole plasma concentrations were measured using HPLC. Pharmacokinetic analysis was performed using NONMEM.
Results: In 54 PK studies, the mean trough concentrations of voriconazole before (C_0) and at the end of dosing interval (C_{12}) were 1.3, and 1.2 ug/ml, respectively. Less than half of the voriconazole plasma concentrations (45.4%) were maintained within 1-6 mg/ml, while 46.2% were below 1mg/ml and 8.4% above 6mg/ml. Voriconazole concentrations normalized to dose (mean±SD, ng/mL/mg) were: C_0 0.006±0.008, C_{max} 0.031±0.022 and C_{12} 0.004 ±0.005 ug/ml. C_0 and C_{12} were similar and correlated well (r^2 = 0.88) indicating

achievement of steady state. The half life ($t_{1/2}$) of voriconazole was 5.09±5.15 hours. The dose normalized (per mg) AUC (mg*hr/ml) was 0.111±0.081. Voriconazole dose did not correlate with AUCo-∞ (r^2 = 0.028). There was a good correlation between AUCo-∞ and C_{trough} (r^2 = 0.94). Population estimates of bioavailability, clearance, apparent volume of the central compartment (Vc) and apparent volume of peripheral compartment (Vp) were 46.5%, 5.76L/hr, 19.4L and 58.8L.

Conclusions: The bioavailability of voriconazole was significantly lower in pediatric BMT patients than in non-transplant adult subjects. The $t_{1/2}$ at steady state tended to be lower than adult patients. Our study suggests that pediatric patients may require dosing higher than 7 mg/kg twice daily. The wide individual variability and the lack of correlation between dose and AUC support therapeutic monitoring of voriconazole and dose adjustments based on steady state blood levels.

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SAFETY AND EFFICACY OF INTRAVENOUS PENTAMIDINE IN CHILDREN AND ADOLESCENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Pneumocystis carnii pneumonia (PCP) is a potentially life-threatening but preventable infection that may occur after hematopoietic stem cell transplantation (HSCT). Although prophylaxis with trimethoprim-sulfamethoxazole has been shown to be effective in the prevention of PCP, the development of neutropenia limits its use in the early post-transplant period. Aerosolized pentamidine is a commonly used second line agent, but the need to have the drug administered via respiratory route may increase the risk of infection. Intravenous pentamidine has been used in the prevention of PCP in the post-transplant period, although there are few trials published in the literature evaluating its safety and efficacy. A recent series studying the use of intravenous pentamidine as secondary prophylaxis in children with cancer receiving conventional chemotherapy reported a breakthrough rate of 1.3%. We evaluated the overall efficacy of intravenous pentamidine, toxicity profile, and overall impact in the prevention of PCP in HSCT recipients.

Patients and Methods: Retrospective review of medical records of children who underwent HSCT from Jan 1, 2005 – October 1, 2011 who received intravenous pentamidine as first line PCP prophylaxis initiated at admission. Demographic, clinical, microbiologic, management, and outcome data was collected.

Results: 170 consecutive pediatric patients were given intravenous pentamidine before myeloablation and then every 28 days until the subject was 6 months post-HSCT, had stable neutrophil recovery (ANC >1000 without growth factor support), had discontinued immunosuppression and did not have evidence of chronic graft versus host disease.). No cases of PCP were seen in this cohort. Ten (6%) had a grade I side effect of nausea/vomiting requiring slower infusion time and 2 (1%) had a grade IV reaction with anaphylaxis and hypotension requiring transfer to the intensive care unit for management.

Conclusions: Our pediatric HSCT patients receiving pentamidine had no episodes of breakthrough PCP, and the incidence of side effects was low. Given the potential neutropenic effects of trimethoprim-sulfamethoxazole, compliance with drug administration, and inferior efficacy of other PCP prophylactic medications, intravenous pentamidine should be considered as first line therapy in the prevention of PCP in children undergoing HSCT.

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IDENTIFYING RELIGIOUS/SPIRITUAL (R/S) PERSPECTIVES OF ADOLESCENTS AND YOUNG ADULTS RECEIVING BLOOD AND MARROW TRANSPLANT: A QUALITATIVE STUDY

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Bone marrow transplant (BMT) or hematopoietic stem-cell transplantation (HSCT) are difficult treatments for life threatening illnesses; the emotional stress experienced by patients of any age is high. Religion/spirituality (R/S) is commonly used by Americans, including adolescents, to cope. Religion can be described as a personal or communal system of religious attitudes, practices and beliefs. Spirituality is generally described as the feelings, experiences, and practices that arise from the search for the sacred or God. We hypothesize that the experience of illness and BMT would affect what adolescents and young adults (A/YA) believe about R/S and their way of using faith to make meaning and to cope. The specific aim was to understand from the patients' perspective how they use R/S and how their R/S changes in the course of their BMT experience. Our goal is to develop a conceptual model of how R/S constructs operate in the experiences of A/YA undergoing BMT and also begin to develop an empirically-based pastoral care intervention. This is a qualitative study of R/S in persons aged 13-29 years undergoing HSCT or BMT. Semi-structured interviews are completed in the first 100 days post-transplant and at 1- year post-transplant. Interviews are audiotaped, transcribed, and coded for common themes using grounded theory methodology. Seven interviews (50% of those eligible) have been completed. Preliminary analysis shows that prayer is the most commonly used R/S practice, and that the majority of participants believe that their illnesses are "part of God's plan". Without the development of evidence for clinical practice, chaplains may offer care which may or may not be effective. We will propose a conceptual model suitable for future testing, and ultimately contribute to a better psycho- social- and spiritual- outcomes for A/YA undergoing BMT or HSCT.

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DRUG INTERACTION BETWEEN ORAL VORICONAZOLE AND ORAL CALCINEURIN INHIBITOR AND ITS RELATIONSHIP WITH BLOOD CONCENTRATION OF VORICONAZOLE IN RECIPIENTS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Drug interaction between calcineurin inhibitors (cyclosporine A (CsA) and tacrolimus) and voriconazole is well known. However, it has yet to be fully evaluated in the setting of hematopoietic stem cell transplantation (HSCT). We have previously shown a wide variability in the drug interaction between voriconazole and calcineurin inhibitors in HSCT recipients, which led to a conclusion that uniform reduction of the dose of calcineurin inhibitors was not recommended on initiating voriconazole. However, in that study, the route of administration of both drugs was not taken into consideration. In the present study, the magnitude of drug interaction between oral voriconazole and oral CsA was examined in HSCT recipients, and its relation with the blood concentration of voriconazole was also evaluated.

Patients and Methods: Nineteen recipients of allogeneic HSCT who had already been on a steady dose of oral CsA, and were started on oral voriconazole (200 mg per body every 12 h) for the treatment or prophylaxis of fungal infection could be evaluated. The concentration/dose (C/D; (ng/ml)/(mg/kg)) ratio of CsA was calculated 7–10 days after initiating voriconazole when the increased blood levels of calcineurin inhibitors had stabilized. The plasma level of voriconazole was measure by high-performance liquid chromatography.

Results: The median C/D ratio of CsA significantly increased to 113.7 (ng/ml)/(mg/kg) (range, 62.4-189.5) after initiating voriconazole administration as compared with that before (63.1 (range, 41.1-189.0): $P<0.001$). Median increased rate of C/D ratios were 83.0% with a range of 0.3% to 224.7%. The plasma level of voriconazole on the day of evaluating C/D ratio was 1.98±0.84 mg/ml. The increased rate of C/D ratio of tacrolimus did not correlate with the plasma level of voriconazole (r = -0.17, P = 0.50).

Conclusion: The magnitude of the drug interaction between oral CsA and oral voriconazole demonstrates a wide variability, whose increased rate of C/D ratio ranged between 0.3% and over 200%. This wide variability could not be explained by the bioavailability of voriconazole. The mechanisms of this variability should be explored in a future study.