IL-2/GM-CSF except for mild flu-like symptoms. The table below summarizes quantitative analysis of immune activation. Values represent means +/- standard error at day 0 (first day of GM-CSF), day 8 (prior to start of IL-2) and day 14 (last day of IL-2 and GM-CSF). P-values are based on paired t-test analysis of day 8 versus day 0 and day 14 versus day 0, respectively. Flow cytometric analysis showed an increase in the numbers of T-lymphocytes (CD3) and T-cell subsets (CD3/CD8 and CD3/CD4) as well as an increase in natural killer cells (CD16/56). Although no differences were seen in the number of dendritic cell subsets, DC1/DC2 ratios decreased with the administration of GM-CSF/IL-2. Limited (n = 4) CD4/FoxP3 analysis did not show change in absolute numbers with administration of GM-CSF/IL-2 (data not shown). In conclusion, cytokine therapy with IL-2/GM-CSF is well tolerated and is an alternative to DLI for relapse after ASCT. Flow cytometry analysis demonstrated a quantitative increase in immune effector cells and polarization to DC2.

Flow Cytometry of Immune Effector Cells

	D0 (Mean ± SE)	D8 (Mean ± SE)	D14 (Mean ± SE)	P-Value (Day 8–0)	P-Value (Day 14–0)
CD3 (K/uL)	309 ± 117	535 ± 103	1306 ± 403	0.034	0.027
CD3/CD8 (K/uL)	94 ± 42	174 ± 33	325 ± 90	0.021	0.029
CD3/CD4 (K/uL)	309 ± 117	404 ± 102	977 ± 310	0.249	0.045
CD16/CD56 (K/uL)	124 ± 60	404 ± 110	496 ± 162	0.029	0.044
CD19 (K/uL)	68 ± 39	89 ± 36	116 ± 31	0.183	0.044
Tot. Lymphs (K/uL)	488 ± 167	942 ± 160	2353 ± 532	0.016	0.013
CD11(DC1) (K/uL)	97 ± 60	46 ± 32	33 ± 27	0.108	0.101
CD123(DC2) (K/uL)	32 ± 7	40 ± 16	45 ± 36	0.694	0.628
DC1/DC2	2.77 ± 1.26	0.68 ± 0.35	0.61 ± 0.07		

SE = Standard Error; DC= dendritic cells.

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WHERE TO BIOPSY IN THE GASTROINTESTINAL (GI) TRACT TO DIAGNOSE ACUTE GRAFT VERSUS HOST DISEASE (AGVHD) IN PEDIATRIC ALLOGENEIC STEM CELL TRANSPLANT RECIPIENTS (AlloSCT)

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Background & Aims: Despite therapeutic advances, GI AGVHD continues to be a serious threat after alloSCT contributing to significant morbidity and mortality (Yacoub-Agha, et al, Transplantation 2004). GI endoscopy, although critical to establishing early diagnosis and grading of AGVHD, poses additional risks such as bleeding and perforation to already immunocompromised patients. The objective of this study was to determine if upper GI endoscopy (ED) with duodenum biopsy (Bx) adds diagnostic accuracy to lower GI ED and colon biopsy in pediatric alloSCT recipients. **Methods:** We performed a retrospective review of pediatric alloSCT recipients who underwent upper (UE) and lower (LE) GI ED at Morgan Stanley Children's Hospital-New York Presbyterian between 2001 and 2005. Biopsies were evaluated by a gastrointestinal pathologist blinded to clinical data to correlate biopsy sites with histological findings of GI AGVHD. To examine which sites were more likely to be diagnostic of AGVHD, six pairwise comparisons were made between different sites, using the McNemar Test with Bonferroni correction so that $p < 0.008$ (=0.05/6) represents statistical significance. **Results:** We evaluated 50 patients (age range 0.8 to 17.6 yr, mean 7.6 yr; M 27, F 23) 24 to 100 days post alloSCT suspected of AGVHD who underwent both upper and lower GI ED. The number of Bx sites per patient ranged from 4 to 10, median 7. For upper endoscopy, 48 patients had both duodenal and stomach biopsies, the duodenum was more likely to be positive than stomach, OR 3.7 ($p = 0.005$). For lower endoscopy cases, there were no significant differences in proportion of positive biopsies between ascending and sigmoid, sigmoid and transverse, or left versus right colon. However, comparing LE to UE, left colon was significantly more likely to be positive than duodenum, OR 12.0 ($p = 0.006$). There were 12 cases where the left colon was positive and duodenum negative and only 1 case where the reverse was true. **Conclusions:** Overall, duodenum and colon are most likely sites to be positive for GI AGVHD. Left-sided colonoscopy and left colon biopsy are more sensitive to detect AGVHD compared to upper endoscopy and gastric and duodenal biopsies. Eliminating concomitant upper endoscopy and biopsies if a lower endoscopy is performed could potentially reduce morbidity in pediatric allograft recipients. However, if upper endoscopy is indicated, duodenal biopsies yield a more accurate diagnosis than gastric biopsies.

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THE PHARMACODYNAMIC ANALYSIS BETWEEN CYCLOSPORINE A (CsA) AND CYTOKINE PROFILES OF CD4+ T LYMPHOCYTES FOR THE DEVELOPMENT OF OPTIMIZED IMMUNOSUPPRESSIVE THERAPY WITH CsA AFTER UNRELATED CORD BLOOD TRANSPLANTATION (CBT)

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Although unrelated cord blood transplantation (CBT) is increasing in number, the optimized immunosuppressive therapy for prevention of graft versus host disease (GVHD) has not been established. Cyclosporine A (CsA) is the most common immunosuppressant used for GVHD prophylaxis and individualization among types of stem cell source by using therapeutic drug monitoring (TDM) is essential to optimize pharmacotherapy. Cord blood lymphocytes are naïve and most of CBT are carried out with a human leukocyte antigen (HLA)-mismatched combination especially in adults. Our retrospective analysis showed CsA can be tapered earlier for recipients of CBT than for those of BMT. To optimize CsA administration in CBT, we analyzed proportion of IL-2 producing cells among CD4+ T lymphocytes using multi-color flow cytometric analysis before and after CsA administration. We analyzed 55 peripheral blood samples from 6 allogeneic BMT recipients as controls and 104 peripheral blood samples from 7 CBT recipients. Cells were cultured in the presence of phorbol 12-myristate 13-acetate, ionomycin, and monensin at 37°C for 4 hrs and then stained for surface markers and intracytoplasmic IL-2. Blood CsA levels were simultaneously measured. We found that the level of IL-2 production in CD4+ T lymphocytes was inversely proportional to blood CsA levels for both BMT and CBT. IL-2 production in CD4+ T lymphocytes of cord blood recipients can be inhibited by relatively lower CsA concentration compared with that of bone marrow recipients. To our most interest, there was dramatic difference in required blood CsA level for inhibition of IL-2 production by days after transplantation (e.g. before and after day45) in recipients of CBT, while there was no difference by days after transplantation in recipients of BMT. This finding can explain why earlier tapering of CsA is possible for cord blood recipients. Further analysis is needed to optimize blood CsA level on different days after CBT for GVHD prophylaxis.

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INCIDENCE AND RISK FACTORS FOR CHRONIC GRAFT-VERSUS-HOST DISEASE (cGVHD) AFTER CORD BLOOD TRANSPLANTATION (CBT)

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Objective: To evaluate the impact of patient and transplant characteristics on the incidence of cGVHD after CBT. **Methods:** Retrospective study of all CBT performed at our institution between 1996 and 2007, excluding primary graft failure cases. 114 patients were analyzed. All had high-risk hematologic malignancies; 59% were in complete remission or chronic phase at transplantation. Median age was 37 years (range 18–67) in the adult group (n = 61) and 7 years (range 0.5–17) in the pediatric group (n = 53).