chimerism. Acute graft-versus-host disease occurred in 9 subjects (2 with grade I, 6 with grade II, 1 with grade III). Chronic graft-versus-host disease occurred in 8 subjects (5 limited, 3 extensive). The overall survival was 66% with a median follow up of 32 months. Four subjects died due to relapse of primary disease (2 leukemia subjects and 1 Omenn syndrome) and acinetobacter septicaemia (1). In conclusion, among malignant diseases, only the patient with chronic myeloid leukemia survived. Chimerism monitoring is essential for post-transplant management of persistent detectable recipient hematopoietic cells. The encouraging result in nonmalignant condition suggests the benefit of reduced transplant related toxicity and satisfactory engraftment.

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ALLOGENEIC BLOOD AND MARROW TRANSPLANTATION IN THALASSEMIA MAJOR CLASS 3: AN EXPERIENCE OF IRAN

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Objective: Our aim for this study was to describe the outcome of blood and marrow transplantation in patients with class 3 thalassemia major. **Method and patients:** Since December 1992 till October 2002, forty-three patients with thalassemia class 3 received blood and marrow transplantation from their HLA-identical siblings. Median age at time of transplantation was 8 years (age range = 3-17), Male/Female = 24/19. Twenty-eight patients received bone marrow and fifteen patients received peripheral blood stem cell transplantation. Conditioning regimen was cyclophosphamide 40 mg/kg/day (from day–5 to -1) and busulfan 4 mg/kg/day (from day –9 to -6). GVHD prophylaxis regimen was cyclosporine A 3mg/kg /day/iv (from day –2 to +5) then 12.5 mg/kg/day/po (from day +5) and methotrexate 10mg/m^2 (day +1), 6mg/m^2 (days +3, +6). **Results:** Median time of absolute neutrophil count $\geq 0.5 \times 10^9$ /L was on day +20 and Median time of platelet recovery $\geq 20 \times 10^9$ /L was on day +25. At present 34 out of 43 are alive and 9 patients died due to aGVHD, cGVHD, rejection, veno-occlusive disease, infection and the others. Thirty-two patients (74.4%) developed aGVHD (grade I = 9, grade II = 7, grade III = 11, grade IV = 5). Seventeen patients (39.5%) developed cGVHD (limited = 5, extensive = 12). Eight year disease free survival in class 3 and 2 were 71% and 63%, respectively (p = 0.3).Eight year overall survival in class 3 and 2 were 78% and 79%, respectively (p = 0.00). **Conclusion:** According to this study, for an acceptable outcome in thalassemia class3. We need better conditioning and GVHD prophylaxis regimens to decrease cardiopulmonary and liver complications. The results of blood and marrow transplantation showed that it is better than supportive therapy such as transfusion and desferal therapy.

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CELIAC DISEASE TRANSMITTED BY CORD BLOOD STEM CELL TRANSPLANTATION (CBST)

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Either BMT or CBST could transmit immune associated diseases such as diabetes mellitus, immune thrombocytopenic purpura and complex autoimmune diseases with Evan's syndrome and transverse myelitis. We observed the occurrence of Celiac disease a year following cord blood stem cell transplantation (CBST) for acute myelogenous leukemia (AML-FAB M2) in complete second remission (CR-2). Patient had not suffered celiac disease prior to CBST and none of family member suffered too. The cord donor was HLA-identical unrelated male donor with HLA types: A3, B7 (w6), DR (B1), DR (B5), HLA DQ A1.0501 and DQ B1.0201 alleles family history was not available for celiac disease. CBST complicated with grade 2 skin Graft versus Host Disease (GVHD), which responded to steroid therapy, a year post transplantation she developed persistent mucous diarrhea with tinge of blood associated with abdominal cramps, work up of infectious causes and studies for CMV enteritis were negative, colonsocopy revealed no GVHD, gastrointestinal symptoms persist and failed to respond to steroid and prograf therapy, duodenal and jejunal biopsy revealed subtotal villous atrophy with cryptic hyperplasia which was suggestive of celiac disease, in addition to, antigliadin IgA, IgG, reticulin IgA, and Endomysial IgA antibodies were elevated. She responded well to gluten-free diet and was symptom-free. Possible causes of her autoimmune illness were 1) transference of autoimmune cells from the donor and 2) patient's predisposition to autoimmune disease secondary to an dysregulated immune system because of myeloablative therapy. Celiac disease is intolerance to certain cereal grains causing small bowel villous atrophy and thus malabsorption. Specifically, the gliadin component of wheat, and the prolamin component of rye and barley are implicated in causing disease by binding to HLA-II class molecules in APC and hence elicit an immune reaction. Celiac disease is associated with an increased risk for non-Hodgkin lymphoma, especially of T-cell type. The propensity to develop T-cell non-Hodgkin lymphoma and transmission of celiac disease by CBST support T cell concept in celiac disease. Celiac disease is strongly associated with some HLA-class II types, including DQA1.0501, and DQB1.0201, in conjunction with the haplotypes A30, B18, DR3, DRw52, and DQ2. Autoimmune enteropathy should be considered in HLA-high risk patients with persistent diarrhea post Stem Cell Transplantation.

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A NOVEL CONDITIONING REGIMEN OF IMMUNE SUPPRESSION WITH CAMPATH-1H, FLUDARABINE AND MELPHALAN IN STEM CELL TRANSPLANTATION FOR NON-MALIGNANT DISORDERS

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Successful allogeneic stem cell transplantation (SCT) benefits many non-malignant disorders. Factors limiting successful transplantation for these conditions are lack of HLA matched donors, toxicities of conditioning, graft rejection, and graft versus host disease (GVHD). Based on the hypothesis that intense immunosuppression targeted at host lymphocytes would allow successful engraftment of stem cells irrespective of source, we used campath-1H, fludarabine and melphalan in a novel fashion as conditioning in a pilot transplant trial for non-malignant disorders. Campath-1H (48 mg total) was administered once daily over 3 days (-21, -20 and -19), fludarabine (30 mg/m^2/day) for 5 days (-8 to -4), and melphalan (140mg/m^2) on day -3. The timing of campath-1H was designed to deplete recipient lymphocytes and macrophages, without prolonged immunosuppression of the graft. GVHD prophylaxis was CSA or FK506 (tapered after 3 months), steroids (1 mg/kg) from day -7 (tapered after 1 month), and short course methotrexate (day +1 [10 mg/m^2], +3 and +6 [7.5 mg/m^2] except in cord transplants). Primary end points of the study were engraftment and treatment related mortality (TRM) at 100 days. The regime was tolerated well. The first 10 recipients are described in table 1. Several recipients with BM failure syndromes were transplanted after several platelet and PRBC transfusions, putting them at high risk for graft rejection. Median follow up was 4 months; range 1-18m. Neutrophils (ANC >500)/cu.mm) engrafted at 12 days (range 8-20d); platelets (>50K/cu mm) engrafted at 22 days (21-30d). Serial immune reconstitution studies revealed profound lymphopenia at 1 month (ALC; NK; T and B cells), recovering after the third month, normalizing at 9 months. Five are off steroids; 2 are off all immunosuppression. All had stable or improved disease parameters. Post transplant complications were predominantly infections. All CMV + recipients (n = 4) reactivated CMV in < 30 days but responded to preemptive therapy. Others included HHV6 (2) and bacterial (7). One UCB recipient developed grade 3 toxicity due to CMV disease and TTP, and died

on day +112. One recipient is pregnant 9 months post transplant. In summary, this regimen is well tolerated, without increased TRM or GVHD, and supports engraftment with varied stem cell sources despite risk factors for graft rejection. Lymphopenia in the early post transplant period requires close vigilance and early intervention for infection.

Table.

Disease	Age (years)	Source	Cell dose (TNC/kg)	Engraftment	GVHD
Hurler's	1.5	BM	3.26 × 10 (8)	donor	0
Langerhan's	19	S BM	3.38 × 10 (8)	donor	Gr1-sk
Thalassemia	10	S BM	2.2 × 10 (8)	BM-d;PB-mixed	0
Evan's	12	UCB4/6	1.3 × 10 (7)	donor	0
Aplastic anemia	12	S PB	1.9 × 10 (10)	donor	Gr1-sk
Adrenoleukodystrophy	3	S PB	4.58 × 10 (8)	donor	0
Sickle cell anemia	2	S BM	3.3 × 10 (8)	donor	0
Aplastic anemia	20	S BM 5/6	4.2 × 10 (8)	NA	0
Hemophagocytosis	3	S BM	3.7 × 10 (8)	NA	0
Aplastic anemia	32	UCB5/6	2.02 × 10 (7)	NA	0

sk = skin; s = sibling; d = donor; NA = Not available.

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FREQUENCY AND MAGNITUDE OF DOSE ADJUSTMENT OF IV BUSULFAN IN TARGETED DOSING STRATEGY FOR PEDIATRIC ALLOGENEIC TRANSPLANTATION

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Busulfan is an important therapuetic agent in pediatric allogeneic transplantation. The recent introduction of IV busulfan (IV Busulfex®, ESPpharma) has descreased the intra-and interpatient dose variations associated with oral absorption and allows for targeted therapy. Children have increased drug clearance and varying degrees of hepatic function both developmentally and associated with the underlying disorders for which they are being treated. Because of this variability, first dose pharmacokinetics were perfomed on all of our patients to ensure the targeted AUC was achieved. In a series of 85 consecutive children undergoing allogeneic transplant at Methodist Children's Hospital/Texas Transplant Institute from June 2001 to October 2003, 45 children received myeloablative doses of busulfan (0.8 mg/kg for patients 3-10 kgs; 1 mg/kg for patients > 10 kgs till age 4 yrs; 0.8 mg/kg for patients > 4 yrs given every 6 hours for 16 doses) as part of a busulfan/cyclophosphamide, busulfan/melphalan or busulfan/fludarabine preparative regimen. 42/45 patients had their actual weight used for dosing calculations. Adjusted IBW was used in 3 patients. All patients received dilantin for seizure prophylaxis. First dose pharmcokinetics were performed by the Clinical Pharmokinetics Lab at Seattle Cancer Care Alliance, targetting an AUC of 900-1300 umol.min, with dose adjustments done starting with dose 7, if needed. Donor source was matched sibling donor bone marrow or cord blood in 10 and unrelated donor sources in 35 (2 marrow and 33 mismatched umbilical cord units). The median age was 4.7 yrs (range 1 month to 17 years). Patients underwent transplant for a variety of conditions: 12 AML, 5 CML, 1 JMML, 9 ALL, 1 lymphoma, 3 HLH, 10 primary immunodefiencies, 4 hematology disorders. No patients developed VOD. 32/33 patients of patients who received a fully myeloabalative preparative regimen engrafted. A targeted AUC (900-1300 umoles.min) was achieved with initial dosing in 50% of the patients. However, many children required dose adjustment to achieve the targeted AUC, mostly dose escalation (see table). Given the variability of metabolism in children, first dose pharmacokintics are recommended. Additionally, the starting dose in infants is lower than the currently recommended dose.

Table.

Age/ Weight	Starting Dose (mg/kg)	AUC μmol · min: Median (range)	Final Dosing (mg/kg): Median (range)	Percent of Patients Requiring Dose Adjustment	Dose Increased/ Dose Decreased
3-10 kg (n = 12)	0.8	1167 (825-1869)	0.93 (0.67-1.25)	50%-6/12 pts	4 ↑ /2 ↓
10 kg-4 years (n = 11)	1	1142 (908-1518)	1 (0.76-1.25)	27%-3/11	2 ↑ /1 ↓
>4 years (n = 22)	0.8	1089 (620-1827)	0.82 (0.57-1.25)	65%-15/23	11 ↑ /4 ↓

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LARGE VOLUME LEUKAPHERESIS FOR AUTOLOGOUS PERIPHERAL BLOOD STEM CELL COLLECTION IN CHILDREN WEIGHTING LESS THAN 25 KG

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Peripheral blood stem cells (PBSC) are the most frequent source of hematopoietic stem cells used to rescue patients from high-dose chemotherapy. The theoretical advantages of PBSC collections are decreased tumor contamination and faster hematological engraftment after the transplant. Small children are usually not eligible for such protocols due to little experience of most Hematotherapy teams, poor venous access and concern with a large extracorporeal volume. In large volume leukapheresis (LVL) three or more blood volumes are processed in the same procedure. LVL is also warranted in pediatric patients to decrease the number of procedures and potentially decrease tumor contamination. Twenty-five patients underwent LVL using a Cobe Spectra® cell separator between 2000-2003. All had the circuit primed with irradiated, filtered and resuspended red blood cells. All patients needed a central venous catheter placed for the procedure. During the procedure, the patients received continuous IV infusion with 10% calcium gluconate 2cc/kg, 10% magnesium sulfate 1 cc/kg, 19.1% potassium chloride 0.3 mEq/kg/hr over four hours to decrease the adverse effects of ADC infusion. They had vital signs, EKG and O2 saturation continuously monitored. Patients were 13M:12F with a median age of 3.5 years-of-age (1-10). The median weight was 14 kg (8-24). Underlying diagnoses were neuroblastoma (21), germ cell tumors (2), non-Hodgkin's lymphoma (1) and alveolar soft tissue sarcoma (1). The median number of procedures was 2 (1-4). The median total nucleated cell count/kg was 16 (5-66) and CD34+/kg 6 (0.6-71). In conclusion, LVL can be safely performed in small children if vital signs are adequately monitored and electrolytes are replaced and promptly corrected.

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AUTOLOGOUS STEM CELL TRANSPLANTATION FOR THE TREATMENT OF PEDIATRIC SOLID TUMORS IN BRAZIL

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High-dose chemotherapy and autologous stem cell rescue can be used in the treatment of poor prognosis responsive pediatric solid tumors. Our objective is to describe the experience of four Brazilian hematopoietic stem cell transplantation (HSCT) centers in