serve as a demonstration that cord blood cells can differentiate into non-hematopoietic tissues.

All children were prepared for transplant with myeloablative chemotherapy consisting of busulfan, cyclophosphamide and anti-thymocyte globulin. Prophylaxis against GvHD was administered with cyclosporine and methylprednisolone. Supportive care was provided with IVIG, G-CSF, low dose heparin for VOD prophylaxis, leukocyte depleted and irradiated PRBC and platelet transfusions, total parenteral nutrition, prophylactic antiviral and antifungal antibiotics and empiric antibiotic therapy for fever. Thirty five young children with Hurler syndrome (MPS I) were transplanted with partially HLA mismatched unrelated donor umbilical cord blood over the past 8 years. All had the severe phenotype. Neutrophil (ANC 500/μL) and platelet (>50k/μL) engraftment occurred in a median of 20 and 63 days respectively. Moderate to severe acute GvHD occurred in 28 % of patients. Extensive chronic GvHD was not seen. Twelve percent of patients had serious events, graft rejection (n = 1), infectious deaths (n = 3), toxic death (n = 1, hyperammonemia). All other patients (87%) are surviving event-free for a median greater than 3 years. All surviving children remain full donor chimeras and have shown increasing velocities of gains of neurocognitive functions. Skeletal growth improved with only 4/11 children with severe kyphosis requiring orthopedic surgery post transplantation therapy. No child developed clinical cardiac disease and corneal clouding improved in all.

Additional children (60) with lysosomal storage diseases including metachromatic leukodystrophy, adrenoleukodystrophy and globoid leukodystrophy (Krabbe disease) have been transplanted with unrelated donor umbilical cord blood over the past 9 years. In asymptomatic children, disease was arrested before the onset of neurologic dysfunction. In symptomatic children disease progression was arrested within 6-9 months of the transplant procedure. In a child with advanced Krabbe disease who died 1 year post transplant, engraftment of donor cells was noted in the brain. Differentiation to oligodendrocytes was demonstrated in vitro and subsequently, in vivo. In a child with MPS III (Sanfilippo syndrome), donor cells differentiated into cardiac myocytes in the heart 6 months post transplant.

These studies suggest that cord blood is capable of transdifferentiation into non-hematopoietic lineages. Further studies are needed to fully define the potential of these cells for cellular therapies and tissue repair.

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UNRELATED DONOR CORD BLOOD TRANSPLANTATION FOR CHILDREN WITH HEMATOLOGICAL MALIGNANCIES

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Cord blood (CB) contains a large amount of hematopoietic progenitors and over the last decade has been largely employed to transplant children with either malignant or non-malignant disorders. Advantages related to the use of CB cells are represented by the low risk of acute and chronic graft-versus-host disease (GVHD), prompt availability of this source of hematopoietic progenitors, which shortens the time needed to locate a suitable donor, and by the possibility of performing transplants in the presence of 1 or 2 HLA disparities in the donor/recipient pairs. Both these latter two factors can be relevant for treating children with malignancies, whose disease, often running an aggressive clinical course, might not allow an extended period of time for finding a suitable unrelated bone marrow donor. Hundreds of children with acute lymphoblastic or myeloid leukemia have received an allograft of unrelated CB cells. The experience derived from these patients has demonstrated that results achieved with this type of transplant are substantially comparable to those obtained in children given bone marrow transplantation. In particular, the risk of leukemia recurrence is not increased after CB transplantation. Disease status at time of transplantation is the main factor influencing patient's outcome, patients transplanted in 1st-2nd remission being those with the best results. Both a higher transplant-related mortality and an increased risk of leukemia recurrence contribute to the worse outcome of patients given the allograft in more advanced disease. As most deaths occurring in children given CB transplantation are due to infectious complications (related to both delayed hematopoietic recovery and lack of adoptive transfer of memory T-cells) strategies able to accelerate both hematopoietic and immune reconstitution could widen the use of CB cells for transplantation.

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THE ROLE OF CORD BLOOD TRANSPLANTATION IN THALASSEMIA

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More than 20 years ago, the first successful cure of β-thalassemia major by bone marrow transplantation was reported. Since then, more than 1500 patients have been treated in this manner. In Pesaro Italy where more than 1000 patients have received marrow transplantation, the 20-year probability of thalassemia-free survival is approximately 70%. Updated results strongly suggest that improved outcomes across risk categories have occurred as effective supportive care and conditioning regimen modifications have been applied to this setting. As with other non-malignant conditions, the alternative of increasingly effective supportive care also impacts upon the decision to pursue transplantation, even when transplant outcomes are very good. Umbilical cord blood (UCB) transplantation, thus, must compare favorably to proven therapeutic alternatives before its use can be expanded. UCB is an attractive alternative to other stem cell sources due to its decreased incidence of graft-versus-host disease (GVHD) and rapid tempo of immunological reconstitution after transplantation. Initial results of UCB transplantation for thalassemia suggest that acceptable outcomes are possible if measures are taken to mitigate the risk of graft rejection. Among 44 patients with sickle cell disease or thalassemia who received augmented conditioning therapy, the event-free survival was 94% compared to 62% among those who received a standard combination of busulfan and cyclophosphamide, with or without horse anti-thymocyte globulin. These early results also support the importance of banking efforts to expand the collection of related and unrelated UCB units. The clinical experience of unrelated UCB transplantation for thalassemia remains very limited. New techniques to prevent GVHD and promote engraftment, coupled with refined donor selection criteria should expand the availability of transplantation for thalassemia major.

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RESULTS OF UNRELATED CORD BLOOD TRANSPLANT IN PATIENTS WITH BONE MARROW FAILURE SYNDROMES

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In Fanconi anemia (FA) patients without an HLA identical bone marrow donor, search for an unrelated cord blood donor is an option, however few results have been reported so far. In the Eurocord registry, we have analyzed 44 patients with FA receiving an unrelated cord blood transplant (UCBT). The median age was 7.7 years and median follow-up 20 months (8-83). At UCBT, the median number of neutrophils was 620/mm^3 and 13 patients had received more than 20 red blood cell transfusions. The cord blood was HLA mismatched in 37 patients (HLA-A and B by serology and DRB1 high resolution typing, 5/6 = 21, 4/6 = 12 and 3/6 = 3). The median number of nucleated cells (NC) at freezing was 5.5 $\times$ 10^7/kg and at infusion 4.7 $\times$ 10^7/kg. Eighteen patients received CY and irradiation based preparative regimens, 12 patients fludarabine (FLU) containing regimen, 6 CY alone and 8 other regimens. GVHD prophylaxis consisted of CSA and MTX (43%) or CsA alone (23%). Results: Neutrophil recovery at day 60 was 56% ± 8%. Two factors were associated with higher probability of neutrophil recovery (cell dose and number of HLA disparities). Acute GVHD (II-IV) was 23% ± 6% (grade II = 7%, III = 7%, IV = 11%) and chronic GVHD occurred in 4/21 patients at risk (19%). Two year survival was 36% ± 7%. In univariate analysis factors associated with better survival were negative CMV serology, NC at freezing or infused, higher neutrophil count at UCBT and FLU containing regimen. In multivariate analysis only two