Increase the quality of banked cord blood units without limiting HLA diversity: how cord blood banks could face this dilemma

We read with great interest the manuscript by Page and colleagues,[1] "Optimizing donor selection for public cord blood banking: influence of maternal, infant, and collection characteristics on cord blood unit quality." We fully agree that identification of donors' characteristics that correlate with higher cord blood unit (CBU) quality should guide operational strategies to increase the yield of high-quality banked CBUs. The suggestion that ethnicity may affect the proportion of collected CBUs with a high number of cells ignores another critical criterion for selection of CBUs by transplant programs, that is, HLA diversity. Focusing only on CBU cell content could thus result in a less diverse representation of HLA phenotypes in the inventory, because of the lower cellularity of CBUs obtained from non-Caucasian donors, which has already been described in the literature,[2-4] and is confirmed in this study.

Public cord blood banks operating in western countries have a high representation of CBUs obtained from women of Caucasian ancestry; they face the dilemma of trying to enrich HLA diversity through collection of new CBUs from women belonging to ethnic minorities, while maintaining a high cellularity of stored CBUs with the view of optimizing the proportion of released and transplanted CBUs. Our cord blood bank operating in the Marseilles metropolitan faces this issue: Marseilles is one of the oldest settlements in France and by its location on the Mediterranean shore has a long history of immigration from neighboring countries. Marseilles public and private birth clinics care for pregnant women from North, East, and Central Africa and Comoros as well as from Eastern Europe; currently, the probability of finding a 10/10 HLA-matched unrelated donor for patients with African ancestry who are candidates for allogeneic transplantation is very low (10%).[5,6] As a consequence, the Marseilles Cord Blood Bank established a strategy and deliberately partnered with one of the Marseilles University Hospital birth clinic that cares for a culturally, sociologically, and ethnically diverse population of pregnant women. Whether this strategy increases HLA diversity and truly offers new allograft possibilities for patients remains to be demonstrated. In accordance with the legislation of each country, the systematic collection of geographical origin of the donor's parents or differential algorithms taking into account the absence or presence of HLA antigens or haplotypes in already registered CBUs may represent an avenue for the future of cord blood banking. Preliminary evidence based on a still relatively low number of stored CBUs suggests, however, that the frequency of released and transplanted CBUs is not negatively affected (seven CBUs released from 493 stored at the time of writing; 1.42%).

Optimization of cord blood bank operations cannot be seen only in terms of productivity as measured by the ratio of validated CBUs to collected CBUs or release of CBUs to stored CBUs. Future evolution of HLA compatibility between donor and recipient could impact the allograft prognosis in ethnic minorities. Indeed, optimal HLA matched cord blood decreases the risk of transplant-related mortality, particularly in children,[7] and consideration of HLA-C matching was recently described to minimize mortality risks.[8] In addition to the HLA haplotypes diversity, differential polymorphisms in genes that are involved in humoral and cellular alloreactivity and in minor histocompatibility antigen have been noted among various ethnic groups and could be responsible, per se, for worse outcome in ethnic origin recipient mismatch.

Thus, trying to increase the representation of CBUs obtained from women that belong to non-Caucasian ethnic groups may be as important as trying to increase the cellularity of banked CBU. Finally, cord blood bank strategies should also be seen in terms of public health and equal access to health care for various populations of patients.

CONFLICT OF INTEREST

The authors report no conflicts of interest or funding sources.

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In reply:

We thank Dr Magalon and colleagues for their insightful comments related to our recent article entitled "Optimizing donor selection for public cord blood banking: influence of maternal, infant, and collection characteristics on cord blood unit quality." We agree with all of the points made by Dr Magalon and colleagues in their letter. To really answer the question of whether it is important to target strategies that increase ethnic and racial diversity of the inventory of public cord blood units, the banking and transplantation communities need to further investigate the impact of race/ethnicity matching on patient outcomes after umbilical cord blood transplantation. These results can then be used to guide cord blood banks in creating algorithms for their operations. Furthermore, we never meant to imply that increasing diversity of public cord blood banking inventory should not be prioritized. Rather, we agree that this is highly important and that it has many implications. The fact that we observed that cord blood units collected from African American infants had lower cellular content compared to Caucasian infants means that additional resources will need to be applied to bank sufficient numbers of units from African American donors. We look forward to ongoing interchanges on this topic as we optimize approaches to cord blood banking.

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Desensitization in allergic transfusion reactions: evidence from the Trial to Reduce Alloimmunization to Platelets

Allergic transfusion reactions (ATRs) occur in up to 3% of platelet (PLT) transfusions,[1] are underreported, and range in severity from mild itching and hives to fatal anaphylaxis. Clinical data have broadly defined factors that may be involved, such as a pathogenic role for plasma. Retrospective data of plasma reduction maneuvers to prevent ATRs to blood products are confounded by selection bias: patients always receive unmanipulated PLTs before being switched to volume-reduced or washed PLTs after ATRs. An individual's risk of ATRs might decrease with increasing numbers of PLT transfusions, independent of PLT product manipulation. Thus, plasma reduction may temporally coincide with, but not cause, a reduction in ATR risk.[2]

To address the question of whether ATR risk varies with increasing PLT transfusion number, we analyzed severe urticarial reaction data from the Trial to Reduce Alloimmunization to Platelets (TRAP).[3] There were 31 severe urticarial reactions reported in 24 subjects in the TRAP study (n = 8770 transfusions). Details about minor allergic reactions or the criteria for defining a severe urticarial reaction were not recorded in the study. Anaphylaxis was an evaluable outcome, but anaphylaxis was not reported after any PLT transfusion. However, three severe urticarial reactions were accompanied by dyspnea or bronchospasm. These reactions meet current criteria for likely anaphylaxis.[4]

Figure 1 shows the frequency of severe urticarial reactions by transfusion number. The risk for a severe urticarial reaction is not constant and is highest among the first five transfusions: 18 severe urticarial reactions