

Peripheral Blood Stem Cell Apheresis in Normal Donors: The Neglected Side

To the Editor:

The letter by Martinez et al in the June 1 issue¹ adds to a short (but growing) list of recent contributions on the impact of cytokine-induced peripheral blood stem cell (PBSC) mobilization and apheresis on the hematopoietic system of normal donors.¹⁻⁵ We wish to elaborate on some of the issues addressed and draw additional attention to some important but frequently neglected aspects of the PBSC procurement procedure.

Accumulating evidence now shows that PBSC collection in normal donors is followed by a transient (and asymptomatic) reduction of several hematologic parameters, in particular leukocyte and platelet count, below baseline levels.¹⁻⁵ Not only thrombocytopenia^{1,3-6} but also transient neutropenia^{2,4} and lymphocytopenia^{1,5} have now been reported. As pointed out by Martinez et al, studies on lymphocyte subsets have shown a transient, generalized reduction in these cells as well.^{1,5} The mechanism(s) underlying these hematologic effects, as well as the relative contribution of mobilization and leukapheresis, have not yet been fully elucidated.

With regard to the absolute neutrophil count (ANC), the nadir is apparently reached approximately 1 to 3 weeks after PBSC donation.^{2,3} Although asymptomatic neutropenia (ANC < 1.5 × 10⁹/L) has been noted, the ANC usually remains above the neutropenic range.^{2,4} The removal by leukapheresis of large numbers of CD34⁺ stem cells from the circulation may conceivably lead to a transient, self-limiting depletion of the CD34⁺ stem cell pool. In disagreement with this hypothesis, however, immunophenotyping of the marrow harvest product in four PBSC donors who had marrow harvesting performed 7 to 10 days after PBSC collection revealed a CD34⁺ cell content within the expected range (data not shown). In primates, the abrupt decrease in leukocyte count and circulating hematopoietic stem cells following granulocyte colony-stimulating factor (G-CSF) discontinuation is virtually abolished by treatment with anti-VLA₄ integrin antibodies.⁷ As cytoadhesion molecules such as VLA₄ integrin are believed to be involved in *in vivo* cell trafficking, this would support the concept that the reduction in leukocyte count may be due to a peripheralization or "homing" effect. Alternatively, some sort of physiologic "downregulation" of the ANC after several consecutive days of leukocytosis and elevated circulating G-CSF levels may ensue. This could be related to the suppression of endogenous production, increased clearance of G-CSF or downregulation of G-CSF receptors, as discussed recently.² Interestingly, the monocyte count seems unaffected.²

The reduction in absolute lymphocyte count, reflected by a decrease in several lymphoid subsets, is probably related to their physical removal by leukapheresis.^{1,5} As lymphocytes are not known to carry G-CSF receptors,⁸ a direct effect of G-CSF on lymphocyte subsets seems unlikely. Lymphocytopenia may persist for up to 3 months after donation,¹ and it would be of interest to evaluate immunologic responses (eg, to vaccines) in these individuals during this period.

Platelet depletion after large-volume leukapheresis has been described before the introduction of cytokines and has been reported consistently after PBSC collection.^{1,3-6} However, an effect of G-CSF administration on the platelet count has also been described.^{6,9} The decrease in platelet count can be substantial after two or three daily

collections. It resolves after approximately 7 to 10 days and has not been associated with bleeding complications.¹⁻⁶ However, less widely recognized is the fact that this undesirable effect can usually be minimized by reinfusing the autologous platelet-rich plasma at the completion of the procedure, as described recently.¹⁰ This should be considered in normal donors with "low" (<100 × 10⁹/L) platelet counts at the end of the procedure.

In conclusion, several reports now suggest that G-CSF mobilization followed by PBSC apheresis in normal donors has a delayed, although self-limiting, impact on their hematopoietic system. Physicians following these donors should be aware of these findings, although their clinical implications and the need for follow-up blood counts remain unclear. However, we believe that, in the absence of clinical indications, routine monitoring of hematologic parameters after donation is not warranted. It may be reasonable, however, to postpone elective vaccinations for at least 2 to 3 months after PBSC donation.

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