Hematopoietic progenitor cell mobilization is more robust in healthy African American compared to Caucasian donors and is not affected by the presence of sickle cell trait

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BACKGROUND: Granulocyte–colony-stimulating factor (G-CSF)-stimulated hematopoietic progenitor cells (HPCs) collected by apheresis have become the predominant graft source for HPC transplantation in adults. Among healthy allogeneic donors, demographic characteristics (age, sex, body mass index [BMI]) and baseline hematologic counts affect HPC mobilization, leading to variability in CD34+ apheresis yields. Racial differences in HPC mobilization are less well characterized.

STUDY DESIGN AND METHODS: We retrospectively analyzed data from 1096 consecutive G-CSF–stimulated leukapheresis procedures in healthy allogeneic African American (AA) or Caucasian donors.

RESULTS: In a multivariate analysis, after adjusting for age, sex, BMI, baseline platelet and mononuclear cell counts, and daily G-CSF dose, peak CD34+ cell mobilization was significantly higher among AAs (n = 215) than Caucasians (n = 881; 123 ± 87 × 10^6 cells/L vs. 75 ± 47 × 10^6 cells/L; p < 0.0001). A ceiling effect was observed with increasing G-CSF dose (10 μg/kg/day vs. 16 μg/kg/day) in AAs (123 ± 88 × 10^6 cells/L vs. 123 ± 87 × 10^6 cells/L) but not in Caucasians (74 ± 46 × 10^6 cells/L vs. 93 ± 53 × 10^6 cells/L; p < 0.001). In AA donors, the presence of sickle cell trait (SCT; n = 41) did not affect CD34+ mobilization (peak CD34+ 123 ± 91 × 10^6 cells/L vs. 107 ± 72 × 10^6 cells/L, HbAS vs. HbAA; p = 0.34). Adverse events were minimal and similar across race.

CONCLUSIONS: AAs demonstrated significantly better CD34 mobilization responses to G-CSF than Caucasians. This was independent of other demographic and hematologic variables. Studying race-associated pharmacogenomics in relation to G-CSF may improve dosing strategies. Adverse event profile and CD34 mobilization were similar in AA donors with and without SCT. Our findings suggest that it would be safe to include healthy AA donors with SCT in unrelated donor registries.
female sex, advancing donor age, lower body mass index (BMI), lower baseline platelet (PLT) counts, and lower G-CSF dose are known to be negatively correlated with CD34+ cell mobilization.5,6

Racial differences in G-CSF–mediated HPC mobilization are less well characterized. Physiologically, lower absolute neutrophil counts (ANCs) are observed in African Americans (AAs) compared to Caucasians. Benign ethnic neutropenia (BEN) is described in about 5% of healthy AAs and is characterized by a decrease in granulocytes and monocytes with minimal differences in other white blood cell (WBC) subsets.7,8 Postulated mechanisms for this phenomenon include a decreased stem cell reserve or fewer G-CSF receptors per cell among AA subjects. An association with the Duffy blood group antigen null phenotype, seen in 67% of AAs, and a consequent decrease in chemokine-mediated WBC recruitment has also been proposed.9-11 Cord blood units collected from AA donors are reported to have lower total nucleated counts and CD34+ cell counts.12 Further, studies show relatively decreased WBC demargination and corticosteroid-mediated WBC egress in healthy AA adults.13,14 Paradoxically, two recent clinical studies noted equivalent or increased G-CSF–stimulated HPC yields among AAs compared to other races.5,15 Healthy AAs also have lower hemoglobin (Hb) and MCV compared to their Caucasian counterparts.16 Low MCV and iron deficiency among healthy donors, which may not affect stem cell mobilization, have been implicated in poor collection efficiencies (due to device-related abnormalities in cell separation mechanics), thus affecting final yields.17

The effect of sickle cell trait (SCT) among AA HPC donors was evaluated in a small study that showed a trend toward better peripheral blood mobilization but poorer apheresis collection efficiencies in sickle trait versus nonsickle trait AA subjects. This resulted in similar CD34+ cell apheresis yields among the two groups. Additionally, no significant adverse events were reported among AAs with or without SCT during the process of G-CSF stimulation and HPC collection.18 Despite these data, healthy AA donors who screen positive for SCT are currently excluded from unrelated donor registries. Our primary objective was to compare G-CSF–stimulated CD34+ cell mobilization and HPC apheresis yields among healthy AA donors compared to Caucasian donors. Further, we evaluated the role of physiologic interracial differences, including that of SCT, in HPC mobilization and apheresis collection outcomes.

MATERIALS AND METHODS

Study subjects
We retrospectively analyzed 1096 consecutive healthy allogeneic-related and -unrelated first-time HPC apheresis donors who self-characterized their race as AA or Caucasian. Given the possibility of biased results due to significant heterogeneity within the following groups, healthy donors who described their race as Hispanic, Asian, Pacific Islander, mixed, and/or other were excluded. All donors were 14 years of age or older and were either healthy siblings enrolled in institutional transplant protocols or unrelated healthy volunteers enrolled in the National Marrow Donor Program (NMDP) or the Department of Transfusion Medicine's research apheresis protocols. Donors underwent G-CSF (filgrastim, Neupogen, Amgen) stimulated HPC collection by apheresis from April 1999 to May 2013. An unstimulated leukapheresis procedure for lymphocyte collection (lymphapheresis) was performed in the 7 days preceding G-CSF administration in 336 subjects. Informed consent was obtained in accordance with the Helsinki Declaration and our institutional review board–approved transplantation and research apheresis protocols. Donor demographic data at the time of HPC collection, including age, sex, weight, and height, were obtained by medical record review.

HPC mobilization, collection, and cryopreservation
Subcutaneous injections of G-CSF were administered for 5 consecutive days at a daily dose of 10 to 16 μg/kg, with the fifth dose given at least 2 hours before the start of the HPC apheresis procedure. The actual dose administered was obtained from a review of pharmacy and nursing records. Apheresis procedures were performed on a continuous-flow apheresis device (either the CS-3000 Plus, Fenwal Division, Baxter, or the COBE Spectra, Terumo BCT), using prophylactic intravenous calcium infusions as previously described.19 CD34+ collection efficiencies were similar using the two devices in our center. Volume processed per procedure ranged from 6 to 33 L for HPC collections (mean ± SD, 19 ± 5 L), depending on the immediate preapheresis CD34+ cell count and the targeted cell dose, and from 3 to 25 L (11 ± 3 L) for lymphapheresis procedures. HPC and unstimulated leukapheresis components were cryopreserved in plasma with 5% dimethyl sulfoxide, 6.5% pentastarch, and 4% human albumin per institutional operating procedures. Details of the study design are shown in Fig. 1.

Laboratory data
Complete blood count including a differential and RBC indices were obtained at baseline, that is, before G-CSF administration or, in patients who underwent lymphapheresis collections, before lymphapheresis, and were repeated on the day of collection, immediately before and after apheresis. Serology records for ABO, Rh, and Duffy RBC phenotype were gathered from the Department of Transfusion Medicine database. Donor Hb electrophoresis data were collected from all AA and selected Caucasian
Fig. 1. Study design. *Within 7 days before HPC collection. C = Caucasian. Peak CD34+ cell enumeration was performed as a stat flow cytometry assay prior to apheresis with results known within 3 hours of starting the procedure.

subjects at baseline to determine the presence of sickle cell and/or thalassemia traits. CD34+ cell quantitation was performed on peripheral blood immediately before apheresis (2 hr after the fifth dose of G-CSF), after apheresis, and on the apheresis product by flow cytometry as previously described.20 Flow cytometric techniques did not change significantly during the 14-year period covered in this review.

Statistical analysis
The total mononuclear cell (MNC) count was calculated as the sum of lymphocyte and monocyte counts reported on the complete blood count differential. Collection efficiencies were calculated using the formula21

\[ \text{CD34+ cell content in product} \times 100 = (\text{Mean of pre- and postapheresis CD34+ counts}) \times (\text{Volume processed}) \]

Summary statistics were calculated for all numerical data. Two-tailed unpaired t tests were used to compare groups of two with a presumed normal distribution. Analysis of variance was used to compare more than two groups. Categorical variables were compared using a two-tailed Fisher exact test. Multivariate analyses were performed using stepwise forward logistic regression, based on variables having significance in univariate analysis, using a commercial statistics program (JMP, Version 7, SAS Institute, Inc.). Results are given as the mean ± SD. A p value of less than 0.01 was considered significant.

RESULTS

Donor demographics
All AA (n = 215) and Caucasian (n = 881) donors with complete data sets were included. Sex ratio was similar among the two groups (45% vs. 52% male; p = 0.09). AAs were younger (39 years vs. 43 years; p = 0.001) and had greater weight (86 kg vs. 81 kg; p = 0.001) and BMI (30 vs. 27; p < 0.0001) than Caucasians. The total daily dose of G-CSF was greater in AAs than Caucasians (920 µg vs. 850 µg; p < 0.0001) but the G-CSF dose/kg was similar in the two groups (Table 1).

Donor race, CD34+ mobilization, and HPC apheresis cell yields
AAs mobilized significantly better than Caucasians with mean peak circulating CD34+ counts of 123 ± 87 × 10^6 cells/L vs. 75 ± 47 × 10^6 cells/L (p < 0.0001; Fig. 2). CD34+ apheresis yield was also significantly greater in AAs than Caucasians (51 ± 35 × 10^6 cells/L processed vs. 32 ± 21 × 10^6 cells/L processed; p < 0.0001), consistent with higher preapheresis counts. Apheresis collection efficiency was similar in the two racial groups (AAs, 64%; Caucasians, 62%; p = 0.11). Lymphapheresis within the 7 days before starting G-CSF was associated with significantly improved CD34+ cell mobilization; however, the effect did not differ by race (Fig. S1, available as supporting information in the online version of this paper).

In a univariate analysis of factors associated with higher peripheral blood CD34+ counts, three factors were overwhelmingly correlated with better peak CD34 mobilization: higher total G-CSF dose, AA race, and greater BMI, followed by higher baseline PLT and MNC counts, prior lymphapheresis, and male sex. After adjustment for total G-CSF dose, AA race was the single variable most strongly correlated with peak peripheral blood CD34+ mobilization. In multivariate stepwise analysis, after total G-CSF dose and race were included in the model, donor BMI lost much of its contribution. Baseline PLT and MNC counts remained highly correlated, and after they were introduced into the model, prior lymphapheresis, male sex, and younger age remained significantly correlated with peak peripheral blood CD34 counts (Table 2). To ensure that confounding factors were not introducing bias, the analysis was repeated by forcing all other variables into the multivariate regression model and retaining race until...
the end; AA race still remained a significant predictor of better CD34 mobilization.

AAs were significantly less likely than Caucasians to be poor mobilizers and significantly more likely to be supermobilizers. A preapheresis CD34+ cell count of less than $20 \times 10^6/L$ was seen in 1.4% vs. 6.1% and a CD34+ cell count of more than $120 \times 10^6/L$ in 39.1% versus 13.5% of AA versus Caucasian donors, respectively ($p < 0.001$ for both comparisons; Table 3).

### Effect of G-CSF on laboratory variables

Hb and mean corpuscular volume were significantly lower among AAs than Caucasians, both at baseline and after G-CSF administration. PLT counts were similar between the two groups and showed a similar degree of decline following G-CSF administration. AAs had lower baseline ANC (3.4 $\times 10^9/L$ vs. 4.0 $\times 10^9/L$, $p = 0.004$) than Caucasians, but demonstrated significantly higher peak WBC and MNC counts after G-CSF administration (Table 4, Fig. 3). Among AA donors with BEN, defined as an ANC of less than 1.5 $\times 10^9/L$, G-CSF stimulation resulted in a significantly higher percentage ANC increase compared to donors with pre-G-CSF ANC in the normal range (mean 23-fold increase in ANC among BEN AA donors; $n = 17$) vs. 13-fold increase in ANC among other AAs ($n = 161$; $p < 0.0001$; Fig. 4). In AA donors with known Duffy phenotype, Duffy antigen expression did not affect CD34 mobilization (peak CD34 counts 114 $\pm 81 \times 10^6$ cells/L vs. 134 $\pm 85 \times 10^6$ cells/L, Fya- $n = 49$ vs. Fya+ and/or Fyb+ $n = 20$; $p = 0.4$). Baseline ANC was similar in AA donors with and without Duffy antigen expression.

### G-CSF dose and CD34+ mobilization in AAs and Caucasians

When stratified by G-CSF dose, at higher doses (16 $\mu g/kg/day$), the difference in mobilization responses between the two groups was less apparent (peak CD34+ counts $123 \times 10^6$ cells/L vs. $93 \times 10^6$ cells/L, AA $n = 33$ vs. Caucasians $n = 881$).

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**TABLE 2.** Regression analysis of factors associated with higher CD34+ cell counts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis (after adjusting for total G-CSF dose) p value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total G-CSF dose</td>
<td>$&lt;10^{-24}$</td>
<td>$&lt;10^{-10}$</td>
<td>$&lt;10^{-10}$</td>
</tr>
<tr>
<td>AA race</td>
<td>$&lt;10^{-23}$</td>
<td>$&lt;10^{-17}$</td>
<td>$&lt;10^{-17}$</td>
</tr>
<tr>
<td>Higher BMI</td>
<td>$&lt;10^{-14}$</td>
<td>$&lt;10^{-9}$</td>
<td>$&lt;10^{-9}$</td>
</tr>
<tr>
<td>Higher baseline</td>
<td>$&lt;10^{-10}$</td>
<td>$&lt;10^{-14}$</td>
<td>$&lt;10^{-14}$</td>
</tr>
<tr>
<td>PLT count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MNC count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior lymphapheresis</td>
<td>0.0004</td>
<td></td>
<td>0.0003</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.0009</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Younger age</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Data are reported as mean ± SD.

**TABLE 3.** Effect of race on preapheresis blood CD34+ cell count

<table>
<thead>
<tr>
<th>Preapheresis blood CD34+ cell count ($\times 10^9/L$)</th>
<th>Caucasian donors</th>
<th>AA donors</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&lt;20$</td>
<td>54 (6.1)</td>
<td>3 (1.4)</td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>74 (8.4)</td>
<td>5 (2.3)</td>
<td></td>
</tr>
<tr>
<td>31-50</td>
<td>162 (18.4)</td>
<td>23 (10.7)</td>
<td></td>
</tr>
<tr>
<td>51-80</td>
<td>256 (29.1)</td>
<td>51 (23.7)</td>
<td></td>
</tr>
<tr>
<td>81-120</td>
<td>216 (24.5)</td>
<td>49 (22.8)</td>
<td></td>
</tr>
<tr>
<td>$&gt;120$</td>
<td>119 (13.5)</td>
<td>84 (39.1)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>881 (100)</td>
<td>215 (100)</td>
<td></td>
</tr>
</tbody>
</table>

* Data are reported as number (%).

**TABLE 4.** Effect of G-CSF on laboratory variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>AAs</th>
<th>Caucasians</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTs ($\times 10^9/L$)</td>
<td>260 ± 65</td>
<td>251 ± 58</td>
<td>0.06</td>
</tr>
<tr>
<td>MNCs ($\times 10^9/L$)</td>
<td>2.46 ± 0.67</td>
<td>2.48 ± 0.69</td>
<td>0.8</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>13.4 ± 1.4</td>
<td>14.2 ± 1.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>85.5 ± 6.3</td>
<td>89.6 ± 4.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13.1 ± 1.7</td>
<td>12.3 ± 1.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PLTs ($\times 10^9/L$)</td>
<td>248 ± 144</td>
<td>231 ± 56</td>
<td>0.09</td>
</tr>
<tr>
<td>MNCs ($\times 10^9/L$)</td>
<td>6.7 ± 2.1</td>
<td>5.8 ± 1.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>12.8 ± 1.5</td>
<td>13.4 ± 1.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>85.8 ± 6.1</td>
<td>90.2 ± 4.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13.0 ± 1.8</td>
<td>12.4 ± 1.3</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

* Data are reported as mean ± SD.
Caucasian \( n = 73; \) \( p = 0.07 \) than at lower doses \((10 \text{ mg/kg/day})\), where peak CD34 counts were \( 123 \times 10^6 \) cells/L \( \text{vs.} \) 74 cells/L, AA \( n = 182 \) \( \text{vs.} \) Caucasian \( n = 808; \) \( p < 0.0001; \) Table S1, available as supporting information in the online version of this paper). Higher G-CSF doses resulted in better CD34\(^+\) mobilization in Caucasian but not in AA donors. Mean peak CD34\(^+\) counts after G-CSF 16 \( \mu g/kg \) versus 10 \( \mu g/kg \) were \( 123 \times 10^6 \) cells/L \( \text{versus} \) \( 123 \times 10^6 \) cells/L \( p = 0.5 \) in AAs and 94 \( \times 10^6 \) cells/L \( \text{versus} \) \( 74 \times 10^6 \) cells/L \( p < 0.001 \) in Caucasians, respectively.

**Effect of SCT on CD34\(^+\) cell mobilization and HPC apheresis yields**

AAs with SCT received significantly higher total G-CSF dose as well as G-CSF dose/kg, by protocol design, related to transplant preparative regimens in those who had siblings with sickle cell disease.\(^5\) Despite this increased dose, in AA donors with known Hbs status, the presence of SCT had no effect on CD34\(^+\) mobilization (peak CD34\(^+\) counts \( 123 \pm 91 \times 10^6 \) cells/L \( \text{vs.} \) \( 107 \pm 72 \times 10^6 \) cells/L, HbAS \( n = 41 \) \( \text{vs.} \) HbAA \( n = 84; \) \( p = 0.34 \)). Although MCV was lower among AAs with SCT, collection efficiency was similar among AAs with and without SCT (Table S2, available as supporting information in the online version of this paper).

**Adverse events**

No significant difference in the incidence of severe adverse events (adverse event \( \geq \) Grade 3 by CTCAE criteria\(^22\)) was seen among AA versus Caucasian donors. Among AA donors with SCT, one subject experienced a more than Grade 3 serious adverse event with diffuse body pain on Days 4 and 5 of G-CSF administration, requiring hospitalization. This patient had a history of rheumatoid arthritis, requiring opiates at baseline. Among AA donors without SCT, one subject was hospitalized overnight (Grade \( > 3 \) serious adverse event) for bleeding from a central venous catheter site. Accurate assessment of Grades 1 and 2 adverse events was unavailable due to inconsistent data collection in our retrospective study. Nonsteroidal anti-inflammatory drug and/or opiate requirement was similar among SCT versus non-SCT AA donors. SCT donors did not demonstrate significant elevations in serum creatinine or transaminases compared to their non-SCT AA counterparts after G-CSF administration. None of 41 HPC components from SCT donors congealed upon thaw.

**DISCUSSION**

Our study demonstrates that healthy AA donors are characterized by significantly more robust CD34\(^+\) mobilization responses to G-CSF than Caucasian donors. This effect was independent of age, sex, BMI, presence of Hbs, and other variables and occurred despite physiologically lower neutrophil counts among AAs than Caucasians before G-CSF stimulation. Other investigators failed to find such robust differences between AA and Caucasian donors, but those studies were smaller and did not take all relevant variables into account in a structured multivariate analysis.\(^15\) A recent study demonstrated findings similar to our study with regard to racial discrepancies in CD34\(^+\) cell mobilization. However, collection efficiencies were dependent on donor BMI and sex.\(^22\) In our experience, preapheresis CD34\(^+\) cell counts were the most important predictors of CD34 yields per liter processed after adjusting for donor demographics, G-CSF dose per kilogram, laboratory variables, and procedure-related variables.

Benign ethnic neutropenia has been associated with the lack of Duffy antigen expression on RBCs, which is
found in 67% of AAs but is rare in Caucasians. Duffy antigen is a chemokine receptor that can inhibit WBC migration. Variability in expression of Duffy antigen thus might be a plausible explanation for the marked difference in HPC mobilization between AA and Caucasian subjects. However, we found no significant differences in HPC mobilization among AA donors with or without Duffy expression on their blood cells. Surprisingly, we found a marked enhancement in neutrophil mobilization in response to G-CSF in AA donors with benign ethnic neutropenia versus those with normal baseline ANC.

Our analysis was limited by small sample size, and our understanding of the actual mechanisms underlying this racial variation in HPC mobilization is speculative. Genomewide association studies have identified variants in the cmlp gene among AAs. MPL is the PLT and megakaryocyte receptor for thrombopoietin (TPO), an essential regulator of megakaryocyte differentiation and PLT production. TPO is also known to regulate the HSC niche. It is possible that MPL variants among AAs may mediate differential responses to G-CSF–stimulated stem cell egress from the marrow niche.

A ceiling effect in response to increased doses of G-CSF (>10 μg/kg) was seen in AAs but not in Caucasians, suggesting that dose titration based on race might be used to optimize HPC yields. From a clinical standpoint, mobilization failures were more common in Caucasians and may result in the need for second-day apheresis collections. Preemptive application of knowledge about racial differences in HPC mobilization may help transplant clinicians plan apheresis collection schedules and use resources more effectively, avoiding overcollection in some cases and averting the need for additional collections in others. The identification of a subgroup of donors more likely to yield robust CD34+ cell collections may also help narrow the choice of donors from unrelated registries. Donors may also be counselled before donation on what to expect based on their demographic characteristics.

Lymphapheresis within the 7 days preceding G-CSF administration was found to enhance CD34+ mobilization and increase HPC apheresis yield. PLT depletion during the prior lymphapheresis procedure may have resulted in a TPO-mediated increase in progenitor cells common to both megakaryocytes and HPCs. The increase was not significant if lymphapheresis was performed more than 7 days before G-CSF administration, suggesting a transient HPC stimulation effect. Interestingly, a marginal decrease in PLT counts was observed after G-CSF administration, suggesting a competitive “steal” of common progenitors toward HPC production. The effects of lymphapheresis and the lowering of PLT counts with G-CSF were independent of race.

CD34+ cell collection efficiency was correlated in prior studies with iron deficiency and low MCV and was related to abnormal cell separation mechanics during apheresis. In our cohort, AAs demonstrated significantly lower MCV and Hb levels than Caucasians both at baseline and after G-CSF administration; however, mean CD34+ collection efficiency was similar in both groups. It is likely that the value of the MCV is less important than the cause of a low MCV in terms of impact on apheresis device performance. Iron deficiency is associated with the presence of RBCs of highly variable size, as reflected in an elevated RBC distribution width (RDW). We have found that a high RDW in the presence of a low MCV is more likely to be associated with impaired leukapheresis collection efficiency than a low MCV alone. Sickle trait subjects had a normal RDW, thus explaining the lack of impact of the low MCV on CD34+ collection efficiency.

Common adverse events due to G-CSF injections include headaches, bone pain, myalgias, and insomnia. Occasionally, more severe adverse events such as splenic rupture, myocardial infarction, and arrhythmias have been reported in healthy donors. Adverse events in our donor cohort were generally of mild to moderate severity and were similar to those reported in prior studies. In contrast, adverse effects of G-CSF can be significant in patients with sickle cell anemia and include cases of life-threatening sickling crisis. One small randomized trial found that G-CSF mobilization and HPC apheresis were as safe in donors with SCT as they were in AA nontrait donors. Yet donors with SCT are excluded from participation in the NMDP registry, based largely on a single case of G-CSF–associated multiorgan failure in a patient with compound heterozygous sickle cell/β+ thalassemia, which, unlike SCT, is a form of sickle cell disease. Since SCT is present in up to 10% of AAs, eliminating these individuals also negatively impacts the unrelated donor pool. Our data include the largest number of consecutive AA donors with SCT yet reported to undergo G-CSF–assisted HPC collection and demonstrate no differences in occurrence of severe adverse clinical events, efficacy of CD34 mobilization, efficiency of CD34 collection, or product loss during cryopreservation and thaw, compared with HPC donations from non-trait AA donors.

In conclusion, racial differences in G-CSF–mediated CD34+ cell mobilization are a novel clinical finding and occur in a direction paradoxical to that predicted by known physiologic mechanisms. Further evaluation of race-associated genetic polymorphisms in relation to G-CSF pharmacokinetics may help improve G-CSF dosing strategies. Clinically, identifying donors at risk for either poor or exceptionally good mobilization may help transplant teams plan ahead and allocate resources appropriately. Finally, the absence of significant adverse clinical events or deleterious changes in product quality among donors with SCT suggests that these individuals may safely be included in unrelated donor registries.

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CONFLICTS OF INTEREST

The authors have disclosed no conflicts of interest.

REFERENCES


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Table S1. Effect of G-CSF dose (10 vs. 16 mcg/kg/d) on CD34+ cell mobilization.

Table S2. Effect of sickle cell trait (SCT) on CD34+ mobilization and apheresis yields in healthy African American donors.

Fig. S1. Effect of prior lymphapheresis on CD34+ cell mobilization. Lymphapheresis within 7 days prior to starting G-CSF was associated with significantly better subsequent HPC mobilization. Data are shown for all donors; no race-specific differences were noted in the lymphapheresis effect. See legend to Fig. 2.