Peripheral blood (PB) CD34+ cells mobilized by granulocyte colony-stimulating factor (G-CSF) administration are potentially useful for transplantation and as a target of gene transfer for therapy of hematopoietic disorders. Efficient harvest and planning for clinical use of PB CD34+ cells ideally requires foreknowledge of the expected mobilization kinetics and yield. We developed a sensitive flow cytometric assay for accurately enumerating CD34+ cells throughout the range seen at baseline to peak mobilization. We used this assay to assess the kinetics of G-CSF-mediated mobilization of CD34+ cells to PB in normal volunteers and in patients with chronic granulomatous disease (CGD) or adenosine deaminase (ADA)-deficient severe combined immunodeficiency disease (SCID). Two dose levels of G-CSF were examined (5 and 10 μg/kg/d for 7 days). Both doses were well tolerated. For normal subjects and patients an increase in PB CD34+ cells was first detected only preceding the third dose of G-CSF (day 3), peaked transiently on day 5 or 6, and then decreased thereafter despite additional doses of G-CSF. With 32 normal volunteers mean peak CD34+ cell counts were 57 and 76 cells/mm3 of blood (5 and 10 μg doses, respectively), whereas for 18 CGD patients the mean peaks were 31 and 40 cells/mm3 of blood. For 2 ADA-deficient SCID patients studied at a G-CSF dose of 5 μg/kg/d, the average peak was 16 cells/mm3 of blood. For both of these patient groups mobilization of CD34+ cells to PB was impaired compared with similarly treated normal subjects (P < .05). By contrast to the kinetics of the CD34+ cell mobilization, the absolute neutrophil count (ANC) increased markedly by 6 hours after the first dose of G-CSF and then increased steadily through day 8. At days 5 and 6 (peak mobilization of CD34+ cells) the mean ANC of CGD and ADA patients was only slightly lower (≤15%) than that seen with normal subjects, whereas the difference in CD34+ cell mobilization was ≥48%. Thus, ANC is not a reliable surrogate to predict peak PB CD34+ cell counts and direct enumeration of PB CD34+ counts should be undertaken in decisions regarding timing and duration of apheresis to harvest a specific number of these cells. Finally, unexpected, but significant differences in the PB CD34+ cell mobilization between normal subjects and patients with inherited disorders can occur and underscores the importance of establishing the expected mobilization of PB CD34+ cells in the planning of treatment approaches using these cells.

**This is a US government work. There are no restrictions on its use.**
were combined immunodeficiency disease (SCID). We therefore obtained similar information about G-CSF mobilization of PB CD34+ cells in normal volunteers and in these two patient groups. CGD is a group of four single gene disorders affecting the function of the superoxide-generating nicotinamide-adenine dinucleotide phosphate oxidase of blood phagocytes resulting in severe recurrent infections.27-31 ADA SCID is a single gene defect resulting in accumulation of toxic metabolites of adenosine causing severe abnormalities in the function of lymphocytes.32-34

We have developed a sensitive and reproducible flow cytometric assay to accurately enumerate CD34+ cells throughout the range of expected levels from baseline to peak mobilization. This assay was used to determine the changes in PB CD34+ cell counts in response to daily G-CSF administration. Our study demonstrates the importance of direct enumeration of PB CD34+ cells rather than absolute neutrophil count to predict G-CSF-induced recruitment and to optimize timing of apheresis harvest of PB CD34+ cells. Unexpectedly, mobilization in CGD and ADA SCID patients was significantly lower than the normal donors and could not be anticipated from the increase in circulating granulocyte counts.

MATERIALS AND METHODS

Normal volunteer and patient populations. Two groups of normal volunteers were studied. The first group contributed a small sample of PB, used to establish the baseline levels of circulating CD34+ cells in whole blood, consisted of 81 healthy normal individuals of both sexes, ages 18 to 65 years. A second group of normal volunteers ages 18 to 58 years of both sexes included 32 individuals who were randomly assigned to be treated with daily subcutaneous (SC) doses of either 5 or 10 μg/kg G-CSF to mobilize CD34+ cells to the PB. In addition to normal volunteers, 18 patients with CGD were also randomly assigned to receive daily doses of 5 or 10 μg/kg G-CSF. CGD patients of both sexes, ages 17 to 38 years of age, except for 3 patients, ages 11, 14, and 15 years. Ten CGD patients had the p47phox-deficient genotype, 6 had the X-linked, gp91phox-deficient genotype, and 1 patient each had the p67phox- or p22phox-deficient genotypes. G-CSF was administered to normal volunteers or CGD patients after informed consent under the auspices of an Institutional Review Board (IRB)-approved protocol for study of G-CSF RECRUITMENT OF CD34+ CELLS 1105

CD2+, CD3+ cell subsets. Evaluation of PB CD34+ cells subset enrichment was performed by flow cytometric analysis of PB CD34+ cell subsets. The CD34+ cell subsets were analyzed from the monofluclear cell-enriched PB obtained from apheresis collections from both nonmobilized and mobilized individuals and from individuals mobilized by administration of G-CSF on standard 5-L procedure for harvesting PB CD34+ cells. The CD34+ cell subsets were not subjected to the apheresis procedure. Side effects were monitored. Most individuals at either dose complained of bone pain and malaise, which was relieved by ibuprofen. The bone pain and malaise was generally more severe with the 10 μg/kg dose. A few individuals at the 5 μg/kg dose noted mild headache. Two normal individuals at the 10 μg/kg dose had headaches of such severity that the last dose of G-CSF was not given. No participants had significant local reactions. All symptoms subsided within 48 hours after the last dose of G-CSF.

Flow cytometric analysis of PB CD34+ cells. CD34+ cells represent rare events in normal PB; hence, it is necessary to establish minimum number of events (cells) that should be analyzed to accumulate 100 CD34+ cells, yielding a count precision that is statistically significant.35,36 Preliminary studies suggested that in normal blood processing of 5 × 10^6 leukocytes fulfilled this criteria. However, data storage and subsequent analysis was performed on the subset of 1 × 10^5 cells collected in a modified mononuclear cell region (gate) that included >99% of CD34+ events.

Two milliliters of peripheral whole blood was collected in a Vacutainer EDTA anticoagulation tube (Becton Dickinson, San Jose, CA). For flow cytometric analysis of PB CD34+ cells, three differently labeled samples were prepared as follows. To a 100-μL aliquot of blood was added 20 μL of Becton Dickinson Leukogate reagent (anti-CD45 fluorescein isothiocyanate [FITC] and anti-CD14 phycoerythrin [PE]). To each of two 200-μL aliquots were added 40 μL of anti-CD34 FITC (anti-HPCA 2, Becton Dickinson) or its FITC subclass antibody control. Samples were incubated for 30 minutes at 4°C in polypropylene tubes prerinsed with 5% fetal bovine serum. Red cells were lysed with fluorescence-activated cell sorter (FACS) lysing buffer (Becton Dickinson), and the remaining leukocytes were washed twice with phosphate-buffered saline (PBS) and resuspended in PBS with 1% paraformaldehyde.

Analysis was performed on a FACScan or FACSort (Becton Dickinson) using a Cytometrics software. Fig 1 fully describes the backgating37 and how the gate for acquisition of CD34+ cells was established. The absolute number of CD34+ cells in normal PB was calculated as follows:

1. Acquire 10^6 events in the gate defined as in Fig 1 using the CD34 antibody and the subclass control to accurately enumerate the small numbers of CD34+ cells in this gate.
2. Subtract the number of subclass control positive cells from the CD34 antibody positive cells to control for any background fluorescent staining with an irrelevant subclass antibody.
3. Multiply the net CD34+ cells in the acquisition gate by the percentage of the total leukocytes within this gate and divide by 10^6.
4. Multiply this number by the separately determined total peripheral blood white cell count per mm^3 to obtain the absolute number of CD34+ cells/mm^3 of whole blood.

Evaluation of CD34+ cell subsets. Evaluation of subsets of CD34+ cells was performed by two-color flow cytometric analysis. The CD34+ cell subsets were analyzed from the mononuclear cell-enriched PB obtained from apheresis collections from both nonmobilized individuals and from individuals mobilized by administration of G-CSF on days 5 or 6 of the study. The apheresis collections (standard 5-L procedure for harvesting PB CD34+ cells) from nonmobilized normal volunteers were obtained by the Department of Transfusion Medicine at NIH after informed consents. All antibodies used were from Becton Dickinson, except CD34 FITC (Amac, Westbrook, ME). For each analysis 200 μL of the apheresis sample was incubated for 30 minutes at 4°C with 40 μL of each of the following monoclonal antibodies except for CD36-FITC where the added volume was 5 μL:

1. CD34 FITC/CD38 PE
2. CD34 FITC/CD2 PE
3. CD19 FITC/CD34 PE
4. CD36 FITC/CD34 PE

The CD34+, CD38- subset likely include the pluripotent hematopoietic...
et al.

**RESULTS**

**FACS enumeration of CD34+ cells in normal PB.** In the top two dot-plot panels of Fig 2 is shown a typical CD34+ analysis of the mononuclear cell gate (defined in Fig 1, see Materials and Methods) for whole blood from a nonmobilized individual. Within the CD34+ region of the CD34 FITC-labeled cells (Fig 2B) there are 160 events, whereas in the subclass control (Fig 2A) in the same region are 12 events, a ratio of <1:10 between control and experimental groups, which is representative for this assay. Fig 2C and D show a similar analysis of the same individual on the fifth day of SC administration of 10 μg/kg G-CSF (within the CD34+ region, 9 events in the subclass control and 1,250 events in the experimental group). Using the same analysis in 81 nonmobilized normal volunteers, the range and mean number of CD34+ cells detected in PB is shown in Table 1.

**Kinetics of CD34+ cell mobilization in response to G-CSF administration.** The two left panels of Fig 3 show for normal volunteers, the average daily absolute neutrophil count (ANC) (upper left), and CD34+ cell count (lower left) after treatment with daily doses of 5 or 10 μg/kg SC G-CSF administered on 7 consecutive days. At both dose levels the ANC increased markedly on the morning of day 2 (about 24 hours after the first dose), but in no individual was any increase in CD34+ cell count noted at day 2. In a subset of individuals ANC and CD34+ cell counts were done at 2 and 6 hours after the first dose of G-CSF. As expected from previously published data, there was already a significant increase in the ANC at 6 hours. However, CD34+ counts were unchanged from baseline at either 2 or 6 hours, ruling out an early transient increase in CD34+ cells in response to the first dose of G-CSF.

The average ANC increased steadily though day 8 (24 hours after the final G-CSF dose) and then dropped precipitously by day 9. Doubling the dose of G-CSF from 5 to 10 μg/kg resulted in 30% increase in ANC (P < .05). By contrast, a rise in CD34+ cell count was first detected on day 3, reaching a peak for the average on day 6 (although some individuals peaked on day 5). Unlike the ANC, the CD34+ cell count decreased on day 7 and day 8 despite a dose of G-CSF given on day 7 and a rising ANC on those days. For those individuals that peaked on day 5, this decrease began on day 6). Although the mean CD34+ cell count on day 6 for individuals receiving 10 μg/kg G-CSF was 36% higher than the mean for those receiving the 5 μg/kg dose, this difference failed to reach statistical significance for the group.

Nine individuals were studied at both doses of G-CSF administered at least 4 months apart with the choice of first dosing administration randomized (Fig 4). When the data from the same individual receiving both dosing regimens (5 and 10 μg/kg G-CSF) was analyzed, CD34+ mobilization averaged 75% higher with the dose of 10 μg/kg of G-CSF (P < .001). The data in Fig 3 includes only the first dosing for these individuals treated twice.

The two right panels of Fig 3 show for patients with CGD, the average daily ANC (upper right) and CD34+ cell count...
We therefore analyzed the relationship between these two values. It can be seen from Fig 3 that the relationship between these two values is changing markedly throughout the mobilization period because the kinetics of both events follow very different curves. We therefore chose to analyze this relationship at a defined time, the day on which the CD34⁺ cell count peaked for each individual. This analysis is shown in Fig 6 where the ratio of peak CD34⁺ cell count to the ANC on the same day is plotted. Of note is that this ratio in the normal subjects at both dosing levels is very similar. In CGD and the ADA SCID patients this ratio is half that of normal at both the doses of G-CSF ($P < .01$). Of note is that several of the CGD patients and one of the ADA patients achieved peak CD34⁺ cell counts of <15 cells/mm³, yet all individuals achieved ANC of ≥20,000 cells/mm³ by that day.

**Effect of G-CSF mobilization on CD34⁺ cell subsets.** Because PB CD34⁺ cells have a number of potential clinical uses, the effect of G-CSF mobilization on certain committed and lineage negative subsets was determined. A number of published reports have suggested that absence of CD38 antigen expression on CD34⁺ cells may indicate pluripotent capacity. Conversely, expression of certain lineage-specific markers on CD34⁺ cells may point to progenitor cells that are committed toward that hematopoietic cell type. The vast majority of CD34⁺ cells are committed toward the myeloid lineage, making small changes in relative percent insignificant. Therefore, in the present analysis we specifically examined the much smaller committed subsets of CD34⁺ cells expressing T-cell (CD2), B-cell (CD19), or erythroid

### Table 1. CD34⁺ Cells in Normal Nonmobilized PB

<table>
<thead>
<tr>
<th></th>
<th>No. of volunteers</th>
<th>Range of CD34⁺ cells/mm³ of whole blood</th>
<th>CD34⁺ cells/mm³ of whole blood*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD34⁺ cells/mm³ of whole blood</td>
<td>81</td>
<td>0.6–4.9</td>
<td>1.46 ± 0.7</td>
</tr>
</tbody>
</table>

* Values are mean ± SD.
Fig 3. Effect of daily administration of SC G-CSF on the kinetics of neutrophils (upper panels) and PB CD34+ cells (lower panels). The normal volunteers are shown in the two left panels (n = 32), and the CGD patients in the right panels (n = 16). The Y axis represents the mean levels of ANC x 10^3/mm^3 in the upper panels and the absolute number of PB CD34+ cells/mm^3 in the lower panels (error bars represent SEM). The X axis represents the day of the study, with day 1 representing the levels just before the first dose of G-CSF.

Fig 4. Mobilization of PB CD34+ cells in the same individuals (— — —, 7 normal volunteers; -- -- -- 2 CGD patients) treated with two different doses of G-CSF (5 and 10 µg/kg/d). For these 9 individuals the mean PB CD34+ cells on day 5 of the study was 33.6 ± 15.7 (SD) with 5 µg/kg dose and 58.7 ± 24.4 with 10 µg/kg dose (75% higher with the 10 µg dose, P = .001).

Fig 5. Shown is a scatter plot of the PB CD34+ cell count on day 5 of G-CSF administration in all studied normal volunteers (5 and 10 µg/kg), CGD patients (5 and 10 µg/kg), and the ADA-deficient SCID patients (5 µg/kg). Both * and ** represent P < .05, comparing the normal volunteers to the patient groups at 5 and 10 µg/kg, respectively.
G-CSF RECRUITMENT OF CD34+ CELLS

CD34+ cell subsets followed a very similar pattern in the CGD patients (data not shown).

Given the increases in the CD34+ subsets expressing T- or B-cell antigens, we also analyzed the effect of G-CSF administration on mature T- and B-cells in circulation. The kinetics of change in T- and B-cells in response to G-CSF followed a pattern similar to the kinetics of CD34+ cells, rising on day 3, peaking at day 5 or 6, and then decreasing thereafter (data not shown). However, the rise in absolute count of T or B cells (normal volunteers and CGD patients) averaged only three- and fourfold over baseline, and not the 10-fold seen with circulating neutrophils or >50-fold seen with PB CD34+ cells.

**DISCUSSION**

Currently, PB CD34+ cells are used widely for autologous transplantation.11-15 These cells are also a convenient target for gene therapy of hematopoietic disorders.16-20 Increasingly, these cells are being considered an appropriate source of stem cells for allogeneic transplantation.16-18 This has led to consideration of establishment of standards for G-CSF mobilization and harvest of these cells from normal donors and patients with inherited disorders of the hematopoietic system. Many of the current expectations and standards for PB CD34+ cell mobilization have been established from information developed by study of patients with malignancies. In such patients, the compounding factors of previously or concurrently administered chemotherapeutic agents and the effects of the malignancy itself may impact on the relevance of data to normal volunteers or patients with nononcologic hematopoietic disorders.

In the present study we established standards for sensitive and accurate enumeration of circulating PB CD34+ cells from baseline levels to peak G-CSF mobilization. As we have demonstrated in the present study, some individuals with inherited disorders may unexpectedly have low levels of PB CD34+ mobilization in response to G-CSF, yet rises in ANC would not be predictive. Particularly for low levels of PB CD34+ mobilization it is essential that CD34+ cells be directly and accurately enumerated to allow determination

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**Table 2. Evaluation of Subsets of CD34+ Cells in Non-mobilized and G-CSF-mobilized PB**

<table>
<thead>
<tr>
<th>CD34+ Subset Cells/mL Blood</th>
<th>Nonmobilized PB</th>
<th>G-CSF-mobilized PB (5 μg/kg)</th>
<th>G-CSF-mobilized PB (10 μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CD34+ cells</td>
<td>1400 ± 700</td>
<td>56,700 ± 20,100</td>
<td>76,500 ± 33,100</td>
</tr>
<tr>
<td>Pluripotent CD34+, CD38+</td>
<td>8.40 ± 5.31</td>
<td>45.4 ± 39.7*</td>
<td>61.2 ± 38.2*</td>
</tr>
<tr>
<td></td>
<td>(0.60 ± 0.38)</td>
<td>(0.08 ± 0.07)*</td>
<td>(0.08 ± 0.05)</td>
</tr>
<tr>
<td>T-cell progenitor CD34+, CD2+</td>
<td>8.70 ± 5.47</td>
<td>3,175 ± 1,644*</td>
<td>3,596 ± 3,213*</td>
</tr>
<tr>
<td></td>
<td>(0.62 ± 0.39)</td>
<td>(5.60 ± 2.90)*</td>
<td>(4.70 ± 4.20)*</td>
</tr>
<tr>
<td>B-cell progenitor CD34+, CD19+</td>
<td>4.60 ± 3.06</td>
<td>805 ± 204*</td>
<td>1,071 ± 918*</td>
</tr>
<tr>
<td></td>
<td>(0.33 ± 0.22)</td>
<td>(1.42 ± 0.36)*</td>
<td>(1.40 ± 1.2)*</td>
</tr>
<tr>
<td>RBC progenitor CD34+, CD36+</td>
<td>72.8 ± 38.1</td>
<td>15,138 ± 10,318*</td>
<td>16,600 ± 7,420*</td>
</tr>
<tr>
<td></td>
<td>(5.20 ± 2.80)</td>
<td>(26.7 ± 18.2)*</td>
<td>(21.7 ± 9.70)*</td>
</tr>
</tbody>
</table>

Values are means ± SD, with % of total CD34+ cell in parentheses.

PB, peripheral blood.

* P < .001, nonmobilized v mobilized PB CD34+ cells.
of the amount of blood processing by apheresis needed to achieve a particular clinical goal. At very low levels of mobilization, a clinical decision might be made not to subject an individual to apheresis at all.

The present study indicates that the level of nonmobilized PB CD34⁺ cells in normal individuals is a tightly regulated parameter, similar to the regulated levels of various other formed blood elements, and may have an important biological function. G-CSF administration resulted in a rapid increase in neutrophils within 6 hours after the first dose of G-CSF, that peaked after the 7th dose. However, the PB CD34⁺ cell count did not change until 48 hours after the 1st dose of G-CSF and peaked before the 5th or 6th dose. This suggests different mechanisms are responsible for the G-CSF mobilization of neutrophils and PB CD34⁺ cells. Furthermore, the delayed effect of G-CSF administration on mobilization of PB CD34⁺ cells, suggests that this effect may be mediated by the production of a secondary cytokine or a cascade of cytokines. Though, the baseline levels of PB CD34⁺ cells in the two patient groups with hematopoietic genetic disorders were similar to normal volunteers, the mobilization of PB CD34⁺ cells at both the doses of G-CSF administration was significantly lower. This result was unexpected, because CGD is a genetic disorder associated with a deficiency of the phagocyte oxidase and is not known to be associated with any abnormality of bone marrow cellular production (27-31). By contrast, the ANC was only slightly lower in the CGD and ADA SCID patients and was not significantly different from the normal volunteers. Specifically, the ratio of the peak PB CD34⁺ cell count divided by the ANC on the same day is about 50% lower in the two patients groups, relative to the normal volunteers. Thus, the ANC count alone would not have provided any indication that the recruitment of CD34⁺ cells was markedly impaired in many of the CGD patients and one of the ADA SCID patients.

In our study, the difference in PB CD34⁺ mobilization between 5 or 10 µg/kg G-CSF administration was not statistically significant in either the normal volunteers and CGD patients, as a group. However, there was a trend towards greater mobilization with the higher dose, (36% greater). Furthermore, in the 9 individuals given both doses of G-CSF there was a significant difference (paired t-test) between the 2 doses, mobilization being approximately 75% higher at the dose of 10 µg/kg of G-CSF. This dose was generally well tolerated in both the normal subjects and CGD patients, hence, we recommend that at least 10 µg/kg dose of G-CSF be used in clinical settings, but dose reduction to 5 µg/kg is acceptable where symptoms become a problem.

Greater mobilization with the dose of 10 µg/kg/d was also reflected in greater CD34⁺ apheresis yields. In normal donors the mean CD34⁺ cell yield was 39 × 10⁶ and 25 × 10⁶ per liter processed for 10 and 5 µg/kg, respectively. As expected from the lower mobilization in CGD patients, the apheresis yields were also lower, 20.8 × 10⁶ with 10 µg/kg and 14.8 × 10⁶ per liter processed with 5 µg/kg dose. The required number of CD34⁺ cells/kg patient bodyweight necessary for complete hematologic reconstitution after myeloablative therapy for allogeneic or autologous bone marrow transplant has not been well established. However, many studies have recommended 1 × 10⁶ to 5 × 10⁶ CD34⁺ cells/kg.⁵,⁶,⁷,⁸,⁹,¹⁰ Our study demonstrates that this level of CD34⁺ cell harvest is readily obtainable with one 10- to 15-L apheresis in normal donors. However, in the two patients groups studied and other patients with inherited disorders of the hematopoietic system may require apheresis for ≥2 days to achieve harvest of sufficient numbers of CD34⁺ cells. This approach to CD34⁺ cell harvesting has the advantage of being less traumatic and not requiring anesthesia, when compared with bone marrow harvesting. The successful application of G-CSF mobilized PB CD34⁺ cells to allogeneic transplantation should help in enhancing the registry of donors for this procedure.

Evaluation of a mobilization regimen in terms of the numbers of pluripotent CD34⁺ cells is important, because gene transfer into these cells may eventually provide a cure for specific hematopoietic disorders. Our study demonstrates that although the percentage of the putative pluripotent cells decrease in the G-CSF mobilized PB CD34⁺ cells, their absolute number increased significantly, making more of these cells potentially available for gene transfer. It is possible that other cytokine combinations might increase the percentage as well as the absolute numbers of the pluripotent cells to a greater extent. A recent study that used the combination of G-CSF and stem cell factor (SCF) demonstrated a two- to three-fold greater mobilization of committed progenitor cells. However, this study did not report the effect of the combination of G-CSF and SCF on the noncommitted stem cell subset.⁴⁷ Furthermore, it is also possible that with G-CSF administration, more noncommitted stem cells may be obtained at earlier days (such as day 3 or 4). These issues on optimal harvesting of the pluripotent or noncommitted stem cells should be examined in future studies. G-CSF administration also resulted in a significant increase in both the percent and absolute number of lymphoid and erythroid committed CD34⁺ progenitors. Gene transfer into these committed progenitors may be helpful in certain disorders involving these lineages. G-CSF administration to normal volunteers and CGD patients resulted not only in a significant increase in the numbers of neutrophils, but surprisingly also in the T, B, and natural killer (NK) cells. This may be important when G-CSF is used for mobilization of PB CD34⁺ cells for allogeneic transplantation, as the numbers of T cells and NK cells may have an impact on engraftment and the incidence and/or severity of graft versus host disease.

In summary, the present study demonstrates that G-CSF administration at a dose of 10 µg/kg is safe and well tolerated, both in normal volunteers and the two patient groups studied. In normal subjects and most, but not all patients this results in mobilization of adequate numbers of PB CD34⁺ cells which can be subsequently harvested by relativelyatraumatic apheresis for transplantation or gene therapy studies. The present study also demonstrates that changes in neutrophil counts do not predict either the kinetics or the peak level of PB CD34⁺ mobilization in response to G-CSF administration, making direct enumeration of PB CD34⁺ cells an essential component of optimum PB CD34⁺ harvest. Finally, the difference in PB CD34⁺ cell mobiliza-
tion between normal donors and the two groups of patients with inherited disorders of the hematopoietic system was unexpected and underscores the importance of determining PB CD34+ mobilization kinetics in a patient population before undertaking specific clinical regimens of gene therapy or other treatments that require CD34+ cell harvest.

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Granulocyte colony-stimulating factor recruitment of CD34+ progenitors to peripheral blood: impaired mobilization in chronic granulomatous disease and adenosine deaminase--deficient severe combined immunodeficiency disease patients

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