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Peripheral blood CD34+ cell counts allow improved management of peripheral blood stem cell collections

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The use of peripheral blood (PB) CD34+ cell counts on the day of, or the day prior to, peripheral blood stem cell harvest (PBSCH) to predict CD34+ progenitor cell yield has been the subject of considerable interest in recent years. Since 1996, we have followed the reports of those who have studied the relationship between PB CD34+ cell counts (and other indicators such as PB white blood cell count [WBC]) and the final CD34+ cell concentration following apheresis. Most reports have demonstrated a correlation between PB CD34+ cell count and harvest yield,[1-9] while one has reported poor correlation.[10]

Between 1996 and September 2002, PB CD34+ cell counts and WBC data were collected on 80 peripheral blood stem cell harvests from 57 patients (38 male, 19 female; age: 18–69; weight: 40–117 kg) with haematological malignancies (non-Hodgkin's lymphoma [NHL; n=33], myeloma [n=9], Hodgkin's disease [n=4], chronic myeloid leukaemia [n=3], acute myeloid leukaemia [n=3], acute lymphoblastic leukaemia [n=1], T-prolymphocytic leukaemia [n=1]) or solid tumours (n=3) immediately preceding the harvest. PBSC CD34+ cell counts were also performed following collection.

CD34 enumeration was performed by flow cytometry (Becton Dickinson FACScan) and the WBC by haematology analyser (Bayer H*1 or Advia 120). The Milan/Mulhouse protocol was used for CD34 enumeration as modified by the Nordic Stem Cell Laboratory Group prior to 1998 and Procount (Becton Dickinson) thereafter.[11]

The harvest day was guided initially by the choice of mobilisation regime (Table 1). Mobilisation was achieved either by cyclophosphamide priming chemotherapy and granulocyte-colony stimulating factor (G-CSF) (harvested on day 10), G-CSF only (harvested on day 5) or salvage therapy (harvested when WBC exceeded 5.0 x 10^9/L).

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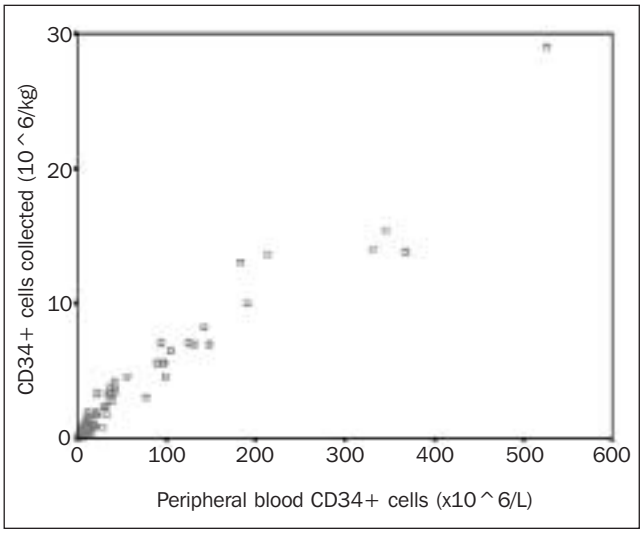

Fig. 1. Correlation between PB CD34+ cell count on the day of the harvest versus CD34+ cells collected (n=80).

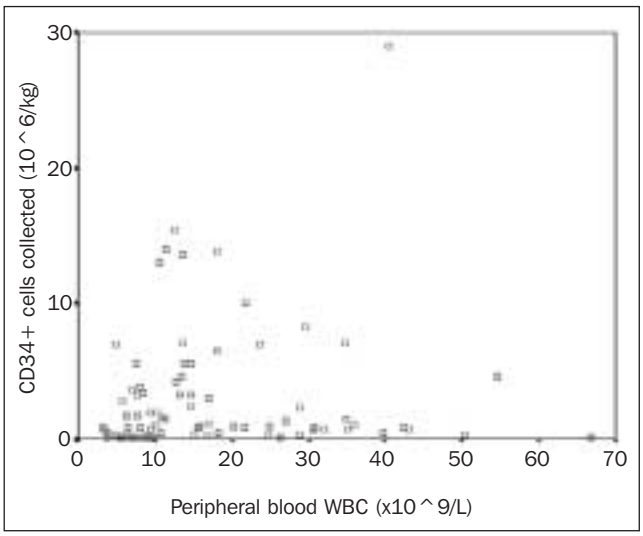

Fig. 2. Correlation between PB WBC on the day of the harvest versus CD34+ cells collected (n=80).

Analysis of data using Spearman's rank (non-parametric) test showed a strong correlation (r=0.94) between PB CD34+ cell count and the final concentration of CD34+ cells collected (Fig. 1). A comparison between PB WBC count and CD34+ cells collected showed only poor correlation (r=0.18) (Fig. 2).

In order to achieve haematopoietic recovery following high-dose chemotherapy, it is necessary to reinfuse sufficient CD34+ cells. The target yield for engraftment in Taunton is at least 2.0 x 10^6 CD34+ cells per kg of patient bodyweight.

The data presented indicate that a PB CD34+ count of ≥ 32.5 x 10^6/L yielded the target dose in a single procedure in all cases, irrespective of the choice of mobilisation regime or weight (range: 48–107 kg). A PB CD34+ cell count of ≤ 20.9 x 10^6/L failed to achieve the target dose in a single collection in all cases, There was some variation between >20.9 and <32.5 x 10^6/L (Table 2).

In addition, the possibility of using a PB CD34+ cell count to predict how many PBSC collections would be required

Table 1. Treatment regimes.

Patient	Diagnosis	Treatment regime
1	Hodgkin's	Mini BEAM salvage/priming chemo Rx – G-CSF 263 μg od
2	Hodgkin's	FLUDAP salvage/priming chemo Rx – G-CSF 263 μg od
3	Maxillary cancer	Adriamycin/cyclophosphamide/etoposide – G-CSF 526 μg od
4	NHL	FLUDAP salvage/priming chemo Rx – G-SCF 263 μg od
5	Myeloma	Cyclophosphamide 4 g/m^2 – G-CSF 263 μg od
6	NHL	Cyclophosphamide 1.5 g/m^2 – G-CSF 263 μg od (10/97) Cyclophosphamide 4g/m^2 – G-CSF 263 μg od (11/97)
7	NHL	Cyclophosphamide 2g/m^2- G-CSF 263 μg od
8	Hodgkin's	Cyclophosphamide 1.5g/m^2 – G-CSF 263 μg od
9	Breast cancer	Cyclophosphamide 4g/m^2 – G-CSF 300 μg od
10	NHL	Cyclophosphamide 4g/m^2 – G-CSF 263 μg od
11	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
12	AML	ADE 8+3+5 consolidation/priming chemo Rx – G-CSF 263 μg od
13	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
14	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od (2/99) G-CSF 526 μg od (9/99)
15	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od (3/99) G-CSF 526 μg od (11/99)
16	AML	DAT 3 + 8 – G-CSF 263 μg od
17	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
18	NHL	G-CSF 526 μg od
19	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
20	NHL	Cyclophosphamide /Adriamycin – G-CSF 263 μg od
21	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
22	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
23	Blast crisis CML	MACE – G-CSF 263 μg od
24	Myeloma	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
25	Myeloma	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
26	NHL	Cyclophosphamide 3g/m^2 – G-CSF263 μg od
27	NHL	Cyclophosphamide 3g/m^2 – G-CSF 526 μg od
28	NHL	G-CSF 263 μg bd
29	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
30	NHL	Cyclophosphamide 3 g/m^2 – G-CSF 526 μg od
31	NHL	Cyclophosphamide 3 g/m^2 – G-CSF 526 μg od
32	AML	FLAG chemo Rx – G-CSF 263 μg od
33	T-PLL	GCSF 600 μg od
34	Seminoma	Paclitaxel/Ifosfamide/Cisplatin – G-CSF 526 μg od
35	Myeloma	Cyclophosphamide 3g/m^2 – G-CSF 526 μg od
36	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
37	Hodgkins	IVE salvage/priming chemo Rx – G-CSF 526 μg od
38	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
39	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
40	NHL	IVAC chemo Rx – G-CSF 263 μg od
41	NHL	Cyclophosphamide 3g/m^2 – G-CSF 526 μg od
42	ALL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
43	NHL	GCSF 263 μg bd
44	CML	GCSF 789 μg od
45	CML	GCSF 789 μg od
46	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
47	Myeloma	GCSF 526 μg od
48	Myeloma	Cyclophosphamide 3g/m^2 – GCSF 263 μg od
49	Myeloma	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
50	NHL	IDARAM salvage chemo Rx – G-CSF 263 μg od
51	Myeloma	Cyclophosphamide 3g/m^2 – G-CSF 526 μg od
52	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
53	Myeloma	GCSF 526 μg od
54	NHL	GCSF 526 μg od
55	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od
56	NHL	Cyclophosphamide 3g/m^2 – G-CSF 263 μg od
57	NHL	IVE salvage/priming chemo Rx – G-CSF 263 μg od

IVE	Ifosfamide, Etoposide, Epirubicin	BEAM	Carmustine, Etoposide, Cytarabine, Melphalan
FLUDAP	Fludarabine, Dexamethasone, Cytarabine, Cisplatin	MACE	Amsacrine, Etoposide, Cytarabine
IDARAM	Idarubicin, Dexamethasone, Cytarabine, Methotrexate	FLAG	Fludarabine, Cytarabine, GCSF
IVAC	Ifosfamide, Cytarabine, Etoposide	DAT	Daunarubicin, Cytarabine, Thioguanine

if one harvest were insufficient was considered. Logarithmic transformation of the data, followed by linearregression,was performed. The resulting model demonstrated that CD34+ cell yield per kg has a direct linear relationship to PB CD34+ cell count (PBSC yield x 10^6/kg = 0.062 x PB CD34 count$^{0.994}$).

Interestingly, although PB WBC did not correlate well statistically with absolute CD34+ cell yield, all except one patient (who did yield the target dose or greater in a single collection) had a PB WBC ≥ 5.0 x 10^9/L and a PB CD34+ cell count ≥ 32.5 x 10^9/L. One other patient, with a WBC of 4.89 x 10^9/L and a PB CD34+ cell count ≥ 32.5 x 10^9/L also achieved the target dose in a single collection. Clinically, this was felt to be so close to the target that further delay could not be justified. Thus, the data presented here indicates that

Table 2. PB CD34+ cell count and achievement of target dose in a single collection (n=80).

PB CD34+ cell count (x 10^6/L)	2.0 x 10^6 CD34+ cells/kg
≤ 20.9	0%
> 20.9 < 32.5	50%
≥ 32.5	100%

a WBC ≥ 5.0 x 10^9/L is a sensible threshold to initiate CD34+ cell counts, and subsequently has been adopted in Taunton.

The PB CD34+ cell count is used to confirm that the harvest will yield sufficient CD34+ cells. If achievement of the target dose is predicted to be unlikely, the linear nature of the PB CD34+ cell count can be used to provide an indication of the number of collections needed.

For example, if 32.5 x 10^6/L predicts a PBSC yield of 2.0 x 10^6/kg, a PB CD34+ cell count of approximately 16.0 x 10^6/L suggests a PBSC yield of half the target dose (i.e.,1.0 x 10^6/kg), suggesting that at least two collections would be required. Similarly, a PB CD34+ cell count of 100 x 10^6/L would indicate a final yield of approximately three times the target yield (i.e., 6.0 x 10^6/kg).

Of course, this assumes that the PB CD34+ cell count will remain stable for the duration of the 'harvest window'. Any decrease in circulating CD34+ cells would extend the number of collections required. Similarly, an increase would reduce the the number of collections needed to achieve the target dose.

Owing to the dynamic nature of PB CD34+ cell mobilisation, the PB CD34+ cell count preceding each harvest was measured if more than one was needed. Updating the predicted yield permits optimum patient management by avoiding harvesting unnecessarily, or allows additional harvests to be performed if the PB CD34+ cell count is seen to be diminishing.

Importantly, we use PB CD34+ cell counts not only to predict the harvest yield on a particular day but also to ensure that stem cell mobilisation has occurred.

With a CD34 count usually available within an hour of receipt of a sample, delays in harvesting are minimal. The cost of routinely performing two or more leucapheresis procedures when one would have been sufficient (or should not have been commenced at all) far outweighs the cost of a CD34 count.

The present study aimed to assess the utility of the PB CD34+ cell count as a robust method to optimise the timing of apheresis in order to achieve the target dose in a single collection, or to provide accurate information about the number of procedures that would be required if one were insufficient (or if CD34+ cell mobilisation had occurred at all). The results showed that PB CD34+ cell counts can predict harvest yield, irrespective of treatment regime or patient weight.

In summary, PB CD34+ cell counts provide a realistic and cost-effective opportunity for improved utilisation of clinical and laboratory resources. A more effective service can be offered to the patient by minimising inconvenience and the need for unnecessary procedures (by avoiding harvesting too early or too late), and by identifying those patients unlikely to yield sufficient CD34+ cells to be of therapeutic value. □

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Placental transfer of measles antibodies in Nigerian mothers

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Measles is a major health problem of childhood in developing countries, despite the immunisation of children against the disease.[1] Factors such as ignorance, malnutrition, non-immunisation, delay in seeking medical attention and intra-uterine fetal infection from the exposed mother have