



## Correspondence

### Bone marrow transplant in Diamond-Blackfan anemia

I would like to elaborate on the topic of bone marrow transplantation for Diamond-Blackfan anemia (DBA), in a follow-up to the article by Bonno *et al.*<sup>1</sup> There are twice the number of transplants for DBA than they cite, with at least 35 cases reported. Some cases are reported more than once.<sup>2-15</sup> Ten of these died, from interstitial pneumonitis, graft rejection, graft failure, acute or chronic graft-versus-host disease and sepsis. The absolute cure rate is 71%, and the projected survival from Kaplan-Meier analysis is 66%. While most of the donors were siblings, one was the mother, and one a matched unrelated donor. In addition to the one reported by Bonno *et al.*, two other cord transplants were done, from a brother<sup>15</sup> and from a matched unrelated donor.<sup>13</sup> Although transplant for a single lineage defect raises ethical concerns for some of us, clearly the experiences with transplant in beta thalassemia and in sickle cell disease<sup>16,17</sup> suggest that purely erythroid diseases can be cured by stem/progenitor cell transplants. All alternative donor sources need to be considered for these conditions.

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### References

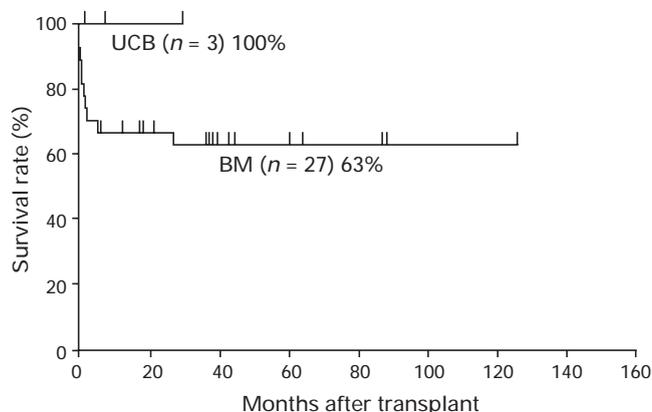
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### Reply

We appreciate Dr Alter's complementary review of transplants for DBA. At the time our patient was transplanted, some of the papers had not yet appeared. Regarding the number of transplants, a patient in Ref. 4 seems also to be included in Ref. 11. Further, we felt separate evaluation of the outcomes of transplanting with bone marrow (BM) or umbilical cord blood (UCB) was important because a high

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rate of engraftment and reduced risk and severity of graft-versus-host disease are reported with UCB.<sup>1,2</sup> Thus, transplants have been performed for at least 31 DBA cases with BM, and at least four cases with UCB including the one recently reported.<sup>2</sup> The absolute cure rates are 68% and 100%, respectively. The projected survival from Kaplan-Meier analysis is 63% and 100% (Figure 1). Although the number is limited, UCB may be a favorable source of hematopoietic cells for DBA and other bone marrow failure syndromes.



**Figure 1** Kaplan-Meier estimate of the probability of survival after transplantation for DBA. UCB 5 umbilical cord blood; BM 5 bone marrow. Cases in which post-transplant survival days were not described were omitted.

### Acute gouty arthritis following recombinant human granulocyte colony-stimulating factor therapy in an allogeneic blood stem cell donor

Of recent interest has been the use of recombinant human granulocyte colony-stimulating factor (rhG-CSF) mobilized peripheral blood stem cells for allogeneic transplantation.<sup>1</sup> While rhG-CSF therapy in normal allogeneic donors has been generally well tolerated, an increasing list of acute complications has been described. We would like to add another acute complication of rhG-CSF in an allogeneic blood stem cell donor, namely acute gouty arthritis.

A 65-year-old male with a history of coronary artery disease was identified as an HLA-genotypically identical stem cell donor for his sister who had acute myeloid leukemia. The donor had a history of asthma, coronary artery disease with two previous angioplastic procedures (in November 1996), degenerative arthritis of the right knee (status post right knee replacement) and hypercholesterolemia. He took pravachol 20 mg daily and one aspirin daily. He had no history of gout. Physical examination prior to administration of rhG-CSF revealed no joint swelling, erythema tenderness or deformities. A baseline uric acid level was 8.2 mg/dl (normal range 3.6 to 8.5). rhG-CSF was begun at a dose of 10 mg/kg per day. On the second day of treatment he noticed tenderness on the back of his heel (in an area of previous Achilles tendon surgery). He saw his private physician who prescribed cephalexin for presumed cellulitis. Over the next several days erythema and tenderness over the heel area progressed. On the morning of intended stem cell donation (following 5 days of G-CSF therapy), examination of left foot was remarkable for marked erythema, warmth and tenderness with fluctuance over the left heel, swelling of the plantar surface of the foot, and erythema and edema of the distal left foot and

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left third toe. His peripheral white blood count was  $33.9 \times 10^9/l$ . A repeat uric acid level was not obtained. A presumptive diagnosis of cellulitis was made and broad spectrum antibacterial antibiotics were begun (nafcillin and ofloxacin). A subsequent needle aspiration of the left heel area however revealed urate crystals. Treatment with colchicine resulted in prompt improvement of symptoms and signs of his arthritis.

This stem cell donor may have been predisposed to gouty arthritis by virtue of having a high normal uric acid level and by taking aspirin. However a rapid rhG-CSF expansion (and turnover) of his myeloid pool probably led to precipitation of acute gouty arthritis and tendonitis.

As discussed in a recent review by Anderlini *et al.*,<sup>1</sup> rhG-CSF therapy is generally well tolerated in normal stem cell donors with only an approximately 1-3% incidence of rhG-CSF discontinuation having been observed. There are, however, anecdotal reports of acute complications following rhG-CSF therapy of normal donors ranging from inflammatory conditions (eg acute iritis),<sup>2</sup> temporally related thrombotic events (cerebrovascular accident, myocardial infarction)<sup>1</sup> and more recently spontaneous splenic rupture.<sup>3</sup> Given the potentially profound acute (and possibly delayed) complications that can occur following rhG-CSF administration in normal donors, we believe that it will be important to monitor complications of this therapy prospectively. The more than 2000 normal donors that Anderlini<sup>1</sup> estimates would have to be followed for 10 years or longer to detect a 10-fold increase in leukemia risk, for example, would seem to be a daunting task. However, given the rapidly increasing application of allogeneic blood stem cell transplantation, this number of donors could probably be accumulated from relatively few transplant centers with high transplant volumes. Several potential advantages of using blood stem cells compared with bone marrow for transplantation (including possibly less complications of stem cell procurement compared with a bone marrow