To the editor:

Lessened severe graft-versus-host after "minitransplantations"

We greatly appreciate Dr Brian Abbott's commentary[1] on the publication by Diaconescu et al,[2] which compared toxicities and non-relapse mortality in patients undergoing HLA-matched related hematopoietic cell transplantation (HCT) following either nonablative or ablative conditioning, and we would like to make 3 points in response to his cautionary notes. First, we recently published very similar observations in patients given unrelated HCT.[3] All nonablative patients in that study received 2 Gy total body irradiation preceded by 3 doses of fludarabine, 30 mg/m^2/d for 3 days. Even though nonablative patients had significantly higher pretransplantation comorbidity scores, were older, and had more often failed preceding ablative HCT and cytotoxic chemotherapies, they experienced fewer grades III-IV toxicities than ablative patients. The 1-year nonrelapse mortality was 20% in nonablative compared with 32% in ablative patients, a difference that was significant after adjusting for pretransplantation differences between the 2 groups of patients ($P = .04$).

Second, while we agree that no long-term follow-up data on disease control are available as yet, early results in patients with multiple myeloma, non-Hodgkin lymphoma, chronic lymphocytic leukemia, and acute myelocytic leukemia look encouraging.[4-7]

Third, the graft-versus-host disease (GVHD) incidence among nonablative recipients was lower than that among their ablative counterparts,[3,8] and this was most pronounced for grades III-IV acute GVHD among unrelated recipients (Figure 1).

Finally, we share Dr Abbott's enthusiasm for the use of the Charlson Comorbidity Index (CCI) to evaluate patients before HCT. Patients with CCI scores of 1 or higher might benefit from undergoing nonablative HCT, regardless of their age.

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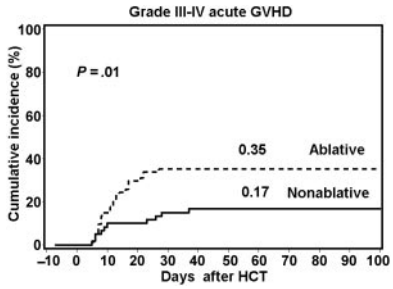

Figure 1. Grades III-IV acute GVHD in concurrent groups of nonablative and ablative patients given unrelated HCT ($P = .01$). Solid line indicates nonablative patients; broken line, ablative patients.

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To the editor:

Down syndrome in Down House: trisomy 21, *GATA1* mutations, and Charles Darwin

At the outer edge of the leafy southeastern London suburbs lies the small village of Downe, nestled in the rolling hills of Kent just 16 miles from the city. The chief attraction of Downe for nonresidents is Down House (the customary spelling for the estate is different from that of the village), the family home of the man who was arguably England's most important contribution to the biological sciences: the great naturalist Charles Robert Darwin (1809-1882). In recent years, Down House has been extensively restored, and the property is now maintained in the public trust by English Heritage. The site is an increasingly popular pilgrimage destination for biologists and others with an interest in the history of the natural sciences.

During a recent visit to Downe, my daughter and I were fascinated by the Darwin family photos scattered about the 19th-century rooms on the ground floor of Down House. I was prompted to read the sensitive and engaging account of Darwin's family life published by his great-great-grandson, Randal Keynes.[1] By all accounts, Darwin and his wife (and first cousin) Emma Wedgewood enjoyed a close, warm, and generally happy domestic existence, limited by Charles' poorly defined chronic ailments—possibly sequelae of Chagas disease contracted during the voyage of the *Beagle*—and broken by the premature deaths of 3 of their 10 children.