CORRESPONDENCE

BONE MARROW DONOR REGISTRIES: DISCORDANCE IN HLA FREQUENCIES BETWEEN DONOR AND RECIPIENT POPULATIONS

To the Editor:

We read with interest the article by Sonnenberg et al describing the relationship between registry size and the probability of finding completely and partially HLA-matched unrelated marrow donors. The effect of a significant difference in HLA profiles between donor and potential recipient populations was simulated by using two groups of different ethnic origin and was shown to drastically alter the probability of successful donor searches from that which would be expected if the populations were similar for HLA. We have investigated whether any significant discordance for HLA actually exists between a random donor population and the population of patients referred to a registry of randomly selected HLA-typed volunteers for an unrelated marrow donor search.

HLA-A, -B, and -DR types were recorded in 750 consecutive patients referred for an unrelated marrow donor search to the British Bone Marrow and Platelet Donor Panel between May, 1984, and July, 1989. Chronic myeloid leukemia (40%), acute leukemia (28%), and aplastic anemia (15%) were the most frequent diagnostic categories. Of the searches, 38% were requested from outside the United Kingdom. HLA-A, -B, and -DR antigen frequencies in this patient group were compared with those in 5,015 UK kidney donors, a random population that can be taken as equivalent to the panel of volunteer marrow donors who were not universally typed for HLA-DR. Statistically significant differences in HLA antigen frequency were detected using Fishers exact test (two-tailed) after correction for the number of HLA antigens compared (multiplication of P values by 50).

Common HLA antigens in the donor group occurred at significantly lower frequencies in the recipient population (Table 1). This is not likely to be the result of any associations between HLA antigens and hematologic malignancy. Racial variation between the populations may play a role, but we think the major factor accounting for this difference is the relatively large proportion of patients (31%) with at least one previous unsuccessful search at another registry. Patients lacking common HLA types are those most likely to require re-referral to a second registry for a further search. Therefore, all registries receiving a significant number of these secondary searches will have their recipient population depleted in common HLA types compared with the healthy donor population. Thus, it is probable that the differences we have observed between the two populations results from the pattern of patient referral.

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REFERENCES

<table>
<thead>
<tr>
<th>HLA Antigen</th>
<th>Recipient Population (n = 750)</th>
<th>Donor Population (n = 5,015)</th>
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RESPONSE

We appreciated the comments of Howard et al regarding the discordance between donor and recipient populations in the experience of the British Bone Marrow and Platelet Donor Panel. The finding of significant discordance is not altogether unexpected, but the conclusion that the discordance is due to referral pattern, rather than to intrinsic characteristics of the recipient population, is surprising although plausible.

We wish to make several points regarding the study of Howard et al. First, they reported the frequency of only single antigen frequencies, which imply discordance, but by themselves do not allow one to calculate the degree to which such discordance would affect the probability of finding a match. Such calculations would require three-allele haplotype data. Second, the impact of discordance on probability of finding matches depends on the quality of matching...
sought. Our study showed that the probability of phenotypically identical matches is affected much more by discordance than is the probability of finding partial matches. Third, the referral pattern of patients will affect the degree of discordance between donors and recipients only if registries are regarded in isolation; if all donors are considered globally, the makeup of the entire donor pool should approximate that of the population from which it is drawn.

Studies like that of Howard et al provide precisely the kind of additional data needed to bring an analysis of operational characteristics of registries from a theoretical plane to a more practical one. We encourage all operating registries to collect and maintain data regarding the HLA characteristics of their donors and recipients and the search history for each prospective recipient. We would further encourage the registries to share this data freely, so that future projections of the success of registries will have the greatest amount of information with which to work.

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Bone marrow donor registries: discordance in HLA frequencies between donor and recipient populations [letter; comment]

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