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HLA MATCHING IN RENAL TRANSPLANTATION

To the Editor: The competing goals of justice and optimal outcome in the allocation of cadaveric kidneys were addressed in the September 22 issue of the *Journal.*[1-3] Takemoto and coauthors accept the premise that current policies place black candidates for transplantation at a disadvantage.[1] They propose a revised HLA-based system with broader categories of acceptable mismatches, allowing more candidates to receive kidneys, and they estimate that such a scheme would improve graft survival for all recipients. However, on closer examination, the proposal offers only marginal improvement in outcomes for black transplant recipients and fails to anticipate the effect of the proposed system on blacks' access to transplantation.

Presumably, even with broadened matching criteria, too few blacks would receive well-matched kidneys from the predominantly white donor pool for a benefit to be documented. One is left to conclude that the primary beneficiaries of improved matching would be white. The authors also note that only after waiting five years will candidates with rare HLA specificities (who are frequently black) accumulate enough points to counterbalance the effects of matching. How often, under this system, would kidneys be allocated to better-matched white candidates rather than less well matched black candidates, who had perhaps waited longer? These shortcomings notwithstanding, by emphasizing broader HLA categories and local distribution, this plan appears more equitable than either the algorithm currently used by the United Network for Organ Sharing (UNOS) or previous proposals to expand HLA-based allocation.[4]

What increment in graft survival is necessary to justify policies with disproportionate adverse effects on certain subgroups of candidates for transplantation? Is it 1 percent or 10 percent or 20 percent? And over what period of time? According to Held et al.,[2] the increment in graft survival to be expected with a national policy of maximal matching is likely to be at most 2 to 4 percent over a period of five years, with a concomitant 33 percent reduction in the access of black candidates to cadaveric kidneys. In our opinion, such a tradeoff is not justified. Unequivocal benefits of HLA matching accrue only to recipients of extremely well matched kidneys (those with no mismatches); in all other circumstances, equity should be the primary determinant of allocation.

Dr. Sanfilippo stresses that "the key to increasing the number of recipients with optimally matched kidneys and reducing waiting time is to increase the number of organs donated, especially from minority groups."[3] To eliminate current inequities, minority donations would need to increase fivefold, an implausible event.[5] He contends that increasing the allocation of poorly matched kidneys to blacks will not result in equitable treatment. Given the complexities of HLA matching, along with the demographics of end-stage renal disease and the donor population, we see no other practical alternatives.

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The authors reply:

To the Editor: Our proposal to change the conventional method of counting mismatched HLA antigens to one that considers fewer but more influential HLA differences offers substantial improvements in both access to and outcome of transplantation for blacks. The estimated 7 percent increase (from 43 percent to 50 percent) in five-year graft-survival rates for blacks cannot be achieved by the use of any other published proposal. As more blacks have received well-matched transplants, graft survival has improved.[1] Under the UNOS system of national sharing of grafts matched for HLA-A, B, and DR, black recipients of matched grafts had an 84 percent rate of graft survival at one year.

With respect to the allocation of mismatched kidneys, national sharing would have a rather small effect in view of the difficulties associated with shipping HLA-mismatched organs.[2] We therefore shifted our attention to matching within local areas. By concentrating on key HLA differences in small local pools, it is possible for as many as 30 percent of blacks to receive well-matched grafts as compared with the rate of 5 percent with the use of conventional methods. A group in Alabama reported similar results.[3]

We believe that the competing goals of improved outcome and justice in allocation of kidneys can be reconciled using the UNOS point system. Our proposal allows patients to accumulate 0.1 point per month of waiting, instead of being allotted the current stepwise increase each year. Candidates will receive kidneys according to how long they have waited, except when a patient lower on the list is a match for the available kidney. The relative number of points given for matching may need to be adjusted according to waiting times in a particular region. Since the average black patient waits slightly more than two years for a kidney, the example of a patient who waits five years and then is skipped over because another patient is a better match for the graft would rarely occur. Patients who wait longer have repeatedly been excluded by positive cross-match tests. According to Cook et al., even for highly sensitized patients, our proposed matching scheme would reduce the frequency of positive cross-matches.[4]

We are dismayed by the conclusion of Gaston et al. that there is no other alternative but to increase the allocation of poorly matched kidneys to blacks. This implies that extra

points would be given to certain patients because they are black.[5] Anyone claiming black ancestry would be pushed ahead in the line from the first day he or she entered the pool. Although our proposal does not solve every problem, it improves the current matching system by projecting an increase in the number of black transplant recipients with longer-lasting kidney function.

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To the Editor: Gaston et al. argue that equity in access to kidney transplantation is an important goal for the transplantation community and that the improvement in five-year graft survival by at most 2 to 4 percentage points does not justify HLA matching except for cases involving no mismatches. The fundamental source of the problem in access to kidney transplantation is the disparity in numbers between kidney donors (living or dead) and needy recipients. With over 22,000 patients on a rapidly growing waiting list and approximately 10,000 transplantations a year, waiting times have increased substantially in recent years. The number of new cases of chronic kidney failure has been growing exponentially, whereas the number of donor organs has essentially been constant for several years.[1]

Black Americans are donating cadaveric kidneys at rates approaching those for white Americans, but their rate of chronic renal failure is nearly four times higher. Therefore, there is no practical way to reduce the disparity. Furthermore, we know of no evidence that blacks have better outcomes with donor organs matched for race than with cadaveric organs that are not so matched. Perhaps the most important disparity in the rates of organ donation is related to donation of kidneys by live persons, which is several times lower among blacks than among whites.[2] Increased donation of organs by live persons could reduce waiting times and improve outcomes for black recipients.

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To the Editor: Gaston et al. appropriately conclude that when no benefit in outcome can be identified, equity should be the primary determinant of donor-kidney allocation. Unfortunately, they inappropriately assume that "unequivocal benefits of HLA matching accrue only to recipients of extremely well matched kidneys (those with no mismatches)." As I discussed in my editorial, transplantation of even suboptimally matched kidneys provides substantial benefits to the recipients, as well as the rest of the recipient pool. These include reduced sensitization and shorter waits for a second transplantation after graft failure, fewer positive cross-matches in presensitized recipients, and improved graft survival, which can be demonstrated clearly when HLA typing is accurate.[1] Furthermore, the improvement in graft survival due to matching reduces the number of patients requiring second transplantations, thus reducing the waiting time for the remaining recipient pool.

It is unclear from their letter whether Gaston et al. believe that to ensure equity kidney allocation should be directed toward specific minority populations or to all patients with prolonged waiting times. The notion of allocating organs on the basis of race, even in an attempt to achieve equity, is discriminatory and would lead to logistic as well as ethical problems in implementation. Allocation on the basis of waiting time is already a key component of the UNOS policy, and as pointed out previously,[2] the main factor leading to prolonged waiting times for blacks is not the HLA-matching policy, but rather differences in ABO blood groups between donors and recipients.

Finally, Gaston et al. attribute to me the statement that "increasing the allocation of poorly matched kidneys to blacks will not result in equitable treatment" and conclude that they "see no other practical alternatives" to this approach. In fact, I stated that "reducing the waiting time for blacks by increasing their allocation of poorly HLA matched kidneys will not result in the type of equitable treatment most desired, especially since graft survival in these patients is already lower than that in whites." Indeed, very recent analyses from UNOS demonstrate that substantial differences in graft outcome between the races at different centers is associated with average HLA matching and is most striking with longer follow-ups (Thompson J: personal communication).

I stand by the above statement and maintain that the only practical means of reaching the dual goals of providing true equity in waiting time and optimal outcome for all patients (including blacks) is to increase the number of organs donated from each population in order to provide better-matched kidneys for all recipients.

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IMPROVEMENT IN CYCLOSPORINE-ASSOCIATED GINGIVAL HYPERPLASIA WITH AZITHROMYCIN THERAPY

To the Editor: Gingival hyperplasia is a known complication of cyclosporine therapy. It appears to be worsened by the concomitant administration of nifedipine or phenytoin.

Two transplant recipients had dramatic improvements in symptomatic gingival hyperplasia after a short course of azithromycin. The first patient was a 49-year-old man with