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EDITORIAL

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A consideration of potential donors with active infection – is this a way to expand the donor pool?

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A cogent argument can be made that one of the landmark achievements of twentieth century biomedical science has been the transformation of organ transplantation from an interesting experiment in human immunobiology to the most practical means of rehabilitating patients with end-stage organ failure. The very success of transplantation has placed a premium on expanding the donor pool, due to the growing disparity between organ availability and the number of individuals who might benefit from organ transplantation. The response to this crisis has been the development of elaborate organ allocation systems (many of which remain controversial), as well as attempts to develop new groups of organ donors, such as nonheartbeating donors [6]. In this issue of *Transplant International*, a paper by Caballero et al. [1] describes the successful transplantation of kidneys from a donor with proven enterococcal endocarditis that had been treated with systemic antibiotics for a relatively short period of time prior to organ procurement. This success suggests that a review of the guidelines for evaluation of donors with active systemic infection is in order as a potential means for carefully expanding the donor pool.

Guidelines based on serologic testing of donors have been developed to prevent the transmission of viral infections, such as hepatitis B and C and the human immunodeficiency virus, with an allograft. Similarly, serologic assays for dormant and latent infections, such as toxoplasmosis, cytomegalovirus, Epstein-Barr virus, and others, have led to a clear understanding of the risk of symptomatic infection after transplantation and form the basis of preventive strategies [11]. The challenge that remains lies in the evaluation of donors with possible or definite systemic infection that has been treated with appropriate antibiotics for a period of time. How long must such therapy be continued before organs can be safely procured and transplanted? Are all infections and therapies of equal efficacy? What guidelines can be put forth to guide the transplant team that is caught between the dilemma of a patient in desperate need of an allograft and a donor who would otherwise be suitable except for the presence of clinically important bacterial or fungal infection?

Two categories of infection merit consideration: bacterial or fungal infection acquired in the terminal stage of the donor's care in an intensive care unit (e.g., vascular access infection, nosocomial pneumonia, bladder catheter-related infection), and systemic infection, as in the Caballero et al. report [1], which was implicated in the donor's demise. The key issue in both of these circumstances is to avoid transplanting an infected organ or an organ from a patient with ongoing bacteremia or fungemia. In both instances, anastamotic suture lines are threatened, with the vascular suture line being at particular risk for the development of mycotic aneurysms and of catastrophic rupture [11].

A relatively large body of literature has reported that cultures of organ perfusate and transport media may be positive in up to 40% of samples. Most such positive cultures are with nonvirulent skin flora; these results have correlated poorly with the occurrence of post-transplant allograft infection. In contrast, when such

surveillance cultures yield gram-negative bacilli, particularly *Pseudomonas aeruginosa,* or *Candida* species, and when such an organ is transplanted, the rate of subsequent infection of the vascular suture line can be rather high [4, 7–11, 13]. The importance of gram-negative infection of the perfusate has been reinforced in a dog renal transplant model in which a perfusate was purposely contaminated with *E. coli* and the kidney subsequently transplanted. All of the recipients died within approximately 4 days of either vascular anastomotic disruption or generalized sepsis [13].

Unfortunately, negative perfusate cultures and careful clinical evaluation of the donor prior to organ procurement do not preclude the possibility of serious allograft infection. We have reported a case of unsuspected donor *Pseudomonas* sepsis causing life-threatening infection in both recipients of kidneys at two separate institutions from a single donor. In the 2nd post-transplant week, emergency graft nephrectomies were performed because of exsanguinating retroperitoneal hemorrhage. At operation, the arterial anastomosis was completely necrotic and disrupted, and grew the same *Pseudomonas* that was isolated from the donor [4]. The incidence of such events, particularly of a less catastrophic nature (e.g., unexplained gram-negative bacteremia), is unknown. The question can and should be raised as to whether the routine administration to donors of broad-spectrum antibiotics for a limited time period prior to organ procurement might offer protection against unsuspected infection. Clearly, recipients of organs from donors with infection should be treated with post-transplant antibodies [2, 3].

Of at least equal concern is the evaluation of potential donors with known systemic infection. In the report by Caballero et al. [1], enterococcal endocarditis was treated with antibiotics for a relatively short period before organ procurement was carried out, far short of the usual 4–6 weeks of therapy recommended for cure of this entity. However, in this instance, this therapy was sufficient to permit the successful transplantation of organs from this donor. With this experience as a point of departure, the challenge is to develop a responsible approach to this problem in the absence of all but anecdotal data. The following would appear to be important variables that warrant consideration:

1. The organism(s): Not all organisms are of equal virulence in terms of adherence to cardiovascular endothelia or the ability to metastasize to organs of interest for transplantation. Thus, enterococci, *Staphylococcus* species, viridans streptococci, and *Pseudomonas aeruginosa* are notable for their ability to adhere to endothelial surfaces, and *Staphylococcus aureus, Salmonella* species, *Candida* species, *Aspergillus* species, and *Pseudomonas aeruginosa* are notable for their ability to establish metastatic infection in organs of interest. In contrast, *E. coli, Enterobacter* species, and *Klebsiella* species generally exhibit neither characteristic [5, 12].
2. Antimicrobial efficacy: Not all antimicrobial strategies are of equal efficacy in terms of eliminating bloodstream infection. For the purposes of cleansing the bloodstream and organs that are potential targets of infection, it would seem logical to require bactericidal (as opposed to bacteriostatic) therapy. Because of the far slower response of fungal infection to antimicrobial therapy, patients with candidemia should require far more extensive therapy than those with acute bacteremia.
3. Time course of infection: The duration and level of bacteremia, and the clinical and microbiologic response to appropriate therapy are important variables to be considered as well. For example, a potential donor with sustained *S. aureus* bacteremia over several days would be an undesirable candidate for this approach. In contrast, acute pneumococcal or meningococcal meningitis, in which appropriate therapy clears the bloodstream in 4–5 days quite reliably, and where metastatic infection to organs such as the kidneys and liver is unusual, might be entities that would lend themselves to an expanded donor pool consideration [2, 3].

With these principles in mind, we would propose the following approach, which is particularly aimed at those patients with systemic infection:

1. The establishment of an international registry in which all situations in which infected donors were utilized – both successes and failures – would be collected, collated, and summarized for the transplant community.
2. The cautious consideration of "infected" donors under the following circumstances:

A. Potential recipients who give informed consent for the receipt of such organs.
B. Bacteremia with a relatively bland organism (e.g., the Enterobacteriaceae with the exception of *Salmonella* species, viridans streptococci) or with an organism that is rapidly cleared from the bloodstream with effective bactericidal therapy (e.g., penicillin-sensitive pneumococci and meningococci) that has been treated with bactericidal therapy for at least 5 days, and where blood cultures have been shown to become negative. Ideally, some evidence of clinical response to such therapy should be present. Patients with undrained, infected fluid collections ("pus under pressure") will require more prolonged treatment regardless of the causative organism.

3. Potential donors with bloodstream infection due to the following organisms and would require a minimum of 2 weeks of bactericidal therapy and then "proof of cure" (i.e., negative blood cultures over a period of a week off antibiotics): *Staphylococcus aureus, Pseudo-*

monas aeruginosa, and infections due to streptococci that have decreased susceptibility to penicillin.
4. Potential donors with bloodstream or invasive tissue infection due to the following more difficult to treat organisms should be eliminated from consideration for the present: Group A streptococcal infection, vancomycin-resistant enterococcal infection, *Streptococcus milleri* infection, *Salmonella* infection, and fungal, nocardial, or active mycobacterial infection.
5. All recipients receiving organs from this category of expanded donors should receive bactericidal antibiotic therapy directed against the donor's organism for a minimum of 10–14 days post-transplant.

Hopefully, this cautious approach, coupled with the collection of clinical data, will allow a gradual and safe expansion of the limited organ donor pool.

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