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INCREASED RISK DONORS: A BIRD IN THE HAND

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Unexpected donor-derived infections (DDI) are relatively uncommon events complicating less than 1% of solid organ transplants (1). Disease can be severe, however, with malignancies and agents that infect the central nervous system carrying a particularly high risk of adverse outcomes (2). In most cases, this risk is managed by a combination of clinical assessment and pre-procurement donor testing.

The area that has received the most attention from public health authorities involves the risk of transmission of blood-borne viruses - human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). In 2013 the Public Health Service (PHS) updated a set of behavioral criteria intended to identify a group of potential donors at increased risk for recent HIV, HCV, or HBV infection. These donors may be in the "window period" –infected with transmissible virus but screening tests not yet positive. According to United Network for Organ Sharing (UNOS) policy, informed consent must be obtained from recipients offered organs from increased risk donors (IRD). Among IRDs, the circumstance of greatest concern is window period HCV infection in donors with active intravenous drug use. Both mathematical modelling and limited data from the UNOS Disease Transmission Advisory Committee (DTAC) required but passive reporting system, suggest that the risk of window period HCV associated with these donors is between 1% and 0.1% (3, 4). Risk of HIV transmission is significantly lower, and only 2 known cases of DDI with HIV have occurred in the U.S. since 2007. Despite these low risks, acceptance of IRD organs varies widely from center to center and between programs within a center. Further, organs from IRD are less likely to be used and one estimate suggests that 313 organs are not used each year due to the IRD designation (5).

Three major changes have occurred over the past decade that should make us reassess the reasoning behind the IRD label. First, since 2014, all increased risk donors undergo nucleic acid testing (NAT) for HIV and hepatitis C. This shortens the window period from 2-3 months (for HCV) to less than two weeks reducing the risk of window period infection compared to antibody screening alone by as much at 10 fold (4). Second, curative HCV treatments are now available and the consequence of HCV transmission is less significant than other risks associated with transplantation

or, for that matter, of prolonging the period of organ failure by declining an IRD donor. Finally, and perhaps most impactful, as a result of the growing opioid epidemic up to 25% of donors (or more in some locations) are now classified as IRD, emphasizing the need to educate both potential recipients and providers regarding the true risk associated with IRD, and, just as importantly, the risks associated with declining and IRD organ offer.

Into this the rapidly evolving situation, the current report by Bowring *et al.* is most welcome. Using 2010-2014 SRTR data, the investigators identified 104,998 potential recipients offered an IRD kidney and compared outcomes of those who accepted and declined the offer (6). Overall acceptance rates were low with only 6251/104,988 (6.2%) accepting their initial IRD, although rates increased from 3.5% in the first year of the study to 7.8% in the final year. The consequences of declining an IRD offer were quite significant. Five years after the offer, 55% of declining recipients had not received a transplant. Those accepting an IRD kidney offer realized a significant survival benefit with a 48% reduction in risk of death 6 months post decision. Crude mortality at 5 years was 14% versus 22.5% among those accepting versus declining the IRD offer. Finally, among those who declined an IRD kidney and eventually received a non-IRD kidney, the KDPI of the non-IRD kidney was significantly worse than the declined IRD kidney (median 52 IQR 30-72) versus (median 21 IQR 10-38).

As the authors point out, the decision to consent to an IRD is not a choice between an organ offer from an IRD and non-IRD kidney, but a choice between a "bird in the hand" and an uncertain wait for an offer from a non-IRD donor. Importantly, the paper illustrates the significant increase in mortality and decrease in median kidney quality that is a consequence of declining an IRD offer. Future studies should be performed to determine if potential recipients of non-kidney organs accrue similar benefits from accepting an IRD offer.

Data from this study needs to be translated into educational content appropriate for counseling potential recipients (and providers), ideally a process that would begin early. In the era of universal NAT testing, curative treatment for

hepatitis C, and a growing pool of donors classified as IRD, this data should encourage the transplant community to rethink the impact of the IRD donor label.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

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