American Society of Transplant Surgeons Comments
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HHS Advisory Committee on Blood & Tissue Safety & Availability (ACBTSA)
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On behalf of the American Society of Transplant Surgeons (ASTS), our members, and the patients we serve, thank you for your consideration in revising the "Public Health Service Guidelines for Reducing HIV, HBV, and HCV Through Organ Transplantation." We greatly appreciate the HHS Advisory Committee on Blood & Tissue Safety & Availability (ACBTSA) conducting this important meeting.

I speak on behalf of the ASTS. The ASTS was established in 1974 and serves approximately 1,800 surgeons, physicians, scientists, and other transplant professionals dedicated to excellence in transplantation surgery. ASTS advocates for comprehensive and innovative solutions to meet the needs of the patients we serve.

The PHS Guidelines currently in use were developed in 2012 and implemented in 2013. ASTS understands the past value of these guidelines. However, our transplant environment has changed in many ways since these were developed. First, the field has a stronger culture that emphasizes patient safety. That means our transplant programs closely monitor results, assess current practice patterns, and re-assess to ensure best practices. Through our emphasis on safety our transplant results have improved, and we transplant more patients. Unfortunately, more patients than ever are awaiting a deceased donor transplant, the wait times are longer, and there are more deaths on the waiting list. In 2018, there were almost 95,000 candidates on the waiting list for a kidney transplant. Less than 16,000 received a deceased donor transplant even though nearly 20,000 kidneys were recovered for transplant. That means almost 20% per cent of the recovered kidneys were discarded. We all agree that we should do everything possible to help more individuals receive the gift of life.

ASTS is very concerned that the current PHS Guidelines are inadvertently contributing to the underutilization of safe and life-saving organs for transplant. Who could have predicted in 2012 when the current policies were developed:

- That the proportion of "increased risk" donors in the US would have increased from 12% to nearly 26% today;
- That the "increased risk" donors are disproportionally in the donor age group, 18-34 years (1);
- That there would be an association between "increased risk" status and a decrease in Organs Transplanted per Donor in the 18-34 age group from 4.2 to 3.9, translating to about 200 fewer organs transplanted annually (1);

- That the decrease in utilization of organs from the "increased risk" donors would fall primarily on the pediatric population awaiting a transplant (1);
- That the collective results in transplant outcomes are actually better in recipients of organs from "increased risk" donors (1);
- That those that turn down a kidney from an "increased risk" donor wait about 9 additional months before they are transplanted and also receive an organ of lower quality (2);
- That there is a nearly perfect screening assay used in virtually 100% of organ donors that will detect these particular viral diseases (2);
- That with donor NAT screening there is very little difference in actual viral disease transmission in comparing standard (approx. 0.1%) versus "increased risk" donors; (approx. 0.18%) (1);
- That these particular viral diseases are all treatable;
- That organs from donors known to have Hepatitis C are now purposefully being transplanted in individuals that do not have Hepatitis C because of the development of safe and effective direct-acting antiviral agents for HCV (2).

The current PHS Guidelines depend heavily on classifying risk based on social history. There are two main concerns about this framework. First, the significance of what we consider to be "risk" and how it should be mitigated back in 2012-3, and today, are probably different. Perhaps it was once necessary to have a "quarantine/absolute prevention" strategy – akin to what is necessary in blood banking. But recent medical advances now make donor screening for these viral diseases more easily detectable and they are all treatable.

Importantly, we are now more acuity aware of the importance of maximizing organ utilization and minimizing organ discards. In the US there are only about 10,000 deceased donors annually that contribute these life-saving organs. With so few, we cannot merely swap out an "increased risk" organ for another unit that is standard risk, as in blood banking. ASTS is concerned about reports that indicate that the utilization rate for these organs is significantly lower than for PHS standard risk organs. (1, 2) This is despite the absolute risk of disease transmission being extremely low and post-transplant survival being equivalent for recipients of PHS-standard and "increase risk" organs (1, 2, 3)

We also appreciate that the risk of end-stage organ disease progression and death without transplantation is significant and may be the greatest risk of all. In fact, from the surgical perspective, there are greater risks with the actual transplant surgery than the morbidity or mortality from these viral disease transmissions. The transplant surgeons do discuss surgical risk and medical risk. But we frame it within a context of events that occur more frequently than 1 in 200, including death. We understand the risk of disease transmission (infection/cancer/etc.) is real and people on the waitlist deserve to receive appropriate risk information ideally in the context of total life risk. It may be prudent to develop a more precise definition of a reasonable likelihood of disease transmission of HIV, HBV and HCV, say between 1:200-1000, in the context of negative NAT screening and, social/medical history, say within 30 days of donation, and not apply the term, "risk", to organ donors. Perhaps the transplant consent process should include a discussion of when "precautionary screening" for viruses will be performed.

The second concern is that the usefulness of social history as an accurate parameter to asses viral disease transmission risk has its limitations. ASTS believes it is time to change the standard to NAT screening

results with social history being contributory only within a very short timeframe of organ donation. The main concern about routine NAT screening is that the rate of false positives may result in excluding an unacceptable number of organ donors. The recent development of newer-generation NAT systems has reduced turnaround time to <4 hours. Using the new machines, in conjunction with repeat/parallel testing protocols, has effectively reduced the false-positive rate to negligible levels, and permit prospective NAT for all organ donors (2). ASTS believes social and medical history gives appropriate context to the interpretation of NAT screening results only when the individual donor is still within the serologic negative/eclipse phase – that the timeframe relative to organ donation that social history is considered useful should be significantly shortened, perhaps changed to 30 days.

The current heavy emphasis on donor social history to label a transplantable organ "increased risk", even when NAT screening is negative, may be misleading the public about the potential for, and adverse effect of, viral disease transmission through transplantation. There is awareness that risk aversion may be particularly pronounced when referring to stigmatized social behaviors and stigmatized diseases like HIV and HCV. This results in individuals refusing to be listed to receive organs from donors currently classified as "increased risk". This is particularly true for pediatric kidney transplant candidates (1). At our institution, for example, no kids waiting for a kidney transplant are listed to receive organ offers from donors classified as, "increased risk", and our center is not alone. Many adult individuals that are contacted about organs from donors classified as "increased risk" sometimes decide not to accept the organ for transplantation even though it is in their best interest of health and wellness to receive the transplant rather than spend even more time on the waiting list. It has been reported that twice as many transplant candidates need to be contacted and offered the organs for transplant when the donor was classified as "increased risk" compared to when organs came from standard donors (4). The social history basis of increased risk when NAT screening is negative also creates needless anxiety and concerns of disease transmission for the patient that does accept it for transplant.

Maintaining a culture of safety is important. Congruent with those values, ASTS believes in post-transplant monitoring of recipients of organs from "increased risk" donors, and immediate adverse event reporting, if it occurs. We appreciate the importance of close monitoring of recipients of "increased risk" organs for *de novo* infection of these viruses in the weeks and months after transplantation. It is reasonable to screen recipients for these viral infections using both serology and NAT testing at 2- and 4-weeks post-transplant, and screening by both NAT and serology at 12 and 48 weeks.

ASTS supports the current systems of donor disease transmission vigilance and surveillance – that is, the importance of immediate reporting and investigating any post-transplant infection in the recipient and notifying other recipients of organs from the same donor to prevent and minimize harm to those exposed. Specifically, that all unexpected, potentially donor-derived disease transmission events be reported to the OPTN/United Network for Organ Sharing, where cases are then reviewed by the Disease Transmission Advisory Committee.

ASTS is pleased that the PHS Guidelines will be re-evaluated. We are here to help move the field forward.

References

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3. Volk ML, Wilk AR, Wolfe C, et al. The "PHS Increased Risk" Label is Associated with Nonutilization of Hundreds of Organs per Year. Transplantation. 101:1666–1669, 2017.
4. Richards VL, Johnson CK, Perkins JD, et al. Willingness to Consider Increased-Risk Donors: A Single-Center Experience in Kidney Transplantation. Ann Transplant. 23: 387-392, 2018.