

# The Changing Scenario of Organ and Blood Donation in the Era of a Cure of Viral Hepatitis

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## **Q. For several years, anti-HCV positivity has been considered an absolute contraindication to blood, tissue and organ donations. Why?**

To answer the question, it might be useful to provide a brief historical background. The global epidemic of hepatitis C emerged in the second half of the 1900s. After the identification of HCV as the etiologic agent, it soon became clear that therapies employing substances of human origin—such as blood transfusion and organ transplantation—had been major determinants of its spread. The adoption of antibody screening of blood, tissue and organ donors was highly effective in preventing the risk of acquiring hepatitis C among recipients. In countries that could afford the costs, the safety of donations was further improved by adding nucleic acid technology (NAT)—based HCV RNA assays. This improved safety of donations and greatly contributed to halting the HCV epidemic, at least in resource rich countries<sup>1</sup>.

It is not surprising, then, that excluding persons with a positive antibody test to hepatitis C has been a mainstay of blood and organ donor selection for almost three decades. Candidate blood donors are permanently deferred in the presence of anti HCV positivity, and to date, organs from infected donors have either been discarded, or allocated to HCV infected recipients only.

## **Q. However, the scenario is now changing, at least for organ transplantation. What are the main reasons?**

The scenario is changing because we are being forced to change, and now we have the right opportunity. The demand for solid organ transplantation has outpaced donor supply in almost all countries. According to the data provided by the Council of Europe, almost 145,000 patients in member states were on waiting lists in 2017 representing an increase of 10% compared to 2013. Six new patients are added to a waiting list every hour across Europe. There are not enough organs to transplant patients, and six thousand patients are dying every year while waiting for a transplant<sup>2</sup>.

Thus, the current tendency is to expand the pool of possible donors, and definitely a better use could be made of organs from donors with markers of HCV infection. We have to consider that candidate donors who are serologically positive for HCV (i.e. those who have antibodies able to recognize viral antigens), do not necessarily harbor HCV RNA which is the marker of an active HCV infection. This lack of viremia can be either

the consequence of a spontaneous clearance after an acute infection due to the host's immune response, or the result of an effective antiviral treatment. In both cases, however, the risk of transmission through organ transplantation is close to zero. Therefore, a consensus panel of the American Society of Transplantation<sup>3</sup> has recently recommended to abandon the definitions "hepatitis C positive" or "hepatitis C negative" for the purposes of organ allocation; rather, candidate donors should be indicated as "hepatitis C viremic" or "hepatitis C nonviremic." The distinction is useful, because organs from hepatitis C nonviremic donors can be safely considered for transplantation, in the absence of other risk factors.

In addition, another option to widen the pool of donors is represented by current HCV treatments based on highly effective and well tolerated direct-acting antiviral (DAA) therapy that can cure more than 95% of patients infected with HCV. This will eventually have a dual beneficial effect on the supply of organ donors. First, the number of safe candidate donors will increase over time as a consequence of sustained virological response. Second, in order to reduce the time spent of severely ill patients on the waiting list we can now use the organs from HCV viremic donors also for never infected patients, and protect them with DAAs. Several studies have been already performed, mainly in the renal transplantation field, indicating that this option is reasonably safe and feasible. The idea of transplanting an organ harvested from a donor with a chronic viral infection into a recipient without that infection does not start now with HCV as it is already in use for other viral agents, for example cytomegalovirus or hepatitis B virus<sup>4</sup>.

### **Q. What are the potential benefits of expanding the eligibility criteria to HCV positive donors?**

The main benefit is that a greater number of patients can have a chance of being transplanted. In a recent analysis from the UK, Patrick Trotter and colleagues<sup>5</sup> showed that over 15 years, the consent for donation was obtained for 244 HCV positive donors, but most of their organs (69%) were declined for transplantation because of concerns about disease transmission. They also estimated that each year a further 17 potential donors were simply not considered for donation due to the presence of HCV markers. New data suggest that expanding the donor pool to HCV carriers would be cost-effective, even considering the cost of DAAs to treat patients who receive HCV RNA-positive organs.

As usual, resistance to change has to be managed. According to a recent study from the US, less than half of candidates to organ transplantation are willing to accept an HCV-positive organ<sup>6</sup>. We should aim at improving patient education, clearly illustrating with this new policy that benefits outweigh risks, especially for those at high risk of death.

### **Q. Will the new approach be applied to blood donations as well?**

It might be useful to stress that at each blood donation donors undergo hepatitis C testing by serology, and in resource rich countries HCV RNA determination is also performed. Obviously, candidate donors who test HCV viremic cannot donate blood. But what about anti-HCV positive, nonviremic individuals? Why should they not be allowed to donate blood?

During the last years several individuals who have been taking DAAs and have been cured from hepatitis C asked us the same questions. Based on what we said earlier, donors who are no longer viremic and have no risk factors for re-infection should not represent a threat for the recipient. However, blood donor selection is based on rigorous regulations that were put into place before there were medical cures for hepatitis C. According to these rules, donors with a positive serology for major transfusion transmittable infections – including HCV – should be permanently deferred.

Transfusion medicine is based on a precautionary principle, which means that a change of deferral policies is problematic, even when evidence supporting their modification exists<sup>7</sup>. And, in the case of blood transfusion from HCV nonviremic blood units, safety has not been formally proven in clinical trials.

However, even if we do not foresee a change of this restrictive policy in the near future, the topic will be the object of further debate within the scientific community. Permanent deferral from donation of all of hepatitis C cured individuals could be perceived as a form of discrimination, especially at a time when transfusion medicine is shifting from general deferral rules based on categories or populations to an individual risk assessment.

## References

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