



POSITION STATEMENT

EARLY PHASE OF vCJD INFECTION IN BLOOD TRANSFUSION RECIPIENTS

Issue

1. The Committee on Microbiological Safety of Blood, Tissue and Organs has requested advice from SEAC on whether a scientific distinction can be drawn between historic and recent blood transfusion recipients in terms of the relative load of the vCJD agent that may be present in the bone, tissues or organs of the blood transfusion recipient. In the context of this question, a recent recipient is defined as having received a blood transfusion within the week prior to bone, tissue or organ donation. A historic recipient is defined as having received a blood transfusion in the more distant past.

Background

2. A pre-symptomatic diagnostic test for vCJD is currently not available. Therefore, blood, bone, tissue or organ donors with a sub- or pre-clinical vCJD infection cannot be identified prior to donation. Two cases of vCJD infection in recipients of blood from donors that subsequently developed vCJD suggest that the disease may be transmitted from asymptomatic individuals via blood transfusion. Epidemiological evidence of iatrogenic transmission of sCJD suggests there is a potential risk of vCJD transmission via tissue/organ transplantation.
3. There are no data on the tissue distribution of vCJD infectivity in humans in the first week following infection by blood transfusion. There is some, albeit very limited, information from mouse studies on prion replication and spread in the early phase of infection. However, these studies used inocula, routes of administration and prion strains not directly applicable to the human blood transfusion situation.

Early phase tissue accumulation of abnormal prions

4. On the basis of the very limited information available, it is considered unlikely that significant prion replication would occur in tissues in the first week following transfusion with infected blood. Thus, the level of abnormal prions accumulating in a tissue would probably correlate with the level of vascularisation of that tissue. Highly vascularised organs such as the liver, lung and spleen, as well as bone, would be more likely to contain the agent compared with other organs. At later times in the incubation period (likely to be well in excess of one week), the accumulation of abnormal prion protein and infectivity would be expected to correlate with the ability of various tissues to support prion replication, with the central nervous system containing the highest levels of infectivity.

Relative risks

5. Data are too limited to allow quantification of the risks of transplant associated vCJD transmission from donors that have received a blood transfusion.
6. The number of pre- and sub-clinical vCJD infections in the population is believed to be small. Therefore, there is a small risk of vCJD transmission from transplantation of tissues/organs from all donors, irrespective of whether they have received a blood transfusion prior to donation. The additional risk resulting from a tissue/organ donor having received a blood transfusion at any time prior to donation is likely to be small. Furthermore, the introduction of precautionary safety measures to protect the blood supply, such as leucodepletion and exclusion of previously transfused blood donors, means that, in general, the risk of blood transfusion-associated transmission of vCJD from tissue/organ donation is, if anything, likely to be lower if the transfusion is recent rather than historic. However, it is not possible to define a threshold of lowest risk in terms of a specific date of, or period of time following, a blood transfusion.

Possible risk reduction measures

7. Screening cadaveric donors for markers of infection would allow, depending on the sensitivity of the test used, pre- or sub-clinically infected donors to be identified prior to the use of the donated tissues/organs. Retrospective screening of donors would also help to inform assessment of transmission risks.

8. On the basis that tissue/organ infectivity levels in the very early stage of infection are associated with the blood content of tissues/organs, washing or perfusing tissues to remove blood could reduce the infectious load. In this respect, it would be important to consider processes that efficiently remove bone marrow and blood from bone.
9. Avoiding the pooling of tissues from different donors to be transplanted into one individual reduces transmission risks to that individual.

Summary

10. There is no clinical evidence that vCJD has been transmitted through tissue/organ transplantation. However, a potential risk of transmission via this route exists. Relevant data are extremely limited but suggest that in the early phase of infection, significant prion replication is unlikely to occur and that, therefore, tissue levels of abnormal prions following recent transfusions are likely to be related to the blood supply to each specific tissue.
11. A risk of transplant associated transmission of vCJD exists from tissue/organ donors that have not received blood transfusions. The additional risk as a result of a donor having received a recent blood transfusion is likely to be very small. Post mortem assessment of donor infection would provide the best method of risk reduction and enable these risks to be quantified.
12. In assessing and communicating the risks a balance must be struck between the small risk of vCJD transmission by transplantation and the benefits to patients receiving a transplant, especially where tissues/organs are scarce and are required for (potentially) life-saving procedures.

SEAC
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