

CJD Risks & Perspectives in Blood Transfusion

The purpose of the Blood Bulletin is to provide regular up-to-date information on the use of blood and blood products in clinical practice.

This issue examines the extremely urgent issue of CJD Risks & Perspectives in Blood Transfusion and was written by Dr. Joan O Riordan. Future issues will update on transfusion reactions and albumin risks. Your comments and suggestions for further topics are always welcome

CJD Risks & Perspectives in Blood Transfusion

The spongiform encephalopathies of man and animal have common properties of transmissibility¹. A virus has never been isolated and the theory with the widest acceptance is that the transmissible spongiform encephalopathies (TSEs) are caused by a protein termed prion (PrP) because of its proteinaceous infectious nature

The Spectrum of Human Prion Diseases

CJD is a disease of older people with an incidence of one in one million, 80% sporadic and 15% familial. The cause of sporadic CJD is unknown. Iatrogenic CJD (approx 5%) has been acquired by the use of cadaveric derived human growth hormone and dura mater grafts, but CJD has also been transmitted by neurosurgical instruments and corneal grafts. In 1996, the first 10 cases of a new form of CJD termed variant (v) CJD was reported². There have been 40 cases of the vCJD reported to date in the UK, one in France and one probable case in Ireland. There is now overwhelming evidence from animal transmission studies that vCJD is caused by the BSE strain^{3,4}, probably acquired through the ingestion of food.

vCJD differs from classical CJD. It primarily affects younger people, has a longer clinical course, often presents with psychiatric symptoms such as severe depression or sensory disturbance or a combination of both and has a different neuropathological appearance.

Genetic Host Factors

Genetic host factors may influence susceptibility to vCJD. Codon 129 is a common polymorphism which occurs at this position of the PrP gene in which either methionine (Met) or valine (Val) is encoded¹. 100% of patients with vCJD are homozygous for methionine at codon 129 in comparison to 37% of the general population. 50% of the general population are Met/Val heterozygotes. In sporadic and iatrogenic forms of CJD, there is also a predominance of homozygosity for Met or Val.

Can CJD be transmitted through blood and blood products?

There are two sources of information to answer this question:

Epidemiological

The epidemiological evidence obtained from case-control studies, look-back investigations and surveillance of individuals exposed to large pools of blood products eg haemophiliacs, led the WHO⁵ and the European Committee for Propriety Medicinal Products (CPMP)⁶ to conclude that there was no proven or even probable instance of transmission of classical CJD by blood transfusion or blood products.

Experimental

Experimental infectivity studies with TSEs in animal models found evidence of low levels of endogenous infectivity in blood and some components following direct intracerebral inoculation⁷. Studies are on-going to see whether intravenous transmission is possible and whether leucodepletion (ie removal of white cells) removes infectivity from blood or plasma.

Strategies to Reduce Risk of Transmission of CJD or vCJD in Blood Transfusion

1. Individuals who are deemed to be at risk of classical CJD are not accepted as blood donors.
2. The transmission characteristics of vCJD may differ from classical CJD. Thus the IBTS, in-line with the CPMP and the FDA, will withdraw any in-date blood products where a donor is later confirmed or is strongly suspected of having vCJD.
3. There are no known criteria for exclusion of donors at risk for vCJD and there is, as yet, no screening test for prions. Because of the predominance of vCJD in the UK, some countries are considering excluding donors who have lived for an extended period in the UK during the peak of the BSE epidemic.
4. The IBTS is in the process of implementing universal leucodepletion of its blood components. This decision was taken because:
 - Abnormal prions have been found in the lymphoid tissues of patients with vCJD.
 - Evidence from an immunodeficient animal model of scrapie suggesting that host lymphocytes and/or follicular dendritic cells may play a role in peripheral neuroinvasion^{8,9}.
 - Evidence from animal models that scrapie can be transmitted by the intracerebral inoculation of buffy coat of blood. There is at present no data on the risk, if any, of transmission of vCJD by blood transfusion or on the effectiveness of leucodepletion in reducing this at present immeasurable risk.
 - There are other possible clinical benefits of leucodepletion with respect to the immunological effects of transfusion i.e. less reactions, reduced post-operative infections.
5. Although the risk is only theoretical, it is prudent that blood should only be given when indicated.

Before prescribing blood for a patient, clinicians should follow this checklist recommended by the WHO.¹¹

- ◆ What improvement in the patient's clinical condition am I aiming to achieve?
- ◆ Can I minimise blood loss to reduce this patient's need for transfusion?
- ◆ Are there other treatments I should give before making the decision to transfuse, such as intravenous replacement fluids?

- ◆ What are the specific clinical or laboratory indications for transfusion for this patient?
 - ◆ Do the benefits of transfusion outweigh the risk for this particular patient?
 - ◆ Have I recorded my decision and reasons for transfusion on the patient's chart and the blood request form?
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 4. Hill AF et al. Nature 1997;389 448-450
 5. WHO Press Release, 27. Spongiform Encephalopathies: New Recommendations on Medicinal Products. Geneva, WHO. 1997.
 6. CPMP position statement on nvCJD. CPMP/201/98
 7. Brown P et al. Transfusion 1998;38; 810-816
 8. Klein MA. Nature 1997; 390:687-90
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 11. Annexes to the WHO Report. Transfusion Today March 1999 ISSN: 1015-3276

The next edition of the Blood Bulletin will update on Transfusion Reactions. If you have any comments or queries on this edition's topic, please forward them to Dr Joan O Riordan, Consultant Haematologist (ex 303). Copies of Issue 1 which examined the topic of Haemovigilance are available from Deirdre Healy(ex 263).