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New insights into Creutzfeldt–Jakob disease

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The prion diseases, including Creutzfeldt–Jakob disease (CJD), have been largely absent from the headlines in the past few years, perhaps giving the impression that they are no longer a major public-health issue. As recent findings illustrate, however, there is still considerable cause for concern.

In a review in this issue, Adriano Aguzzi and Markus Glatzel highlight three cases of transmission of variant CJD (vCJD) through blood transfusion. Before these cases came to light, blood was not believed to be a significant route of transmission for prion proteins, so these findings raise important questions about the safety of blood products. Moreover, one of the blood recipients had a genetic trait that was previously thought to protect against vCJD infection. All of the individuals who apparently contracted vCJD through eating contaminated beef had the 'MM' genotype (homozygous for methionine at codon 129 of the prion protein gene *PRNP*). One of the individuals who contracted vCJD from a blood transfusion, however, had the MV genotype (methionine/valine heterozygous at codon 129). Interestingly, this patient did not develop the symptoms of vCJD, and died of an unrelated cause. Therefore, although the MV genotype can no longer be considered a barrier to vCJD infection, it might still protect against development of the symptoms.

Support for this idea was provided by a recent animal study, which was published in *The Lancet Neurology* (Bishop MT *et al.* [2006] *Lancet Neurol* [doi:10.1016/S1474-4422(06)70413-6]), and also widely reported in the press. In this study, transgenic mice were generated that recapitulated the human MM, MV and VV (homozygous for valine at codon 129) genotypes. The authors found that vCJD could be transmitted to mice of all three genotypes, with MM and MV mice showing approximately equal susceptibility to infection. Only the MM mice developed symptoms of vCJD within their lifetimes, however. If these findings can be extrapolated to humans, they raise the possibility that some individuals with the MV or VV genotype could become asymptomatic carriers of vCJD. Consequently, the prevalence of vCJD infection in the human population might have been underestimated.

The prevalence of vCJD in the human population might have been underestimated

Although no cases of vCJD have been observed in VV individuals, this genotype is associated with certain forms of sporadic CJD (sCJD). VV1 sCJD shares many clinical characteristics with vCJD, and from a public-health standpoint, it is vital to be able to distinguish between the two conditions. In a Practice Point in this issue, Surachai Suppattapone and Judy R Rees comment on a recent study that characterized the features that distinguish VV1 sCJD from vCJD. They recommend that VV1 sCJD should be included in the differential diagnosis of vCJD.

If, as recent findings indicate, there are likely to be asymptomatic carriers of vCJD in the human population, what steps could be taken to ensure the safety of blood and blood products without drastically depleting the donor pool? Attempts to detect prions directly in blood have met with little success, but surrogate molecular markers that are indicative of prion disease, such as a reduction in the level of erythrocyte-differentiation-related factor, are available. Another approach is to develop filtration devices that can remove prions from blood. As Aguzzi and Glatzel discuss in their review, such devices have already proved to be successful in animal studies, and clinical trials are now underway in the UK and Ireland.

HB Wood is the Editor of Nature Clinical Practice Neurology.

Competing interests
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