New variant Creutzfeldt–Jakob disease and the blood supply: Is it time to face the music?

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Within the next few months British blood services will stop using most plasma products manufactured from blood collected in the UK and will begin leukodepletion processing of donated blood. These decisions were taken on the basis of evidence that the “hypothetical” risk that new variant Creutzfeldt-Jakob disease (nvCJD) is transmissible by blood “cannot be fully discounted” and that the causative agent — believed to be a prion — may have an affinity for leukocytes. Because there is no means of detecting nvCJD in asymptomatic people, and in view of the presumably very long incubation period for the disease, it is a theoretical possibility that some — and possibly many — blood donors in the UK are inadvertently contaminating the blood supply with nvCJD.

These measures have been described as a precautionary, better-safe-than-sorry response to the uncertainties that surround the infectivity of nvCJD. There is no epidemiologic evidence that CJD has ever been transmitted through the blood supply. CJD has not been found in recipients of blood donated by people who were subsequently diagnosed with the disease, and there are no confirmed cases of CJD among recipients of clotting factor concentrates, a high-risk population that receives plasma products pooled from a huge number of donors. We are unaware of any reports of nvCJD associated with the receipt of blood or blood products.

Nevertheless, the UK authorities are justifiably worried. Some of the evidence on the potential for CJD and nvCJD to be transmitted by blood has been reviewed in these pages. Recent studies have shown that the prion protein (PrP) associated with nvCJD can be detected in tonsillar biopsy tissues from patients with nvCJD and have implicated B lymphocytes as being potentially capable of transporting it. If, as this suggests, the putative causal agent can be carried in the lymphatic system, then blood is a potential vector for transmission.

Much is still unclear about the infectivity of nvCJD, such as whether it can cross the blood–brain barrier, the dose that would be required to cause infection, how that dose is affected by the route of infection and, for that matter, what accounts for its disturbing propensity to cross species barriers. In the face of these unknowns, we cannot dismiss the theoretical possibility that asymptomatic individuals harbouring nvCJD may be able to infect others through blood donation.

The question of the prevalence of undetected disease must also enter into the assessment. As of June 30, 1998, there had been 27 definite and probable cases of nvCJD in the UK. The incubation period for CJD is thought to be long (perhaps as much as 10–20 years), and appears also to be several years for nvCJD. The 27 cases may be only the beginning of a much larger epidemic. A recent worst-case estimate of the number of people unknowingly infected with nvCJD in the UK is about 80 000. Among those who are infected, many will give blood. It is impossible to distinguish donors harbouring nvCJD from those who are not, although a recently developed monoclonal antibody that can discriminate between the normal and the disease-specific forms of PrP may eventually lead to the development of a diagnostic test.

The risk of receiving blood from a donor infected with nvCJD is relatively low when the transfusion is limited to a single unit or a very few units of blood. The problem with fractionated plasma is that it is made not only from pooled dona-
tions but from pooled production runs derived from donations from as many as 100 000 people. Thus the odds that the pool will contain a contaminated unit are much higher. The chance of a recipient being exposed to an infected unit depends, of course, on the concentration of infective particles and on the effect (if any) of fractionation procedures on prion concentration. The chance of becoming infected depends in turn on factors such as the minimum infective dose and all of the other factors that influence transmission that we do not yet understand.

What bearing does all of this have on the Canadian situation? If we accept the possibility that plasma-derived products have the potential to be a vector for nvCJD, we must consider the potential for blood donors in Canada to be harbouring nvCJD. Few people dispute that the main risk factor for acquiring nvCJD is the consumption of beef products in the UK during the BSE epidemic that began in the mid-1980s and continued until after the use of offal as cattle feed was banned in 1989. First, the prion associated with BSE has been demonstrated to be identical with that found in the brain tissue of people who died from nvCJD. Second, despite the considerable difficulty of obtaining a dietary history, there is some evidence that the relative risk of nvCJD increases substantially with the amount of beef consumed.18 Second, despite the considerable difficulty of obtaining a dietary history, there is some evidence that the relative risk of nvCJD increases substantially with the amount of beef consumed.

Close to 600 000 Canadians visit the UK every year, presumably, a large proportion of these visitors eat beef. Of those who visited the UK during the BSE epidemic, how many may have consumed contaminated beef? How many will donate blood while they are still asymptomatic?

We must pose the question: if the UK is banning the fractionation of plasma donated in the UK, shouldn’t we do the same for plasma donated in Canada? Or, at least, should we refuse donations from people who can recall visiting the UK during the window period of risk (approximately 1981 to 1997) and who ate beef?

Following the UK’s lead on this has some risks.20 Banning potential donors in Canada will increase an already worrying shortage of plasma and necessitate the purchase of plasma from other markets — which, in view of the shortage, may become less able or willing to accommodate us. (The UK will have to purchase 600 tons of plasma annually at a cost of £57 million in order to meet demand us. (The UK will have to purchase 600 tons of plasma from other markets — which, in view of the risks but will not completely eliminate them. And, of course, purchasing plasma on the open market is costly and will become more so as suppliers bow out.

In addition to considering a ban on plasma use from Canadian donors who have lived in or visited the UK during the window period, we must also consider the immediate implementation of leukodepletion of all donated blood. This issue requires urgent consideration by those responsible for the safety of our blood system: the Canadian Blood Agency and the Health Protection Branch of Health Canada. We urge the Blood Safety Council to assess without delay the risks posed by nvCJD, to make their deliberations open to public participation and scrutiny and to provide clear recommendations. The tragic contamination of the Canadian blood supply with HIV and hepatitis C, together with Justice Horace Krever’s careful inquiry, has taught us that there are no simple answers in risk assessment and that zero risk, although desirable, is never attainable. What the public and physicians want is wise management of the blood supply and to be informed of emerging risks now rather than later.

References