

Development of mathematical Models for estimating the Risk of VCJD transmission by Blood and Surgery

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Background:

The new variant Creutzfeldt Jakob Disease (vCJD) is the human form of the mad cow disease or the Bovine Spongiform Encephalopathy (BSE). Both are subset of a larger group of neurodegenerative disorders called Transmissible spongiform encephalopathies (TSEs). Those disorders are caused by non-conventional infective proteins called prions. Infective prions (PrP^{Sc}) are misfolded forms of the normal prion protein (PrP) that are expressed different tissues particularly the central nervous system. The etiology of vCJD has been linked to the consumption of BSE-contaminated beef. Other animal TSEs include chronic wasting disease (CWD) in the deer and elk population of the US and Canada, transmissible mink encephalopathy (TME) of mink, and other sporadic cases in domestic cats and zoo animals. Other forms of TSE in humans include the classical Creutzfeldt- Jakob disease (CJD) which occurs as sporadic, genetic and iatrogenic. A good review of these diseases can be found in Liberski, (2008) (1).

Like BSE, vCJD is an infectious disease typified by long incubation period and asymptomatic infections, two factors making epidemiological investigations particularly difficult. Primary infections are associated with the ingestion of infectious materials. Secondary infections are associated with blood transfusions and surgical procedures.

Prions, the causative agents of vCJD have been shown to be resilient to traditional cleaning measures. Recently, decontamination procedures using special enzymes have come to market. These new technologies for infectivity reduction may affect both the parameters and the structure of the models. There are a number of papers regarding the science and policy surrounding the issue of prion decontamination.

Secondary transmission of vCJD is controlled through a number of measures. Mitigation of surgical transmission has been mostly handled through the limitation of reuse of surgical instruments especially through high-risk procedures. Risk of vCJD in the blood system is basically controlled by means of donor deferral policies, treatment of blood products (leukodepletion, for example) and the use of a detailed tracking system in the case of suspected vCJD infection. The cost of donor deferrals on the blood system is fairly well studied.

Models and methods from the literature:

The most cohesive and comprehensive body of work involving epidemiological and risk models for primary vCJD comes from the stream of papers by Ghani et al (2), Clarke and Ghani (3). Models for the secondary VCJD infection via blood can be found in Clarke et al. (4), Dietz et al. (5) and via surgery Garske et al. (6) and Bennett et al. (7).

Our Proposed Model

Our Proposed model would address the issue of the risk of secondary transmission of vCJD by blood transfusion and surgery knowing that no cases of primary vCJD has been diagnosed in Canada but there is a potential risk since until now a total of 16 cases of mad cow disease have been detected in Canadian cattle and it is possible that some infected cattle have been slaughtered for human consumption. Our model would include the following variables. We need to consult MITACS about the appropriate approach to build a model and what parameters to include and how to model them. Examples of parameters:

- probability distribution of risky surgical operations in Canada by age
- probability of prion transmission from tissues to surgical instruments
- transmission probability of prions from surgical instruments to exposed patients
- rate of growth of prion in infected tissues and tissue distribution
- rate of reuse of medical instruments
- size of the population exposed
- probability of prion inactivation given they are sterilized or reduction due to multiple use (wash-out)
- efficacy of prion inactivation by steam sterilization or chemical sterilents.

Modelling the dynamics of vCJD secondary (i.e. human-to-human iatrogenic transmission) involves a careful consideration of a wide variety of (secondary) transmission routes. We must also choose a sufficiently rich description of the statespace: a population of susceptible individuals, infective individuals and vectors of infection. To begin with however, we need to construct a simple model in the context of an unstratified population.

The full picture of secondary vCJD involves a structured population which captures the variations in risk associated with different age groups and genetic sub-populations. Nonetheless, these simple unstratified models provide a complete understanding of the mathematical framework for a branching process analysis even in the more complex situation. Furthermore, the qualitative behavior of the stratified system should correspond to that of a simpler system for an appropriate choice of an effective parameter.

References:

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