Variant Creutzfeldt-Jakob disease and the potential for its accidental transmission following surgery with contaminated instruments: The risk of transmission in Australia

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We present a simple model for the quantitative risk assessment of vCJD transmission following surgery. Factors that affect the transmission of the disease are prevalence of the disease, concentration of prions in tissues, genetic susceptibility, the number and type of surgical procedures and the effectiveness of decontamination procedures. The main sources of uncertainty are the number of people currently incubating vCJD in Australia and the effectiveness of the decontamination processes for surgical instrumentation. The model serves as a guide for predicting the number of possible vCJD transmissions following individual surgical procedures. It is the uncertainty of the epidemic that poses a challenge to the public health scientist. Greater certainty of the pathogenesis and progression of the disease will only come with increased years of surveillance.

key words: vCJD, transmission, contaminated instruments

INTRODUCTION

In this article we discuss the evidence for surgical transmission of variant Creutzfeldt-Jakob disease (vCJD), a human form of the transmissible spongiform encephalopathies (TSE) or prion diseases. We propose a simple model for the quantitative risk assessment for the transmission of vCJD following surgery. The model takes into account the various uncertainties in the analysis of the risk of surgical transmission, which makes absolute predictions vary by many orders of magnitude.

POPULATION STUDIES

Prevalence of CJD

In the UK, over the period Jan 1970–Dec 2000, 888 cases of sporadic CJD were identified, of which 7 cases were still alive in December 2000. Of these cases, 689 (78%) were classified as definite cases and the remainder classed as probable. Over the period 1990–2000 the average annual mortality rate from sporadic CJD per million population was 0.75 in England, 1.00 in Wales, 0.86 in Scotland and 0.46 in N. Ireland. If allowance is made for age and sex, the variation in mortality between areas is not statistically significant. The annual mortality rate (from 1993–2001) for sporadic CJD varies from 0.2–2.7 per million in the world (data from Eurocjd, Neurocjd).

By April 2002, 117 cases (approximately 2/million) of definite or probable vCJD had been identified in the
UK (110 definite and probable vCJD deaths and 7 probable cases still alive). The median age of disease onset was 26 years and the median age at death 28 years. The youngest case was aged 12 years and the oldest 74 years (UK CJD surveillance unit). The mortality rates were analysed as quarterly incidence of vCJD deaths, and the fitted line predicted a total number of deaths of 36 in 2001. This is to be compared with the observed 20 deaths in 2001 (Department of Health, UK). A further 5 cases of vCJD were reported in France, one case of vCJD in Ireland and one case in Italy (Promed April 2002). A single case of vCJD was reported in Hong Kong in 2001 [18].

The epidemic patterns observed suggest age-related incubation period or susceptibility and exposure. This is because vCJD generally presents at a younger age. One reason can be that comparatively popular and inexpensive beef items might be consumed more by children and young adolescents. The genetic and environmental factors responsible for the possible preference for the disease for this age group are still poorly understood.

The vast majority of cases of BSE (more than 99% in 1999) have been reported from the United Kingdom. BSE was first identified in dairy cows in the spring of 1985. Over the years the number of affected cows increased sharply to a peak in the year of 1992. As the ban on ruminant feed was imposed in the UK in 1988, the number of cases had gradually decreased by the year 2000. However, endemic cases have also been reported in other European countries, including the Republic of Ireland, Switzerland, France, Liechtenstein, Luxembourg, the Netherlands, Portugal and Denmark (Office International Des Epizooties, Nov 2001). Although the outbreak of BSE in the UK now seems to be under control, data from the OIE suggests that in Europe the numbers of infected cattle are increasing, albeit from a low number. As a result, there is mounting concern that there is a possibility of transmission to humans in these countries as well. In the USA, the possibility of TSE in hunters who consume venison from deer or elk with chronic wasting disease has been suggested, though evidence for a causal link has not been found [2].

In Australia the number of cases of CJD recorded on the CJD National Registry (up to Jan 2001) is stated as: definite CJD 236, probable CJD 160, possible CJD 1, incomplete CJD 89. The term incomplete delineates possible examples of CJD awaiting further information before classification. When all cases on the registry are considered, the annual incidence of the disease is approximately 1.1/million during the period 1988 to 2000. The composition of the cases on the register is 91.2% sporadic, 6.3% familial and 2.5% iatrogenic. The number of iatrogenic cases was: 1 (growth hormone recipient), 4 (pituitary gonadotrophin recipient), 5 (dura mater recipients). There has been an approximate doubling of the annual incidence of TSE since the mid 1980s, probably secondary to improved reporting and diagnosis. Until the present day, Australia remains free of vCJD.

Predictions of variant CJD in the UK

Predicting the course of vCJD and the size of the epidemic has been difficult. In many instances, the width of the confidence intervals of the predictions varies by many orders of magnitude, making interpretation difficult.

The calculations on which the numbers are based are similar. The number of cases of vCJD cases diagnosed during 2002 will be a result of the time of infection and the incubation period distribution (IPD), expressed as (number infected in 1987 × probability of progressing to disease during the 15th year after infection) + (number infected in 1988 × probability of progressing to disease during the 14th year after infection) + etc. Knowledge of any two of these three quantities allows the other to be estimated. For the current vCJD epidemic neither the numbers infected nor the incubation period is known, hence absolute predictions are clearly impossible. For example, the current case data could have arisen from a small number of infections and short IPD (predictions will be small) or a large number of infections and long IPD, (predictions will be large). Age, sex and genetic susceptibility will further complicate the relationship.

The question remains regarding the size of the final epidemic.

(i) Anderson’s team in Oxford [13], explored more than 5 million combinations, based on a wide range of assumptions, regarding the distribution of the vCJD incubation period, the relative infectivity of cattle by incubation stage, and the effectiveness of control measures at reducing human exposure to infected material. Table 1 is a summary of their results, if the average number of cases in 2000–2002 exceeds 20.

A further analysis by the same authors [11] estimated the 95% confidence interval for future vCJD deaths during the years 2001–2080 to be 40–90,000, with up to 400 deaths occurring during the period 2001–2005.

If the spread of BSE in sheep was non-self-sustaining, the projected total number of vCJD cases was similar to the vCJD epidemic modelled on BSE in cattle alone. In the worst case scenario for the spread of BSE
within and between flocks of sheep, the total number of vCJD cases increased to 110–150,000 cases. Thus with the presence of BSE in sheep, the upper bound is substantially increased only if BSE is capable of being endemic in sheep. The authors also suggest that combined tissue- and age-based restrictions can reduce public health risk by at least 80% in sheep BSE scenarios. Kao et al. [17] also suggest that, although there are large uncertainties in the parameter estimates, indications are that the current prevalence of BSE in sheep is low. However, should horizontal flock-to-flock transmission occur, this would eventually cause a large epidemic. Krebs et al. [20] review both papers and state that, given the uncertainties and assumptions, quantitative details cannot be taken literally.

(ii) The team at the London School of Hygiene and Tropical Medicine used a back calculation approach, which calculated the number of infections from case numbers. Allowing for a flexible incubation period distribution, the authors found that the cases observed were almost equally compatible with any number of infections up to several millions. However, when a large number of infections was considered, the model indicated that the average incubation period was likely to be extremely long and in most instances well beyond the human life span. As a result, the corresponding epidemic may range from a few hundred to a few thousand cases. The authors state that considerable uncertainty surrounds the number of primary vCJD infections that have occurred. Whether a few hundred or many more people have been infected has important consequences for public health and in particular for the risk of secondary surgical transmission [6].

(iii) Valleron’s group [28] assumed that the risk of developing the disease in susceptible exposed subjects decreases exponentially after the age of 15, that all infections occurred between 1980–1989 and that the distribution of the incubation period is log normal. With an estimated mean incubation period of 17 years, the total number of cases was predicted as 205 (with an upper limit 95% CI of 403). The authors also predict that the age distribution of vCJD cases will be bimodal.

Other factors that may complicate predictions are that (i) from 1990, more than 5 million people have died in the UK from non-CJD causes and some of them would have been infected; (ii) to date all vCJD patients have been homozygous for methionine at codon 129. If the entire population is susceptible, other than 40% methionine homozygotes, the worst-case scenario will have to be multiplied by 2.5. Other genetic factors, unrelated to the PrP gene, may also affect susceptibility.

The following points are relevant to risk management strategies:

- There is uncertainty about the number of people infected and the incubation period of the disease;
- Data limitations allow assumptions to influence epidemic projections; and
- Greater certainty on the total number of vCJD cases will only come with additional years of surveillance.

In the UK, two retrospective studies were set up to examine 15,000–20,000 appendectomy and tonsillectomy specimens stored in the archives. Analysis of the first samples (approximately 3000 appendix and 95 tonsils) did not reveal any positive cases. One disadvantage of the study is that the length of the incubation period at which PrP^Sc infectivity becomes positive in the tissues studied is not known. By the use of mathematical models, the authors suggest that if the tests are able to detect infection in the last 75% of the vCJD incubation period (with 100% sensitivity and specificity) then the upper limit on the epidemic size is reduced from several million cases to about 150,000 cases. However, if tests are only able to detect infection in the last 50% of the incubation period, the results do not decrease the previous uncertainty in epidemic size. Clearly, at this stage, larger studies are required [16].

Predictability of vCJD cases in Australia

For the purposes of risk evaluation, the population at risk will be limited to those who have travelled to and/or lived in the United Kingdom. The Australian Bureau of Statistics recorded a total of 500,706 arrivals from the UK, during the periods 1984–1997, the period believed to cover increased risk of exposure to the BSE agent. Those arrivals consisted of migrants to Australia, Australians returning from long-term residence (> 12 months) in the UK and long-term visitors from the UK (resident in Australia for longer than 12 months). The latter group are included as there is a likelihood of this group undergoing surgery while in Australia.

<table>
<thead>
<tr>
<th>Mean incubation period (years)</th>
<th>Projections for the total number of vCJD cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>120–630</td>
</tr>
<tr>
<td>20–30</td>
<td>120–2900</td>
</tr>
<tr>
<td>30–60</td>
<td>200–6000</td>
</tr>
<tr>
<td>≥ 60</td>
<td>1,300–136,000</td>
</tr>
</tbody>
</table>

Table 1. Predicted number of vCJD cases
If similarity in environment, age distribution and genetic susceptibility of both populations in the UK and the Australian-UK travelling population is assumed, then the projected epidemic in Australia may approximately be \( \frac{1}{100} \) that expected in the UK. This assumes a population of 55 million people in Britain. If the projected number of new vCJD deaths in 2001 is 36 in the UK (UK CJD surveillance data), the expected number of cases in Australia will be 36/100, that is, less than one. This does not allow for the incubation period and the pre-clinical vCJD cases among the population at risk in Australia. It is not possible to detect all carriers in the prodromal phase nor is it possible to identify the number of persons incubating sporadic CJD and vCJD. The possibility of transmission by this group has to be considered in risk management strategies.

Iatrogenic infection

Physicians have inadvertently transmitted CJD by a variety of procedures. Known sources of infection have been improperly sterilised depth electrodes, transplanted corneas, human growth hormone, gonadotrophins derived from cadaveric pituitaries and dura mater grafts.

In recorded case histories, CJD developed in two young patients 16 and 20 months after they underwent surgery to excise epileptic foci. At the time of surgery, EEG exploration was undertaken with electrodes that had been previously implanted in a patient with known CJD. The electrodes had been 'sterilised' with 70 percent alcohol and formaldehyde vapour. Two years later, these electrodes were implanted into a chimpanzee in which the disease developed subsequently [3]. Brown et al. [4] summarised the number of cases of iatrogenic CJD in the world (Table 2)*.

The corneal transplant patients are classified as one definite, one probable and one possible case.

The three case reports in the literature describing human-to-human transmission of CJD via corneal transplantation are described below.

**Case I:** The donor was a 55-year-old man who was later confirmed to have pathologically confirmed CJD. The recipient was a 55-year-old woman who developed symptoms of lethargy, nausea and ataxia 18 months after surgery, and died after a further 9 months. Post mortem confirmed she had CJD and a chimpanzee developed CJD when injected with her brain homogenate. Though the transplanted cornea was not studied, this is considered a definite case of transmission [8].

**Case II:** Clinical features of CJD developed approximately 30 years following corneal transplantation from a donor who had autopsy-confirmed CJD. Although the recipient developed dementia and myoclonic jerks, no histological proof of the diagnosis of CJD was ever found, and this remains a probable case of transmission [15].

**Case III:** A 63-year-old woman developed autopsy proven CJD 15 months after a corneal transplant. Details of the donor are not given, and this was considered a possible case of transmission [27].

Rizzo et al. [24], as well as others [30], raised concerns about applanation tonometry following three patients undergoing the procedure during the early phases of CJD. The concern associated with the transmission of CJD through ophthalmic procedures is illustrated by the recent case of ocular tissue transplanted into 3 separate patients from a donor who was later found to have sporadic CJD. Two of these patients accepted explantation of the ocular tissue [1]. The degree of public concern with iatrogenic transmission of CJD was also reflected in the official policy of Health Canada, which supported blood recall from donors at risk of developing CJD [33].

### Transmission of TSE through surgical instruments

There is evidence from case studies that prion diseases can be transmitted via stainless steel instruments. In addition to the report by Bernoulli et al. [3], contaminated neurosurgical instruments have been suspected as modes of transmission in other patients. An early paper by Nevin et al. [23] described three patients with spongiform encephalopathy who had been operated on by the same neurosurgeon in the same neurosurgical unit during an eight-month period. Will et al. [32] later reviewed these cases and confirmed the relationship between theatre operation lists and the diagnostic procedures on cases with proven CJD and

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**Table 2. Iatrogenic cases of cCJD**

<table>
<thead>
<tr>
<th>Modes of infection</th>
<th>No. of patients</th>
<th>Median incubation period (months)</th>
<th>Clinical signs on presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal transplant</td>
<td>3</td>
<td>16, 18, 320</td>
<td>Dementia/cerebellar</td>
</tr>
<tr>
<td>EEG</td>
<td>2</td>
<td>16, 20</td>
<td>Dementia/cerebellar</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>5</td>
<td>17 (12–28)</td>
<td>Visual/dementia/cerebellar</td>
</tr>
<tr>
<td>Dura mater graft</td>
<td>114</td>
<td>6 (1.5–18) years</td>
<td>Cerebellar/visual/dementia/cerebellar</td>
</tr>
<tr>
<td>Growth Hormone</td>
<td>139</td>
<td>12 (5–30) years</td>
<td>Cerebellar</td>
</tr>
<tr>
<td>Gonadotrophin</td>
<td>4</td>
<td>13 (12–16) years</td>
<td>Cerebellar</td>
</tr>
</tbody>
</table>
the operative procedures later carried out on the three patients. Another probable case of neurosurgical transmission has been identified [10]. Using model systems for contaminated surgical instruments, infectivity has been shown to persist on steel surfaces following formaldehyde treatment [12, 34].

Case control studies have investigated the role of surgery (and other causes) as risk factors for sporadic CJD, though results have not been consistent. Collins et al. [5] found that a large range of surgical treatments were associated with a significantly increased risk of sporadic CJD. Davanipour et al. [7] and Kondo et al. [19] found a positive association between surgery and CJD, although, in the former study, the association was only significant for procedures involving the head, face and neck. Other studies [14, 29, 31] do not support an association between surgery and increased risk of CJD. The differing results between the studies may be the result of methodological differences. Selection bias is possible through non-response in patients and control subjects, as well as the selection of control subjects in the various studies.

Transmission of TSE during surgery

Clearly there is a risk of infection from surgery. PrPSc has been detected in various tissues and there is evidence of contaminated material adhering to a set of surgical instruments. The question is of evaluating the extent of the risk of person-to-person transmission through surgery.

The first stage is to approximate the risk of a prion-infected patient presenting for surgery. The annual incidence of classical CJD is approximately 1 case per million. Thus approximately 20 new cases of classical CJD will be expected to occur in Australia annually. No cases of BSE have been reported in Australia, and allowing for the fact that the UK-exposed Australian population is approximately 1/100th the total UK population, an approximation may be that 1/100th the vCJD cases diagnosed in the UK, i.e. 1–2 cases would be expected in Australia, by the year 2002–2003. Patients presenting with clinical symptoms characteristic of prodromal CJD, cognitive changes, speech abnormalities, cerebellar findings and myoclonus can be recognised by using clinical examination and travel history screening criteria. This does not take into account patients without neurological symptoms, who cannot be screened for using currently available methods. There is uncertainty, currently, on the future of epidemic size and the number of people currently incubating vCJD.

Procedures on the CNS, eye, GIT, lymph nodes and spleen will encounter infective material. As lymphoreticular material is widely distributed, it is likely that most general surgical procedures may disturb lymphoreticular tissue. For CNS surgery, procedures that breach the dura mater and do not use disposable instruments are at risk.

For risk-reduction strategies the following points need to be considered:

- There is potential for secondary infections to result from a wide range of procedures on the nervous system. Procedures on the brain, spinal cord and meninges come into contact with tissues with a higher level of abnormal prion and consequently have a higher risk of transmission of vCJD;
- Surgery involving the lymphoreticular tissue (tonsil, spleen, lymph node, Peyers patch and probably appendix) and the gastrointestinal tract can be considered as procedures with a high risk of transmission. Other surgical procedures may also disturb lymphoreticular tissue and are at risk for vCJD transmission;
- Risk reduction measures can either selectively target procedures in the high risk category or use an across-the-board approach and target all surgical procedures;
- The presence of PrPSc in blood, the possibility of PrPSc in muscle and of subclinical prion disease suggest that all surgical procedures are at risk of onward vCJD transmission. The level of prion encountered, though, may be $10^{-2}$ to $10^{-4}$ fold lower in some operations and the risk of transmission, consequently lower.

Secondary transmissions arising from previous infections following surgery

The feedback effect depends on the number of transmissions following surgery (prevalence of disease, tissue infectivities, decontamination effectiveness) and the frequencies of re-operations.

The number of secondary transmissions will depend on the number of infected individuals undergoing more than one operation. A tonsillectomy may mean that there is no chance of having another operation, however an operation to remove a malignant tumour is often followed by further operations. Life expectancy following surgery may also affect the chances of undergoing another surgery. Those infected need also to have another operation before showing clinical symptoms or dying. Other factors that may affect secondary transmission are the nature of the operations, as transmission through the CNS route is more likely than the peripheral route. The incubation period may also depend on the route of infection, which may be shorter after intracerebral infection. Of relevance are the conditions under which re-infection will cause a self-sustaining outbreak [9].

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Decontamination of surgical instruments

TSE infection is not associated with consistent biochemical, haematological or gross pathological abnormalities associated with the disease. Early diagnosis depends on the recognition of clinical signs, EEG or MRI imaging techniques. Sensitive tests to detect vCJD during early stages of infection are still at the development stage. Protection of public health, therefore, rests on decontamination and infection control procedures to reduce the risk of secondary transmission.

The argument remains that instruments used for ophthalmic surgery on unrecognised vCJD sufferers can become contaminated with the agent. The ability of steel surfaces to bind scrapie prions was demonstrated by placing steel wires in scrapie-infected brain homogenates and inserting them into the brain of indicator mice. The procedure resulted in transmission of disease [34].

The wire model can serve as a model for the sterilisation of surgical instruments. There is a need to conduct sterilisation experiments using vCJD prions, with appropriate second hosts. The area of contact between the instrument and the tissue should reflect the surface area of the surgical instruments.

Though several studies of prion inactivation by ger- micides and sterilisation procedures have been conducted, the experimental conditions do not always reproduce procedures in a hospital setting. In some cases, studies have been conducted with brain homogenates and the prion protein inactivation curve may be different on steel surfaces [25]. Methods that have been used to reduce instrument decontamination (bleach, NaOH) are corrosive to instruments and prolonged autoclaving may not be suitable for large instruments.

Brain homogenates from CJD hamsters were tested with guanidine thiocyanate. CJD infectivity was reduced more than 10^3-fold in crude tissue. 4 M guanidine thiocyanate also showed no corrosive effects with surgical instruments [22]. Further work with the wire model, mouse prions and indicator mice showed that exposure to 1M NaOH for 1h, or 4 M guanidine thiocyanate for 16 h rendered the wires completely ineffective by the mouse bioassay [12].

Prion proteins are unusually resistant to conventional chemical and physical decontamination methods. It is accepted that steam under pressure at the standard temperature and pressure settings used in healthcare establishments or other commonly used methods (dry heat, ethylene oxide, hydrogen peroxide) are not suitable for reprocessing items contaminated with prion proteins. Rutala et al. [25] summarise other disinfection and sterilisation procedures, shown to be more effective with the infectious agents for CJD.

The WHO infection control guidelines for TSE recommend that the most stringent methods for decontamination be applied to instruments in contact with high infectivity tissues of a person with a known TSE (WHO/CDS/CSR/APH/2000.3). The procedures required for sterilisation of more complex surgical instruments remain controversial. Not all surgical instruments can withstand the complete decontamination processes currently recommended. This is particularly relevant to ophthalmic surgery and endoscopic procedures.

Recommendations depend on inactivation data for prions as well as a review of worldwide practice. Decontamination procedures have been in place for patients at risk for iatrogenic (recipients of dura mater grafts and pituitary hormones) and classical forms of CJD. The Australian Guidelines on patient management and infection control (Sept 2001) for the management of patients with classical CJD are published in the Infection Control Guidelines for Creutzfeldt-Jakob disease and other human transmissible spongiform encephalopathies.

A summary of relevant issues for risk management strategies:

- Methods currently in use for decontamination, reduce prion titres by approximately 3–5 logs;
- Further research into newer methods of decontamination using more relevant model systems are required;
- There are still many unknowns in the equation. Decontamination strategies may vary with advancing technology and increasing knowledge of prion diseases.

Infectivity transmitted through instruments: illustrative scenarios

Clinically symptomatic vCJD patients can be identified and the surgical instruments quarantined. The uncertainty lies with the number of pre-clinical patients, who may be incubating CJD, who also present a potential risk. The nature of ‘infectivity’ in other than a clinically symptomatic patient also becomes relevant if tissues become infective late in the incubation period.

The maximum number of infections, per year, will depend on the prevalence of infected patients, the effectiveness of the first and subsequent decontamination cycles and the number of times instruments are reused.

Number of procedures

The number of surgical procedures that require to be carried out before a single vCJD patient is encountered will depend on the number of infections in the population.
The expected total number of ‘at risk’ operations (E) will be:

\[ E = \frac{x \times y \times l}{20,000,000} \]

If the total Australian population is approximated to 20 million and where
- \( x \) = number of vCJD cases in Australia (approximated to 1/100\(^\text{th}\) of the total UK infections)
- \( y \) = number of relevant operations per year
- \( l \) = infectious period for vCJD

The annual probability of encountering an ‘infected patient’ is given in Table 3. The probability increases linearly each year if allowance is made for the infectious period of vCJD. The above scenario shows that the total number of procedures determines the potential for encountering a patient who may harbour CJD. It is likely that the numbers of each surgical procedure has to exceed 2000 before a single infected patient is likely to be encountered.

**Expected infections per operation**

Analysis of the risk of surgical transmission following surgery requires the following inputs [9]:

(i) Mass and infectivity of material picked up on the instrument, and the transfer of infectivity from instrument to patient at each subsequent use;

(ii) The number of infections resulting from one relevant operation;

(iii) The number of infective patients undergoing the operation (the prevalence of the disease);

(iv) The efficacy of the ‘decontamination procedure’.

The models assume a linear dose response. (1 ID\(_{50}\) transferred to one patient would have the same effect as transferring 0.01 ID\(_{50}\)s to 100 patients — i.e. 0.5 expected infections). This model is to be taken as an **illustrative example** only, and emphasises the uncertainties in any risk-assessment procedure.

All possible models in this scenario are subject to large uncertainties. Again, it is to be emphasised that it is not possible to formally validate the models, because of inadequate data on the number of primary infections.

**Example 1.**

**Tonsillectomy**

(i) for a total of 30,000/year procedures on the tonsils with a baseline tissue infectivity of \(10^7\) ID\(_{50}\)/g;

(ii) with 20 instruments used per operation, and a mean of 10 mg of tissue initially picked up on each [26];

(iii) and a transfer proportion of 10%;

(iv) decontamination efficacy of the first cycle of \(10^4\);

(v) subsequent decontamination efficacy as a factor of 10.

In a simple model:

In which an ‘infected’ patient is operated on, the mass (10 mg) picked up by each instrument will contain \(10^5\) ID\(_{50}\) units.

Following cleaning and sterilisation, 10 ID\(_{50}\) units will remain on the instrument.

An instrument used again will transfer 1 ID\(_{50}\) unit.

If 20 instruments are used as a batch on a single patient, then this patient will be exposed to 20 ID\(_{50}\) units and will be infected. If the instruments are used on 20 different patients, then each patient will receive 1 ID\(_{50}\) unit and 10 will be infected. That is, a maximum of 10 patients will be infected or 1 patient will be infected should the instruments stay together.

If the number of people incubating vCJD in Australia is 1, 10 or 100, 1000 or 10,000.

As shown below the predicted number of transmissions will vary with disease prevalence.

The expected number of transmitted infections per year will be:

\(\text{(The number of people incubating the disease/Total Australian population) \times 30,000 \times 10 as maximum if the instruments are mixed in a pool or} \)

### Table 3. Potential scenarios

<table>
<thead>
<tr>
<th>Number of primary infections in the UK</th>
<th>Estimated number of primary infections in Australia (approximately 1/100(^\text{th}) of the number in the UK)</th>
<th>Number of surgical procedures/year before a single patient incubating vCJD is encountered</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 million</td>
<td>10,000</td>
<td>2000</td>
</tr>
<tr>
<td>500,000</td>
<td>5,000</td>
<td>4000</td>
</tr>
<tr>
<td>100,000</td>
<td>1,000</td>
<td>20,000</td>
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<tr>
<td>10000</td>
<td>100</td>
<td>200,000</td>
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<tr>
<td>1000</td>
<td>10</td>
<td>2000,000</td>
</tr>
<tr>
<td>100</td>
<td>1</td>
<td>20,000,000</td>
</tr>
</tbody>
</table>
(The number of people incubating the disease/Total Australian population) × 30,000 × 1 as maximum if the instruments are used as a set.

If the number of people incubating vCJD in Australia is 1, 10, 100, 1000 or 10,000, scenarios are given in Table 4.

If, following the first decontamination, the level of contamination is reduced by a factor of 10.

Following cleaning and sterilisation 1.0 ID50 units will remain on the instrument.

An instrument used again for surgery will transfer 0.1 ID50 units during the operation.

If 20 instruments are used, then there is a potential for 1.0 patients to be infected. If instruments continue to lose infectivity with subsequent operations, the number of patients infected will decrease with the number of decontamination cycles (Fig 1).

### Example 2

**Caesarean delivery**

(i) for a total of 30,000/year Caesarean deliveries with a baseline tissue infectivity of $10^6$ ID50/g;

(ii) with 20 instruments used per operation, and a mean of 10 mg of tissue initially picked up on each;

(iii) and a transfer proportion of 10%;

(iv) decontamination efficacy of the first cycle of $10^4$;

(v) subsequent decontamination efficacy as a factor of 10.

In the simple model:

In which an ‘infected’ patient is operated on, the mass (10 mg) picked up by each instrument will contain $10^4$ ID50 units.

Following cleaning and sterilisation 1 ID50 unit will remain on the instrument.

An instrument used again will transfer 0.1 ID50 units.

If 20 instruments are used as a batch there is potential for a single patient to be infected.

If the number of people incubating vCJD in Australia is 1, 10, 100, 1000 or 10,000.

As shown below the predicted number of transmissions will vary with disease prevalence.

The expected number of transmitted infections per year will be:

(The number of people incubating the disease/Total Australian population) × 30,000 × 1.

Suppose that each patient infected with contaminated instruments had a 1 in 4 chance of undergoing another operation. The resulting number of transmissions from each infected patient will be (the number of transmissions from each infected patient) x (proportion of patients undergoing re-operation). The model shows that self-sustaining epidemics are possible only when (the number of transmissions from each infected patient) x (proportion of patients undergoing re-operation) is > 1 (Table V, Fig 2).

### Precautionary measures as risk management

For transmission of vCJD, scientific evaluation does not allow risk to be determined with certainty. When evidence-based medicine fails to give a clear picture, a conservative approach is taken to health policy development.

Difficulties encountered with surgical instrument cleaning have been reported [21]. Instruments cleaned by the standard method (visual inspection of gross soiling, ultrasonic cleaning, hot wash, rinse air dried and steam sterilised), still showed blood or tissue when inspected by dissecting microscope. The study indicates a need for effective cleaning of surgical instruments. In the UK, a survey of decontamination procedures across

### Table 4. Possible number of transmissions following tonsillectomy

<table>
<thead>
<tr>
<th>Number of people incubating vCJD</th>
<th>Number of transmissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0015–0.015</td>
</tr>
<tr>
<td>10</td>
<td>0.015–0.15</td>
</tr>
<tr>
<td>100</td>
<td>0.15–1.5</td>
</tr>
<tr>
<td>1000</td>
<td>1.5–15</td>
</tr>
<tr>
<td>10,000</td>
<td>15–150</td>
</tr>
</tbody>
</table>

**Figure 1.** Reduction in the transmission of vCJD cases with increasing numbers of decontamination cycles.
hospitals observed that some hospitals initially did not meet acceptable standards. (UK Dept of Health, Decontamination Survey). An inspection of decontamination facilities in Australian hospitals has not been carried out. It may be required to adopt the highest decontamination methods feasible. Other control procedures that can be introduced are measures to enable all reusable instruments to be traced. Not all expensive instruments can be decontaminated using relatively harsh procedures. The possibility of using disposable instruments requires exploration, although this may be limited by the quality of the available instruments. In the latter situation, allowing for the uncertainty of patients harbouring vCJD, pre-operative screening of the travel history of patients who have been exposed to vCJD may be an option.

Other approaches to decrease the risk of prion transmission would be to increase research in areas related to prion surveillance. Areas of active research are the development of screening tests for prion infectivity in tissues and investigation into effective decontamination procedures for surgical instrumentation.

Possible strategies for reducing the risk of transmission of vCJD are:

- Upgrading decontamination facilities in hospitals;
- Use of single use/disposable surgical instruments;
- Tracking procedures for tracing re-usable instruments;
- Patient screening for travel history to countries in which BSE is endemic;
- Encourage research into methods for (i) detection of vCJD during the clinically asymptomatic period; (ii) more efficient decontamination methods for surgical instruments.

### CONCLUSIONS

This review examines the evidence for the potential transmission of vCJD following surgery. Human transmission of TSE has already been described following iatrogenic exposure to infectious tissue. The simple models presented in this paper demonstrate the various scenarios possible following surgical transmission of vCJD. The uncertainty lies with the number of people currently incubating vCJD in Australia. The scale of the problem will only become clearer as we begin to understand the disease and the prognosis regarding further development of vCJD cases.

### REFERENCES