

Report of the consensus workshop

Creutzfeldt-Jakob disease: preventing transmission in the health care setting

Implementing the Infection Control Guidelines

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‘As a consumer, what’s important to me is knowing that people in health services are not being negligent with issues like CJD. Transparency is really important, and when something has gone wrong, to have that honesty to the public, and to know that whatever procedures are undertaken, health care workers are not being negligent or cutting corners to reduce costs –it’s good to know that.’

Workshop participant

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Executive summary

Creutzfeldt-Jakob Disease (CJD) is a unique disease that, despite its rarity, causes significant community concern. It may be difficult to diagnose, may be transmitted from person to person in the course of medical treatment, and challenges some of the conventional infection control wisdoms. CJD is resistant to all of the conventional cleaning, disinfection and sterilisation methods that are routinely used for medical equipment.

Australian guidelines for preventing the transmission of CJD in health care establishments were first published by the National Health and Medical Research Council in December 1995. Since then they have been extensively revised and updated. The Department of Health and Ageing published revised guidelines in June 2004. Given the rarity of CJD, there are few opportunities to test the CJD guidelines in a practical setting—yet it is only when we apply these guidelines that we can identify the challenges in implementing them. Recent events in Victoria have highlighted this, raising issues that those working in the clinical setting are struggling with CJD; this ultimately led to the convening of the CJD Consensus Workshop, held in Melbourne on 26 November 2004.

The goal of the CJD Consensus Workshop was to develop a clear, reasonable and achievable approach to implementing the guidelines. The workshop covered three broad areas: risk assessment and screening; cleaning, disinfection and sterilisation of instruments and equipment; and adverse event management. More importantly, the CJD Consensus Workshop process is intended to build community confidence that everything possible is being done to prevent exposures, and that the risk of transmission of CJD in the Victorian health care system is, in fact, immeasurably low.

This document summarises the materials presented at the CJD Consensus Workshop, and the discussions that resulted. The introductory material in each section is drawn from the discussion paper distributed to participants before the workshop. It is intended that this document will be used by hospital managers, infection control, operating room and sterilisation services staff and will be used to assist in the development of local practices and processes intended to reduce the risk of CJD transmission. The document should be read as a supplement to the Australian Guidelines.

Recommendations

Identification of CJD risk

1. That a standardised approach to identifying CJD risk be introduced for all patients undergoing elective surgery involving potentially high infectivity tissues. Groups for CJD risk assessment would include those undergoing neurosurgery, spinal surgery, posterior eye surgery, pituitary surgery and complex dental surgery. The responsibility for risk assessment resides with the surgeon responsible for the planned surgery.
2. That a risk assessment include the following questions:
 - a. Have you considered the possibility of CJD in this patient?
 - i. Does the patient have a family history of CJD?
 - ii. Does the patient have a progressive neurological disorder of less than 12 months duration?
 - b. Is the patient a recipient of a dura mater graft prior to 1990?
 - c. Does the patient have a history of receiving human pituitary-derived hormones for infertility or short stature (prior to 1985)?

Public Health is able to provide further information regarding the management of a person requiring a medical or dental procedure and who has been identified as a possible CJD risk. Public Health can be contacted on 1300 651 160.

3. That each health service has a process in place to ensure that the risk assessment has been undertaken; for example, the assessment may be linked with the operating suite or hospital booking process.

Managing instruments and equipment

4. That all Victorian hospitals and health services that perform procedures affecting higher infectivity sites including brain, pituitary gland, spinal cord, cerebrospinal fluid, retina, and optic nerve, and companies that provide surgical equipment for use in these procedures, work towards having a system that will identify individual instruments to individual patients.
5. That in the event that CJD is identified retrospectively in a patient who has undergone surgery or other procedures, including endoscopy, all equipment potentially contaminated through use on the patient be treated as follows:
 - a. In the case of procedures in which brain, pituitary gland, spinal cord, cerebrospinal fluid, retina or optic nerve tissues are exposed, all instruments that have come into direct contact with the tissue shall be withdrawn pending a decision from the CJD Incidents Panel.
 - b. In flexible endoscopic procedures, equipment that has contact with brain, pituitary gland, spinal cord, cerebrospinal fluid, retina and optic nerve tissues shall be withdrawn pending a decision from the CJD Incidents Panel.
 - c. In all other surgery and endoscopic procedures—that is, procedures that do not involve brain, pituitary gland, spinal cord, cerebrospinal fluid, retina and optic nerve—equipment should not be withdrawn, and should be cleaned and sterilised as per normal procedures.

6. That there are operational difficulties associated with the implementation of the guidelines recommendation concerning maintenance of a one-way flow of surgical instruments as defined by perioperative nurses. The guideline writing group have been asked to review this recommendation to clarify its intent.

Adverse event management

7. That in order to support health services in managing a CJD-related adverse event, the department will convene an incident team comprising health service administrators and clinicians, public health experts and other Department of Human Services representatives as required. This group will be responsible for co-ordinating the convening of the CJD Incidents Panel. The Department will undertake to produce an information kit on CJD risk management for consumers and health care workers.

Conclusion

The strategies for the prevention of CJD transmission is a rapidly developing area, and it is recognised that the process of guideline development and interpretation will need to be iterative, with annual reviews, as the evidence base continues to build. The Victorian Advisory Committee on Infection Control will undertake an annual review of this document in order to maintain its currency. It is anticipated that as the Australian Guidelines evolve, they will supersede this state-based document.

Introduction

CJD is a unique disease that, despite its rarity, causes significant community concern. It is difficult to diagnose, may be transmitted from person to person in the course of medical treatment, and challenges some of the conventional infection control wisdoms. CJD is resistant to all of the conventional cleaning, disinfection and sterilisation methods that are routinely used for medical equipment.

Guidelines

Australian guidelines for preventing the transmission of CJD in health care establishments were first published by the National Health and Medical Research Council in December 1995. The following year saw the publication of the first national infection control guideline. Over the past four years, both documents have been extensively revised by the Communicable Diseases Network of Australia and the National Health and Medical Research Council (NHMRC) Special Expert Committee on Transmissible Spongiform Encephalopathies. Revised guidelines were endorsed at the Australian Health Ministers Advisory Committee in January 2004 and were published by the Department of Health and Ageing in June 2004. The complete document, *Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting* (the guidelines) is available at

www.health.gov.au/internet/wcms/publishing.nsf/content/icg-guidelines-index.htm

The guideline document has a broad scope and aims to establish nationally accepted standards for infection control. The guidelines are designed to provide a basis for hospitals and other health care settings to develop methods and protocols according to local needs (Department of Health and Ageing 2004).

The primary goal in developing guidelines at the national level is to help health care workers improve the quality of health care. Guidelines, then, can be defined as directing principles or outlines of policy or conduct, which should not be regarded as rigid standards. Guidelines facilitate the setting of standards, but should also respect the autonomy of each hospital or health care setting and recognise the governing body's (for example, the hospital board's) authority and responsibility in establishing local standards of care. Where scientific evidence is lacking, the consensus of experts may be used to formulate a recommendation (Health Canada 2002).

Given the rarity of CJD, there are few opportunities to test the CJD guidelines in a practical setting—yet, it is only through applying the guidelines that we can identify challenges to implementing them. Recent events in Victoria have highlighted this, raising issues that those working in the clinical setting are struggling with CJD; this ultimately led to the convening of the CJD Consensus Workshop, held in Melbourne on 26 November 2004.

The CJD Consensus Workshop

The purpose of a consensus development workshop is to evaluate the available scientific information on a particular subject and develop a statement that advances the understanding of the issue in question, and that will be useful to health care professionals and the public. The National Institutes of Health in the USA developed the consensus conference methodology that has been in place since 1977. The consensus development conferences have proven to be particularly useful for providing guidance when a controversy exists over preventative, therapeutic or diagnosis options, or when the issue is of public as well as professional interest.

A broad-based independent planning committee was convened to develop an initial discussion document and to plan the workshop program. The membership of this group can be found at appendix A.

The goal of this consensus workshop was to develop a clear, reasonable and achievable approach to implementing the guidelines. The workshop covered three broad areas:

1. risk assessment and screening
2. cleaning, disinfection and sterilisation of instruments and equipment
3. adverse event management.

Health services across Victoria that provide neurosurgical services were invited to nominate representatives to participate in the workshop; they were asked to nominate from neurosurgery, operating rooms, infectious diseases, microbiology, infection control and sterilisation. Names were then collated and divided according to occupational group, and those to participate in the CJD Consensus Workshop were then randomly selected. This approach was taken to ensure that each group was well represented and that no one group would dominate the discussion. A number of interest groups and professional associations were also asked to provide a nominee to participate, and the list of represented groups is included at appendix C. Consumer participants were identified from the Australian CJD Support Group and the Health Issues Centre Consumer Participation Program.

Prior to the CJD Consensus Workshop, a discussion paper was developed by the workshop planning committee and was circulated to all participants. At the workshop, papers were presented by a variety of experts to provide participants with an overview of current research and clinical issues (the program is included at appendix B).

At the completion of the presentations, workshop participants were split into 13 groups and each group was asked to discuss one of the discussion areas and recommendations. Groups were asked to focus on the practical application of the recommendations. At this end of this process, the whole group discussed each topic and recommendation. The recommendations were either accepted or rejected. Following the workshop, transcripts of the day were collated and summarised, and an expert panel was convened to synthesise this information—along with occasionally conflicting interpretations of the data—into clear and concise recommendations.

The Australian Guidelines recognise the difficult ethical issues relating to lookback investigations and identifying patients at increased CJD risk, as identified in section 3 of this document. While outside the workshop's main focus, participants' views on these ethical issues were also canvassed to inform future policy development and action at state level. It is recognised that the process of guideline development and interpretation will need to be iterative, with annual review, as the evidence base continues to build.

This document

This document summarises the materials presented at the CJD Consensus Workshop, and the discussions that resulted. The introductory material in each section is drawn from the discussion paper distributed to participants before the workshop. It is intended that this document will be used by hospital managers, infection control, operating room and sterilisation services staff, and will be used to assist in the development of local practices and processes intended to reduce the risk of CJD transmission.

The document is the report of the consensus workshop and is not a policy statement of the State Government; the expert panel is not an advisory body to the Victorian Government. The document should be read as a supplement to the Australian Guidelines.

This is a rapidly developing area and the Victorian Advisory Committee on Infection Control will undertake an annual review of this document in order to maintain its currency. It is anticipated that as the Australian Guidelines evolve, they will supersede this state-based document.

Background

The Australian context

CJD in Australia

The incidence of CJD in Australia is approximately one case per million, per year. As of September 2001, the Australian National CJD Registry had recorded 405 persons as having died from probable or definite CJD. Of these, 90.4 per cent were classified as sporadic, 7.4 per cent as familial and 2.2 per cent (10 cases) as health-care associated. Health-care acquired CJD is thus very rare (Boyd et al. 2001).

Of the 10 Australian cases of health-related CJD transmission, five were associated with the use of cadaver-derived human pituitary hormone (for fertility or short stature) and five were associated with cadaver-derived human dura mater graft. Pituitary hormone ceased to be used in July 1985 and the product licence for Lyodura (dura mater graft) was withdrawn in 1987 (Brooke et al. 2004).

Recent issues

Over the past four years in Victoria, there has been a small number of potential and actual surgical exposures to CJD. In most cases, the surgery was performed on patients who were subsequently identified as possibly having CJD. In two events, lookback investigations were required to identify and notify patients who may have been exposed to potentially contaminated surgical instruments. The most recent was the case at the Royal Melbourne Hospital in September 2004, where more than 1200 people were contacted to notify them of possible exposure. The significant media attention has highlighted that the community believes there is a substantial risk of CJD associated with surgery, though a sane and balanced editorial in *The Age* (15 September 2004), beginning 'Providing accurate, non-inflammatory news about health risks is a public duty,' set the tone for responsible media reporting of the incident.

One aim of the CJD Consensus Workshop process was, therefore, to build community confidence that everything possible is being done to prevent exposures, and that the risk of transmission of CJD in the Victorian health care system is, in fact, immeasurably low. These recent issues have also highlighted the difficulties faced by hospitals and health services trying to apply the CJD Infection Control Guidelines retrospectively.

Variant CJD

There have been no reported cases of Variant Creutzfeldt-Jakob Disease (vCJD) in Australia, but over 150 cases have been identified worldwide, chiefly in the United Kingdom, where, as of 1 April 2005, 155 definite or probable cases have died. There is strong evidence that vCJD is causally linked to bovine spongiform encephalopathy (BSE) (Will et al. 2000).

Patients with vCJD exhibit a number of distinctive features compared with classical CJD. These include a much younger age of onset; longer disease duration; prominent psychiatric symptoms; absence of characteristic EEG abnormalities and, in many cases, distinctive MRI abnormalities; and presence of the prion protein (PrP) in tonsillar tissue. There are also some pathological differences from classical CJD.

It has been estimated that about 80 000 people in Australia lived in the United Kingdom around the time of the BSE outbreak. When vCJD first appeared in the United Kingdom in the mid 1990s, a major epidemic was considered possible, but the magnitude of the epidemic has been far less than predicted.

The Australian Guidelines (section 31.1) note that ‘the risk of transmitting vCJD in Australia in the course of health care delivery is extremely remote and does not warrant additional precautions beyond standard precautions’. The guidelines ‘specifically address classical CJD, and provide a firm foundation for additional recommendations that may be necessary for the control of vCJD in the future’.

An update on the state of the science

Dr Michael Gonzales, Anatomical Pathologist, Royal Melbourne Hospital

Prion protein is present in many organs and tissues, including the brain, spinal cord and eye of healthy humans and animals. The CJD agent is believed to be an abnormal form of a prion protein that causes surrounding prion proteins to change their structure to the abnormal conformation. The two forms of this protein are referred to as:

1. PrPC, the normal (cellular) form
2. PrPSc, the disease-associated form.

The diseases prions cause—the transmissible spongiform encephalopathies (TSEs)—are fatal degenerative diseases of the brain that affect both humans and animals. Clinical diagnosis can be difficult because of the myriad possible presentations, including sporadic, inherited and ‘infectious’ sub-types. Regardless of presentation, all of these diseases are associated with the presence of deposits of the abnormal prion protein in the brain.

The major difference between these two forms of protein is structural. The normal protein consists mostly of corkscrew-like structures; whereas the abnormal protein changes and takes on a folded or pleated structure. Deposits of the abnormal protein are insoluble and extremely resistant to destruction by heat or chemicals, and it is the structural difference that accounts for the resistance to conventional methods of disinfection and sterilisation.

Classification of human prion diseases

The diseases can be classified into three broad groups:

1. **Sporadic**—these occur spontaneously at a rate of one new case per million per year, and include CJD and sporadic fatal insomnia. It is thought that sporadic disease is the result of spontaneous change to the conformation of the prion or non-heritable mutations in the prion protein gene. It is the commonest form of CJD, accounting for about 85–90 per cent of the disease.
2. **Inherited**—these familial forms are inherited between generations and occur at a rate of about one new case per 10 million per year. The principle familial prion diseases are:
 - a. Familial CJD
 - b. Gerstmann Sträussler Scheinker Syndrome
 - c. Fatal familial insomnia
3. **Acquired prion ‘infection’**—where exogenous abnormal forms of the prion enter the brain. Examples are:
 - a. Kuru
 - b. Variant CJD (vCJD)
 - c. Iatrogenic CJD (iCJD)

Iatrogenic disease

Iatrogenic prion diseases occur either through:

- contact with contaminated tissues; for example, dura mater grafts, human growth hormone or human gonadotrophin. There have only been a small number of cases in each of these categories in Australia.

- contact with contaminated instruments. There are a few examples, including one well-documented case, in the literature of contamination of deep electrodes used in patients for the treatment/diagnosis of epilepsy. There have been no proven cases of transmission in this way since 1970, despite substantially increased surveillance. Although the reasons for this are uncertain, modern sterilisation techniques are like to have had a substantial impact on this very low risk.

Pathology and spread of prion disease

The pathology of the different forms of prion disease is typical:

- In sporadic CJD, there is characteristic sponge-like appearance within the surface brain tissue. The diagnosis is usually confirmed by demonstrating the presence of the abnormal prion protein, and this is most easily identified post mortem. It can be missed in a random biopsy because the sponge-like changes may not be evenly distributed throughout the brain.
- In vCJD there are heavy deposits of the abnormal protein in the brain, forming what are called florid plaques.

There are currently two theories to explain the spread of prions. The first is the protein unfolding/misfolding model, which proposes that the abnormal protein is formed from the normal protein; that is, when the abnormal protein is present, it influences the normal protein to partially unfold and refold into the abnormal form. In this model, it is proposed that abnormal protein appears because of a spontaneous genetic mutation. This is thought to be an infrequent event, and probably occurs at about the same rate as the sporadic disease; however, this theory does not explain the rapid increase in the concentration of abnormal protein that is visible as the disease develops.

The second and preferred model is the ‘seeding’ model. This proposes that the normal and abnormal proteins are in equilibrium, but that equilibrium is heavily weighted towards the normal protein. The abnormal protein is stabilised only when it forms a crystal-like seed, or aggregate, to which monomers are then added in very rapid progression. In this model, the exponential increase in concentration is explained by the fact that aggregates break down and offer further surface area for accretion of further monomers.

Issues for instrument reprocessing

Both the National Health and Medical Research Council and the World Health Organization have produced a list of tissues that have a high or low potential for contaminating surgical instruments. The profile is somewhat different in vCJD, which affects a large number of peripheral tissues, particularly lymphoid tissues, in addition to brain, spinal cord and retina. In vCJD, tissues highly likely to contaminate instruments are tonsil, lymph nodes, spleen, appendix, and lymphoid tissue associated with the gut. The abnormal prion has been found in the nerves that supply the gut.

There have been some recent reports that strongly suggest transmission of vCJD by blood transfusion. In one case, vCJD occurred in an individual who had received a transfusion from an apparently healthy donor who later died of vCJD. In the second case, the abnormal prion was found in the spleen and cervical lymph nodes in a person who was not displaying any neurological disease, but had died from a ruptured aortic aneurysm. This person had also had a blood transfusion five years earlier from a blood donor who later developed vCJD.

These reports suggest that vCJD might be transmissible through means such as blood transfusions even before the individual is showing any evidence of the disease.

Current research

The principle of prion decontamination is to try to alter the actual structure of the protein so it can no longer interact with the normal protein to form abnormal protein. There have been some interesting experimental models developed recently which supposedly simulate the situation of contact between surgical instruments and brain tissue. These have involved taking surgical-quality stainless steel wires and:

- immersing them in a mixture of brain tissue containing the abnormal protein, or inserting a wire directly into the brain of a prion-sick animal for periods of time ranging from five minutes to five days
- subjecting the wires to a variety of physical and chemical decontamination procedures, then
- re-implanting those wires into brains of healthy animals for periods varying from five minutes to continuous, and monitoring those animals for disease.

The findings from these experiments suggest that the abnormal prion is stabilised on a stainless steel surface and appears to be resistant to the partial in vivo denaturing that is observed when brain homogenates are inoculated into experimental animal brains, and is more effective in promoting conversion of the normal to abnormal prion. In addition, the findings show that contact between a stainless steel surface and brain tissue for as little as five minutes is sufficient to contaminate the surface with a load of abnormal prion capable of transmitting disease, and if effective decontamination is not achieved, the surface will remain 'infectious' for a prolonged period of time.

The present World Health Organization-recommended chemical protocols were found to be effective. There was no infection transmission in wires treated with sodium hypochlorite and sodium hydroxide, and there was a very significant reduction in the log of infectious particles. The recommended World Health Organization sterilising protocol—sterilising at 134°C for 18 minutes—was partially effective and did not produce such a large reduction in activity. When the wires were immersed in water during the sterilising procedure, however, there was 100 per cent effectiveness. This suggests that some modification to the recommended protocol is probably required. Finally, some enzymatic cleaners, when combined with vaporised hydrogen peroxide, are also very effective. A summary of the experiments can be found at appendix E.

Questions and discussion arising from the presentation

Testing for CJD

Brain tissue from biopsy can be tested, but diagnosis cannot be assured. The abnormal protein is not always evenly distributed throughout the brain, so a sample of brain tissue may not show the typical pathology. In addition, there may not be sufficient abnormal protein for the test to be accurate.

Another test that is used is for the cerebrospinal fluid (CSF) 14-3-3 protein. These proteins are present in any neurological disease where there is destruction of brain cells, including CJD. This test cannot be used as the sole diagnostic tool. A positive CSF 14-3-3 protein test combined with compatible clinical features in the patient adds to the diagnostic probability of CJD; however, the test does not conclusively confirm or exclude CJD.

While the CSF 14-3-3 protein is a useful test, a positive result should be interpreted with caution. When used as a diagnostic tool, a positive result has approximately 90 per cent sensitivity and specificity. This means that some patients who have CJD will have a negative CSF 14-3-3 protein, and some who don't have the disease, will have a positive result. These false positives have been recognised in various diseases, such as stroke and encephalitis. For these reasons, the test should only be used when based on the clinical findings of a neurologist, that there is a reasonable expectation of CJD. Use of the protein test for screening is not recommended. It seems unlikely that a specific non-invasive diagnostic test will be developed in the near future.

Decontamination of surgical materials

Some experiments suggest that a dry steel surface stabilises the prion protein so that it does not come off easily. It is necessary to maintain a wet surface to get the accretion of the protein off the surface.

There has been very little experimentation done with surgical plastics and other non-metal surfaces.

Experiment design

How well can we transfer the results from these experiments to the real world of instrument reprocessing? Some clinical experts expressed the opinion that if similar studies were conducted after instruments had been cleaned and sterilised using the methods routinely used in our hospitals, the results would show little evidence of contamination and the risk of transmission would be minimal.

CJD—a national perspective

Professor Graeme Ryan, Chair, NHMRC Special Expert Committee on Transmissible Spongiform Encephalopathies

The Australian Government established the Special Expert Committee on Transmissible Spongiform Encephalopathies in December 2000. It is an interactive committee, regularly hearing updates from the various agencies involved with the committee and other interested individuals. Its work is wide-ranging and encompasses:

- assessing and minimising the potential risk of transmission of TSEs
- infection control
- ethical and legal issues
- links with national and international committees
- contingency planning/risk management planning
- advice to governments and non-government agencies

The expert committee is now accepted as the national peak body for the provision of expert scientific advice regarding BSE and CJD (including variant CJD), ensuring that government agencies are receiving the best possible scientific advice. Key achievements include:

- advice that supported the development of safer animal feeding practices (for example, ruminant feed ban), stronger approaches to surveillance, and the national BSE contingency plan
- advice and community consultation that has supported the implementation of blood donor deferral decisions
- advice that has supported decisions in relation to human therapeutic goods (for example, vaccines, plasma products, insulin, Lyodura)
- advice that has supported decisions in relation to the importation of human food products
- advice in relation to organ and tissue donation
- advice in relation to infection control practices
- advice in relation to ethical and legal issues, particularly in relation to the operation of the Australian National CJD Registry
- advice in relation to the implications of the BSE outbreak in Canada and the USA
- advice that supported the development of the Commonwealth contingency plan should a case of vCJD be confirmed in Australia
- advice leading to the establishment of the National CJD Incident Panel.

Discussion arising from the presentation

Blood supply

Internationally, there are some discrepancies in recommendations for screening of blood donors for vCJD. In the USA, in particular, there are significant restrictions placed on who can donate blood. In Australia, a consensus conference was held early in 2003 to discuss a rationale and acceptable standard, and it was agreed to continue recommending donor deferral for those who had lived in the UK for six months or more between 1980 and 1996. Six months is a compromise figure that balances two factors: a statistical calculation that the risk is multiplied the longer the period of possible exposure, and the risk involved in substantially decreasing the number of people who are able to donate by making the time period shorter.

The NHMRC Expert Committee holds that screening is appropriate only where informed consent on the part of the recipient is not possible. This applies to blood and tissue donations. Organ donation requires informed consent, so that living in the UK does not disqualify a person from being an organ donor providing that the matter is discussed with the recipient. Where an informed consent process cannot be assured, donor restrictions are required. The restrictions on blood donations are designed to prevent the transmission of vCJD; there is no evidence that sporadic CJD is transmitted via blood.

Discrimination and 'at risk' individuals

Concerns were raised about individuals nominated as 'at risk' for CJD experiencing discrimination and trouble accessing the health services. It was agreed that guidelines exist, but each case should be assessed on its merits. There is awareness that 'at risk' individuals may experience discrimination and that this is an issue that will continue to require attention.

Guidelines for vCJD

The NHMRC Expert Committee has formulated initial vCJD guidelines, but more work is needed. While there is considerable public concern about the emergence of vCJD in Australia, it is unlikely that the number of people who develop the condition will be very large and it is unlikely to pose a large public health risk.

Other issues

There was discussion about the merit of establishing a basic standard of care that applies to all, and thus eliminating the need to categorise people at risk. By concentrating on the science of sterilisation and managing instruments, and recognising that no system is perfect, it would be possible to provide the community with an assurance of high level of safety.

Recently, at the Royal Melbourne Hospital, a number of patients were exposed to instruments used on a patient who was subsequently diagnosed with CJD. Of these patients, many will have surgery in the future. What risk category do these patients fit into and what are the recommendations for sterilising and disinfecting the instruments used on them?

The Australian Guidelines are clear that, when a case is confirmed, instruments that have been used on a high-risk tissue must be destroyed. Lack of clarity emerges when the guidelines are applied retrospectively—that is, CJD risk is identified at some time after surgery, and the instruments have been used and processed many times. There is no answer to this at present, although we learn something after each event.

Lookback investigations

The general view at the workshop was that people who have potentially been exposed to CJD should be warned of this potential exposure. The issue, however, is not clear cut. In Canada's first vCJD case, the person had had an endoscopy and the endoscope was then used on a number of people. It was decided to call in and advise everybody potentially exposed. This caused considerable concern across population in that province. Whether this was appropriate is questionable. This is where the CJD Incidents Panel can help to provide support on a case-by-case basis as to the extent of a lookback. It is not a black and white area and one needs to err on the side of conservatism. Ultimately, as we gain more experience with CJD, we may do things differently.

Section 1: Risk assessment and screening

Recommendations

1. That a standardised approach to identifying CJD risk be introduced for all patients undergoing elective surgery involving potentially high infectivity tissues. Groups for CJD risk assessment would include those undergoing neurosurgery, spinal surgery, posterior eye surgery, pituitary surgery and complex dental surgery. The responsibility for risk assessment resides with the surgeon responsible for the planned surgery.
2. That a risk assessment include the following questions:
 - a. Have you considered the possibility of CJD in this patient?
 - i. Does the patient have a family history of CJD?
 - ii. Does the patient have a progressive neurological disorder of less than 12 months duration?
 - b. Is the patient a recipient of a dura mater graft prior to 1990?
 - c. Does the patient have a history of receiving human pituitary-derived hormones for infertility or short stature (prior to 1985)?

Public Health is able to provide further information regarding the management of a person requiring a medical or dental procedure and who has been identified as a possible CJD risk. Public health can be contacted on 1300 651 160.

3. That each health service has a process in place to ensure that the risk assessment has been undertaken; for example, the assessment may be linked with the operating suite or hospital booking process.

Background

Managing risk

The guidelines approach to managing the risk of health care-associated transmission of CJD is to identify individuals who pose a risk in the health care setting, and manage them under conditions that prevent disease transmission to other patients or care providers. Patients with diagnosed or suspected CJD pose the highest risk for transmission of prion disease. Risk assessment should include two dimensions in order to determine the infection prevention and control measures:

1. the probability that a patient has or will develop CJD
2. the level of infectivity of the patient tissues. The risk of transmission varies according to the infectivity of the tissue, with central nervous system tissue being the most highly infective (see table 31.1, p. 31–6, of the Infection Control Guidelines).

Iatrogenic risk

Contaminated tissue

The major part of iatrogenic risk is accounted for by contaminated corneal and dura mater grafts, and human growth hormone and human pituitary gonadotrophin (Rutala and Weber 2001). As discussed earlier, in Australia there have been 10 reported cases of iatrogenic transmission of CJD: five associated with dura mater grafts and five with human pituitary gonadotrophins (Boyd et al. 2001). According to the Australian Guidelines (section A9.5), approximately 2000 people in Australia received cadaver-derived human pituitary hormones in treatment for infertility or short stature before this practice ceased in 1985.

Use of Lyodura (dura mater graft) ceased in Australia in 1987, by which time some 2478 sheets may have been used, based on the manufacturer's records (Brooke et al. 2004). It is not known exactly how many patients this equates to. The Australian Guidelines (section A9.5) state that 'An estimated 5,000-10,000 people received dura mater grafts in a variety of surgical procedures. Of these, 95% had neurological procedures requiring grafting, and it is this group that has a documented, increased risk of CJD.' This was an initial estimate by the Commonwealth Department of Ageing and the Therapeutic Goods Administration, but Brooke et al. believe the number is fewer than 2500.

Contaminated equipment

With stereotactic electroencephalography electrodes and neurosurgical instruments, the risk, though it cannot be excluded entirely, is infinitesimally small. There have been no cases in Australia, and worldwide there have been none for over 20 years (Will 2003).

Familial risk

There are currently 17 pedigrees (families) with familial CJD, with 34 affected individuals. In aggregate, the Australian population is thought to include possibly fewer than 200 at-risk first-degree relatives.

Sporadic CJD

Sporadic CJD, by definition, has no known cause and no known risk factors, and can only be identified where symptoms are already present. It is the most common form of human prion disease, comprising 85-90 per cent of all human transmissible spongiform encephalopathies. Death occurs after a median illness of four months.

Screening of blood donors

Blood donors are screened for CJD risk, primarily for variant CJD, because there is some evidence that transmission of this disease is possible via blood transfusion (Pincock 2004; Sibbald 2004). Given that blood donors comprise a large population of healthy people, and blood products are pooled and concentrated before being distributed, the risk, though small, can be managed by excluding certain donors. The same does not apply to surgery.

Infection Control Guidelines recommendations

The Australian Guidelines recognise that the highest risk of health-care associated CJD transmission is when the central nervous system is exposed in a patient with CJD (section 31.7.5). The guidelines advise, however, that all hospital patients should, in effect, be screened for CJD risk:

When individuals are being admitted to hospital or presenting at an outpatient/ emergency unit or health care waiting room, a detailed medical history should be collected from them or their carers. Triage staff should use a checklist to assess patients for conditions that require additional (infection control) precautions, as well as for prioritising those who may require urgent attention or immediate treatment. Using a triage checklist may also reveal a medical history relating to CJD for example:

- *a pre-existing neurological disease that requires further evaluation;*
- *a family history of two or more first-degree relatives with CJD or other undiagnosed neurological illness;*
- *a history of receiving human pituitary-derived gonadotrophin (for infertility) or growth hormone (for short stature); or*
- *a dura mater graft in a neurosurgical or other surgical procedure before 1990.*

(Department of Health and Ageing 2004, section 31.12.1)

An undiagnosed neurological illness might, for example, be a rapidly progressing dementia or other undiagnosed brain disease of less than 12 months duration with no known cause. The guideline recommendations are based on laboratory evidence that CJD prion may be detected outside the central nervous system, and an Australian case-control study suggesting that surgery in general, not just neurosurgery, is an independent risk factor for the development of CJD (Collins et al. 1999).

Comprehensive pre-operative: screening risks and benefits

Special precautions are imperative when patients known to have CJD, and those with a recent-onset neurological condition as yet undiagnosed, undergo surgery in which high-risk tissue is contacted. The recommendation in the Infection Control Guidelines to screen all patients undergoing procedures, while superficially attractive, is fraught with difficulty. The example in the following presentation illustrates the point.

Screening: a view from a health service

Associate Professor Paul Johnson, Deputy director, Infectious Diseases Unit, Austin Health

The Australian Guidelines recommend that, to reduce the risk of inadvertent transmission of classical CJD, risk stratification of all patients undergoing procedures should be undertaken. Risk stratification entails 'screening' and some organisations in Victoria are already doing this, even for endoscopy.

Screening is the process by which you look for a needle in a haystack. It is the application of a tool (for example, a test or a set of questions) to sort through the haystack and find the needle. The perfect screening tool will be 100 per cent specific and 100 per cent sensitive; that is, it will find all of the needles (sensitivity) and never mistake a strand of hay for a needle (specificity). Most screening tests are not this good!

Because there is no screening blood test for CJD, we have to rely on a set of screening questions. Everyone uses slightly different questions, but in general these are the ones that the guidelines recommend:

- Do you have CJD?
- Do you have an undiagnosed progressive neurological illness of less than 12 months duration?
- Do you have two or more relatives with CJD or a CJD-like illness?
- Have you had a dura mater graft?
- Have you had growth hormone or fertility hormone?

These are the best questions we have, but they are impractical in many situations. What do you do in an emergency; where the patient is unconscious, or does not speak English and no interpreter is available; the patient is actually developing a dementing illness; or whose educational level is such that they do not know about CJD? What is the definition of a rapidly dementing illness, and how do you distinguish it from Alzheimer's disease, or other dementias? These uncertainties must mean that this screening tool is likely to have a specificity considerably less than 100 per cent. How would such a tool work in practice?

By way of example, imagine that we have 2000 people, only one of whom has CJD. We apply our screening tool (the above set of questions) but accept that the tool is only, say, 95 per cent specific. When we screen our 2000 hypothetical patients, we will end up with 100 positive tests, but only one will be a true positive. This situation happens frequently with screening tests (with HIV, with syphilis in pregnancy): the first test you use is intended to be very sensitive (so as not to miss anyone), and for those who test positive, you use a second test to check and confirm the diagnosis. But for CJD, there is no second test. You could argue that a lumbar puncture could be used, but this is not 100 per cent specific either, and you would have to do 100 lumbar punctures to find the positive case. As cCJD only has an annual incidence of 1 in 1.5 million, if you use a screening tool with a 95 per cent specificity to screen the general public, on average you will generate 75 000 false positives for every true case.

Assuming you have all the resources to do it, is it a good way finding all cases? Would we find every one? If we assume that the test *sensitivity* is 100 per cent (a big assumption), and we sort carefully through the 75 000 positive tests (diverting resources from, say, Methicillin resistant Staphylococcus aureus control) and identify all the *identifiable* cases, would we be protecting everyone else from CJD?

I would argue not. If 85 per cent of CJD is sporadic—that is, there are no risk factors that could be found with the screening questions—and if the patient hasn't yet developed symptoms, and we assume that CJD is transmissible by neurosurgery for, say, three years before the onset of symptoms, then the following arithmetic applies, assuming:

- a test with 95 per cent specificity and 100 per cent sensitivity
- a general hospital that does 15 000 general surgical procedures per year (the Austin does 13,000, so this is a reasonable model)
- an incidence of CJD that is 10 times higher in the general (non-neurological) hospital population than in the general population.

Based on these assumptions, it would take an average of 10 years before a single case of CJD would be identified at this hypothetical institution. In this time, there would be 7,499 false positives (an average of 14 per week) that would have to be followed up, and you would have operated on three asymptomatic cases that you did not know about.

What about high-risk procedures?

There are definitely procedures in which there is a higher prior probability, if the person has CJD, of encountering very high concentrations of prions—in the brain, cord, and posterior eye. Also, in people who have been brought into hospital to investigate neurological symptoms, the incidence of CJD is likely to be much higher than the background rate. The screening arithmetic may become a little more sensible in that situation; however, I have spoken to several neurosurgeons, and they are already informally screening for CJD before planning procedures.

One possible recommendation for this conference to consider is that, if systematic screening is to be used, it should be restricted to high-risk procedures (brain, spinal, posterior eye). It should be recognised that screening would not have prevented the recent incident at the Royal Melbourne Hospital.

Discussion arising from the presentation

The introduction of screening as it is currently recommended in the guidelines is likely to be labour-intensive and not very effective. People do not fill out forms, and the forms do not get into the patient medical record, or they are overlooked. There was strong support for the notion of developing a universal approach to transmission prevention, which was seen to be a more effective approach than trying to screen all patients. Given the very low probability of CJD, the screening tool has to be much better than the rather vague questions proposed, before it could be practically applied to the general population.

Screening for CJD risk: epidemiological principles and the role of the registry

Steven Collins, Co-director, Australian National CJD Registry

There are considerable difficulties for the Australian National CJD Registry in trying to track a very rare disorder. Accurate diagnosis is the first requirement. Case definition criteria are still not perfect, and the registry actively seeks post-mortem—the gold standard—for all suspect cases. The CSF 14-3-3 test is non-specific, and was developed as a diagnostic confirmatory test. There is now clear evidence that it can become positive during the disease rather than being invariably positive earlier on. The test was not designed for screening, and when used in this way, its sensitivity and specificity drop right down.

Despite the difficulties, and the differences in surveillance methods from those used in other countries, Australian surveillance figures are very much in keeping with those in Europe, reassuring us that what we are doing is probably adequate.

Over the last few years, the number of new cases of sporadic CJD in Australia has varied from about 20 to 28 cases per year. Familial cases are also an important group. Some of the mutations mimic sporadic CJD entirely and are difficult to pick, requiring genetic testing. Surprisingly, only 30 per cent of people with genetically determined CJD have a positive family history.

Management of the risk of CJD transmission is straightforward when that risk is overt and able to be clearly identified and validated. The difficulty arises when there is possible covert transmission.

Overt risk

The concern about neurosurgery is largely based on a handful of cases. The first recognised was back in 1977, when two young patients had CJD transmitted to them by use of depth electrodes which had been previously used on a patient for myoclonus. The patient, who died the next day, may have had a genetically determined CJD, given that the person's father had died of a similar illness at the age of 70. The electrodes went through standard cleaning processes used at that time, with alcohol and formaldehyde vapour. Despite that, both patients went on to develop CJD within 20 months. One of the two depth electrodes was subsequently implanted into a chimpanzee, that died of CJD 18 months later. Retrospectively, Colin Master and Bob Will found a few other cases in which there is the likelihood of neurosurgical instruments transmitting disease. There was a patient in 1956 that had neurosurgery on the same day as a patient with CJD, and went on to develop CJD within 20 months.

The other mode of transmission is via corneal and dura mater grafts and human pituitary hormones. As of March 2004, there were 170 recorded dura mater graft-related transmissions, mostly in Japan. The incubation period has ranged from 18 months to 23 years. Although most are related to a brand called Lyodura, there is now at least one report from another brand, and a couple of patients with CJD from in-house processed dura mater. There are also a couple of reports of transmission from the use of Lyodura in peripheral embolisation, suggesting peripheral transmission. There is even a possibility of transmission via a pericardial graft used for tympanic membrane repair.

Worldwide, there have been 174 cases of transmission via human cadaveric pituitary hormones. The vast majority of these cases are in France. There was an international moratorium on the use of these hormones in 1985, but France alone decided to continue their national pituitary harvesting program. The incubation period is up to 30 years—very long. There is even a case of a person who received test doses of hormone for a few days and developed CJD 37 or 38 years later. It is tentative, but raises the possibility that even extremely small doses can transmit.

In Australia, there have been five Lyodura-related cases of CJD, four related to human pituitary gonadotrophin, and one possible growth hormone-related case. There have been no recognised cases for the last three years.

Covert risk

I now want to talk about the more difficult area of covert transmissions: the unsuspected cases that may pose risks that we do not really appreciate. While 85 per cent of CJD appears to be sporadic, and only about 1 per cent in humans is related to recognised transmission, there is growing concern about the possibility of a natural reservoir of sub-clinical infection. Although the present understanding is that sporadic CJD probably occurs from a spontaneous misfolding of the prion protein, another possibility is that, for some patients with sporadic CJD, transmission is unrecognised.

A case control study we did a few years ago looked at a number of risk factors for sporadic CJD. The study included 240 cases and 780 community controls. It found positive associations with surgery: the risk of CJD increased with increasing numbers of operations, and it became quite significant with three or four operations. The operations associated with this rise in risk were all peripheral surgery. We also found an association with long-term residence in a rural setting, a finding we do not understand. We found a number of negative associations, adding some support to the reliability of the data with respect to surgery. Negative associations included blood transfusion, close personal contact with a non-relative with dementia, major dental work, transplant, and living in the United Kingdom for more than one month in the 1980s.

Control study for sporadic CJD in Australia

Study design

- cases all known to National CJD Registry
- controls—3:1 ratio with cases
- community based (compared with most prior studies)
- sourced over a single weekend in August 1997
- random telephone survey
- very abridged questionnaire prompting yes/no answers
- 241 definite and probable cases—January 1970–October 1997
- 784 controls
- aimed at identifying risk factors for sporadic CJD based on their a priori relevance, especially iatrogenic exposures

Medico-demographic variables: risk of sporadic CJD

- positive associations
- surgery
- work of residence on farm/market garden for more than 10 years

No association

- dialysis, chemotherapy, radiotherapy, arterial embolisation
- blood transfusion
- close personal contact with non-relative with dementia
- major dental work
- transplant recipient
- lived in United Kingdom for more than one month in 1980s
- types of surgery associated with increased risk
- cardiac, hysterectomy, haemorrhoids, gall bladder, hernia repairs, cataract/eye, varicose veins, carpal tunnel

In summary, high risk patients—a current focus of concern in relation to surgery—are usually recognised and, therefore, do not, in my opinion, pose health risks. The problem is with the people who are pre-symptomatic, who are not being recognised as having potential for high infectivity. Use of a screening question may at least provide a prompt to think about each patient and make a more informed decision about whether there really is a risk.

Discussion arising from the presentation

The question was raised about how concerned we should be about the possible hidden transmission of CJD. It was noted that CJD is a very rare disorder and, if it was highly contagious in the hospital setting, we might be seeing a lot more neurosurgery-related cases. It seems likely that routine sterilisation reduces transmissibility to levels that do not effectively transmit the disease.

Recommendations: risk screening

The discussion paper presented two recommendations for discussion at the workshop:

Recommendation 1: That the CJD consensus conference participants endorse option 1 for implementation in the Victorian health care setting

Recommendation 2: That a screening tool be developed based on the triage checklist from the Infection Control Guidelines.

The options presented were as follows:

- Option 1:** Screen only some groups using a risk-screening tool. Groups for screening would include those undergoing neurosurgery, spinal cord surgery, posterior eye surgery and pituitary surgery.
- Option 2a:** Screen everyone presenting for surgery by asking a single question: ‘Does this patient have a dementing illness or other progressive neurological condition of less than 12 months duration that could be CJD?’
- Option 2b:** Screen everyone presenting for surgery and endoscopy by asking a single question: ‘Does this patient have a dementing illness or other progressive neurological condition of less than 12 months duration that could be CJD?’
- Option 3a:** Screen everyone presenting for surgery using a risk-screening tool.
- Option 3b:** Screen everyone presenting for surgery and endoscopy using a risk-screening tool.
- Option 4:** Screen no one.

There was a range of opinion the topic of screening. Emerging themes included the following:

- Screen no one—screening questions are too inaccurate and could cause harm to large numbers of people who would be labelled without being able to be diagnosed. Screening would divert resources from more important issues, and there is no convincing evidence that CJD incidence is rising and that surgery is transmitting the disease. This position, if adopted, should be regularly reconsidered in the light of new data on increasing rates of disease, or the availability of a much better screening tool.
- Screen everyone (as per the guidelines)—screening reassures the public and satisfies management. The group who proposed this have actually been doing it and argued that it is not difficult to do once it is incorporated into the system.
- Screen patients having high-risk procedures (for example, neurosurgery, spinal surgery), using either the full set of questions (provided as an example in the discussion paper), or with a single question regarding dementia. This process would produce fewer false positives than universal screening.

Those who did not support universal screening recommended that the guidelines be changed because of the low likelihood of accuracy of the screening test. Some supported the use of a narrow screening tool, for all patients undergoing high risk procedures, to look for some very specific risks (for example, familial), although the question of an evidence base for such a screening tool was not addressed. It was suggested that the screening tool comprise two questions (to the patient or, if not capable, to a family member): ‘Do you have two or more direct family members with CJD?’ and ‘Have you/your relative been diagnosed with CJD? If yes, has the case been notified to public health?’ The supporters of this level of screening argued that it should be complemented by increased and improved cleaning, disinfection and sterilisation, to provide a safety net.

Others agreed with option 1 as presented in the background report (see above). People supporting this course of action also noted the need for a greatly improved sterilisation/decontamination process, and for a clear and well resourced process for managing the screening.

It was noted that screening in any form would require having protocols and practices in place that ensure that patients who answer ‘yes’ to any of the questions are not subject to discrimination, and those administering the screening tool know what action is required.

In general, there was support for option 1 as a minimum standard to provide safe care. It was agreed that a standardised screening tool for this purpose should be developed.

Section 2: Managing instruments and equipment

Recommendations

4. That all Victorian hospitals and health services that perform procedures affecting higher infectivity sites including brain, pituitary gland, spinal cord, cerebrospinal fluid, retina and optic nerve, and companies that provide surgical equipment for use in these procedures, work towards having a system that will identify individual instruments to individual patients.
5. That in the event that CJD is identified retrospectively in a patient who has undergone surgery or other procedures, including endoscopy, all equipment potentially contaminated through use on the patient should be treated as follows:
 - a. In the case of procedures in which brain, pituitary gland, spinal cord, cerebrospinal fluid, retina or optic nerve tissues are exposed, all instruments that have come into direct contact with the tissue shall be withdrawn pending a decision from the CJD Incidents Panel.
 - b. In flexible endoscopic procedures, equipment that has contact with brain, pituitary gland, spinal cord, cerebrospinal fluid, retina and optic nerve tissues shall be withdrawn pending a decision from the CJD Incidents Panel.
 - c. In all other surgery and endoscopic procedures—that is, procedures that do not involve brain, pituitary gland, spinal cord, cerebrospinal fluid, retina and optic nerve—equipment will not be withdrawn and should be cleaned and sterilised as per normal procedures.
6. There are operational difficulties associated with the implementation of the guidelines recommendation concerning maintenance of a one-way flow of surgical instruments as defined by perioperative nurses. The guideline writing group are to be asked to review this recommendation to clarify its intent.

Background

CJD transmission via surgical instruments

There are case reports of the transmission of CJD on contaminated neurosurgical equipment (Rutala and Weber 2001; Will 2003), but evidence of transmission in this way is limited. Worldwide, the most recent reported case was more than 20 years ago, in 1980 in France (Foncin et al. 1980), and there have been no reports of cases of CJD transmitted in this manner in Australia.

If a patient's risk categorisation for CJD is known before the procedure, management of instruments and equipment requires some planning but is relatively straightforward. Complexities arise when CJD is diagnosed after surgery. When this occurs (for example, in the recent exposure the procedure had been performed more than 12 months before the possibility of CJD was raised), the instruments and equipment may have been processed using routine methods many hundreds of times. The risk of continued prion contamination of this equipment cannot be excluded entirely, but must be extremely low.

In addition, as discussed earlier (see 'Covert risk'), the suggestion has been made, based on two large case control studies, that an uncertain but potentially significant number of CJD cases classified as sporadic occur as a consequence of unrecognised low-level contamination events arising from invasive medical care, especially surgery. While both the studies have methodological limitations, the suggestion, if substantiated, has potentially wide-ranging implications; therefore, it deserves serious consideration (Lewis et al. 2002).

Infection Control Guidelines recommendations

The Australian Infection Control Guidelines recommendations are as follows:

The standard method of preventing transmission of CJD is to identify individuals who pose a risk in the health care setting and manage them under conditions that prevent disease transmission. This approach is not only expensive and resource intensive, but may lead to discrimination against people in recognised risk groups for CJD by limiting their access to health care services. An alternative viable and cost-effective method of minimising disease transmission is to apply more stringent methods of instrument processing and use less invasive clinical procedures when they are available. (Section 31.9) Equipment used on high infectivity tissues in a patient in the higher or lower risk categories for CJD should be destroyed, quarantined until diagnosis is confirmed and then destroyed, or kept for use for that patient only. (Department of Health and Ageing 2004, table 31.4, p. 31.16)

The guidelines also specify that:

Systems should be in place to track reusable items of equipment used on high-infectivity sites, especially for procedures where transmission of infection has been known to occur. Instruments that have been in contact with neural or ocular tissue (such as brain, spinal cord, retina, optic nerve and pituitary) should not only be tracked but also handled in such a way as to avoid cross-contamination of any other instruments (for example, by maintaining a one way flow of instruments during surgical procedures and by separating instruments potentially contaminated with CJD infectious agents from other instruments). (Department of Health and Ageing 2004, section 31.8.1)

The Australian Standard (AS/NZS 4187, 2003) states:

There shall be protocols for inventory control. These may include...recall, where necessary. Bar coding or similar systems will provide information for identification of area of use and patient identification in case of malfunction or misadventure. (section 8.5.1, p.63)

Procedures should be in place to link sterilizer cycle batch information to items that have been sterilized, to the patient. (section 8.5.2.1)

One of the steps required by the Standard in compiling a recall report is: "Identifying the number of patients potentially exposed and the actions taken". (section 8.5.7)

Variation in recommendations

There is substantial variation internationally in recommendations regarding the degree of the reprocessing required in order to render surgical equipment safe for reuse after use on a patient at CJD risk. All guidelines strongly recommend that instruments used on high risk patients during a procedure on high-risk tissue be destroyed, but some countries (for example, Canada) offer reprocessing alternatives for instruments that an institution is unable or unwilling to dispose of. There is also variation in recommendations on reprocessing for lower risk patients and procedures.

The UK guidelines (ACDP/SEAC 2003) have now abandoned an earlier recommendation for enhanced reprocessing of certain surgical instruments in particular circumstances. The regime previously recommended is now known to not be reliably effective and may even render the instrument more difficult to decontaminate. They provide recommendations for instrument management for known CJD risk patients: essentially, instruments are to be either destroyed, quarantined until diagnosis is known, or reprocessed according to best practice (that is, 134°C for three minutes), depending on the level of CJD risk of the patient and the procedure being performed.

The Canadian guidelines (Health Canada 2002) offer a range of options for instruments used on at-risk patients. The preferred option is disposal of instruments; however, for instruments that are heat-resistant and that the institution is unwilling to incinerate, the option is to clean the instruments, immerse them in chemical solution for one hour, rinse, then place them in an open pan of water and sterilise for one hour on a liquid cycle (121°C). Alternatively, after soaking in the chemical solution, the instruments may be rinsed then transferred to an open pan and sterilised for one hour at either 134°C or 121°C. The guidelines do not specify that patients or the public be informed about the reuse of such instruments.

Different definitions of 'contaminated'

In a perioperative setting, the notion of asepsis requires that all instruments opened from their sterile packaging be considered contaminated. In the disease transmission context, only those instruments that have a sufficient volume of tissue that is considered to have an infective dose of agent are considered contaminated. These differing definitions lead to problems in applying guideline recommendations. For the purposes of CJD management, an agreed definition of 'contaminated' instruments is needed. This definition could be one of the following:

- all instruments used in a procedure where high infectivity tissue is exposed
- only those instruments directly used on the high infectivity tissues
- instruments that may have come in direct contact with in situ high infectivity tissue.

Instrument tracking

A recent publication notes that batch tracking was not sufficient in managing an adverse event, and suggests the need for instrument-level tracking (Cooper and Blamey 2003). Patient-level instrument tracking is not currently a standard practice in health care, although some hospitals and health services have begun to implement systems of this type. Some instruments cannot be marked for tracking so would automatically be earmarked for disposal.

Loan and consignment stock

Consignment and loan stock is surgical equipment owned by a company but lent to hospitals or health services for use during a particular procedure. Such equipment may raise management and logistical issues for tracking. Companies would have to be notified if such instruments were to be either destroyed or quarantined. Companies would also require good tracking of both instrument sets and prostheses, to enable them to be tracked in the same way as hospital-owned instruments. Loan arrangements between hospitals of neurosurgical instruments and equipment is common practice, highlighting the need for a common sterilisation standard.

Single-use items

Single-use items have been suggested in some cases; however, routine use of single-use equipment in surgery is expensive. More importantly, single-use instruments are generally of a lower quality (both in materials and function) than reusable ones and may result in more frequent surgical accidents through equipment failure. The risks associated with equipment failure far outweigh the risk of transmission of CJD on surgical instruments. In the United Kingdom, for example, single-use tonsillectomy instruments caused deaths, and the risk of death was much higher than the risk of iatrogenic vCJD. A device alert was released in December 2001 by the medical devices authority in the United Kingdom, advising hospitals to revert to reusable instrumentation (Device Alert 2001).

Flexible endoscopes and other heat-sensitive equipment

Recommendations are needed for the management of heat-sensitive equipment. None of the currently available low temperature disinfection/sterilisation methods are considered effective in destroying prion.

Endoscopes provide particular challenges in their cleaning and reprocessing in that their lumens and channels cannot be visually inspected to ensure adequate cleaning has occurred and they generally cannot withstand steam sterilisation methods or other additional methods of reprocessing for CJD.

In general, endoscopy procedures would not be performed on patients with confirmed CJD; however, endoscopes may be used on patients with neurological illness—for example, to locate a primary tumour—where it is suspected that the patient's symptoms are due to metastatic disease that is not visible by imaging.

The Australian Guidelines also provide for 'instruments that cannot be adequately reprocessed, because of their design or the limitations of current reprocessing technology'. These include endoscopes, bronchoscopes, cystoscopes, other fiberoptic scopes (for example, laparoscopes), diagnostic ultrasound transducers, and certain ophthalmic and optometric equipment. Diagnostic or therapeutic procedures using these instruments on patients in the CJD higher-risk category should be avoided where possible (section 31.14.5).

Where such a procedure is considered essential, the guidelines are as follows:

Group A patients: higher risk patients and symptomatic lower-risk patients. All parts of instruments that cannot be adequately reprocessed and that come into contact with low-infectivity tissue should be destroyed. This would include, for example, bronchoscopes, endoscopes and colonoscopes, and instruments that come in contact with the anterior components of the eye (section 31.14.5).

Group B and C patients: asymptomatic lower-risk patients and those with no identified CJD risk, respectively. Instruments should be 'kept immersed in an anionic detergent before being manually cleaned in accordance with procedures outlined in section 31.14.3, followed by routine reprocessing'.

The recommendation to destroy any endoscope used on low-infectivity tissue in group A patients is based on the problems with cleaning and reprocessing and the concern that lymphoid tissue may be encountered during the procedure; however, research to date provides no indication that endoscopes used on low-infectivity tissues are a transmission risk in classical CJD. The limited published research data suggest that 'prions, if present at all, are only found infrequently and/or in low titres in the gastrointestinal tracts of patients with cCJD'.

At the same time, for surgical equipment that can be processed at higher temperatures for longer times, incineration is not required following use on low infectivity tissues in higher risk patients, although uncertainty remains about the effects of the sterilisation regime.

Equipment reprocessing—current research

Dr Victoria Lawson, Senior Research Officer, Department of Pathology,
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There is limited human information about the transmission of CJD on instruments. Case reports where CJD transmission was proven are old and involve methods of disinfection and sterilisation no longer used; their conclusions, while valid, do not really help us. Research has to rely on experimental models. Our current understanding is based on research using different strains of transmissible spongiform encephalopathy, from different animal hosts, using different methodologies and different forms of tissue (intact tissue, macerates, homogenates and surface bound). All models have inherent problems, and there is no perfect method for replicating the experience of an operating room. Using such experimental models, it has been demonstrated that a wide range of chemicals are ineffective –that is, over one hour, they do not reduce infectivity by more than three logs. This list includes:

- phenolics
- iodine
- formaldehyde
- sodium deoxycholate
- SDS
- teogo
- urea
- alcohol
- hydrogen peroxide
- chlorine dioxide
- potassium permanganate
- Triton X-100
- glutaraldehyde
- ammonia
- hydrochloric acid
- peracetic acid

Some of these agents (for example, formaldehyde) may actually fix tissues onto the instrument, making it impossible to decontaminate.

The list of reagents shown to be effective (that is, greater than three log reduction in one hour) is short:

- chlorine
- phenolic LpH
- sodium hydroxide
- formic acid–formalin fixed tissue

Then there are physical methods of decontamination. We know that neither irradiation nor dry heat works; and that as a general rule, the efficacy of steam sterilisation increases with increasing temperatures, and with increasing time. There is one caveat to this: within different prion strains there may be a sub-population that is resistant to heat and, in some rare cases, inappropriate heating may actually increase the stability of the prion. There appear to be multiple strains of sporadic CJD and we do not know their thermostability profiles. This knowledge supports the argument for using two deactivation methods—chemical followed by steam sterilisation. Another important point is that most of the recommended decontamination methods are harsh and, while this does not pose a problem for experimental studies because surgical equipment is not being used, these methods are not appropriate for surgical equipment.

Equipment reprocessing is an area of significant interest and there have been many publications of alternative methods of decontamination in the last 12 months. Areas of study include:

- Proteases—enzymes that degrade the protein. In general, proteases alone are not sufficient, they need to be in the presence of a detergent or high heat or alkaline pH. This may or may not work within an instrument-processing system.
- Enzymatic detergents—several have been tested. In a study published earlier this year, one was shown to be minimally effective on its own (Yan et al. 2004). Another reduced infectivity associated with prion-contaminated steel wire by 3.5 logs (Fichet et al. 2004), but did not clear all the infectivity.
- Alkaline cleaners—these have been found to reduce detectable levels of infectivity.

More recent studies have used surface-bound prions as the model for decontamination in a surgical setting; a surgical steel wire is contaminated with prions and the infectivity associated with the wire is assessed, using an animal model. This model probably represents the best example of transmission in a surgical setting by taking into account the fact that instruments are cleaned before sterilisation. The prion-contaminated surgical wire is treated using the decontamination method under study (steam sterilisation, chemical, or cleaning) and then implanted into the indicator mouse for testing. The infectious dose associated with the wire is based on the incubation time to the development of disease, and the log decrease in infectivity is calculated.

A recent study found that surface-bound prions on a steel wire were inactivated by both sodium hypochloride and sodium hydroxide, and also by steam sterilisation immersed in water. Steam sterilisation in a dry environment was less effective.

Discussion arising from the presentation

What is the effect of manual cleaning on the reduction of infectivity? There was discussion about the methods of manual cleaning, keeping instruments moist after use before processing, manual cleaning with brushes and then the use of the automatic industrial washers called tunnel washers. There was some concern that equipment used for cleaning prion-contaminated surgical instruments may themselves become contaminated and potentially capable of transmitting the disease.

A recently published paper showed that the researchers could wash off some of the infectivity, and when they looked for the prion protein in the wash fluid, it was there at detectable levels. It is difficult to know how this translates into infectivity, and particularly infectivity that may contaminate another set of instruments. This is a new technology and it is likely that we will considerable research in the area in the coming years.

One participant noted that this is an important area of research, but had the following comment: 'Isn't the best test that for the last 30 years we have not had any cases of CJD caused by transmission on surgical instruments?' (*Workshop participant*). This was acknowledged.

Equipment reprocessing—issues in practice

Michele Cullen, Infection Control Consultant Disease Control and Research, Public Health Department of Human Services

Key issues in implementing the Australian Guidelines in the operating room include the following:

- ‘One-way flow’ of instruments—the guidelines recommend that a ‘one-way flow’ of instruments be maintained in operations involving high-infectivity tissues. Surgical instruments move back and forth between the patient and trolley as the surgeon uses them. A one-way flow would require that after an instrument is used, it is handed off and out of the operative site. Logistically, this system would require an enormous number of instruments and, in practical terms, would be difficult to implement.
- Additional processing for heat-sensitive equipment—while rigid endoscopes can be reprocessed using conventional methods, in endoscopy, flexible endoscopes will not withstand the processes recommended.
- Loan equipment and implantable items—this is a vexed issue. Implants should be packaged separately to prevent damage to them. There should be processes in place to ensure that loan instrumentation is processed and monitored to the same standard as the hospital-owned instrumentation.
- Defining ‘contaminated equipment’ in the context of CJD exposure.
- Cleaning of instruments during operative procedures—this keeps the instruments and the removed tissue (which may contain infective prion) moist; therefore, the infective load may well be much less or very low compared to that being used in current research. The moist instruments may also prevent prion from adhering to the instrument. The cleaning of instruments during an operative procedure means that if the prion load is less, the current cleaning and sterilisation methods may be sufficient to prevent transmission.

Instrument tracking has been an issue for a long time. Batch tracking has been standard for many years, and tracking to individual patients is recommended in the Australian Standard, but is not mandatory—in part, because we have not yet worked out how to do it. A lot of hospitals and health services have moved to implement tracking to individual patients by set or pack, and by individual instruments.

Sterilisation practices have improved out of sight, particularly since 1994, when the first sterilising standard, AS 4187, came into being. Since that time, each new edition of AS/NZS 4187 has further raised the standard of reprocessing.

Discussion arising from the presentation

There was extensive discussion about wet sterilisation methods and how these might be achieved. Sterilisation of fluids is technically difficult but not impossible. Problems with communication with companies that provide loan instruments were also discussed.

Recommendations: managing instruments and equipment

The discussion paper presented three recommendations for discussion at the workshop. Each of these is discussed below.

Tracking systems

The discussion paper presented the following recommendation and options to the workshop:

Recommendation 1: That the CJD Consensus Workshop participants endorse option 2.

Option 1: That all instrumentation used on higher infectivity tissues is either designated for single use only, or is routinely subjected to additional sterilisation methods, regardless of patient CJD risk status.

Where additional equipment processing is in place routinely, destruction or quarantining of instruments will not be required in the event that an exposure is identified retrospectively.

Option 2: That all Victorian hospitals and health services that perform procedures affecting higher infectivity tissues are required to have a tracking system that will track individual instruments to individual patients. In the event that an exposure is identified retrospectively, all equipment used on that patient will be withdrawn and destroyed.

There was broad support for option 2, with some caveats:

- Tracking cannot be standardised. Several systems are available, and the system to be used in a given establishment should be selected in consultation with industry and the sterilising department.
- The tracking system adopted needs to be able to capture all patients, loads, instruments/trays, reprocessing occasions, departments, areas, and sites; and a search of the system needs to be able to be initiated from any of these elements.
- Some instruments, including some neurosurgery instruments, cannot be marked. Guidelines are needed on this. The cost impact means that it is not practical to dispose of all instruments.
- Two of the 13 discussion groups felt that equipment used on a patient who is subsequently diagnosed with CJD should be quarantined and kept, rather than disposed of, pending the possible validation of decontamination. If research shows that a particular decontamination regime is effective, the equipment could then go back into circulation. Another table, which had not considered this possibility, felt that any set of instruments identified as having been used on a patient with confirmed CJD should be disposed of. Consumers were divided on the issue.

Consumer comment:

'Destruction of so much equipment in the Royal Melbourne Hospital incident seemed like a knee jerk reaction, and it seems that most people today feel that the equipment issue should have been handled differently.'

Consensus workshop participant

'From my point of view, if it was a known case of CJD, I'd want it to go in the bucket, not in the cupboard.'

Consensus workshop participant

Segregation and one-way flow of instruments

The discussion paper presented the following recommendation to the workshop:

Recommendation 2: That all Victorian hospitals and health services undertake to implement systems that allow segregation and one-way flow of instruments that come into contact with high infectivity tissues, regardless of risk status of the patient.

This recommendation was rejected. All agreed that these recommendations are not feasible. In practice, for perioperative nurses a one-way flow of instruments refers to the movement of instruments within the sterile field, and a one-way flow cannot be maintained in practice. Another interpretation of the expression 'one-way flow' could be taken to mean the movement of instruments through a reprocessing cycle; that is, from designated 'clean' to 'dirty' areas within the operating suite. A clear definition of this terminology is required to eliminate confusion. The handling of instruments by scrub personnel was considered to contaminate all equipment.

Defining contamination

The discussion paper presented the following recommendation to the workshop:

Recommendation 3: That contamination of instruments and equipment, in the context of CJD transmission risk, is defined as only those instruments that come into direct contact with any high infectivity tissue.

This recommendation was rejected. The definition of 'contamination', therefore, should be 'all instruments used in procedures where high infectivity tissue is exposed'.

Other discussion

There was universal agreement on the need for better validation of decontamination/sterilisation processes for CJD, and increased funding for research in this area, to underpin future equipment management. In particular, research and better information are needed on:

- washing and mechanical cleaning processes
- the effects of multiple reprocessing.

The importance of washing/mechanical cleaning was emphasised, and this raised the need to consider the potential contamination of equipment used in cleaning—brushes, sinks, etc. There was agreement across the room that, if research validated certain types of cleaning (for example, using particular enzymes), then this should form part of standard precautions for all surgical instruments.

One group advocated the use of additional sterilisation/decontamination methods for instruments used on all high infectivity tissue, but could not reach any agreement on what these methods should be. Another group suggested that a working party be convened to review cleaning agents and provide recommendations for standard cleaning agents to be used in all health services, with a particular focus on validating methods of mechanical cleaning.

Section 3: Adverse Event Management

Recommendations

7. That in order to support health services in managing a CJD-related adverse event, the department will convene an incident team comprising health service administrators and clinicians, public health experts and other Department of Human Services representatives as required. This group will be responsible for co-ordinating the convening of the CJD Incidents Panel. The Department will undertake to produce an information kit on CJD risk management for consumers and health care workers.

Background

The infectious agent of CJD, the prion, may not be destroyed by the routine instrument reprocessing and sterilisation methods used in health care facilities. The Australian Guidelines recommend, therefore, that instruments used on patients at risk of CJD be destroyed.

Given the lack of a test to detect infection before the onset of symptoms, it is possible for a procedure to be performed on a person who subsequently develops symptoms of CJD. It is also possible for breaches of infection prevention protocols to occur where instruments are not disposed of. A possible scenario, therefore, is that surgical instruments used for a patient with CJD (either symptomatic or asymptomatic) might subsequently be reused on other patients after routine reprocessing methods, with the potential risk of CJD transmission via the instruments. Risk of transmission is highest when the central nervous system is exposed during surgery. Worldwide, there have been some documented cases of CJD transmission via surgical instruments (stereotactic EEG and neurosurgical instruments) (Brown et al. 2000), but none at all in Australia, and none worldwide since 1980 (Will 2003).

Should infection prevention protocols be breached, advice is required for:

- the management of the instruments involved
- the identification of the people who require contacting.

Infection Control Guideline recommendations

The Australian Guidelines are not specific on the issue of identifying the people that require contacting in the event of a breach of infection protocols. They state:

The health care establishment, in consultation with the State or Territory health authority, is responsible for tracing individuals suspected of exposure to CJD. Health care establishments should develop a look-back contingency plan... The plan should allow for the tracing of potentially exposed individuals and assessment of their level of risk, and consider the ethical, legal and counselling requirements. (section 31.16.2)

The guidelines recognise the difficulty of balancing the real risk of psychiatric injury and the hypothetical risk of contracting CJD. They note that:

if...exposures are suspected, there is an ethical obligation to investigate the incident and to look back and trace the individuals concerned, and to notify and counsel them about the level of the risk and its potential implications. ...In determining the need for a lookback study, consideration should be given to the benefit of informing individuals of a hypothetical risk of CJD and their 'right to know', against the real risk of psychiatric injury and their right 'not to know' about the risk of developing a disease that has no treatment or cure. (section 31.16.2)

CJD Incident Panel

In September 2004, the Australian Government established a National CJD Incident Panel, auspiced by the NHMRC Special Expert Committee on Transmissible Spongiform Encephalopathies. The panel, modelled on the UK Incident Panel (established in 2000), is to provide expert advice in the event of an adverse event involving CJD. When an incident occurs, the relevant health department initiates involvement of the panel which, in collaboration with the state/territory health department, will have responsibility and accountability for determining action to be taken, including the scope of a lookback investigation.

CJD: a local perspective

Professor Andrew Kaye, Divisional director, Neurosciences, Royal Melbourne Hospital
Department of Neuroscience

A patient at the Royal Melbourne Hospital who had undergone surgery for the removal of malignant melanoma of the brain twice in 2003, died mid-2004 after being diagnosed with CJD. The last operation was performed six months before symptoms of the CJD became apparent. CJD was not suspected until the patient was readmitted with rapidly developing dementia and other signs indicative of CJD. The patient's family was advised and they consented to a post mortem autopsy of the brain. This examination of the brain is a highly specialised investigation and takes approximately two months to perform. In September 2004, the National Neural Tissue Resource Centre confirmed the diagnosis of CJD.

The National CJD Incident Panel was then notified immediately, and it met the next day—Wednesday. There were extensive discussions with representatives of the panel, the Department of Human Services and the Royal Melbourne Hospital about which patients to tell and what to do with the instruments. Initially, it was decided that all neurosurgery patients who had been operated on following those two cases would have to be notified, and more specific notification would have to wait until later.

By Friday afternoon, the panel had decided that the instruments that had been used in the operations had to be quarantined. There was further debate about the number of sterilisation cycles the instruments had been through, and whether there was any other possible way of sterilising them. A conservative approach was recommended. This created enormous logistical and access problems in maintaining the emergency surgery throughput of the unit. Contingency plans, such as using loan equipment, were made to minimise the impact of this recommendation.

It was decided to notify the media and the patients on the same day. A 1800 telephone line set up for concerned patients was well used, taking many thousands of calls. A media conference was held on the same day.

The next priority was to stratify the affected patients for the level of risk of exposure. Approximately 2000 patient medical records were reviewed to identify if the dura had been penetrated, and whether the operation had occurred within the three months following the affected patient's tumour operations. The three-month time frame was based on the calculation that all the instruments would have been sterilised at least 12 times in the six weeks following the initial tumour operations, and three months allowed a further six weeks' safety margin.

Patients received further letters and phone calls alerting them to their updated risk status. Those patients identified as being at higher risk were interviewed and received a 'medical in confidence' letter outlining the risks.

Discussion arising from the presentation

The lookback was enormous and the relative merits generated a lot of debate and contention. One workshop participant suggested that this particular event could not have been managed any other way—to do so would have given the appearance of covering things up and thus causing even more concern in the community.

The question was raised as to why action was not taken when the suspicion of CJD was first raised. With the benefit of hindsight, this would seem to be a reasonable comment, but it was emphasised that the patient's clinical presentation was such that CJD was still not likely—it is a very rare event for a person with malignant melanoma of the brain also to have CJD. It should also be remembered that by the time the possibility was raised all of the surgical instruments had been cleaned and sterilised many hundreds of times, and the risk of any remaining prion being present was seen to be infinitesimally low.

The psychological impact of contacting patients was discussed. One consumer participant recounted the following story.

In 1990 I was doing some patient research with infertility patients, and had a phone call from a woman who had been told she had a 1 in 200 risk as a result of taking infertility drugs in the early 1980s. She was extremely distressed – years later, she was crying on the phone, telling me how being told that news had destroyed her life. I would like to think, if you look at a continuum, that she was at the far end of an extreme of repercussion – but for a lot of people, this has a huge impact on their lives, they live with this cloud over them, ... thinking this could happen to me, wondering, every time they forget something, is it coming on? ... There are huge repercussions on a day-to-day basis, so when we make these things public, when we tell so many people they are at risk, the balancing has really got to be very clearly and carefully looked at. I'm hearing today that there is a very low risk of these people ending up with CJD, but their lives have been so badly affected. I'm also thinking that 85% of cases are sporadic, so whatever things you put in place, the vast majority of cases are simply ones you cannot prepare for. Workshop participant

The role of instrument-tracking systems was discussed. Had a patient-level instrument tracking system been in place at the Royal Melbourne Hospital in 2003, the numbers of patients included in the lookback would have been substantially less.

Adverse event management

Dr Bill Shearer, Director, Critical Care Services, Southern Health

We are talking today about a group of events, the consequences of which are catastrophic; the events are likely to recur, and they require state and/or national action. They are issues that you should discuss with your chief executive officer, who will talk to the Department of Human Services. The Department needs to have a plan for communicating with the media and the community.

Phase 1: Immediate action

First, you have to decide how severe the problem is and who is going to be in charge of managing it. You must then decide what to do immediately to prevent further harm. You need to plan during that first 24 hours in order to maintain your focus, so that you don't get distracted and overreact or react to outside influences. Set up an event management team. Initially—in the first 24 hours—this should be an internal team of:

- context experts—people that know a lot about issue at hand
- health management experts—people that can work the system for you
- communication experts—people that are best able to communicate to patients and their relatives, the Department of Human Services, the media, and the wider community.

The responsibility of the event management team in the first 24 hours is to *prevent further harm*.

Phase 2: 24 hours to 2 weeks

The primary question is: are our patients safe and is it safe to come into our organisation? You need to ensure that your staff is supported and that you have spoken with all of the right people.

Phase 3: Definitive action, 2 weeks to 3 months

This phase addresses three questions:

1. Have we developed and implemented strategies to prevent this or similar events happening again?
2. If not, will we detect the event as early as possible, contain the damage, and manage the event better?
3. Have we communicated what we have learnt that is relevant to other areas or other organisations; for example, other hospitals?

Root Cause Analysis (RCA) provides a tool for doing this. There are many models for RCA, but what is important is that you have a methodology for a structured review of critical events.

The actions that come out of the review of an adverse event should build better systems to anticipate and detect error. When you make recommendations, you can do one of three things:

1. eliminate the problem—not as easy as one might think
2. control the problem—so that the damage is likely to be less if you detect it early or the like
3. accept the problem—there is a flavour in the room with regard to CJD that some of the risks may have to be accepted.

Discussion arising from the presentation

The role of the National CJD Incident Panel would be during phase 2, where they would be helping with the nuanced judgement and classifying patients. It would be reasonable to expect timely support within 24 hours to 2 weeks of an event occurring. The panel would need to have expertise with regard to both adverse event management and CJD.

One participant raised the concern that conflicting organisational priorities would affect the adverse event management plan; however, workshop participants felt that as we understand more about adverse clinical events, our organisational leaders will be more inclined to want to know, rather than to not want to know about adverse events. Insurers would probably be included in the event management team, so if they were not notified within the first 24 hours, they would certainly be notified within the first 48 hours.

Consumers are extremely important stakeholders in all of this, and bring an important viewpoint to adverse events management. Community advisory committees within hospitals provide a means whereby health consumers can be asked to join this adverse events panel.

Recommendations: adverse event management

The discussion paper presented three recommendations for discussion at the workshop. Each of these is discussed below.

State adverse management group

The discussion paper presented the following recommendation to the workshop:

Recommendation 1: That a state adverse events management group be established, with clinical, administrative and public health expertise and representation from the Office of the Chief Clinical Advisor, to liaise with the National Incident Panel, and to develop a policy that takes into account the ethical issues relating to lookback investigations.

There was general support for this recommendation, but with some qualifications and caveats:

- Presuming the state group to be CJD-specific, there was concern that there might be a proliferation of such adverse management groups, and it was suggested that the Department of Human Services should consider the establishment of a generic adverse management group. This group could be formed under the auspice of the existing Clinical Risk Management Reference Group.
- There was also concern about duplicating the role of the national panel, the spread of responsibility for decision making across national, state and hospital levels, and potential communication problems by adding an extra layer. There needs to be a combination of local and external control in event management, with clearly defined responsibility at the hospital concerned, and at the Department of Human Services. Further, the people designated to hold responsibility need to have the power to act within their organisations.

Expectations of the national incident panel

The discussion paper presented the following recommendation to the workshop:

Recommendation 2: That the CJD Consensus Workshop group define its expectations of the National Incident Panel.

This recommendation was not widely considered or discussed. One group, however, considered the recommendation explicitly and defined their expectations as:

- a timely response
- a multidisciplinary approach
- technical and scientific expertise, including assessment of risk to consumers, and provision of evidence-based advice
- risk management advice
- recognition of the views and wellbeing of the various stakeholders—consumers, institution, clinicians.

Scientific and technical experts may not be experts in adverse event management; however, it was suggested that the latter may be provided by the State Adverse Events Panel.

A CJD risk management kit

The discussion paper presented the following recommendation to the workshop:

Recommendation 3: That the Department of Human Services undertake to produce standard information/a management kit on CJD risk management for consumers and health care workers.

There was unanimous agreement on this recommendation.

One consumer expressed the view that there is not enough understanding of CJD in the community. Information is needed in plain language, and the Department of Human Services should consider involving consumer groups in producing such information. Another consumer cited the distress caused to patients by a lack of knowledge on CJD among health care workers.

One group suggested the kit might comprise two parts, one on information on CJD, and the other a risk management kit. The very successful Legionella Risk Management Plan was cited as a potential model.

Lookback investigations

In relation to lookback investigations, the Workshop identified the need for:

- **further consideration of the ethical issues in lookback investigations**–There is a need to balance the patient’s/consumer’s right to know or not to know, and the public health risk. Consumers identified the need for consumer input into the process of lookback investigation, which could be achieved via the consumer advisory committees at each hospital.
- **evaluation of the impact on the people involved in lookback investigations**– This would inform future action. It was suggested that the Royal Melbourne Hospital lookback investigation cohort is an important group to follow and undertake research on the impact of notification of exposure risk.
- **consistent advice on lookback investigations**–This acknowledges that the science is soft, but ensures that when a CJD-related adverse event happens, people know what to do.

One group felt that lookback investigations should be carried out through a cooperative approach between the Department of Human Services and the hospital, with the Department providing the expertise on how to carry it out, and the actual work largely done by the hospitals.

All agreed that standardised Victorian advice should be provided for notifying people. Patients should be informed by a personal telephone call following a standardised script, followed by a letter and/or face-to-face appointment. The communication should come from the hospital/health service concerned, rather than the Department of Human Services, because they have an existing relationship with the patient. At the same time, there was concern that standard advice would not work because each patient is an individual, and that higher risk people, in particular, will need an individualised approach. A standardised information kit will help after the news has been delivered.

In addition, a 1800 call centre should be set up, with training for personnel staffing the phone lines. Community education is needed, including a pamphlet written in plain English.

Appendix A: CJD Consensus Workshop Steering Committee

The CJD Consensus Workshop Steering Committee has comprised:

Ms Judith Brett, Infection Control Consultant, Southern Health Monash Medical Centre

Miss Michele Cullen, Infection Control Consultant Public Health, Department of Human Services

Ms Glenda Gorrie, Manager, Infection Prevention and Surveillance Service, Royal Melbourne Hospital

Ms Laurene Graham, Project Officer, Clinical Governance Unit, Office of Chief Clinical Advisor, Department of Human Services

Associate Professor Paul Johnson, Deputy Director, Infectious Diseases Department, Austin Health

Ms Alison McMillan, Manager, Clinical Governance Unit Office of Chief Clinical Advisor, Department of Human Services

Dr Melissa Morgan, Public Health, Department of Human Services

Ms Verna Ramsay, Infection Prevention and Surveillance Service, Royal Melbourne Hospital

Dr Graham Rouch, Chair, Victorian Advisory Committee on Infection Control

Dr Norman Swan, Norman Swan Medical Communications

The steering committee also acknowledges input from:

Dr Jenny Bartlett, Chief Clinical Advisor, Department of Human Services

Associate Professor Steven Collins, Co-director, Australian National CJD Registry

Professor Stephen Davis, Head of Neurology, Royal Melbourne Hospital

Dr Robert Hall, Chief Medical Officer, Public Health, Department of Human Services

Professor Andrew Kaye, Department of Neurosurgery, Royal Melbourne Hospital

Dr Angela Kirsner, Writer/Editor in Medical and Health Sciences

Professor Colin Masters, Co-director, Australian National CJD Registry

Professor Graeme Ryan, Chair NHMRC Special Expert Committee on Transmission Spongiform Encephalopathies

Dr Bill Shearer, Director of Critical Care Services, Southern Health

Appendix B: CJD Consensus Workshop program

- 08.00 **Opening**
- The Honourable Bronwyn Pike MP, Minister for Health
- 08.10 **Welcome and overview of program**
- Dr Norman Swan
- 08.15 **An update on the state of the science**
- Dr Michael Gonzales, Melbourne Health
- 08.35 **CJD: a national perspective**
- Professor Graeme Ryan, Chair of the NHMRC Special Expert
Committee on Transmissible Spongiform Encephalopathies
- 08.50 **CJD: a local perspective**
- Professor Andrew Kaye, Melbourne Health
- 09.05 **Adverse event management**
- Dr Bill Shearer, Southern Health
- 09.25 **Screening and risk assessment**
- Associate Professor Paul Johnson, Austin Health
- 09.40 *Morning tea 1*
- Equipment Processes**
- 10.00 - Dr Victoria Lawson, Department of Pathology,
University of Melbourne
- 10.15 - Ms Michele Cullen, Public Health, Department of Human Services
- 10.30 **Screening for CJD risk, epidemiological principles**
- Assoc Professor Steven Collins, Australian National CJD Registry
- 10.50 *Morning tea 2*
- 11.00 Morning session
- **Screening and risk assessment**
- 12.30 *Lunch*
- 13.15 Afternoon session 1
- **Adverse event management**
- 14.45 *Afternoon tea*
- 15.05 Afternoon session 2
- **Equipment processes**

Appendix C: Special interest and professional groups represented at the workshop

Australian Association of Neurologists
Australian CJD Support Group
Australian Dental Association
Australian National CJD Registry
Chronic Illness Alliance
Dental Health Services, Victoria
Health Issues Centre
LIFEGift
Royal Australasian College of Pathologists
Royal Australasian College of Surgeons
Sterilization and Research Council of Australia
Victorian Infection Control Professionals Association
Victorian Managed Insurance Authority
Victorian Perioperative Nurses Group
Victorian Surgical Consultative Council

Appendix D: List of CJD Consensus Workshop participants

Ms Silvana Afrasiabi	Austin Health	Dr Tatiana Emelianova	Dental Health Services, Victoria
Dr Vin Amerena	Australian Dental Association	Ms Melissa Evans	St Vincent's Health
Dr Paul Armstrong	NSW Health	Mr Gavin Fabinyi	Austin Health
Dr Eugene Athan	Barwon Health	Ms Sue Flockhart	Ballarat Health Services
Ms Wendy Bacalja	Latrobe Regional Hospital	Mr David Fogarty	Wimmera Health Care Group
Ms Helen Backway	Goulburn Valley Health	Ms Lois Foley	Northeast Health Wangaratta
Ms Kaylene Baird	Department of Human Services	Mr Bruce Fowkes	VACIC–Department of Human Services
Ms Pam Balstrup	Bayside Health	Dr Michael Gonzales	Royal Melbourne Hospital
Ms Helen Barallon	Victorian Perioperative Nurses Group	Ms Glenda Gorrie	VACIC–Department of Human Services
Dr Dianne Barrington	S.A. Department of Health	Ms Laurene Graham	VACIC–Department of Human Services
Dr Jenny Bartlett	Department of Human Services	Ms Kaye Grant	Dental Health Services, Victoria
Ms Jan Beaton	Western Hospital	Ms Ruth Griffiths	Royal Melbourne Hospital
Ms Glenis Beaumont	Bendigo Health Care Group	Ms Leonie Handford	East Grampians Health Service
Dr Jim Black	Royal Melbourne Hospital	Ms Anne Hardy	Knox Private Hospital
Mr Stephen Blamey	VACIC - Royal Australasian College of Surgeons	Ms Sheila Hargrave	Consumer Representative
Ms Marion Borlase	Western Hospital	Ms Cath Harmer	Department of Human Services
Dr Shirley Bowen	WA Department of Health	Ms Leanne Houston	Bayside Health
Dr Neil Boyce	LIFEGift	Dr Simon Hawke	Australian Association of Neurologists
Ms Alison Boyd	Australian National CJD Registry	Ms Annette Hinton	Cabrini Health
Ms Judith Brett	Southern Health	Prof Geoff Hogg	VACIC–MDU Public Health Laboratory, University of Melbourne
Ms Fiona Brooke	Department of Health and Ageing	Ms Bronwyn Holbeche	Melbourne Pathology
Dr Sheena Broughton	Peninsula Health	A/Prof Paul Johnson	Austin Health
Ms Gwenda Bunting	Dental Health Services, Victoria	Prof Megan-Jane Johnstone	RMIT–Bundoora Campus
Ms Mal Butler	Epworth Hospital	Ms Riemke Kampen	ACT Health
Mr Bob Button	Peninsula Health	Ms Anna Kane	Cabrini Health
Ms Christina Caws	Royal Victorian Eye & Ear Hospital	Prof Andrew Kaye	Royal Melbourne Hospital
Dr John Carnie	Department of Human Services	Ms Jacqui Kennon	VACIC–Bayside Health
Ms Joanne Cocks	St Vincent's Health	Ms Elaine Khaw	Eastern Health
Prof Steven Collins	Australian National CJD Registry	Dr Angela Kirsner	Department of Human Services
Ms Pauline Connelly	Royal Victorian Eye & Ear Hospital	Dr Tony Korman	Southern Health
Mr Eric Cooper	Cabrini Health	Dr Garry Lane	Western Hospital
Ms Elizabeth Cooper	Southern Health	Dr Victoria Lawson	University of Melbourne
Ms Simone Corin	Royal Melbourne Hospital	Ms Annie Lyon	HICMR
Ms Sue Cornish	VACIC–Mayfield Education Centre	Dr Steve Macfarlane	Peninsula Health
Ms Michele Cullen	VACIC–Department of Human Services	Mr Roger Magnusson	University of Sydney
Mr Peter Dohrman	Epworth Hospital	Ms Carol Makhoul	Consumer Participation Policy Reference Group
Mr Clinton Dunkley	VACIC–Department of Human Services		

Ms Janine Malcolm	Werribee Mercy Hospital	Dr Tony Weaver	Barwon Health
Mr Greg Malham	Bayside Health	Ms Evelyn Webster	Health Issues Centre
Ms Rhea Martin	Austin Health	Ms Audrey Williams	Barwon Health
Ms Michelle Martin	South West Healthcare	Ms Theresa Williamson	Royal Melbourne Hospital
Ms Mathew Mason	VICPA	Ms Carol Wilson	CJD Support Group
Ms Samantha Maxwell	Peninsula Health	Dr Margaret Young	Queensland Health
Dr Alistair McGregor	Royal Hobart Hospital	Dr Phillippe Zimet	Australian Dental Association
Dr. Shane McGuire	Dental Health Services, Victoria		
Ms Kellie McIntosh	Southern Health		
Ms Alison McMillan	VACIC–Department of Human Services		
Mr Kevin Moon	VACIC–Hospital Engineers		
Dr Melissa Morgan	Department of Human Services		
Ms Jill Muir	Dental Health Services, Victoria		
Dr Cathryn Murphy	NSW Health		
Mr Helen Musgrove	Mayne Health		
Mr Denis O'Leary	Austin Health		
Dr Mary O'Reilly	Eastern Health		
Ms Renza Peruch-Pullicino	Consumer Representative		
Ms Marion Place	VACIC–Department of Human Services		
Ms Michelle Pratt	Bayside Health		
Ms Verna Ramsay	Royal Melbourne Hospital		
Ms Robyne Renton	Cabrini Health		
Dr Mike Richards	Royal Melbourne Hospital		
Dr Graham Rouch	VACIC–Department of Human Services		
Mr Jonathan Rush	Victorian Surgical Consultative Council		
Prof Graeme Ryan	Bayside Health		
Ms Sue Scott	Royal Children's Hospital		
Dr Bill Shearer	Southern Health		
Ms Vicky Siler	Royal Children's Hospital		
Dr Renato Simionato	Australian Dental Association		
Ms Isobel Smith	Eastern Health		
Ms Suzanne Solvyns	CJD Support Group		
A/Prof Denis Spelman	Bayside Health (VACIC)		
Ms Iva Steinke	Chronic Illness Alliance		
Ms Pam Sykes	Royal Hobart Hospital		
Ms Joanne Tamlyn	Chronic Illness Alliance		
Ms Coralie Tyrell	West Gippsland Health Care Group		
Ms Sophie Waller	St Vincent's Health		

Appendix E: Synopsis of disinfection methods

Abstracted from Fichet et al., 2004, 'Novel methods for disinfection of prion-contaminated medical devices', *The Lancet Neurology*, vol.364, pp.521-526.

Treatment	Transmission frequency (%)	Log reduction in infectious titre
NaOCl 20,000 ppm, 20°C, 1 hour	0	>5.6
NaOH 1N 20°C, 1 hour	0	>5.6
Dry Autoclaving 134°C, 18 minutes	60	4-4.5
Wet autoclaving 134°C, 18 minutes	0	>5.6
Klenzyme (STERIS) + Vaporized Hydrogen Peroxide	0	>5.6
Alkaline Cleaner (STERIS)	0	>5.6

Glossary of terms and acronyms

bovine spongiform encephalopathy (BSE): a **transmissible spongiform encephalopathy (TSE)** affecting cattle, more commonly known as mad cow disease (see also **Variant Creutzfeldt-Jakob disease**)

Creutzfeldt-Jakob disease (CJD): a rapidly progressive neurologic disorder, one of the subacute **TSEs** caused by **prions**. Clinical features include progressive abnormalities of gait.

Classical Creutzfeldt-Jakob disease (cCJD): an alternative name for all forms of CJD excluding variant CJD

dementia: an organic mental disorder occurring after normal intellect is achieved characterised by a general loss of intellectual abilities involving impairment of memory, judgement and abstract thinking as well as changes in personality

dura mater: the outermost of the three membranes covering the brain and spinal cord

dura mater graft: one commercial source of dura mater was manufactured by a West German firm under the trade name Lyodura. The material is primarily used in neurosurgery. It consists of dura mater harvested post-mortem, which has been lyophilised and irradiated.

exposure: contact with brain tissue and spinal cord fluid from infected patients

gonadotrophins: any hormone that has a stimulating effect on the gonads, such as hormones secreted by the pituitary gland

holding time: the time for which all of the articles in a steam or dry heat steriliser must be held at the selected sterilising temperature. Holding time includes pressure level for steam sterilisation, as well as temperature.

iatrogenic CJD: A rare form of CJD caused by accidental transmission to a patient as the result of a medical procedure in which there has been exposure to infectious tissue

infectivity: relates to the probability that a disease will be transmitted. High infectivity sites for CJD are those sites shown to be consistently infectious in a person who has CJD. Low infectivity sites are those sites that have been shown to be infectious, but not consistently.

lookback investigation: the process of identifying, tracing, recalling, counselling and testing patients or health care workers who may have been exposed to an infection, due to a breakdown in infection control procedure or protocols

monomer: a molecule that repeats itself to form a polymer

NHMRC: National Health and Medical Research Council

pituitary hormone: hormone derived from the pituitary gland, such as growth hormone and follicular stimulating hormone

prion protein: a protein that is present in many organs and tissues, including the brain, spinal cord and eye of healthy humans and animals. The CJD agent is believed to be an abnormal conformation of the prion protein that causes surrounding prion proteins to change their conformation.

PrP: prion protein (PrP^c is the normal cellular protein, PrP^{Sc} is the pathogenic abnormal conformation)

sterilisation: a process that is intended to kill or remove all types of micro-organisms with an acceptably low probability of an organism surviving on any article (Gardner and Peel 1998)

transmissible spongiform encephalopathies (TSEs): rare, fatal degenerative disorders of the nervous system that occur in a wide variety of animals, including humans. The term describes the pathology produced in the brain, and infection occurs by specific forms of direct contact, with an incubation period usually measured in years.

VACIC: Victorian Advisory Committee on Infection Control

Variant Creutzfeldt-Jakob disease (vCJD): a new form of TSE that emerged in the United Kingdom in 1996, thought to be the human presentation of bovine spongiform encephalopathy (BSE), or ‘mad cow disease’

14-3-3 protein: a protein released from the brain into the cerebrospinal fluid in CJD and other neurological conditions. It is thus a non-specific, ante-mortem marker of central nervous system neuronal injury or death.

14-3-3 protein test: this entails testing CSF for the protein. Based on international experience in carefully selected patients, a positive result has approximately 90 per cent sensitivity and specificity for sporadic Creutzfeldt-Jakob disease. False positives are recognised in various disease processes; for example, encephalitis, encephalopathies and recent cerebral infarcts. Unselected sampling is consequently less reliable if the 14-3-3 protein CSF test is used to screen for a possible diagnosis of CJD.

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