NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedures consultation document

Reducing the risk of transmission of Creutzfeldt–Jakob disease (CJD) from surgical instruments used for interventional procedures on high-risk tissues

Creutzfeldt–Jakob disease (CJD) is caused by abnormal proteins (prions) that infect the brain. It is very rare and there is no cure. It causes brain damage and leads to death. Symptoms include depression, anxiety, delusions, hallucinations, tremors and loss of co-ordination. There is a chance that surgical instruments could spread CJD from 1 patient to another, even when they have been properly washed and disinfected. This is because prions are very difficult to remove or destroy. Special safety measures are needed for instruments that are used on tissues at high risk of containing prions.

NICE is looking at reducing the risk of transmission of Creutzfeldt–Jakob disease (CJD) from surgical instruments used for interventional procedures on high-risk tissues. This is a review of NICE's interventional procedures guidance on patient safety and reduction of risk of transmission of Creutzfeldt–Jakob disease (CJD) via interventional procedures.

NICE's interventional procedures advisory committee met to consider the findings in the report from the School of Health and Related Research (ScHARR) and the opinions of the CJD advisory subcommittee members, who are specialists with knowledge of the topic. The committee also considered the cost effectiveness of potential management strategies to reduce the risk of transmission of CJD. This document contains the draft guidance and summarises the evidence on which it is based. It has been prepared for public consultation. Your views are welcome, particularly:

- comments on the draft recommendations
- identification of any factual inaccuracies
- additional relevant evidence, with references if possible.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

This is not NICE's final guidance on this procedure. The draft guidance may change after this consultation.

After consultation ends, the committee will:

- meet again to consider the consultation comments, review the evidence and make appropriate changes to the draft guidance
- prepare a second draft, which will go through a resolution process before the final guidance is agreed.

Please note that we reserve the right to summarise and edit comments received during consultation or not to publish them at all if, in the reasonable opinion of NICE, there are a lot of comments or if publishing the comments would be unlawful or otherwise inappropriate.

Closing date for comments: 17 July 2019

Target date for publication of guidance: October 2019

This guidance is for interventional procedures on tissues considered at high risk of transmitting CJD. These procedures on high-risk tissues are intradural surgery on the brain (including the pituitary gland) and spinal cord, neuroendoscopy, and surgery on the retina or optic nerve (see appendix D for a complete list).

Note that the abbreviation 'CJD' is used for both sporadic and variant CJD (vCJD) including surgically transmitted CJD (stCJD), unless otherwise specified.

The recommendations do not apply to any interventional procedures done on patients already known to have or thought to be at increased risk of CJD as defined by the Advisory Committee on Dangerous Pathogens and Spongiform Encephalopathies Advisory Committee. For these patients, the guidance on transmissible spongiform encephalopathy agents, safe working and the prevention of CJD, part 4

must be followed. The guidance on transmissible spongiform encephalopathy agents, safe working and the prevention of CJD, part 4 must also be followed when the risk of CJD cannot be ascertained by questioning the patient or when a diagnosis of CJD cannot be excluded.

1 Draft recommendations

Decontamination

1.1 All surgical instruments that have come into contact with high-risk tissues during an interventional procedure must be kept moist until decontamination. This improves the efficacy of the decontamination process and is highly cost effective.

Set integrity and tracking

1.2 Surgical instruments that come into contact with high-risk tissues must not be moved from 1 set to another and must remain within their individual sets. Maintaining set integrity reduces the risks associated with instrument migration and means that it can be traced back to the patient it was used on. Systems must be in place to ensure sets of instruments are tracked (set traceability).

Supplementary instruments

1.3 Supplementary instruments that have come into contact with high-risk tissues must remain within the individual set to which they have been introduced. Supplementary instruments are those that were not part of a specific instrument set. If supplementary instruments are used with different sets, this compromises set traceability.

Neuroendoscopy

1.4 Rigid neuroendoscopes (rather than flexible neuroendoscopes) should be used if possible. They should be of a type that can be autoclaved and must be thoroughly cleaned and autoclaved after each use.

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Single-use instruments

1.5 The evidence on cost effectiveness does not support using sets of single-use instruments to reduce the risk of CJD transmission.

Systems specifically for people born after 1996

1.6 The evidence on cost effectiveness does not support introducing systems to maintain separate sets of neuroendoscopes and reusable surgical instruments for use on high-risk tissues for people born after 1996.

1.7 There is insufficient evidence to make a recommendation on whether existing systems that keep separate sets of neuroendoscopes and reusable surgical instruments for use on high-risk tissues for people born after 1996 should be maintained. However, removing the requirement to use different instruments on high-risk tissues for people born after 1996 would not markedly increase the risk of surgical transmission of CJD.

Other relevant guidance

1.8 This guidance should be used with:

- the Advisory Committee on Dangerous Pathogens Transmissible Spongiform Encephalopathies risk management subgroup's guidance on minimising risk of transmission of CJD and vCJD in healthcare settings
- the Department of Health and Social Care's 2016 Health Technical Memorandum 01-01: Decontamination of surgical instruments.

Further research

1.9 NICE may update this guidance after 3 years or sooner if important new information becomes available including evidence on:

- the epidemiology of CJD, including data on the prevalence of CJD and its infectivity in the UK population
- the transmission of CJD by surgical instruments, including cases of CJD in which surgery is a possible route of transmission
- the cost effectiveness of single-use instruments for use in interventional procedures on high-risk tissues
- commercially available decontamination methods that are safe and cost effective against prions
- the cost effectiveness of maintaining existing systems for integrity and traceability of instrument sets.

2 Indication

The condition

2.1 CJD is a progressive, fatal neurological disease affecting the brain. It is caused by pathological accumulation of an infectious form of protein called a prion. CJD belongs to a wider group of neurodegenerative disorders known as transmissible spongiform encephalopathies that affect both humans and animals. People with CJD typically present with rapidly progressive dementia, usually accompanied by myoclonus and cerebellar ataxia. Most people die within 4 months of disease onset, in a mute and immobile state.

Epidemiology of CJD

2.2 The incidence of any type of CJD (based on published surveillance studies) is 1 to 2 cases per million of the population worldwide. There are 4 aetiological CJD categories:

- **Sporadic** CJD (sCJD) accounts for 85 to 90% of cases worldwide. The aetiology is not known. It has an annual incidence of 1 to 2 deaths per million of population per year. The general rate of age-adjusted detection of sCJD is increasing in

the UK. Reasons for this include improved case ascertainment and an ageing population.

- **Inherited** (genetic or familial) CJD accounts for 5 to 15% of cases or about 10 deaths in the UK per year. It is associated with pathogenic mutations in the prion protein gene.
- **Variant** CJD (vCJD) is a novel form of human prion disease, first recognised in the UK in 1996. It is believed to result from consumption of food derived from cattle infected with bovine spongiform encephalopathy (BSE), a fatal neurodegenerative disease that causes sponge-like changes in the brain. vCJD is characterised by extensive lymphoreticular tissue involvement and a young age at onset (the mean age at death is 28 years, compared with 66 years for sCJD). The clinical course of vCJD is distinct from that of sCJD. People with vCJD frequently present with sensory and psychiatric symptoms that are uncommon in people with sCJD. They develop progressive neurological signs such as gait disturbance, ataxia and tremor. The median duration of illness is longer than that for sCJD (14 months compared with 4 months). By 2016 there had been 178 cases of vCJD in the UK. Three cases are considered to have occurred through blood transfusion and 175 cases were related to dietary exposure to BSE. The prevalence of non-clinical vCJD (abnormal prion accumulation in tissues without clinical symptoms) in the general UK population is estimated to be 240 per million, based on retrospective analyses of appendix specimens.
- **Iatrogenic** CJD (iCJD) accounts for less than 1% of cases. It is the transmission of prions through surgical or medical procedures (neurosurgery, intradural surgery on the brain and spinal cord including the pituitary gland, neuroendoscopy, and posterior eye procedures that involve the retina or optic nerve) or human derived products (growth hormones, gonadotropin, dura

mater grafts, and packed red blood cells). Surgically transmitted CJD (stCJD) is theoretically possible through prion-contaminated instruments (including endoscopes, laryngoscopes and electroencephalograph needles) that have been previously used on patients with CJD. This includes patients who are asymptomatic but infectious because neural tissue has a high infectious load, and there are difficulties in eradicating prions from surgical instruments. The most common causes of iCJD are human growth hormones and dura mater grafts, according to a review of worldwide iCJD cases published in 2012. In the UK, 85 iCJD cases were identified between 1970 and 2016. Eight were from dura mater grafts, 1 was from human gonadotrophin and 76 were from human growth hormones. There were 4 cases of possible stCJD through contaminated neurosurgical instruments between 1952 and 1974; 3 in the UK and 1 in France. The ScHARR report indicates that the risk of stCJD is currently low and no cases were reported between 2005 to 2018. However, there is uncertainty about the future risk of stCJD because of the potentially long incubation period of CJD, difficulties in eradicating prions from surgical instruments, the sub-clinical prevalence in the general population, and high levels of infectivity in the brain. Neurosurgical instruments used on people who are possibly carriers of CJD are handled in accordance with the Advisory Committee on Dangerous Pathogens Transmissible Spongiform Encephalopathies risk management subgroup's guidance on safe working and the prevention of infection.

Incubation periods

2.3 Evidence from retrospective data in the ScHARR report shows that the incubation period of CJD ranges from 1 to 42 years but shorter durations have been reported in cases of stCJD. Incubation times

might be affected by the recipient's genotype and the infecting prion strain or subtypes of the CJD.

Infectivity

2.4 The infectivity of CJD is likely to be moderated by a number of factors including the recipient's genotype, the infecting prion strain, and the route of transmission. There are limited data about infectious dose or infectious titre in humans. Animal studies indicate that an infection dose (ID) greater than 10^8 ID_{50}s is possible. The ID_{50} is the dose that would give the person receiving it a 50% chance of becoming infected. High values are expressed in log or factor-of-10 terms. For example, a gram of brain tissue has an ID_{50} of 10^8 (8 log). This means it carries a dose of 100,000,000 ID_{50}s. Intracranial transfer of 0.01 microgram of such brain tissue would result in the recipient having a 50% chance of becoming infected with CJD.

3 Committee considerations

Issues considered in this guidance

3.1 The following issues of clinical and decontamination practice were considered in terms of clinical and cost effectiveness, patient safety and the extent to which they reduce the risk of CJD transmission:

- use of reusable and single-use instruments in surgical procedures
- use of reusable and single-use endoscopes, laryngoscopes and related accessories
- arrangements for cleaning, sterilising and tracking of reusable surgical instruments and endoscopes.

Issues not considered in this guidance

3.2 The following issues were not considered in this guidance:

- transfusion of blood or blood products, including occupational exposure to blood or body fluids. Several organisations provide advice on measures to reduce the risks from blood transfusion and exposure to blood in the workplace, including the Department of Health Advisory Committee on the Microbiological Safety of Blood, Tissues and Organs for Transplantation, the Spongiform Encephalopathy Advisory Committee, and the Advisory Committee on Dangerous Pathogens Transmissible Spongiform Encephalopathies risk management subgroup
- extracorporeal life-support machinery, including cardiopulmonary bypass, haemodialysis and ventilator equipment
- the risk of CJD and vCJD transmission through drugs and other materials of human or bovine origin, which is regulated by the Medicines and Healthcare products Regulatory Agency (MHRA)
- the safety of transplant grafts, which is the responsibility of the Department of Health Advisory Committee on the Microbiological Safety of Blood, Tissues and Organs for Transplantation
- the decontamination and reuse of single-use instruments, for which the MHRA has issued guidance advising against the reuse of such items
- general dentistry.

The evidence

For detailed information on the evidence, see the ScHARR report.

3.3 The ScHARR report consists of the following evidence:

- eight systematic reviews on the incidence and prevalence of CJD in the general population in the UK, risk of transmission through surgery, incubation periods, infectivity, efficacy of decontamination procedures, adherence to NICE guidance by keeping surgical instrument sets together, complications from single-use instruments, and the likelihood of patients who have

had high-risk surgery returning for further surgery. Direct evidence is limited because of the rare nature of CJD. So the systematic reviews use historical case reports of stCJD, observational data, case-control studies and animal studies. They are mostly descriptive and no formal critical appraisal of study quality was done

- an updated version of the model used in NICE's previous appraisal of patient safety and reduction of risk of transmission of CJD (IPG196) to assess the cost effectiveness of potential strategies to reduce the risk of stCJD. The updated model assumes that all genotypes are susceptible to stCJD infection, patients with stCJD can be misdiagnosed with an alternative neurodegenerative disease, and calibration of predicted model inputs with the number of possible stCJD cases observed between 2005 and 2018. All assumptions were agreed with the CJD advisory subcommittee. A formal elicitation exercise with members of the CJD advisory subcommittee, was used to update the parameters used in the modelling.

3.4 Organisations representing patients provided submissions and representation at the CJD advisory subcommittee meetings.

4 Committee comments

4.1 The committee emphasised the importance of continued surveillance for all forms of CJD to identify trends in incidence rates. It noted that there are effective systems for doing this in the UK.

4.2 The committee noted that the economic modelling suggests that keeping surgical instruments moist is the most cost-effective strategy, because it saves money and potentially increases societal health. Additional strategies aimed at reducing the future risk of stCJD do not appear to be cost effective.

4.3 The committee encouraged further research into the development of cost-effective decontamination methods that remove or destroy prions from instruments.

4.4 The committee noted that single-use instruments are the only way of completely avoiding the potential for the transmission of CJD infection by surgical instruments.

4.5 The committee emphasised that clinicians must comply with the Department of Health and Social Care's Health Technical Memorandum (HTM) 01-01: Decontamination of surgical instruments and other relevant guidance and standards.

4.6 The committee emphasised that this guidance applies to procedures on high-risk tissues and not to people at risk of CJD as defined in the Advisory Committee on Dangerous Pathogens and Spongiform Encephalopathies Advisory Committee's guidance on transmissible spongiform encephalopathy agents: safe working and prevention of CJD: part 4.

Tom Clutton-Brock
Chair, interventional procedures advisory committee
June 2019

Appendix A: CJD advisory subcommittee members and NICE project team

CJD advisory subcommittee members

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Professor Graham Medley

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Appendix B: Contributors

These organisations provided specialist advice and comments:

- CJD Support Network
- Child Growth Foundation

Appendix C: Related advisory groups

A number of advisory committees, expert groups and academic units are addressing issues related to CJD including developing the scientific basis of our understanding of the disease, improving decontamination practices across the NHS and minimising the risk of transmission. NICE has made every effort to coordinate with these groups to ensure that this guidance takes account of, and builds on, their work. Some members of the CJD advisory subcommittee are also members of other CJD committees, working groups and academic units. NICE has been represented on some of these groups.

These are some of the organisations working on CJD in the UK:

- Department of Health
- Medical Research Council Prion Unit
- University College London Hospitals National Prion Clinic
- University of Edinburgh National CJD Research & Surveillance Unit
- Public Health England
- Health Protection Scotland

Appendix D: High-risk procedures

The OPCS-4 codes for intradural operations on the brain are:

Neurosurgery

A01 Major excision of tissue of brain

A02 Excision of lesion of tissue of brain

A03 Stereotactic ablation of tissue of brain

A04 Open biopsy of lesion of tissue of brain

A05 Drainage of lesion of tissue of brain

A07 Other open operations on tissue of brain

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A08 Other biopsy of lesion of tissue of brain

A09 Neurostimulation of brain

A10 Other operations on tissue of brain

A12 Creation of connection from ventricle of brain

A13 Attention to component of connection from ventricle of brain

A14 Other operation on connection from ventricle of brain

A16 Other open operations on ventricle of brain

A20 Other operations on ventricle of brain

A22 Operations on subarachnoid space of brain

A24 Graft to cranial nerve

A25 Intracranial transection of cranial nerve

A26 Other intracranial destruction of cranial nerve

A29 Excision of lesion of cranial nerve

A30 Repair of cranial nerve

A31 Intracranial stereotactic release of cranial nerve

A32 Other decompression of cranial nerve

A33 Neurostimulation of cranial nerve

A34 Exploration of cranial nerve

A36 Other operations on cranial nerve

A38 Extirpation of lesion of meninges of brain

A39 Repair of dura

A42 Other operations on meninges of brain

B01 Excision of pituitary gland

B02 Destruction of pituitary gland

B04 Other operations on pituitary gland

B06 Operations on the pineal gland

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L33 Operations on aneurysm of cerebral artery

L34 Other open operations on cerebral artery

Posterior eye surgery

The OPCS-4 codes for high-risk operations on the posterior eye are:

C01 Excision of eye

C79 Operations on vitreous body

C81 Photocoagulation of retina for detachment (only when the retina is handled directly)

C82 Destruction of lesion of retina

C84 Other operations on retina