TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES (TSE) or PRION DISEASES

KEY POINTS

Patients with degenerative central nervous system disease without a clear diagnosis, or a likely diagnosis or proved CJD must not have any invasive disease procedure, especially endoscopy, without telling the Infection Control Team.

1.0. INTRODUCTION

The Transmissible Spongiform Encephalopathies are rare conditions caused by abnormal folding of a protein in the brain. This abnormal protein is able to cause disease when inoculated into animals. These transmissible agents are called prions (Protein Infectious agent) and the “infectivity” cannot be inactivated by the usual methods of killing “living” organisms (sterilisation and disinfection).

CJD IS RECOGNISED IN FOUR FORMS

Classical (cCJD) divided into:
- Familial (fCJD) associated with a family history in a first degree relative.
- Sporadic (sCJD) occurs with no known risk factors for other forms.
- Iatrogenic (iCJD) associated with exposure to contaminated tissues or instruments from a known case of CJD.

Variant (vCJD) is:
- Causally associated with the epidemic of BSE in cattle and is clinically and pathologically distinguishable from cCJD.

The TSE/prion diseases include Creutzfeldt-Jakob Disease (CJD), scrapie of sheep, bovine spongiform encephalopathy (BSE) manifest as variant CJD in man, and kuru (restricted to members of the Fore Tribe, Papua-New Guinea.

Sporadic prion disease is most commonly seen as a rapidly progressive dementia in elderly patients.

Some diseases are inherited (eg Gerstmann-Straussler-Scheinkler syndrome (GSS) and fatal familial insomnia (FFI). 10-15% of cases represent the inherited forms of prion disease, which are transmissible in animal models. Inherited prion disease is diagnosed on the basis of an abnormality of prion protein gene analysis and there is often, though not always, a family history of neurodegenerative disease. The commonest presentation of inherited prion disease is a progressive ataxic syndrome or progressive cognitive impairment.

The pathological process is a slow one with progressive neurological disease following a very
long incubation period. Each of these diseases have rather different clinical presentations, although the eventual outcome is always a fatal global cortical degeneration.

Prions elicit no detectable immune response and are resistant to the usual methods of decontamination.

2.0. TRANSMISSIBILITY

Ordinary person-to-person transmission of CJD in any form has not been recorded.

There are several known instances worldwide of patient-to-patient transmission following neurological procedures on classical CJD, the use of human pituitary growth hormone to treat dwarfism, dura mater patches and corneal transplantation. The only likely source of infection from cases of classical CJD is implanted nervous tissue.

It is presumed that vCJD is acquired by eating contaminated food of bovine origin from an affected animal. This risk is currently assessed as being very low.

In addition, vCJD prion is known to involve the lymphoreticular system early in the course of incubation. The number of asymptomatic individuals harbouring the prion is not known. Therefore vCJD is of particular concern as an infection risk. Any procedure involving either the lymphoreticular system or nervous system of a patient with vCJD is regarded as a risk for transmission. Blood and blood products could be contaminated with vCJD prions and a recent report suggests that at least three incidents of transfer from donor to recipient has occurred. In the UK, all products involving human plasma are sourced from non-UK donors, and blood from transfusion is routinely leucodepleted. Organs or tissue for transplantation are not taken from any cases with suspect or proven CJD of any form. Avoiding unnecessary procedures on patients who have, or might have any form of spongiform encephalopathy is the most certain way of preventing iatrogenic infections.

3.0. GUIDELINES FOR DIAGNOSIS AND CARE

These guidelines are based on current UK Guidelines (http://www.dh.gov.uk/)

These guidelines are being continually reviewed in the light of new knowledge, particularly with respect to vCJD. The Infection Control Team must be informed of all procedures involving high risk patients (known or suspected), to ensure that the most recent advice is taken into account.

STATEMENT OF DIAGNOSIS

Only a Consultant Neurologist can label a patient as having suspected (possible or probable) CJD. If in doubt, seek expert advice. Do not perform any invasive procedure on a patient with neurodegenerative disease without considering the possibility of a diagnosis of prion disease. (Quarantine instruments used in emergency procedures)
MAKING A DIAGNOSIS

If a case is suspected

and

Before doing a procedure on a patient with degenerative neurological disease,

Those in charge of the patient must contact the local Infection Control Team

Before cerebral biopsy in patients with dementia, seek a second opinion from an expert in prion disease (see website for a list of contacts)

PATIENT CARE

The Department of Health publication “CJD: Guidance for Healthcare Workers” states that any patient diagnosed with prion disease is to have a key worker identified. This key worker will be constantly involved in the co-ordination of the patient’s care, in both the hospital and community settings. When a patient is given a confirmed diagnosis of prion disease, a member of the team responsible for their care will inform the infection control nurse.

Because of the continuing media interest in prion disease, staff need to be particularly aware of issues concerning patient confidentiality.

WARD CARE

Routine ward care of patients with, or suspected of having prion disease, does not require special precautions, other than those routinely used in the safe handling of patients, their excreta, sharps and body fluids. Patients do not need to be nursed in isolation for infection control.
4.0. CLINICAL INVESTIGATIONS

Diagnostic Procedures
Diagnostic departments in the hospital (neurophysiology, neuroradiology, etc) routinely follow procedures to minimise the risk of cross-infection from patients with undiagnosed, preclinical prion disease. Where a patient has confirmed prion disease, these departments follow different procedures which add considerably to their workload. For invasive procedures, instruments must not be reused but will be discarded.

Pathology Tests
Precautions are taken in the transport system and in the laboratories to reduce the risk of harm to staff from all pathological specimens as far as possible.

Pathological Specimens
“High-risk” or “Danger of Infection” stickers must be affixed to all request forms and specimen containers from patients known to have or suspected of having prion disease.

5.0. SHARPS INJURY

Accidental injuries or inoculation wounds should be thoroughly washed in running water immediately, and further treatment given as appropriate to the type of injury.

It is essential that the normal procedure is followed (see full Sharps Injury Policy at www.infectioncontrolservices.co.uk/sharps_intro.htm). Essentially, blood (clotted and sequestrene/EDTA) from the patient with TSE (ie the Donor) must be sent to virology for appropriate tests. In the case of an incompetent patient not being able to give consent to have their blood taken and tested in this way, permission may be granted by the Consultant in charge of the case or a Consultant Infection Control Doctor. The injured recipient’s blood is also saved.

All accidents should be reported in the usual way. The incident is recorded in the patient’s notes. The injury is reported to Occupational Health. Advice on whether further action is necessary can be sought from the National Prion Clinic.
6.0. PROCEDURES

PRECAUTIONS TO BE TAKEN FROM KNOWN, SUSPECT OR AT-RISK PATIENTS WITH TSE

When procedures are undertaken which carry a risk of contamination with CSF, brain, blood or lymphoid tissue, the following precautions must be taken.

WARD PROCEDURES

Access to CSF (eg by lumbar puncture)

All Patients

All lumbar punctures and access to cerebrospinal fluid must be performed with “single use only” equipment. This applies to all procedures involving access to the subarachnoid space and, for example, access to ventriculo-peritoneal shunts. The rule includes spinal anaesthesia and diagnostic neuroradiology.

- Lumbar puncture (including radiological and other procedures during which CSF is withdrawn)
- Attending to extraventricular and lumbar drains
- Venepuncture and administration of injections
- Dressing wounds and bed sores
- Wear disposable gloves, plastic aprons and eye protection
- Use disposable drapes, instruments and other equipment
- All used equipment must be incinerated after use (see below)
THEATRE PROCEDURES

Biopsies (especially neural tissue)

Neurosurgical procedures

General principles
Inform infection control nurse and theatre manager before ANY procedure. Warn the neuropathologists if a diagnostic brain biopsy is to be taken.

The greatest risk of transmission of prions from one patient to another arises from transplantation of tissue (e.g., cornea). There is also theoretically a high risk from re-using instruments on the brain and other neural tissue.

Biopsies of tissues such as nerve, muscle, skin or lymph nodes may also provide a risk for the transmission of variant CJD. Where there is any risk that the patient may have any form of prion disease, the biopsy should be performed with disposable instruments. Where this is not possible, or where the diagnosis is in doubt, the instruments must be quarantined until a definitive diagnosis is reached. A record of patient, pathological diagnosis and fate of instruments will be kept by the operating theatre manager. Formal notification of decisions regarding instruments should be made to the operating theatre manager.

Wherever possible, any surgical procedure on a patient known or suspected to be suffering from prion disease should be performed at the end of the list, to allow the theatre to be cleaned afterwards. The minimum number of staff possible should be present in theatre and proper personal protective equipment must be worn.

Action

1. Brain biopsies

   All brain biopsies for diagnostic purposes (whatever the clinical diagnosis) will be performed with a disposable set of instruments with the exception of the Pistol drill. Turbine drills must not be used.

   The disposable instruments will be destroyed by incineration. The Pistol drill will be washed under water by a trained operative wearing full protective clothing (including domestic rubber gloves, apron and visor), and then sent for routine processing in CSSD.

2. Other surgery on patients with known or suspected CJD

   Known cases of classical CJD (or GSS or FFI)

   OR

   Known case of variant CJD

For surgical procedures on classical CJD patients involving brain or spinal cord, eye, and
excluding invasive dental procedures and
For surgical procedures on vCJD patients involving CNS, brain, spinal cord, the eye and lympho-reticular system; (e.g. tonsillectomy, appendicectomy);

**Dress code:**
Members of the operating team should wear the following single use, disposable protective clothing:
- A disposable plastic apron under the operation gown
- Non-wettable operation gown
- Gloves, masks, cap, over-shoes, and suitable eye protection (visor or goggles).
The procedure should be scheduled last on the list.

**Instruments and drapes**
Disposable drapes and dressings must be used and destroyed after use. All instruments must be disposed of in plastic sealable containers after use. These will be incinerated.

**Additional measures**
Where the surgical procedure involves the brain (e.g. cortical biopsy), spinal cord or eye, the following additional precautions should be taken:
- The least possible number of persons should take part in the operation.
- A one-way flow of instruments should be maintained.
- Single use disposable instruments should be used whenever practical.
- All instruments in contact with neural tissue must be destroyed by incineration.
These are sensible precautions in any event.

**Suspected case of CJD (all forms including GSS or FFI)**
The precautions above must be observed when neurological procedures, or procedures where lymphoreticular tissue is involved are carried out on patients in whom the possibility of any form of CJD enters into the differential diagnosis. All re-usable instruments must be placed in quarantine (see below) until a confirmed diagnosis is obtained.

Patients with classical CJD and inherited forms: the prion protein has not been found in reticulo-endothelial tissue so the instruments may be re-used after normal decontamination. However, it would be wise to check this before performing a procedure, then quarantining the instruments before re-use.
7.0. DIAGNOSTIC TONSILLAR BIOPSY FOR SUSPECTED VARIANT CJD

A tonsil biopsy may be considered in an individual with the following symptoms either in combination or in isolation:

- Psychiatric symptoms
- Progressive cognitive impairment
- Ataxia or pyramidal signs
- Unexplained sensory symptoms (e.g. limb pain or dysaesthesiae)
- Unexplained movement disorder
- MRI with Pulvinar sign

Forward planning is of great importance. When a patient arrives in hospital for such a biopsy, all the agencies involved with have been warned to expect the case.

The National Prion Clinic physician will decide whether it is necessary to do a tonsillar biopsy. The NHNN Prion Clinical Nurse Specialist will then make arrangements for admission and liaise with the Consultant ENT surgeon and Consultant Neuro-Pathologist. The date for the procedure will be organised with the Theatre Manager.

Admission will be for two nights around the biopsy. Patients will be admitted by the neurology SpR and Prion Clinical Fellow, and the ENT SpR informed when the patient arrives.

The Prion Clinical Fellow will arrange:

- Routine pre-operative blood samples
- Research blood
- Urine samples

and tell the tissue biopsy group of the approximate time of the procedure.

In theatre:

- Biopsies are to be placed in a dry pot with no formalin.
- Label pot with the patient’s name and “High Risk” and double bag.
- Neuropathology Research Support Scientist will collect the specimen personally.
- The specimen will be processed in the National Prion Unit under the supervision of Prof Brandner and Dr. Wadsworth.
Post-operative care:

- Hand over care to appropriate SHO on-call for post-operative management (analgesia, fluids, etc).
- Monitor clinically for pain, difficulty breathing or swallowing.
- Nursing staff to maintain proper observations.
- Normally the patient will be ready for discharge on the day after biopsy.
- Plan obtaining and communicating the result of the biopsy (Prion Clinical Fellow)
- Results will be collated and reported by the clinicians in the NPU to the consultant in charge of the case and to the co-ordinator of the CJD Working Group.

8.0. INSTRUMENT QUARANTINE PROCEDURE

(SEE "TSE AGENTS: SAFE WORKING AND THE PREVENTION OF INFECTION, [SEE REFERENCES])

Designated training staff will deal with the instruments wearing appropriate protective clothing including protective gloves and either a visor or goggles. Care must be taken to avoid penetrating injuries.

Re-usable instruments should be washed to remove gross soil. Care should be taken to avoid splashing and generating aerosols by holding instruments below the surface of the water in a sink into which water is running and draining continuously. Instruments should not be held directly under a flowing tap as this is likely to generate splashes.

Instruments should be placed in disposable instrument tray and allow to air dry. They should then be placed in an impervious rigid plastic container with a close fitting lid. The lid should be sealed with tape (e.g. autoclave tape) and labelled with the patient’s identification (i.e. hospital number, name, and date of birth), the date of the procedure, the surgical procedure in which the instruments were used and the name of the responsible person (e.g. the theatre superintendent). The sealed box should be stored indefinitely in a suitably designated place (a locked cupboard) until the outcome of any further investigation is known. The instrument tray must be disposed of by incineration.

Decisions about whether to destroy instruments will be made by the CJD Working Group, NHNN.

If the patient is later confirmed as suffering from CJD, the box and its contents must be incinerated without further examination. If an alternative, definitive diagnosis is confirmed, the instruments may be removed from the box by the responsible person (or named deputy) and sent to the Sterile Services Department (SSD) for processing in the usual way. Recent changes in guidance may result in a requirement NOT to incinerate instruments used outside the nervous system in patients with confirmed classical CJD. The working group will make this decision.

Records must be kept of all decisions, and the SSD must be told of the decision before the
instruments are sent for routine processing.

Prolonged autoclaving or supplemental disinfection is not necessary for instruments removed from quarantine, which had been used on a patient not suffering from CJD of any type.

9.0. ENDOSCOPIC PROCEDURES

Gastro-intestinal endoscopy on patients with known vCJD or suspected CJD (classical or variant) should not normally be performed. Where clinical need dictates such a procedure on a case of KNOWN vCJD, then a designated CJD endoscope MUST be used. Such a scope is available via a member of the Infection Control Team. All endoscope accessories will be destroyed by incineration after use.

Because of the potential risk of contamination of endoscopes, patients referred for GI endoscopy must have a note from their consultant in their medical records, stating the position with regard to prion disease. It is recommended that the ward SpR responsible for the patient contacts the team performing endoscopy to discuss the possible risks involved. It should be remembered that, in case of suspected diagnosis, the instruments used for the endoscopy should be quarantined until the diagnosis is ascertained. Insertion of PEG tubes non-endoscopically can be arranged via the National Prion Clinic.

Where clinical need dictates a requirement to endoscope a patient with suspected prion disease (classical or variant), the endoscope and all re-usable accessories will need to be quarantined as described above until a definitive diagnosis is available. Single use accessories will be destroyed by incineration.

10.0. MANAGEMENT OF SPECIMENS

Biopsy specimens and specimens of blood and CSF must be placed in appropriate containers enclosed in plastic bags and labelled “Danger of Infection”. The suspected diagnosis must also be stated on request forms.

11.0. TRANSPLANT AND TISSUE DONATIONS

Patients with any degenerative neurological disease and those with clinically definitive CJD of any type must not be accepted as donors of tissues used for transplant purposes.

In the case of corneal grafts, a member of the ophthalmological team responsible for collecting the cornea should be instructed to make specific enquiries to exclude such cases. Corneas should not be taken from demented patients nor from patients who die from obscure neurological diseases.

Materials from such patients must not be used for the preparation of thromboplastin, growth hormone or other biological extracts used as reagents or for treatment.
12.0. POST MORTEM

Special procedures are to be followed to prevent accidental inoculation of neural tissue or inhalation of homogenised neural tissue. See National Guidelines below.

- Only trained staff should undertake necessary autopsies.
- It is recommended that only three people are present: the pathologist, the technician and a circulating assistant.
- Proper personal protection will be worn.
- For examinations restricted to the brain, wadding is used to soak up CSF, blood and loose brain tissue. Sawing is performed in a plastic bag.
- The bag acts as a receptacle for bone dust.
- Full scale autopsies must be done in an approved designated suite.
- Bodies are placed in waterproof body bag and any wadding used is left in the bag.
- Samples should be labelled high-risk.
- After performing the autopsy, clean surfaces with 20,000 ppm free chlorine solution left for one hour.
- Run wounds under cold water but do not squeeze or scrub. Report Sharps Injuries to Occupational Health (see Occupational Health and Sharps Injuries policies).

13.0. RESEARCH

The CJD Working Group is keen to facilitate the availability of tissues for research, particularly where patients are having post-mortems performed. Where it is considered appropriate by the consultant in charge of the case, and the patient and/or their next of kin agree, the appropriate consent forms should be discussed and signed. These forms may be obtained from Professor Sebastian Brandner, who will also be pleased to provide further advice. NB these forms provide consent only for tissues to be used for research. The conventional post-mortem consent form must ALSO be signed.
14.0. FURTHER INFORMATION AND REFERENCES

Advice may also be obtained from, and referrals for all suspect prion disease cases should go to:

The National Prion Clinic at NHNN
Phone: 020 7405 0755
Fax: 020 7061 9889
E-mail: help.prion@uclh.nhs.uk
Website: www.nationalprionclinic.org

Research Units
MRC Prion Unit
www.prion.ucl.ac.uk

The UK CJD Surveillance Unit (Edinburgh)
www.cjd.ed.ac.uk/index.htm

Patient support groups
The Human BSE Foundation (vCJD)
www hbsef.org

The CJD Support Network (other forms of prion disease)
www.cjd support.net

Advice on the care of patients with prion disease or vCJD is available at:
TSE Agents – Safe Working and the Prevention of Infection
www.advisorybodies.doh.gov.uk/acdp/tseguidance/

Creutzfeldt-Jakob disease guidance for health workers
www.dh.gov.uk