



## STERILIZATION CONSENSUS

# Sterilization issues in vCJD—towards a consensus

## Meeting between the Central Sterilizing Club and Hospital Infection Society

12th September 2000

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### Background

Creutzfeldt-Jakob Disease first described by Jakob in 1921, is one of four transmissible spongiform encephalopathies (TSEs) found in man. The others being Gerstmann-Straussler-Scheinker Syndrome, Kuru (associated with cannibalism in Papua New Guinea) and Fatal Familial Insomnia. TSEs are rare, fatal neurodegenerative diseases that cause degeneration of the brain resulting in loss of co-ordination and faculties. The infectious agents are thought to be unique proteins and are termed 'prions'. Prions replicate by transforming normal cellular prion proteins into abnormal isoform proteins. These abnormal prion proteins PrP<sup>res</sup> then accumulate in the central nervous system causing spongiform changes in grey matter where they trigger neurological symptoms.

Sporadic CJD occurs worldwide. It is a rapidly progressive and ultimately fatal disorder of the central nervous system with a long incubation period of 15 months to over 30 years. There are approximately 0.5 to 1 new cases per million of the population per year. The similarities between TSEs found in different animal species (e.g. bovine spongiform encephalopathy, BSE) and those found in man suggest that the disease, in some form or another, may be able to cross the species barrier. Sporadic CJD usually presents in late middle age, mean age 66 years (range 16–95 years) with progressive dementia, a duration of illness of < 4 months (range 1–74 months). Diagnosis is based on clinical signs and characteristic waveforms when recording electrical events in the brain (EEG), and as no treatment is available for CJD, medical management remains limited to supportive care.

The new variant of Creutzfeldt-Jakob disease (vCJD) was described in UK in 1996 after the occurrence of 10 atypical cases of CJD in patients under 40 years of age, nine of them under 30. Median age is 28 years (1–74 years). All these patients

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had common features: young age, a special clinical presentation with psychiatric features at onset, an abnormal duration in the evolution of the disease (14 months on average compared with two to six months in classical cases of CJD), and a pathognomic neuropathology. Particular neuropathological features were amyloid plaques surrounded by vacuoles (florid plaques) whose distribution in the central nervous system was remarkably similar from one patient to another; a potent PrP immunostaining was identified in the injured areas, and the presence of PrP<sup>res</sup> was found by Western blot. Moreover, all these patients were homozygous methionine/methionine to codon 129 of the human *PRNP* gene, and did not have a medical history to suggest an iatrogenic or familial origin of disease. In addition, unlike sporadic CJD, no periodical electrophysiological abnormalities were observed; further the protein 14-3-3, a nonspecific marker usually found positive in sporadic forms of CJD, was not detected. Finally, hyperdense signals to cerebral MRI have been described in the post-hypothalamus area (Pulvinar sign, not seen in sporadic) and can be a helpful diagnostic feature in cases with suggestive clinical picture.

This form of CJD was suspected to be the consequence of infection in man with the BSE agent as no other aetiological hypothesis could reasonably be considered. The evidence that this is indeed the case is compelling, with BSE manifesting itself as a novel human prion disease—variant Creutzfeldt-Jakob Disease (vCJD), with temporal association with consumption of bovine central nervous system material in food. First exposure was thought to have occurred in 1983, peak exposure 1989, last exposure in 1995. First cases of variant CJD, identified retrospectively, occurred in 1993. Incubation of vCJD is governed by infective dose and methionine/methionine at codon 129. Experimental transmission of BSE and vCJD in bovine transgenic mice have shown similar brain pathology characteristics (possibly satisfying Koch's postulates).

### **Infection control—department of health viewpoint**

Despite many sensational reports in the media, TSEs although infectious, are not easily transmissible as this requires specific material from the affected individual's tissue from or adjacent to their central nervous system. For this reason isolation of sufferers is not necessary. Recent guidance issued by the Department of Health reinforces the previous advice

recommending thorough cleaning and sterilization of surgical instruments, and specific precautions for instruments used on known or suspected CJD cases. Cases of iatrogenic transmission of classical CJD have been reported. At this time there is no evidence implicating iatrogenic transmission of vCJD.

### **Department of health guidance/documents**

- (i) TSE agents:—Safe Working and the Prevention of Infection (1998). Advisory Committee on Dangerous Pathogens (ACDP) Spongiform Encephalopathy Advisory Committee (SEAC).
- (ii) MDA AN 1999 (02) July 1999—Use of trial contact lenses on multiple patients.  
Action: Do not re-use contact lenses issued to patients for a trial wearing.
- (iii) MDA AN 1999 (03) October 1999—Single patient use of contact lenses: implications for clinical practice.  
Action: Do not use contact lenses, including trial contact lenses fitting sets (diagnostic lenses fitting sets), on more than one patient.
- (iv) MDA AN 1999 (04) October 1999—Single patient use of ophthalmic medical devices: implications for clinical practice.  
Action: Components of ophthalmic devices that touch the surface of the eye should be restricted to single patient use wherever practicable and where this does not compromise clinical outcome.
- (v) HSC 1999/178 Variant Creutzfeldt-Jakob Disease (vCJD)—Minimizing the risk of transmission.

This circular highlights the risks of transmission of vCJD from one patient to another. It details the action that health organizations and clinicians should already be taking to reduce the risk of transmission and recommends some further precautionary measures. It should be read in conjunction with HSC 1999/179 and HSC 1999/123. It has implications for effective and thorough cleaning of surgical instruments and single-use instruments, and states unequivocally that 'devices designated for single episodes of use must not be reused under any circumstances whatsoever'.

- (vi) HSC 1999/179 Controls Assurance in Infection Control—Decontamination of Medical Devices. The purpose of this circular is to emphasize the importance of implementing existing guidance on the cleaning and sterilization of medical devices. A CD-ROM titled 'Decontamination

Guidance' draws together the extant Department of Health guidance on the complete process relevant to the decontamination of medical equipment (<http://www.doh.nhsweb.nhs.uk/health/decontamination-guidance.htm>)

- (vii) HSC 2000/032 Decontamination of Medical Devices.

This circular identifies the immediate and medium-term actions required to ensure that decontamination is carried out effectively. It also sets out the information needed to gather a robust picture of decontamination provision nationally and describes the support available to assist NHS Trusts, Health Authorities and Primary Care Trusts in delivering the actions required.

- (viii) MDA DB 2000/04 Single-use Medical Devices: Implications and Consequences of Re-use, (August 2000).

Section 5 deals with prion disease and states that most chemical and physical means of cleaning, disinfection and sterilization of medical devices are only partially effective at inactivating prion proteins. Research on the most effective method of inactivating the protein is still ongoing, and will be made available once complete.

### **Risk stratification—what is the extent of the problem? Is it the same for sporadic CJD as vCJD**

#### **Extent of problem**

This is unknown. In the year 2000 there was a significant increase in incidence of disease and number of deaths resulting from vCJD. Total now approximately 100 in the United Kingdom, three in France and one in Ireland (this patient did live for some time in the UK). Doctors are better at diagnosing the disease since the first patient's death in 1995. Future numbers, time scale and number of people exposed are all unknown. Exposure occurred until the early 1990s. First results from a study of stored human tissue have shown no evidence of the abnormal prion protein associated with CJD. A total of 3170 specimens of tonsil and appendix tissue were examined for traces of the protein as part of a study designed to help assess the number of cases of vCJD that may be incubating in the adult UK population.

Modelling experts from the Wellcome Trust Centre for the Epidemiology of Infectious Diseases

in the University of Oxford commented on the tonsil/appendix study in January 2000. The main assumption underlying their model is that the test can detect infection in the last three-quarters of the incubation period with 100% sensitivity and specificity. Detecting no infections in a sample of 2000 specimens of appendix tissue would indicate at most 217 000 cases. Zero positives in 5000 specimens would give an upper limit of 70 000 cases.

#### **Stratification**

Sporadic CJD and vCJD can be stratified according to clinical criteria, magnetic resonance imaging scans, tonsillar biopsy. In patients with sporadic CJD one is not concerned with tonsillar or gut interventions. Endoscopes are purely a vCJD problem. For known cases guidelines exist but do not at present distinguish between sporadic CJD and vCJD (SEAC Document 1998). At risk groups for iatrogenic sporadic CJD are finite: growth hormone (ceased 1985) dura mater grafts (ceased 1992), corneal grafts—only three cases in world; no vCJD to date.

For the wider population adopt a generic approach as for ophthalmic operations. Corneal grafts from neurological patients ceased in 1994. There is no evidence of placental transfer of either sporadic or vCJD at this moment in time. A child born in West Midlands from a vCJD mother showed no evidence of vCJD.

At the moment numbers of sporadic CJD cases exceed those of vCJD. Tissue distribution of vCJD differs from other human prion diseases. vCJD is not restricted to the central nervous system. Prion is present in lymphoid tissue from early pre-clinical onset time (<15 years). In scrapie the prion is present early in tonsils and spleen. Established facts about infectivity in the blood of human beings and animals with TSEs are as follows:

- Blood, especially the buffy-coat component, from animals experimentally infected with scrapie or CJD, and from either a clinical or pre-clinical incubation phase, is consistently infectious when bioassayed by intracerebral or intraperitoneal inoculation into the same species
- In naturally infected animals (sheep and goats with scrapie, mink with transmissible mink encephalopathy, and cows with BSE), all attempts to transmit disease through the inoculation of blood have failed

- Blood from four of 37 human beings with clinically evident sporadic CJD has been reported to transmit the disease after intracerebral inoculation into guinea-pigs, mice or hamsters. But each success has been questioned on technical grounds and has not been reproducible
- Epidemiological data have not revealed a single case of CJD that could be attributed to the administration of blood or blood products among patients with CJD, or among patients with haemophilia and other congenital clotting or immune deficiencies who receive repeated doses of plasma concentrates.

No comparable information about vCJD is available. However, as lymphoreticular organs, such as tonsils, have been shown to contain the prion protein (which is an excellent index of infectivity), whereas, it is not detectable in patients with sporadic CJD, there is some reason to suspect that blood from individuals incubating vCJD might be infectious. Data from studies into the ability of blood from experimentally infected rodents and primates with vCJD to transmit the disease will not be available for months or years.

The Department of Health has introduced measures to protect the safety of blood and plasma on a precautionary basis. These include:

- As from 1 November 1999, all blood (red cells and platelets) collected is universally leucodepleted (white cells removed).
- All blood products manufactured by the UK plasma fractionation centres use from non-UK plasma.

### Methods of decontamination

There is incomplete inactivation of prions by chemicals, gases, physical methods and problems with cleaning instrument prior to autoclaving. More sensitive protein detection systems, e.g., use of fluorochromes are needed.

The following are not effective:

- Chemicals: alcohols, detergents, formalin, glutaraldehyde, ammonia, hydrogen peroxide, iodophors, peracetic acid, phenolics,  $\beta$ -propiolactone, chlorine dioxide, hydrochloric acid.
- Gases: ethylene oxide, formaldehyde.
- Physical Methods: boiling, dry heat, UV/ionizing radiation, steam using conventional parameters.

### Specific recommendations

#### Incineration

- suitable for all waste
- suitable for disposing of contaminated tissues
- suitable for single use instruments
- surgical instruments in contact with brain

However, recommendations are not the same in all countries.

#### Quarantine

See HSC 1999/178. This should apply to all procedures where CJD is suspected. Instruments are quarantined until a definitive diagnosis is obtained.

#### Autoclave

- 134–137°C  $\times$  18 min or six cycles of 3 min/cycle not completely effective. Thermostable variants of BSE/Scrapie are known to exist.

#### NaOH

- 1 M for 1 h
- not suitable for aluminium
- preferred method for surfaces.
- This is the recommended method of the World Health Organisation. There are some 60 different types of stainless steel that are affected differently by NaOH. Over time, several percent of bulk of steel is lost. Some instruments are composed of several types of stainless steel and other metals.

#### Sodium hypochlorite

- 20 000 ppm free chlorine  $\times$  1 h
- causes corrosion of some metal surfaces

#### Formic acid

- 96%  $\times$  1 h
- suitable for use in Histopathology

### Points to consider

- Combination protocols for inactivation—chemical exposure, then steam autoclaving
- Large quantities of tissue versus smaller quantities
- Apparent thermostability of prions at higher temperatures

- Do not let instruments dry out prior to tissue removal and further reprocessing
- Some agents, for example aldehydes, may fix protein on to surfaces
- Decontamination procedures that do not involve protein fixation may be more effective than those that do
- Use of processes to remove prions are not wholly reliable, and therefore in practice may be impractical.

**Specific recommendations—(presently under review by ACDP/SEAC joint working group)**

**Combination cleaning**

- clean with NaOH, soak in NaOH × 1 h autoclave × 134°C × 18 min
- may be suitable for settings where incineration considered and rejected

**Boiling in NaOH 1 min**

- may be suitable for settings where incineration considered and rejected

**Instrument reprocessing based on tissue contact and patient history**

**A. High-risk tissues, high-risk patient**

- Discard single use devices and those instruments that are impossible to clean
- Use non-powered drills and saws
- Quarantine all other instruments until diagnosis confirmed. Discard if diagnosis is CJD

**B. Exceptionally, and following expert advice:**

- Steam autoclave cleaned instruments
  - \* 134°C for ≥ 18 min—prevacuum or porous load unit
  - \* 121–132°C for 1 h—gravity displacement unit
- Instruments that are difficult to clean
  - Soak 1 h in hypochlorite (20 000 ppm) available chlorine or in 1 N NaOH
  - Rinse, clean and autoclave as listed above

**C. Medium- to low-risk tissues, high-risk patient**

- Discard single-use devices and those instruments that are impossible to clean
- Reusable instruments and devices should be cleaned (twice) thoroughly and decontaminated in a washer/disinfector compliant with HTM 2030 (washer–disinfector) followed by being disinfected or sterilized as appropriate using conventional protocols

**Quarantining of surgical instruments**

- Tracking of surgical instrument trays and endoscopes should now be available. Quarantined instruments must be fully identified within the tracking system, from patient's case notes to processing and subsequent storing
- Single-use instruments to be incinerated
- Rinse re-usable instruments under running water, below surface
- Do not generate splashing or aerosols
- Operatives to wear personal protective clothing, including domestic grade gloves, mask and eye protection
- Air-dry instruments on disposable tray
- Secure in an impervious rigid plastic container
- Label box with patient details and name of responsible person
- Sealed box to be securely stored until definitive diagnosis available

**Outcome**

- Confirmed CJD—incinerates. Whether instruments used outside the nervous system should be destroyed in cases that are not vCJD, is currently under discussion
- If not—return instruments to normal use, following standard decontamination procedures

**CJD infection control—endoscopy**

- There are no documented cases of CJD being transmitted during endoscopy
- There is no need to destroy an endoscope after performing a procedure on a known case of classical CJD patient
- There is no basis for denying a patient this procedure if it is medically indicated, however,

a dedicated scope is required for patients with known vCJD

- Follow current standard procedures and protocols for cleaning and disinfecting the endoscope

All endoscope disinfectants, whatever type, fix prion proteins. Endoscopes are available for proven vCJD if required e.g., to create PEG site for feeding. These are based in Edinburgh and University College Hospital (UCLH) London. Endoscopes in ENT and Neurosurgery are just a visual system, and do not have channels. A sheath for nasendoscopes is available and should be used. All endoscopes must be traceable, and the identity of the scope recorded in the patient's case notes. There is concern about the traceability of accessories.

There is an argument for keeping instruments wet, to aid adequate washing and removal of organic matter. The question of where to wash was considered. In a General Practitioner's surgery, which would be at low risk, e.g., speculums; however a dedicated sink must be available. Problems were foreseen for remote hospitals using a central Sterile Supplies Department (SSD). Ultrasonics were essential for jointed instruments or healthcare premises remote from a SSD. Considered the best way forward was washing to be performed centrally under controlled conditions, quickly, all washed twice.

### **Traceability of instruments used on the patient**

Most important aspect of infection control.

### **Central tracking**

- Flexible endoscopes—this is a requirement but there are problems with accessories
- Rigid endoscopes—if processed centrally this is possible. Probably difficult if done in operating theatres
- Track sets—the sets do actually stay together (less than 10% turnover). This is the preferred option
- Track instruments—in the future: readability of instruments in theatres; possibly bar codes in operating notes; big education programme is needed

### **Dentistry**

- General—no problem
- Known cases—single-use—send to central dental hospitals

- What to do with at risk groups
- Need for generic guidance
- Impact on primary care. Dentists deal with cranial nerves, root canal work, reamers, dental instruments
- Animal studies show scrapie can be transmitted via dental pouches from hamster to hamster
- General approach to oral surgery

### **Eye**

Problems identified

- Corneal transplants (anterior eye surgery is considered of lower risk compared with posterior eye)
- Tonometers
- Risk assessment/stratification
- Retinal and posterior eye surgery highest risk
- Risk reduction
- Guidelines yet to emerge

### **CJD—environmental infection control**

- There is no evidence that CJD is transmitted from environmental surfaces (i.e., walls, floors, counter tops)
- Do not soak or wet the surfaces with 1 N NaOH
- Conventional detergents, disinfectants and procedures
- Hypochlorite (10 000 ppm available chlorine) can be used to spot-decontaminate visible tissue residues on surfaces

### **Conclusions**

Effective and thorough cleaning of surgical instruments before disinfection or sterilization makes the major contribution to risk reduction. It is therefore essential that all existing cleaning and sterilization procedures operate to the highest standards in line with extant guidance. Instruments designated for single episode of use should be discarded after use and never reprocessed.

### **Addendum**

- (1) A CJD Incident Panel has been created in the UK under the Chairmanship of Professor Michael Banner to respond to all incidents of exposure of patients to CJD.

- (2) The 16 volume report of the public enquiry chaired by Lord Phillips, into the handling of the BSE crisis, which resulted in the slaughter of 177 390 cattle on 35 103 farms, and deaths of at least 85 people was published on the 27<sup>th</sup> October 2000.
- (3) 4 January 2001 the Government announced the investment of £200 million over two years to modernize NHS decontamination and sterilization facilities. The money is to ensure that surgical equipment is cleaned and sterilized to the highest possible standards to protect patients from a theoretical risk of vCJD.
- (4) Following advice from SEAC, the Department of Health introduced single-use instruments for tonsil surgery during 2001, further to minimize the theoretical risk of transmission of vCJD. It is calculated that the cost of single use instruments for tonsil surgery (approximately 70 000 in

- England annually) will be £25 million per year. This will create an extra 100 tonnes of metallic surgical instruments for disposal by incineration. However the Government performed a U-turn in December 2001, because, following the change from re-usable surgical instruments, surgeons found more patients than before were being harmed during surgery. Most incidents involved increased bleeding and a single-use diathermy forceps tool, which cauterized the wound to halt bleeding, was suspended from use on 4 December 2001 following the death of a patient. The Department of Health said that given the balance of actual (bleeding) vs. perceived (vCJD) risks, surgeons could return to using re-usable surgical equipment, decontaminated and sterilized in the normal way!
- (5) The Government's interim response to the Phillips' Report was published in January 2001.