参考資料 2

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WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies

Report of a WHO Consultation

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Contents

Section 1. INTRODUCTION

Transmissible spongiform encephalopathies (TSEs), also known as prion diseases, are fatal degenerative brain diseases that occur in humans and certain animal species. They are characterized by microscopic vacuoles and the deposition of amyloid (prion) protein in the grey matter of the brain. All forms of TSE are experimentally transmissible.

The following guideline on the prevention of iatrogenic and nosocomial exposure to TSE agents was prepared following the WHO Consultation on Caring for Patients and Hospital Infection Control in Relation to Human Transmissible Spongiform Encephalopathies, held in Geneva from 24 to 26 March 1999. The meeting was chaired by Dr Paul Brown. Dr Martin Zeidler and Dr Maurizio Pocchiari kindly agreed to be Rapporteurs. The full list of participants is given in Annex I. Presentations made at the Consultation are listed in Annex II.

This document provides guidance upon which infection control practitioners, healthcare practitioners, medical officers of health, and those involved in the care of persons suffering from TSE can base their care and infection control practices, to prevent events which are either extremely rare (e.g. transmission of TSE through a surgical procedure) or hypothetical (e.g. transmission of TSE to a healthcare worker or family member). Throughout the document there is specific and assumed reference to country or region-specific guidelines for matters which lie within the legal jurisdiction of that country or region, i.e. International Air Transport Association (IATA) regulations for transportation of hazardous goods, or bio-safety containment levels for laboratories. Readers should be familiar with such requirements for their own country or region.

Issues on which the consultants could not agree, or where the consultants did not feel there was sufficient expertise to render an opinion, have been noted. The consultation recognized that its recommendations to ensure maximum safety to care-givers and the environment may under some circumstances be regarded as impractical. However, they urged personnel involved with TSE patients or tissues to endeavour to comply as far as possible. There is no reason for a patient with a TSE to be denied any procedure, as any associated risks should be reduced to negligible levels by following the recommendations in this document.

Section 2. GENERAL CONSIDERATIONS

2.1 Transmissible Spongiform Encephalopathies in humans and in animals

Human TSEs occur in sporadic, familial, and acquired forms. The most common form, sporadic Creutzfeldt-Jakob disease (CJD), has a worldwide death rate of about 1 case per million people each year, and typically affects people between 55 and 75 years of age. The disease usually begins with a progressive mental deterioration that soon becomes associated with progressive unsteadiness and clumsiness, visual deterioration, muscle twitching (myoclonus), a variety of other neurological symptoms and signs, and is often associated with a characteristic periodic electroencephalogram. The patient is usually mute and immobile in the terminal stages and in most cases, death occurs within a few months of onset of symptoms. TSEs are invariably fatal and there is no proven treatment or prophylaxis.

Table 1 Human TSEs

Human TSE	First Reported
Creutzfeldt-Jakob Disease (CJD):[1]	
Sporadic (85-90%)	1921
Familial (5-10%)	1924
Iatrogenic (<5%)	1974
Variant (vCJD)	1996
Gerstmann-Sträussler-Scheinker Syndrome (GSS)	1936
Kuru	1957
Fatal Insomnia	
Familial	1986
Sporadic	1999

Similar neurodegenerative diseases also occur naturally in some animal species (scrapie in sheep and goats, chronic wasting disease in deer and elk), or as a result of exposure of susceptible species to infected animal tissues (transmissible mink encephalopathy, bovine spongiform encephalopathy, and spongiform encephalopathy in domestic cats and a variety of captive zoo animals).

TSE agents exhibit an unusual resistance to conventional chemical and physical decontamination methods. They are not adequately inactivated by most common disinfectants, or by most tissue fixatives, and some infectivity may persist under standard hospital or healthcare facility autoclaving conditions (e.g. 121°C for 15 minutes). They are also extremely resistant to high doses of ionizing and ultra-violet irradiation and some residual activity has been shown to survive for long periods in the environment. The unconventional nature of these agents, together with the appearance in the United Kingdom, Republic of Ireland and France of a new variant of CJD (vCJD) since the mid-1990s, has stimulated interest in an updated guidance on safe practices for patient care and infection control.

2.2 Diagnosis of Human Transmissible Spongiform Encephalopathies

The February 1998 Report of a WHO Consultation the Global Surveillance, Diagnosis and Therapy of Human Transmissible Spongiform Encephalopathies[2,3] provides a guideline for diagnostic criteria of human TSEs. Readers should be aware of efforts to revise diagnostic criteria for CJD and vCJD due to the introduction of new diagnostic tests and intense surveillance efforts. Surveillance case definitions (which may not be the same as diagnostic criteria) for both forms of the disease may also be subject to change.

2.3 Iatrogenic transmission

TSEs are not known to spread by contact from person to person, but transmission can occur during invasive medical interventions. Exposure to infectious material through the use of human cadaveric-derived pituitary hormones, dural and cornea homografts, and contaminated neurosurgical instruments has caused human TSEs. The Report of a

[1] Percentages vary somewhat from country to country.

[2] All cited WHO reports and consultations are available at the WHO Web site http://www.who.int/emc/diseases/bse/.

[3] WHO Consultation on Global Surveillance, Diagnosis and Therapy of Human Transmissible. Spongiform Encephalopathies. WHO/EMC/ZDI/98.9 Geneva, 9-11 February 1998.

WHO Consultation on Medicinal and other Products in Relation to Human and Animal Transmissible Spongiform Encephalopathies[4] can be consulted for more information and guidance on these issues.

2.4 Evaluating risk in healthcare environments

When considering measures to prevent the transmission of TSE from patients to other individuals (patients, healthcare workers, or other care providers), it is important to understand the basis for stipulating different categories of risk. Risk is dependent upon three considerations:

- the probability that an individual has or will develop TSE (see Section 2.4.1);
- the level of infectivity in tissues or fluids of these individuals (Section 2.4.2);
- the nature or route of the exposure to these tissues (Section 2.4.3).

From these considerations it is possible to make decisions about whether any special precautions are needed. Specific TSE decontamination procedures are described in Section 6. If TSE decontamination is required, the question remains as to how stringent it should be. The specific recommendations are described in sections devoted to Patient Care (Section 3), Occupational Injury (Section 4), Laboratory Investigations (Section 5) and Management After Death (Section 8).

2.4.1 Identification of persons for whom special precautions apply

Persons with confirmed or suspected TSEs are the highest risk patients. They must be managed using specific precautions which will be described in this and subsequent sections. All precautions recommended in the body of this document apply to the care of confirmed or suspect cases of TSE, or the handling of tissues from such patients, and unless otherwise noted, no distinction will be made between confirmed and suspect cases.

However, the concept of 'persons at risk for TSE' is useful in infection control, as it allows for the development of intermediate precautionary measures. The following persons have been regarded as 'at risk' for developing TSEs. The bracketed numbers are the number of reported occurrences of CJD transmitted through that route:

- recipients of dura mater (110 cases);
- recipients of human cadaver derived pituitary hormones, especially human cadaver derived growth hormone (130 cases);
- recipients of cornea transplants (3 cases - 1 definite, 1 probable, 1 possible);
- persons who have undergone neurosurgery (6);
- members of families with heritable TSE (5-10% of all cases of TSE are heritable, but the number of families varies widely from country to country).

The discussion and recommendations for healthy asymptomatic individuals considered to be at risk for TSE are described in Annex IV and referred to in Table 9.

The consultants did not extensively discuss the management of persons who have confirmed or suspected vCJD, due to the absence of specific data for review and the

[4] Report of a WHO Consultation on Medicinal and other Products in Relation to Human and Animal Transmissible Spongiform Encepalopathies. Geneva, World Health Organization, 1997. WHO/EMC/ZOO/97.3 or WHO/BLG/97.2.

geographical isolation of the current cases. The discussion and their recommendations are described in Annex V and Table 9.

2.4.2 Tissue infectivity

From published and unpublished information, infectivity is found most often and in highest concentration in the central nervous system (CNS), specifically the brain, spinal cord and eye. This document will refer to these tissues as 'high infectivity tissues'.

Infectivity is found less often in the cerebrospinal fluid (CSF) and several organs outside the CNS (lung, liver, kidney, spleen/lymph nodes, and placenta). This document will refer to these tissues as 'low infectivity tissues'.

No infectivity has been detected in a wide variety of other tested tissues (heart, skeletal muscle, peripheral nerve, adipose tissue, gingival tissue, intestine, adrenal gland, thyroid, prostate, testis) or in bodily secretions or excretions (urine, faeces, saliva, mucous, semen, milk, tears, sweat, serous exudate). Experimental results investigating the infectivity of blood have been conflicting, however even when infectivity has been detectable, it is present in very low amounts and there are no known transfusion transmissions of CJD. This document will classify these tissues as having no detectable infectivity ('no detectable infectivity tissues') and, for the purposes of infection control, they will be regarded as non-infectious.

Table 2 Distribution of infectivity in the human body[5]

Infectivity Category	Tissues, Secretions, and Excretions	
High Infectivity	Brain Spinal cord Eye	
Low Infectivity	CSF Kidney Liver Lung Lymph nodes/spleen Placenta	
No Detectable Infectivity	Adipose tissue Adrenal gland Gingival tissue Heart muscle Intestine Peripheral nerve Prostate Skeletal muscle Testis Thyroid gland Blood[6]	Tears Nasal mucous Saliva Sweat Serous exudate Milk Semen Urine Faeces

[5] Assignment of different organs and tissues to categories of *high* and *low infectivity* is chiefly based upon the frequency with which infectivity has been detectable, rather than upon quantitative assays of the level of infectivity, for which data are incomplete. Experimental data include primates inoculated with tissues from human cases of CJD, but have been supplemented in some categories by data obtained from naturally occurring animal TSEs. Actual infectivity titres in the various human tissues other than the brain are extremely limited, but data from experimentally-infected animals generally corroborate the grouping shown in the table.

[6] See discussion this Section and Section 5.2.

The consultants agreed that an international effort to identify stored tissues from persons who later developed CJD or that were collected during the investigation for CJD (sporadic, iatrogenic or familial) should be initiated. These specimens should be tested in order to clarify the extent and level of infectivity during the pre-clinical phase of disease. Collections of these tissues, which are potentially infective, should be properly labelled as to their source and potential infectivity and appropriately stored to avoid cross contamination.

2.4.3 Route of exposure

When determining risk, infectivity of a tissue must be considered together with the route of exposure. Cutaneous exposure of intact skin or mucous membranes (except those of the eye) poses negligible risk; however, it is prudent and highly recommended to avoid such exposure when working with any high infectivity tissue. Transcutaneous exposures, including contact exposures to non-intact skin or mucous membranes,[7] splashes to the eye,[8] and inoculations via needle[9,10] or scalpel and other surgical instruments[11] pose a greater potential risk. Thus, it is prudent to avoid these types of exposures when working with either low infectivity or high infectivity tissues. CNS exposures (i.e. inoculation of the eye or CNS) with any infectious material poses a very serious risk, and appropriate precautions must always be taken to avoid these kinds of exposures.

Section 3. PATIENT CARE

3.1 Care of patients in the home and healthcare settings

3.1.1 Patient care

Normal social and clinical contact, and non-invasive clinical investigations (e.g. x-ray imaging procedures) with TSE patients do not present a risk to healthcare workers, relatives, or the community. There is no reason to defer, deny, or in any way discourage the admission of a person with a TSE into any healthcare setting. Based on current knowledge, isolation of patients is not necessary; they can be nursed in the open ward using Standard Precautions.

As the disease is usually rapidly progressive, the patient will develop high dependency needs and require ongoing assessment. It is essential to address the physical, nutritional, psychological, educational, and social needs of the patient and the associated needs of his or her family. Co-ordinated planning is vital in transferring care from one environment to another.

Private room nursing care is not required for infection control, but may be appropriate for compassionate reasons. Patient waste should be handled according to country, regional or federal regulations. Contamination by body fluids (categorized as no detectable infectivity tissues) poses no greater hazard than for any other patient. No special precautions are required for feeding utensils, feeding tubes, suction tubes, bed

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[7] TSE can be experimentally transmitted to healthy animals by exposing abraded gingival tissue to infected brain homogenate.

[8] By analogy with cornea transplants.

[9] A documented route of transmission in humans, from contaminated human cadaver extracted pituitary hormones (hGH and gonadotropin).

[10] Intraperitoneal, intramuscular and intravenous administration of *low infectivity tissue* extracts can cause transmission of TSE in experimental animals.

[11] By analogy with transmissions following neurosurgical procedures.

linens, or items used in skin or bed sore care in the home environment. Section 7 provides detailed information on disposal of medical waste.

3.1.2 Psychiatric manifestations

Caregivers both in the home and healthcare setting should be made aware and anticipate the possibility of labile psychiatric symptoms e.g. mood swings, hallucinations, or aggressive behavior. For this reason, training and counselling of professional and non-professional caregivers is recommended.

3.1.3 Confidentiality

Current heightened awareness requires special sensitivity to confidentiality of written and verbal communications. Special measures to safeguard the privacy of the patient and family are essential.

3.2 Dental procedures

Although epidemiological investigation has not revealed any evidence that dental procedures lead to increased risk of iatrogenic transmission of TSEs among humans, experimental studies have demonstrated that animals infected by intraperitoneal inoculation develop a significant level of infectivity in gingival and dental pulp tissues, and that TSEs can be transmitted to healthy animals by exposing root canals and gingival abrasions to infectious brain homogenate. The consultants agreed that the general infection control practices recommended by national dental associations are sufficient when treating TSE patients during procedures not involving neurovascular tissue. The committee was unable to come to a consensus on the risk of transmission of TSEs through major dental procedures; therefore, extra precautions such as those listed in Table 3 have been provided for consideration without recommendation.

Table 3 Optional precautions for major dental work

1.	Use single-use items and equipment e.g. needles and anaesthetic cartridges.
2.	Re-usable dental broaches and burrs that may have become contaminated with neurovascular tissue should either be destroyed after use (by incineration) or alternatively decontaminated by a method listed in Section 6 (Annex and III).
3.	Schedule procedures involving neurovascular tissue at end of day to permit more extensive cleaning and decontamination.

3.3 Diagnostic procedures

During the earlier stages of disease, patients with TSE who develop intercurrent illnesses may need to undergo the same kinds of diagnostic procedures as any other hospitalized patient. These could include ophthalmoscopic examinations, various types of endoscopy, vascular or urinary catheterization, and cardiac or pulmonary function tests. In general, these procedures may be conducted without any special precautions, as most tissues with which the instruments come in contact contain no detectable infectivity (see sub-Section 2.4.2). A conservative approach would nevertheless try to schedule such patients at the end of the day to allow more strict environmental decontamination (see Section 6.3) and instrument cleaning (see Section 6.2). When there is known exposure to high or low infectivity tissues, the instruments should be subjected to the strictest form of decontamination procedure which can be tolerated by the instrument. Instrument decontamination is discussed in more detail in Section 6.2 and decontamination methods are specifically described in Annex III.

3.4 Surgical procedures

Before admission to a hospital or healthcare facility, the infection control team should be informed of the intention to perform a surgical procedure on any person with confirmed or suspected TSE. Every effort should be made to plan carefully not only the procedure, but also the practicalities surrounding the procedure, e.g. instrument handling, storage, cleaning and decontamination or disposal. Written protocols are essential. All staff directly involved in these procedures or in the subsequent re-processing or disposal of potentially contaminated items, should be aware of the recommended precautions, and be adequately trained. The staff should be made aware of any such procedures in sufficient time to allow them to plan and to obtain suitable instruments and equipment (such as single use items), and it may be useful to schedule the patient at the end of the day's operating list. Staff must adhere to protocols that identify specifics regarding pre-operative, peri-operative and post-operative management of the patient, disposable materials, including bandages and sponges, and re-usable materials. Ancillary staff, such as laboratory and central instrument cleaning personnel, must be informed and appropriate training provided.

Basic protective measures are described in Table 4. Recommendations listed in Section 6 and Annex III for decontamination of equipment and environment, and in Section 7 for disposal of infectious waste should be followed. Supervisors should be responsible for ensuring that the appropriate procedures are followed and that effective management systems are in place.

Table 4 Precautions for surgical procedures

Wherever appropriate and possible, the intervention should:

1. be performed in an operating theatre;
2. involve the minimum required number of healthcare personnel;
3. use single-use equipment as follows:
   i) liquid repellent operating theatre gown, over a plastic apron
   ii) gloves
   iii) mask
   iv) visor or goggles
   v) linens and covers;
4. mask all non-disposable equipment;
5. maintain one-way flow of instruments;
6. treat all protective clothing, covers, liquid and solid waste by a method listed in Section 6; and Annex III; incineration is preferred
7. mark samples with a "Biohazard" label;
8. clean all surfaces according to recommendations specified in Section 6 and Annex III.

Procedures which are normally carried out at the bedside (e.g. lumbar puncture, bone marrow biopsy) may be performed at the bedside, but care should be taken to ensure ease of environmental decontamination should a spillage occur.

3.5 Handling of surgical instruments

3.5.1 General measures

Methods for instrument decontamination are fully discussed in Section 6. Determination of which method to use is based upon the infectivity level of the tissue and the way in which instruments will subsequently be re-used. For example, where surgical instruments contact high infectivity tissues, single-use surgical instruments are strongly recommended. If single-use instruments are not available, maximum safety is attained by destruction of re-usable instruments. Where destruction is not practical, re-usable instruments must be handled as per Table 5 and must be decontaminated as per Section 6 and Annex III.

Although CSF is classified as a low infectivity tissue and is less infectious than high infectivity tissues it was felt that instruments contaminated by CSF should be handled in the same manner as those contacting high infectivity tissues. This exception reflects the higher risk of transmission to any person on whom the instruments would be re-used for the procedure of lumbar puncture.

Table 5 General measures for cleaning instruments and environment

1.	Instruments should be kept moist until cleaned and decontaminated.
2.	Instruments should be cleaned as soon as possible after use to minimize drying of tissues, blood and body fluids onto the item.
3.	Avoid mixing instruments used on no detectable infectivity tissues with those used on high and low infectivity tissues.
4.	Recycle durable items for re-use only after TSE decontamination by methods found in Section 6 and Annex III.
5.	Instruments to be cleaned in automated mechanical processors must be decontaminated by methods described in Section 6 and Annex III before processing through these machines, and the washers (or other equipment) should be run through an empty cycle before any further routine use.
6.	Cover work surfaces with disposable material, which can then be removed and incinerated; otherwise clean and decontaminate underlying surfaces thoroughly using recommended decontamination procedures in Section 6 and Annex III.
7.	Be familiar with and observe safety guidelines when working with hazardous chemicals such as sodium hydroxide (NaOH, 'soda lye') and sodium hypochlorite (NaOCl, 'bleach') (see Annex III for definitions).
8.	Observe manufacturers' recommendations regarding care and maintenance of equipment.

Those instruments used for invasive procedures on TSE patients (i.e. used on high or low infectivity tissues) should be securely contained in a robust, leak-proof container labelled "Biohazard". They should be transferred to the sterilization department as soon as possible after use, and treated by a method listed in Annex III, or transferred to the incinerator as per Section 3.5.2. A designated person who is familiar with this guideline should be responsible for the transfer and subsequent management.

The consultation did not address the issue of post-exposure notification in the event that an instrument used on a high-risk tissue and/or high-risk patient was subsequently re-used without adequate decontamination.

3.5.2 Destruction of surgical instruments

Items for disposal by incineration should be isolated in a rigid clinical waste container, labelled 'Hazardous' and transported to the incinerator as soon as practicable, in line with the current disposal of clinical waste guidance described in the Teacher's Guide: Management of Wastes from Health-care Facilities[12] published by WHO. To avoid unnecessary destruction of instruments, quarantine of instruments while determining the final diagnosis of persons suspected of TSEs may be used.

3.5.3 Quarantine

If a facility can safely quarantine instruments until a diagnosis is confirmed, quarantine can be used to avoid needless destruction of instruments when suspect cases are later found not to have a TSE. Items for quarantine should be cleaned by the best non-destructive method as per Section 6 and Annex III, sterilized, packed, date and 'Hazard' labelled, and stored in specially marked rigid sealed containers.[13] Monitoring and ensuring maintenance of quarantine is essential to avoid accidental re-introduction of these instruments into the circulating instrument pool. If TSE is excluded as a diagnosis, the instruments may be returned to circulation after appropriate sterilization.

3.6 Anaesthesia

3.6.1 General anaesthesia

TSEs are not transmissible by the respiratory route; however, it is prudent to treat any instruments in direct contact with mouth, pharynx, tonsils and respiratory tract by a method described in Annex III. Destruction by incineration of non re-usable equipment is recommended.

3.6.2 Local anaesthesia

Needles should not be re-used, and in particular, needles contacting the CSF (e.g. for saddle blocks and other segmental anaesthetic procedures) must be discarded and destroyed.

3.7 Pregnancy and childbirth

TSE is not known to be transmitted from mother to child during pregnancy or childbirth; familial disease is inherited as a result of genetic mutations. In the event that a person with TSE becomes pregnant, no particular precautions need to be taken during the pregnancy, except during invasive procedures as per Section 3.4. Childbirth should be managed using standard infection control procedures, except that precautions should be taken to reduce the risk of exposure to placenta and any associated material and fluids. These should be disposed of by incineration. Instruments should be handled as for any other clinical procedure (Table 5). In home deliveries, the midwife (or any other persons in charge of delivery) should ensure that any contaminated material is removed and disposed of in accordance with correct procedures for infected clinical waste.

[12] Pruess A, Townend WK. Teacher's Guide: Management of Wastes from Health-care Activities. Geneva, World Health Organization, 1998. WHO/EOS/98.6.

[13] Although the intention of quarantine is to avoid destruction of instruments and will permit the re-introduction of instruments only if TSEs are not diagnosed, the use of a decontamination method for TSEs will confer additional safety should an instrument unintentionally come in contact with staff or patients.