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# Prion Disease and Its Implication for Dentistry

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**Abstract**

Prion Diseases are a group neurodegenerative disease which is fatal and rapidly progressive. By now, it has not definite cure. There is a theoretical, yet real risk of prion disease transmission via dental instruments and dental treatment, although the magnitude of the risk has yet to be determined as prions are highly resistant to conventional sterilization methods that we practice in dentistry field.

**Keywords**-Prion, prion disease, dental instrument, sterilization, Creutzfeldt-Jakob disease (CJD), occupational exposure

## INTRODUCTION

A prion in the Scrapie form ($PrP^{sc}$) is an infectious agent composed of protein in a misfolded form [1]. Since 1982, prion has been used to differentiate it from infectious agents (e.g. viruses and bacteria) that contain nucleic acids (either DNA, RNA, or both) [2]. Prion is like viruses, they are not actually alive although both can reproduce by hijacking the functions of living cells [3]. If prion enters a healthy organism, it induces existing, properly folded proteins to convert into disease-associated – prion form. Prion also acts as template to guide the misfolding of more protein into prion form. These newly formed prions can then go on to convert more protein themselves.Therefore, it triggers a chain of reaction that produces large amount of prion form [4]. Prion diseases are caused by this transformation of normal cell glycoprotein into conformationally-altered isoform (PrP). This confers PrP with partial resistance to proteolytic degradation and detergent insolubility [2]. This review article provides an overview of characteristics, risk of transmission, potential of infection, as well as the infection-control considerations of prions in dentistry.

## GENERAL CLINICAL ASPECT OF PRION DISEASE

Human prion disorders are classified into Creutzfeldt Jakob Disease (CJD), Gerstmann-Straussler-Scheinker (GSS) syndrome, and Kuru. It also further subclassified into 2 main etiologic catergories:

i. Inherited Prion Disease
   It accounts for approximately 15% of all human prion disorders. They comprise GSS syndrome and a group of other familial human prion disorders.
   At least 30 pathogenic mutation of prion protein-coding gene have been described. They are all inherited in an autosomal dominant manner [2].
ii. Acquired Prion Diseases

Kuru, an incurable. Degenerative, neurological disorder (brain disease) that is a type of transmissible spongiform encephalopathy (TSE) found in humans. It is believed to be caused by prions and related to CJD. Kuru has long incubation period, it causes physiological and neurological effects that ultimately lead to death. It is characterized by cerebellar ataxia, preceded by headaches, joint pains, shaking of the limbs, with the clinical stage lasting an average 12 months [2, 5].

Classic CJD is a neurodegenerative disorder. This disease is rapidly progressive and always fatal. It leads to death usually within 1 year of the onset of illness. It is also known as sporadic CJD (sCJD), due to the sporadic appearance, caused by spontaneous transformation of normal prion protein into abnormal prions [2].

Variant CJD (vCJD) is a rare and fatal neurodegenerative condition. It is classified as TSE because of its characteristic spongy degeneration of brain and its ability to be transmitted.

Before the identification of vCJD, CJD was recognized to exist in only 3 forms [5,6,7]:

a) Sporadic cases, which have an unknown cause and occur throughout the world at the rate of approximately 1 per 1 million people, and account for 85% of CJD cases.
b) Familial cases are associated with a gene mutation. It make up 5-10% of all CJD cases.
c) Iatrogenic cases (iCJD), results from the accidental transmission of causative agent via contaminated surgical equipment or as a result of cornea or dura mater transplants, or the administration of human-derived pituitary growth hormones [7]. It only accounts less than 5% of CJD.

The prion is acquired via cadaver-derived growth hormone, pituitary gonadotropins, dura mater homografting, corneal grafts, or inadequate sterilized intracerebral surgical equipment.

## DENTAL IMPLICATION OF PRION DISEASE

### *Oral manifestations of prion disease*

Oral symptoms occur rarely in patients with prion disease [8]. But oral manifestations are commonly seen in prion diseases. In human TSEs, oral manifestations are dysphagia (difficulty in swallowing) and dysarthria (speech disorder as characterized by poor articulation). In vCJD, orofacial dysesthesia (abnormal sensations experienced in the absence of stimulation), paresthesia (tingling, pricking, or numbness of skin) [9,10], or loss of taste and smell (only one case has been reported so far) [11].

### *Infectivity and transmission risk from oral cavity*

Experimentally, prions have been easily transmitted to animal gingival tissues from endodontic files which contaminated with suspensions of contaminated human brain tissues, [12] which prove that endodontic files could be vector. However, the infectivity of dental pulp tissue in

individuals suffering from clinical or subclinical vCJD (i.e., endodontic files might carry some tissues) is not known [12,13]. In animal forms and models of prion disease, $PrP^{res}$ has been found in serous and mucous glands on the posterior surface of the dorsum of the tongue [14], in nerve fibres, taste cells, and even in straitified squamous epithelium in fungiform papillae [15]. Meanwhile in all human forms of CJD, $PrP^{res}$ has also been detected in the skeletal muscles [16].

Since dental pulp originates from the richly-innervated tissue of neural crest, theoretically, it is reasonable to presume that the dental pulp of patients infected with vCJD, SCJD, and familial CJD might be infectious [18,19]. In studies of transmission of prion diseases, when infection occurs via oral route in the experimental animal, $PrP^{res}$ first appears in Peyer's patches and other gut-associated lymphoid tissue [15]. $PrP^{res}$ next appears in serous and mucous glands in oral cavity [15]. Lymph system is expected for transferring to mucosally associated lymphoid tissue because gut-primed lymphoid and myeloid cells are known to home to oral mucosally associated lymphoid tissues [17]. Neuronal routes are responsible for transferring from oral cavity to olfactory bulb and brainstem [15].

So far, only 2 possible mechanisms for the transfer of vCJD infectivity via dental instruments have been risk assessed [13].

i. Accidental abrasion of the lingual tonsil, known to carry infectivity in vCJD cases. Such a chance is extremely low ($10^4$ to $10^9$ times less likely to transmit vCJD than tonsillectomy)

ii. Contact with dental pulp: as mentioned above, dental pulp originates from the richly-innervated tissue of neural crest, theoretically, it is reasonable to presume that the dental pulp of patients subclinically infected with vCJD, SCJD, and familial CJD might be infectious. [18-22]

And yet, there is little data to indicate that prions are transmitted within the dental clinic setting, mirroring knowledge of the transmission of HIV [20] and hepatitis C virus [21]. Oral tissues are considered to be of low infectivity, and regarded by World Health Organization (WHO), people who are liable to acquire iCJD (e.g. recipients of dura mater, corneal transplants, and human pituitary hormones, and those who have undergone neurological procedures) are being at low risk of developing prion disease [22].

### *Potential of transmission*

Community transmission

By now, there has been no evidence to show that CJD is transmissible from person to person by normal contact, airborne droplets, or sexual contact [22,23].

Transfusion of blood

There is no evidence reveal that sCJD can be transmitted by blood or blood products in past studies. To date, there have been 4 instances of possible transmission of vCJD infection through blood transfusion. In these cases, donors were at a preclinical phase of disease at the time of donation [24,25]. The extended incubation period of prion diseases results in a long asymptomatic period in infected patient should be aware [26].

Occupational exposure

There is no risk of transmission of TSE to health care workers, including medical doctors and dentists through clinical contact or noninvasive clinical investigative procedure. A total of 24 cases of sCJD have been reported in health care workers as of 2005 [21]. Theoretically, it is possible to acquire prion disease from affected patients through needle stick injuries. However, there is no epidemiological evidence to prove an association between occupational exposure and sCJD. In case of an occupational exposure while performing dental procedures on TSE patients, World Health Organization (WHO) has recommended "common sense" actions [22] as shown in table 1:

**Table 1: Common sense actions in case of an occupational exposure by WHO, 2000 [22]**

| Incident of occupational exposure | Common sense actions |
|---|---|
| i. Contamination of unbroken skin with internal body fluids or tissues | Wash with detergent and abundant quanlities of warm water, rinse and dry. Exposure to 0.1N NaOH or 1:10 dilution of bleach for 1 minute can be considered for maximum safety. |
| ii. Needle sticks or lacerations | Gently encourage bleeding. Wash with warm soup water, rinse, dry andcover with a water proof dressing. Further treatment like suturing should be appropriate to the type of injury. Report the injury according to normal procedures of your hospital or health care facility. Records should be kept for no less than 20 years. |
| iii. Splashes into eye or mouth | Irrigate with either saline (eye) or tap water (mouth). Report according to normal procedures for your hospital or health care facility. |

### *Infection control in Dentistry*

The general infection control practices recommended by National Dental Association are sufficient for treatment of TSE patients with procedures not involving neurovascular tissue [22,27,28]. However, when certain invasive interventions are performed on patients who are at risk, it is essential to implement proper infection control to reduce the possibility of transmission of TSEs via dental instruments [22,28].

The single-use items and equipment such as disposable needles and anesthetic cartridges are strongly recommended and also represented the safest method for minimizing the risk of residual infectivity. Despite inability to make every health care workers obey the rule, World Health Organization (WHO) did provide a guideline for reusable endodontic files, matrix bands, burs that might become contaminated with neurovascular tissue [27] as shown in Table 2:

**Table 2: Infection control guideline for TSE by WHO, 2000 [22].**

| Category | Methods |
|---|---|
| i. Incineration | - Use for all disposable instruments, materials and waste.<br>- Preferred method for all instruments exposed to high infectivity tissues. |
| ii. Autoclave and chemical methods for heat-resistant instruments | - Immerse in sodium hydroxide (1 N NaOH) and heat in a gravity displacement autoclave at 121°C for 1 hour; clean and subject to routine sterilization.<br>- Immerse in NaOh or sodium hypochlorite (20,000 ppm available chlorine) for 1 hour; transfer instruments to water; heat in a gravity displacement autoclave at 121°C for 1 hour; clean and subject to routine sterilization.<br>- Immerse in NaOh or sodium hypochlorite for 1 hour; remove and rinse in water, then transfer to open pan and heat in a gravity displacement (121°C) or porous load (134°C) autoclave for 1 hour; clean and subject to routine sterilization.<br>- Immerse in NaOH and boil for 10 minutes at atmospheric pressure; clean, rinse in water and subject to routine sterilization.<br>- Immerse in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for 1 hour; clean, rinse in water and subject to routine sterilization.<br>- Autoclave at 134°C for 18 minutes (to be used for worst-case scenario; i.e., brain tissue bake-dried on surfaces). |
| iii. Chemical methods for surfaces and heat-sensitive instruments | - Flood with 2 N NaOH or undiluted sodium hypochlorite; let stand for 1 hour; mop up and rinse with water.<br>- For surfaces that cannot tolerate NaOH or hypochlorite, thorough cleaning will remove most infective agents by dilution, and some additional benefit may be derived from the use of one or another of the partially effective methods (chlorine dioxide glutaraldehyde, guanidinium thiocyanate [4 mol/L], iodophors, sodium dichloro-isocyanurate, sodium metaperiodate, urea [6 mol/L]). |
| iv. Autoclave or chemical methods for dry goods | - Small dry goods that can withstand either NaOH or sodium hypochlorite should first be immersed in one or the other solution and then heated in a porous load autoclave at ≥ 121°C for 1 hour.<br>- Bulky dry goods ordry goods of any size that cannot withstand exposure to NaOH or sodium hypochlorite should be heated in a porous load autoclave at 134°C for 1 hour. |

However, the best infection control procedure is quarantining instruments, linen, gowns, gloves and masks in a rigid leak-proof combustible clinical waste container after use, and transferring the container to the incinerator as soon as practicable [21,27,28,29].

In 2001, Federation Dentaire Internationale (FDI) suggested a universal precautions, a precise case history for every dental patient and appropriate continuing education for dentists about the control about controlling of cross-infection in dental practice, regarding the prevention of TSEs [30].

## GUIDELINE FOR DENTAL MANAGEMENT OF PATIENTS WITH PRION DISEASE

Existing guidelines for the clinical management of patients with prion disease do not address dental health care in any detail [22,28]. Generally, the suggested infection control procedures for dental management of patients with prion disease are similar those of all other patients but with certain important modifications.

Instruments must not be reused but discarded appropriately

The current UK guidance stated that all health care instruments employed in the treatment of patients with prion disease should be discarded [22,28]. Single-use instruments are highly recommended, and these will come into increasing use for al patients as new legislation comes into force.

Dental unit waterlines must be inactivated

Dental unit waterlines are a potential source of nosocomial infection. Dental unit waterlines can become contaminated with prions when the dental handpiece is connected to the waterline. Therefore, to avoid the risk of retraction of prions into waterlines due to the impossibility of inactivating prions, coolant provided by syringe is used instead.

Retraction of oral fluids into dental handpieces and the waterline is common, indeed as much as 800µL of fluid can pass into the handpiece [32]. Biofilms of microorganisms derived from both the water source of the unit and retracted oral fluids develop within 8 hours within waterlines [31]. Thus, it would seem sensible not to inactivate warerelines when patients with known prion disease require restorative dental care.

An independent suction and spittoon other than those of dental unit should be used

Due to the difficulties of disinfection, the suction system of dental unit cannot be used by patient with prion disease; instead a stand-alone suction unit should be used. The reservoir of the suction unit must be disposable bowl, not a spittoon. Then, it should be discarded directly into the clinical waste bin for incineration.

## CONCLUSION

There is a theoretical, yet real risk of prion disease transmission via dental instruments and dental treatment, although the magnitude of the risk has yet to be determined. Health care workers should understand these emerging diseases so that practical and reasonable changes to dental public health and infection control policies can be implemented. A proper and precise case history should be taken before any dental treatment is given to the patient. And also due to the difficulty to define the risk of CJD at present because it is unrelated to family history, therefore, to reduce the risk of prion disease transmission, the best practice is to treat every person as potentially infectious. By improving universal infection-control precautions for decontamination of instruments and waste in dental practice is now the best way to prevent current prion disease trends.

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