

# Prions in Dentistry — What Are They, Should We Be Concerned, and What Can We Do?

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## ABSTRACT

**Objective:** To briefly review the characteristics of prions, the risk of transmission and implications for infection control in dentistry.

**Methods:** The literature on prion disease in the context of dentistry up to March 2005 was reviewed using the PubMed, MEDLINE, Cumulative Index to Nursing & Allied Health Literature, Google Scholar databases and the Web sites of the departments of health of countries affected by the disease.

**Results:** The sporadic form of Creutzfeldt–Jakob disease (CJD) is the most common human prion disease; the mean age of those affected to date is 68 years, the mortality rate is 85% within 1 year, and the average death rate is 1 per million persons. Variant CJD (vCJD) affects people (mean age 26 years) with a history of previous extended periods of residence in certain countries, mainly in the United Kingdom. Currently, there is no evidence of human-to-human transmission of CJD or vCJD following casual or intimate contact or blood transfusion, nor is there evidence of iatrogenic transmission of vCJD in a health care setting. Furthermore, there is no evidence indicating increased occupational risk of CJD or vCJD among health workers or clustering of vCJD among people associated with a dental practice. The risk of transmission of prions through dentistry is unknown but is thought to be very low if appropriate infection control measures are taken.

**Conclusions:** The theoretical risk of transmission of prion disease through dental treatment emphasizes the need to maintain optimal standards of infection control and decontamination procedures for all infectious agents, including prions.

**MeSH Key Words:** dental care; infection control, dental; prion diseases/transmission; risk factors

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Prion diseases were first discovered by Stanley B. Prusiner, who won the 1997 Nobel Prize in Physiology or Medicine. Prusiner defined prions as infectious, transmissible proteinaceous particles that lack nucleic acid and are composed exclusively of a modified isoform of the noninfectious cellular prion protein (PrP<sup>C</sup>). The pathogenic (also called scrapie or PrP<sup>Sc</sup>) form of the prion protein (PrP) has the same amino acid content but a higher  $\beta$ -sheet content than PrP<sup>C</sup>.<sup>1</sup> Prions cause a group of fatal neurodegenerative diseases in humans and animals called transmissible spongiform encephalopathies (TSEs). Upon post-mortem examination of

those who die from these diseases, the brains appear normal.<sup>2</sup> However, histopathologic examination reveals an accumulation of PrP<sup>Sc</sup> in the central nervous system and microscopic vacuoles within the grey matter, resulting in widespread spongiform morphology of the brain.<sup>2,3</sup> The various forms of TSE are summarized in Table 1.

The prevalence of prion disease in North America is very low, so dental practitioners must learn from the experience of countries that have already been affected by the disease, to ensure the security and safety of patients as well as staff.

**Table 1** The prion diseases

Disease	Mechanism of pathogenesis
<b>Human diseases</b>	
Kuru (Fore people)	Infection through ritualistic cannibalism
Iatrogenic Creutzfeldt-Jakob disease	Infection through prion-contaminated HGH, dura mater grafts, and so forth
Variant Creutzfeldt-Jakob disease	Infection through bovine prions?
Familial Creutzfeldt-Jakob disease	Germline mutations in PrP gene
Gerstmann–Sträussler–Scheinker disease	Germline mutations in PrP gene
Fatal familial insomnia	Germline mutations in PrP gene (D178N and M129)
Sporadic Creutzfeldt-Jakob disease	Somatic mutation or spontaneous conversion of Pr <sup>PC</sup> into Pr <sup>Sc</sup> ?
<b>Animal diseases</b>	
Scrapie (sheep)	Infection in genetically susceptible sheep
Bovine spongiform encephalopathy (cattle)	Infection with prion-contaminated MBM
Transmissible mink encephalopathy (mink)	Infection with prions from sheep or cattle
Chronic wasting disease (mule deer, elk)	Unknown
Feline spongiform encephalopathy (cats)	Infection with prion-contaminated MBM
Exotic ungulate encephalopathy (greater kudu, nyala, oryx)	Infection with prion-contaminated MBM

HGH = human growth hormone; MBM = meat and bone meal feed  
 Reprinted with permission from Prusiner.<sup>2</sup> Copyright 1997 AAAS.

Although the risk of transmission of Creutzfeldt–Jakob disease (CJD) through dentistry is unclear, the theoretical risk of transmission through any contaminated instruments provides some insight. Prions are highly resistant to inactivation and can survive autoclaving even at high temperatures; therefore, dentists and members of their dental teams should be aware of the precautions and principles of appropriate infection control to minimize iatrogenic transmission of prions.

The literature search for this article covered studies of human and animal TSEs relevant to the field of dentistry up to March 2005, on the basis of the PubMed, MEDLINE, Cumulative Index to Nursing & Allied Health Literature, Google Scholar databases and the Web sites of the departments of health of countries that have been affected by the disease. This review article is intended to provide dentists with a brief overview of the characteristics of prions, the risk of transmission and the implications for infection control in dentistry. Although animal forms of TSEs — bovine spongiform encephalopathy (BSE) and scrapie — are important diseases, this review is limited to human forms.

### Human TSEs

CJD is actually a group of diseases divided into sporadic (sCJD), inherited (Gerstmann–Sträussler–Scheinker syndrome and fatal familial insomnia) and acquired (iatrogenic, kuru, variant CJD [vCJD]) forms. Eighty-five per cent of cases of CJD are sporadic; up to 15% are

familial, linked to genetic mutations of PrP, and less than 1% are iatrogenic.<sup>4</sup>

As of May 1, 2004, the incidence of CJD death reported to the Creutzfeldt–Jakob Disease Surveillance System (CJD-SS) of Health Canada was 31 in 1999, 35 in 2000, 30 in 2001, 36 in 2002, and 29 in 2003.<sup>5</sup> The Canadian epidemiological rate is the same as the worldwide rate of about one death per million persons, adjusted for age.<sup>5,6</sup> Table 2 summarizes the clinical features of human prion diseases.

### Sporadic Form of CJD

Sporadic cases of CJD occur spontaneously, without any apparent reason. The mean age of patients with sCJD is 68 years.<sup>10</sup> The mortality rate is 85% within 1 year, and the diagnosis is best ascertained during the final stages of the disease, at or near the time of death.<sup>6,10</sup>

### Acquired Forms

#### Kuru

Kuru, first described in the 1950s, is an acquired human TSE, geographically restricted to the Okapa area of the eastern highlands of Papua New Guinea. It resulted from cannibalism (specifically the consumption of deceased relatives' tissues as a form of respect).<sup>7</sup> Cannibalism was banned in 1956, which resulted in a decrease in the annual incidence from approximately 1% in 1957 to the current rate of about 5 cases per annum.<sup>11</sup>

**Table 2** Clinical features of human prion diseases

	Age at onset (yr)	Incubation time (yr)	Duration of disease (mo)	Clinical stages	
CJD	60–69	Not recorded	3–6	Early	Lapses in memory, mood swings (similar to depression), lack of interest, social withdrawal and unsteadiness
				Late (neurological)	Blurred vision, sudden jerking movements and rigidity in the limbs, slurred speech, difficulty swallowing, progressive mental deterioration, and, eventually, immobility and muteness
vCJD	20–29	> 4	9–35	Early (psychiatric)	Mostly depression, with (less often) a schizophrenia-like psychosis; for half of cases, unusual sensory signs, such as “stickiness” of the skin
				Late (neurological)	Unsteadiness, difficulty walking and involuntary movements as the illness progresses; in final stages, complete immobility and muteness
Kuru	>20	Mean: 12	6–36	Early	Cerebellar syndrome; communication difficulties due to severe dysarthria
				Late	Progression to total incapacitation and death in final stages

CJD = Creutzfeldt–Jakob disease, vCJD = variant Creutzfeldt–Jakob disease.  
 Source: Will,<sup>7</sup> Kompoliti and others,<sup>8</sup> Porter<sup>9</sup>

### Variant Creutzfeldt–Jakob Disease

In 1996, the National Creutzfeldt–Jakob Disease Surveillance Unit in the United Kingdom identified 10 cases of CJD with a specific neuropathological profile and called them variant CJD. These patients had a lower age at onset (median age 26 years) than was the case for CJD,<sup>10</sup> unusual clinical findings and an absence of the typical electroencephalographic (EEG) changes of CJD.<sup>12</sup> Young age, methionine homozygosity at codon 129 of the PrP gene and residence in the United Kingdom are among the risk factors for vCJD.<sup>7</sup> Consumption of food contaminated with tissues from animals with BSE is likely to initiate vCJD in humans.<sup>13</sup>

By November 2003, a total of 143 confirmed and probable vCJD cases had been recognized in the United Kingdom. Another 10 cases of vCJD had been recognized elsewhere: 6 in France and single cases in Ireland, Italy, Canada and the United States, each with a history of extended periods of residence in the United Kingdom.<sup>14,15</sup> Because of the ease of global travel and Canada’s open immigration policy, it is possible that other vCJD cases will be seen in Canada.<sup>14</sup>

### Inherited Forms

Gerstmann–Sträussler–Scheinker syndrome (GSS) and fatal familial insomnia (FFI) are both very rare, with an annual incidence of 1 per 10 million to 100 million people.<sup>16</sup> They occur in people with an apparent hereditary predisposition.<sup>17</sup> However, the mutations responsible for GSS are different from those causing FFI.

### Diagnostic Tests

A number of tests and investigations can be used to diagnose vCJD, including blood tests (for inherited prion diseases), EEG (for sCJD), cranial magnetic resonance imaging (for sCJD and vCJD), cerebrospinal fluid tests (sCJD) and tonsillar biopsy (vCJD). However, the definitive diagnosis of vCJD is made at autopsy.<sup>18</sup>

### Potential Risks

#### Blood Transfusion

It is not currently possible to firmly conclude that vCJD can be transmitted through blood transfusions or plasma derivatives; as such, this risk is theoretical.<sup>19–22</sup>

**Table 3** Categorization of patients by risk

Patient group	Risk criteria
Symptomatic patients	<ul style="list-style-type: none"> <li>• Patients who fulfill the diagnostic criteria for definite, probable or possible CJD or vCJD</li> <li>• Patients with neurological disease of unknown cause who do not fit the criteria for possible CJD or vCJD, but in whom the diagnosis of CJD is being considered</li> </ul>
Asymptomatic patients at risk for familial forms of CJD linked to genetic mutations	<ul style="list-style-type: none"> <li>• Individuals who have or have had 2 or more blood relatives affected by CJD or another prion disease or a relative known to have a genetic mutation indicative of familial CJD</li> <li>• Individuals who have been shown by specific genetic testing to be at significant risk of CJD or another prion disease</li> </ul>
Asymptomatic patients potentially at risk because of iatrogenic exposure <sup>a</sup>	<ul style="list-style-type: none"> <li>• Recipients of hormone derived from human pituitary glands, e.g., growth hormone, gonadotropin</li> <li>• Individuals who have received a graft of dura mater (people who underwent neurosurgical procedures or operations for a tumour or cyst of the spine before August 1992 may have received a graft of dura mater and should be treated as being at risk, unless there is evidence that dura mater was not used)</li> <li>• Patients who have been identified as potentially at risk because of exposure to instruments used on, or receipt of blood, plasma derivatives, organs or tissues donated by, a patient who went on to develop CJD or vCJD<sup>b</sup></li> </ul>

CJD = Creutzfeldt–Jakob disease, vCJD = variant Creutzfeldt–Jakob disease.

Adapted with permission from the U.K. Department of Health.<sup>31</sup>

<sup>a</sup> A decision on the inclusion of corneal graft recipients in the “iatrogenic at risk” category is pending completion of a risk assessment.

<sup>b</sup> The CJD Incidents Panel, which gives advice to the local team on what action is needed when CJD or vCJD is diagnosed in a patient who underwent surgery or donated blood, organs or tissues before the disease was identified, will identify contacts who are potentially at risk.

Transmission of BSE to a single animal through blood transfusion was recently reported,<sup>23–25</sup> but further studies are needed to identify an actual iatrogenic risk.<sup>26</sup> However, at this time, because of the extremely small risk of acquiring vCJD in Canada<sup>27</sup> and the current incidence (one case to date), the risk of transmission of vCJD by blood seems extremely low.

### **Iatrogenic Factors**

Iatrogenic transmission of CJD is a rare situation caused by cross-contamination with material in or adjacent to the brain. Examples of cross-contamination include corneal transplant (3 associated cases), contaminated neurosurgical devices (7 cases worldwide, of which 2 are considered probable and 5 possible), contaminated EEG depth electrodes (2 cases), human pituitary growth hormones (about 130 cases worldwide), human gonadotropin (4 cases) and human dura mater grafts (about 110 cases worldwide).<sup>7,16,26</sup>

### **Human-to-Human Contact**

Currently, there is no evidence of human-to-human transmission of CJD or vCJD following casual (touching or kissing) or intimate (sexual) contact.<sup>11,19</sup>

### **Assessment of a Patient’s Risk for CJD**

The World Health Organization (WHO) Consultation on Infection Control Guidelines for Transmissible Spongiform Encephalopathies, held in March 1999, defined patients with diagnosed or suspected CJD as having high risk; recipients of human dura mater grafts, corneal grafts and human pituitary hormones, as well as members of families with familial CJD, GSS and FFI, were defined as at risk (but only under conditions in which there could be exposure to their high-infectivity tissues, including cerebrospinal fluid).<sup>28</sup> However, the current incidence of CJD in Canada does not justify classifying people who have undergone neurosurgical procedures as being at risk.<sup>27</sup>

### **Risk among Health Care Workers**

Although there is no epidemiological evidence indicating increased occupational risk of CJD or vCJD among health care workers, including dental practitioners, the possibility cannot be excluded.<sup>28</sup> Currently, there is no evidence of clustering of vCJD in people associated with a dental practice,<sup>29</sup> nor is there evidence of iatrogenic transmission of vCJD, although it could be masked by the

long incubation period.<sup>30</sup> At present, there is no evidence that saliva is infective.<sup>31</sup> At autopsy, vCJD PrP has not been detected in the alveolar nerve, tongue, dental pulp, gingiva or salivary glands.<sup>16,31,32</sup> However, animal studies have shown that the oral tissues can become infected with prions and can be a potential source of infection for other animals.<sup>29</sup>

## TSEs and Dental Patients

### *Oral Manifestations of Prion Disease*

Pseudobulbar palsy may cause dysphagia and dysarthria in patients with TSEs. Orofacial dysesthesia or paresthesia, as well as loss of taste and smell (in one case), have been reported in patients with vCJD.<sup>29,33</sup>

### *Assessing the Risk of Transmission through Dentistry*

At the time of this review, the risk of acquiring vCJD in Canada was extremely small.<sup>27</sup> The risk of transmission of prions through dental treatment is unknown, but it is thought to be very low if optimal standards of infection control and decontamination are maintained.<sup>34</sup>

Sogal and Tofe<sup>35</sup> conducted a risk analysis to assess the possibility of TSE transmission from a commercially available bovine-derived xenogenic bone substitute that is popular in clinical dentistry. They concluded that the risk of TSE transmission was insignificant, given the strict protocols followed in the sourcing and processing of raw bovine bone for human use.

The UK Department of Health reported that the potential risk of vCJD transmission through re-use of instruments in dental surgery (via tonsillar abrasion) is very low. Even in the most pessimistic scenario of infectivity of dental pulp, the per-operation risk of transmitting vCJD would be at least 10 times lower than that of tonsillectomy, which, in turn, is lower than that of a surgical treatment involving the central nervous system.<sup>36</sup>

Several case-control studies have found no relationship between tooth extraction, dental surgery or major dental work and human TSEs.<sup>20,22,37</sup>

In a study conducted in 2003, Head and others<sup>32</sup> were unable to detect disease-associated PrP in dental tissues at autopsy of 5 patients with vCJD. In contrast, the tonsils were positive for prions in all cases.

Blanquet-Grossard and others<sup>38</sup> analyzed proteinase-K-treated homogenates from the brain and dental pulp of 8 patients with confirmed sCJD. Using Western blotting with the monoclonal 3F4 antibody, they were unable to detect any signal of characteristic proteinase-resistant PrP from approximately 10 mg of dental pulp tissue, but they did detect the signals in 0.01 mg of brain tissue. They pointed out, however, that because the sensitivity of Western blotting is lower than that of the animal bioassay test, the risk of iatrogenic contamination by endodontic surgery could not be rejected.

### *Animal Studies*

In 1978, Adams and Edgar<sup>39</sup> assessed the possibility of transmission of scrapie through dental burs. They traumatized the gingival tissue of healthy mice using dental burs that had been contaminated with gingival tissue of infected scrapie mice. Despite the infectivity of the gingival tissue of the infected mice (as confirmed by intraperitoneal injection), they found no clinical or histological findings of scrapie when the healthy mice were killed and examined 15 months later. However, there is some evidence that a significant level of infectivity develops in the gingival and dental pulp tissues of infected animals, and that “TSEs can be transmitted to healthy animals by exposing root canals and gingival abrasions to infectious brain homogenate.”<sup>28</sup>

In 1982, Carp<sup>40</sup> applied brain homogenates from scrapie-infected mice to the gingiva of 2 groups of healthy mice, one group previously scarified with forceps and scissors and the other not. He reported that 71% of the nonscarified mice became infected, whereas all of the scarified mice became infected; in addition, the incubation period for the second group was significantly shorter than that of the first group. After intracerebral injection of fluid from oral lavage of scarified gingiva of scrapie-infected mice into 31 healthy mice, 3 mice became infected. Carp concluded that the risk of transmission of scrapie through the oral route was high when the scrapie agent was applied in high concentration and the gingiva was scarified.

In 1999, Ingrassio and others<sup>41</sup> conducted a study on the possibility of prion infection through dental procedures. They found a significant level of infectivity in the trigeminal ganglia and in the gingival and pulpal tissues of scrapie-affected hamsters after intraperitoneal inoculation, suggesting possible transmission from the central nervous system through trigeminal nerves toward the oral cavity. They also injected the scrapie agent into the dental pulp of a group of Syrian hamsters, all of which developed the disease. Although these results cannot be generalized to humans affected by TSEs, they point to the possibility that inadequately decontaminated dental instruments may represent a potential route of infection, specifically in vCJD, with has greater infectivity in peripheral tissues than CJD.

### *Infection Control in Dentistry*

Table 3 shows the patient risk categorization of the joint working group of the Advisory Committee on Dangerous Pathogens/Spongiform Encephalopathy Advisory Committee.<sup>31</sup>

That working group stated that for treatment of TSE patients with procedures not involving neurovascular tissue, the general infection control practices recommended by national dental associations are sufficient.<sup>4,28,31</sup> However, when certain invasive interventions are performed on patients who are at risk, it is essential to implement proper

**Table 4** World Health Organization infection control guidelines for transmissible spongiform encephalopathies

Category	Methods
Incineration	<ul style="list-style-type: none"> <li>• Use for all disposable instruments, materials and wastes.</li> <li>• Preferred method for all instruments exposed to high infectivity tissues.</li> </ul>
Autoclave and chemical methods for heat-resistant instruments	<ul style="list-style-type: none"> <li>• Immerse in sodium hydroxide (1 N NaOH) and heat in a gravity displacement autoclave at 121°C for 30 min; clean; rinse in water and subject to routine sterilization.</li> <li>• Immerse in NaOH or sodium hypochlorite (20 000 ppm available chlorine) for 1 h; transfer instruments to water; heat in a gravity displacement autoclave at 121°C for 1 h; clean and subject to routine sterilization.</li> <li>• Immerse in NaOH or sodium hypochlorite for 1 h; 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 h; clean and subject to routine sterilization.</li> <li>• Immerse in NaOH and boil for 10 min at atmospheric pressure; clean, rinse in water and subject to routine sterilization.</li> <li>• Immerse in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for 1 h; clean; rinse in water and subject to routine sterilization.</li> <li>• Autoclave at 134°C for 18 min (to be used for worst-case scenario; i.e., brain tissue bake-dried on surfaces).</li> </ul>
Chemical methods for surfaces and heat-sensitive instruments	<ul style="list-style-type: none"> <li>• Flood with 2 N NaOH or undiluted sodium hypochlorite; let stand for 1 h; mop up and rinse with water.</li> <li>• 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]).</li> </ul>
Autoclave or chemical methods for dry goods	<ul style="list-style-type: none"> <li>• Small dry goods that can withstand either NaOH or sodium hypochlorite should first be immersed in one or the other solution (as described above) and then heated in a porous load autoclave at <math>\geq 121^\circ\text{C}</math> for 1 h.</li> <li>• Bulky dry goods or dry 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 h.</li> </ul>

Source: World Health Organization.<sup>28</sup>

infection control to reduce the possibility of transmission of TSEs via dental instruments.<sup>4,31</sup>

Although participants in the WHO Consultation on Infection Control Guidelines for Transmissible Spongiform Encephalopathies were unable to reach agreement on the risk of iatrogenic transmission of TSEs through major dental work, they suggested that single-use items and equipment such as disposable needles and anesthetic cartridges represented the safest method for minimizing the risk of residual infectivity. Despite inability to make a strong recommendation, they did provide a guideline for reusable endodontic files, matrix bands and burs that might become contaminated with neurovascular tissue (Table 4).<sup>28</sup> However, the best infection control procedure

(whenever possible) 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.<sup>4,28,31,33</sup>

In 2001, the Fédération Dentaire Internationale (FDI) announced a policy statement regarding the prevention of TSEs in dentistry,<sup>42</sup> suggesting universal precautions, careful history-taking for every dental patient and appropriate continuing education for dentists about the control of cross-infection in dental practice. For at-risk patients, referral to specialist clinics or hospitals and incineration of all instruments and extracted teeth were recommended. It was suggested that animal-derived graft materials not be used in oral or periodontal surgery unless the safety of the

product has been certified. Also, caution should be exercised in the use of heterologous human graft materials.

Recently, the Centers for Disease Control and Prevention (CDC) released guidelines for infection control in dental health care settings that differ in some aspects from the WHO guidelines. When treating patients with known CJD or vCJD, the CDC recommended that dental items that are difficult to clean (such as endodontic files, broaches, and carbide and diamond burs) be discarded after one use. For heat-resistant dental instruments, they suggested thoroughly cleaning and steam-autoclaving the instruments at 134°C for 18 minutes.<sup>43</sup>

Patients with confirmed prion disease should be scheduled at the end of the day to permit more extensive cleaning and decontamination.<sup>4,28</sup> It is preferable to avoid activating waterlines because of the risk of retraction of prions in oral fluids. Also, a stand-alone suction unit with disposable reservoir, rather than the suction component of the dental unit, and a disposable bowl instead of the dental unit spittoon should be used.<sup>16,29,33</sup> To avoid environmental contamination, dental equipment should be adequately shielded using disposable, impermeable cover sheets.<sup>28</sup>

## Conclusions

Recently, there has been an increase in scientific and public awareness about prion disease. Although the prevalence of the disease in North America is low, global travel and Canada's open immigration policy raise the possibility that other vCJD cases will be seen in this country, and these may pose a risk of secondary iatrogenic transmission. The theoretical risk of transmission of prion disease through dental treatment points to the importance of maintaining optimal standards of infection control and decontamination for infectious agents, including prions. ♦

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