Prion Disease: The Implications for Dentistry

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Abstract

The aim of this article was to provide the dental community with a brief overview of the characteristics, risk of transmission, and the infection-control implications of prions in dentistry. MEDLINE, EMBASE, CINAHL, The Cochrane Library, and relevant databases were searched, and a targeted internet search was conducted up to July 2007. Transmissible spongiform encephalopathies (TSEs) are a group of fatal neurodegenerative diseases that are rapidly progressive and always fatal, with no approved cure, and their definite diagnosis can only be obtained at post mortem autopsy. The causative agent, prion protein, resists conventional sterilization methods especially when infected tissue becomes dried onto glass or metal surfaces. To date, there are no reported definite or suspected cases of disease transmission arising from dental procedures, and there seems to be no correlation between dental treatment and TSEs. Because there is a theoretical but real risk of transmission of prion disease from dental instruments (although it is extremely low, especially in North America), as a general rule, appropriate family and medical history (including the risk for prion diseases) should be obtained from all patients, before all dental procedures. TSE research regarding diagnosis, transmission, treatment, and inactivation of prions and other transmissible amyloidoses are ongoing, and, thus, dental professionals should maintain optimal and up-to-date standards of knowledge, infection control, and decontamination. *(J Endod 2008;34:1158–1166)*

Key Words

Dental, dental care, infection control, prion diseases

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Prion proteins (PrP) are infectious, transmissible proteinaceous particles that lack nucleic acid and are composed exclusively of a modified isoform of the noninfectious cellular prion protein (PrP^{C}) (1, 2). The noninfectious protein is a component of a common cellular receptor. The normal function of PrP^{C} remains unclear but is thought to be involved in copper metabolism and transport (3). It has been found at elevated levels in human odontoblasts and may be involved in dentine deposition (4). The pathogenic isoform of PrP (PrP^{Sc} or PrP^{res}) has the same amino acid content but a different three-dimensional conformation with a higher β-sheet content than PrP^{C}, that reduces the solubility of the protein and leads to the deposition of insoluble fibrils in amyloid plaques (3). Posttranslational changes that occur after proteins are synthesized on the ribosome are poorly understood but PrP^{res} is thought to act as a template that promotes the misfolding of newly formed PrP^{C} (5). When accumulated in the central nervous system of humans and animals, PrP^{res} can cause a microscopic vacuolization of the brain tissue called spongiform degeneration (Fig. 1), characteristic of a group of fatal neurodegenerative diseases called transmissible spongiform encephalopathies (TSEs) (2). It is likely that prion disease is one of a subset of transmissible amyloidoses, protein conformational diseases that are the result of pathologic depositions of fibrillar misfolded proteins (6). Other amyloidoses proteins, such as transthyretin and lysozyme have a high β-sheet content in their native form (6), but the native PrP^{C} has only a small β-sheet portion in the membrane-proximal carboxyterminal of the protein (7). However, the PrP^{res} isoform misfolds forming a large β-sheet section and trimers of PrP^{res} molecules stack to form stable insoluble fibrils (Figure 2) (3).

Variations in the conformation of different isolates of PrP^{res} change the stability of the misfolding process leading to isolates with differing infectivities and varying "incubation" periods (8). The "incubation" period seems to depend on the dose, the stability of the misfolded protein conformation, and the susceptibility of the host (8). There is evidence that other amyloidosis conditions may also be transmissible (9–11).

This article aimed to provide the dental community with a brief overview of the characteristics, the risk of transmission, and infection-control implications of prions in dentistry.

Methods

Search Strategy for the Identification of Studies

The literature search (from the earliest record up to July 2007) for relevant articles was performed using Ovid MEDLINE (R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE (R) Daily, Ovid MEDLINE (R), Ovid OLDMEDLINE (R), Cumulative Index to Nursing & Allied Health Literature (CINAHL), Evidence Based Medicine of Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, EMBASE, Health and Psychosocial Instruments, HealthSTAR/Ovid Healthstar, International Pharmaceutical Abstracts, and PubMed. Table 1 shows the Key words and combinations of the Key words used. Moreover; the targeted internet search was performed on the following web sites for any other relevant evidence: CDC and CJD Surveillance; Public Health Agency of Canada; UK Department of Health; New York State Department of Health; Centers for Disease Control and Prevention (CDC); New York City Department of Health and Mental Hygiene; National Prion Disease Pathology Surveillance Center; World Health Organization; Creutzfeldt-Jakob Disease Foundation; Inc.; The UK Creutzfeldt-Jakob Disease Surveillance Unit; The Spongiform Encephalopathy Advisory Committee (SEAC); Stanley Prusiner; MD; Structural Studies of Prion Disease; Alberta Prion Research Institute Memory and Aging Center; University of California; San Francisco; Division of Neurological Science; Tohoku University; The Australian National CJD Registry; Communica-

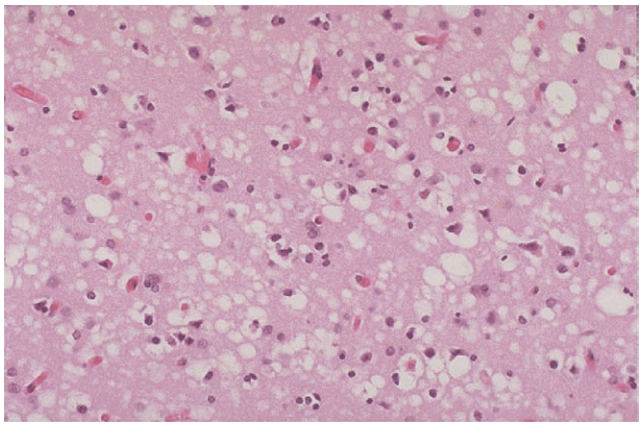

Figure 1. Spongelike lesions in the brain tissue of a classic CJD patient. Courtesy of Ermias Belay with permission from Prion Disease Office of the Center for Disease control and Prevention (23).

ble Diseases Network of Australia; National Prion Disease Clinic; London; CJD Resource Centre of National Institute for Biological Standards and Control; and Scottish Dental Clinical Effectiveness Programme.

Methods of the Review

Limiting the searches to articles in English resulted in some 365 articles being identified. No other exclusion criteria were set at the initial stage to ensure finding all potentially relevant articles that include the search Key words. After removing duplicates; 106 articles were searched for relevancy; determined by the article title. Articles were excluded that did not address the characteristics; the risk of transmission; and infection-control implications in dentistry for prions or provide background information (review articles). Further articles were identified by reviewing the references and bibliographies of articles obtained by the search strategy.

Results

Animal TSEs

Animal TSEs include scrapie in sheep and goats; bovine spongiform encephalopathy (BSE) or mad cow disease in cattle; transmissible mink encephalopathy in farmed mink; chronic wasting disease in North American mule deer, white-tailed deer, elk, and moose; feline spongiform encephalopathy in domestic cats and captive exotic felines; spongiform encephalopathy in captive exotic ungulates; and a reported spongiform encephalopathy in a French zoologic collection (2, 12, 13).

BSE or "mad cow disease," a progressive neurologic disease, is a massive common-source epidemic in dairy cows that first appeared in UK cattle in 1986 (14). BSE appears to have originated from scrapie, an endemic and naturally occurring TSE disease of sheep and goats that has been recognized in Europe since the mid-18th century (15–17).

Prion-infected animal feed appears to have been the major cause of BSE transmission and, thus, the number of cases in the United Kingdom decreased with the implementation of a governmental order in 1988 (18), banning the use of rendered sheep or cattle offal from the dietary protein supplement of domestic animals. These prevention strategies resulted in a relatively rapid decline of BSE cases in the United Kingdom. As of May 2007, 14 cases of BSE have been identified in North America, 3 in the United States, and 11 in Canada (19). Currently, public health control measures, such as surveillance, culling sick animals, or banning specified risk materials, have been instituted in many countries in order to prevent potentially BSE-infected tissues from entering the animal feed and human food chains (19). To prevent BSE from entering North America, both the Canadian and the US governments have implemented safeguards, placing severe restrictions on the importation of beef products and live ruminants, especially from countries at risk of BSE (20, 21).

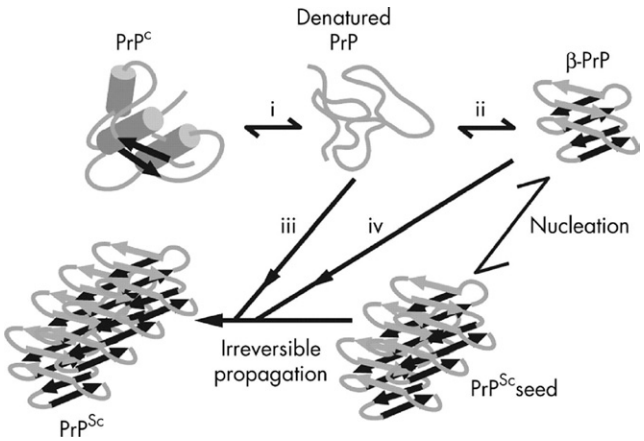

Figure 2. Possible mechanism for prion propagation. Largely α-helical PrPC proceeds via an unfolded state (i) to refold into a largely β-sheet form, β-PrP (ii). In physiological salt concentrations, β-PrP stacks into aggregates. Unfolded PrP (iii) or β-PrP monomers (iv) are irreversibly added to the stacks because PrP is most stable when it is stacked. Reproduced with permission from Collinge J. Molecular neurology of prion disease. J Neurol Neurosurg Psychiatry 2005;76:906.

Human TSEs

Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is the most commonly occurring human TSE. CJD patients experience a rapid onset of dementia as well as a range of neurologic symptoms including walking difficulties, sudden jerky movements, and, sometimes, visual deficits (22). At the moment, there is no approved cure for any type of CJD, although clinical evaluations of quinacrine and related 9-aminoacridine compounds for the treatment of human prion diseases are in progress. The disease is rapidly progressive and always fatal, usually 85% within 1 year of onset of the illness (23, 24).

TABLE 1. Search Strategy

#	Search History	Results
1	(oral biology or dentist$ or oral health or dental care or dental or oral care).mp. [mp=ti, ot, ab, nm, hw, kw, it, tx, sh, ct, de, tn, dm, mf, ac, rw]	670,147
2	(Prion or Kuru or Creutzfeldt-Jakob or Creutzfeldt Jakob or Gerstmann Straussler Scheinker or Fatal familial insomnia or Scrapie or Bovine spongiform encephalopathy or Transmissible mink encephalopathy or chronic wasting disease or Feline spongiform encephalopathy or Exotic ungulate encephalopathy or CJD or vCJD or v-CJD or sCJD or s-CJD).mp. [mp=ti, ot, ab, nm, hw, kw, it, tx, sh, ct, de, tn, dm, mf, ac, rw]	36,317
3	1 and 2	365
4	Remove duplicates from 3	282
5	Screening the titles of the relevant articles	106
6	Updating the search strategy from 2007-2008 following the steps before	9
7	Total relevant articles screened	115