Potential Risk of Prion Transmission during Periodontal Surgeries

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ABSTRACT

Prion diseases are a cluster of neurodegenerative diseases seen in both animals and humans and are often invariably fatal. The defining characteristic of prion diseases are the accumulation of abnormal prion proteins in the central nervous system. The prion proteins are not decontaminated with conventional sterilization procedures and persist on metal instruments in contact with infected materials, thus giving rise to queries on cross-contamination during periodontal surgical procedures. This article is a review of literature of prion diseases, collected using the search engines of PubMed and Medline, to analyze the oral manifestations of prion diseases and to investigate the possibility of cross-contamination during periodontal therapy. We conclude by highlighting the need for awareness of prion diseases by periodontists and suggest appropriate decontamination procedures to prevent iatrogenic spread.

Key message: Iatrogenic transmission during regenerative periodontal surgeries with alloplasts and zoografts along with cross-contamination from previously used inadequately disinfected surgical instruments constitutes a very real risk for prion infection transmission in the periodontal office.

Keywords: Cross-contaminations, Iatrogenic infections, Periodontal surgeries, Periodontitis, Prion diseases, Prions.


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INTRODUCTION

Prion diseases have recently exploded as a significant health care problem worldwide. They are a group of neurodegenerative diseases, invariably fatal and seen in both animals and in humans. They are also called transmissible spongiform encephalopathies (TSEs) which comprise variants like human spongiform encephalopathy, bovine spongiform encephalopathy (BSE), Kuru disease, and the most infectious of the lot – Creutzfeldt–Jakob disease (CJD). They are caused by abnormal protein-like particles that lack nucleic acids and form widespread plaques in the nervous tissues of infected persons. Although they predominantly localize in the central nervous tissue and the lymphoreticular tissues, the mode of infection is through oral route and hence the need for awareness of accidental iatrogenic spread. As the abnormal prion proteins are resistant to inactivation by conventional surgical decontamination and sterilization procedures, the possibility of cross-contamination in an iatrogenic setting is an ever-increasing threat. Although the literature does not describe any iatrogenic transmission of prion infections during periodontal surgical procedures, the theoretical possibilities of such occurring in the near future should be kept in mind. Hence, this article reviews the published literature on PubMed and Medline with reference to oral localization and uses the data obtained to describe a brief overview of the current issues involved in iatrogenic transmission and infection control protocols for prevention of the same during periodontal surgical procedures.

ETIOPATHOGENESIS

Prion proteins, the infectious agent which causes prion diseases, were first purified by Stanley B Prusiner who won the Nobel Prize in medicine in 1997 for it. Prion diseases which are now known as TSEs occur naturally in both animals and humans. All have long incubation periods of months to years, leading to death over a short period after the onset of the symptoms of acute neurological disease. There is no host immune response but only a noninflammatory pathologic process in the central nervous system (CNS). The vacuolation of the grey matter of CNS gives rise to the descriptive term “spongiform” encephalopathy. Although the infectivity of the proteinaceous particles is found to be highest in nervous tissue and it is also present in peripheral tissues (reticulolymphoid tissues), the literature is silent on its presence in body fluids, including saliva.

Prusiner who was the first to isolate them, defined prions as infectious, transmissible proteinaceous particles that lack nucleic acid. The infectious agents are unique in containing no detectable nucleic acids and are composed of an abnormal isoform of a host membrane...
sialoglycoprotein called “prion protein”—PrP. The normal or cellular form of the prion protein (PrPc) exists as a soluble, protease-sensitive cell-surface protein on many cells, especially in the CNS and lymphoreticular tissue.3

This normal cellular prion protein (PrPc) is encoded by the PrPc gene, which is located on the short arm of chromosome 20. Prion protein has predominantly alpha-helical structure, is soluble, and proteinase sensitive. The normal function of PrPc is not well known, but the suggested functions are signal transduction, cell adhesion, regulation, and distribution of acetylcholine receptors.4

Prion protein is transformed into abnormal isoform of the protein (PrPSc) due to posttranslational modification or mutation in the PrPc gene. Prion protein has predominantly beta structure, is insoluble, and partially proteinase resistant.5 This mutated PrPSc gives rise to TSEs, including BSE in cattle, scrapie in sheep and goats, and CJD in humans. These diseases are characterized by vacuolization of the gray matter, and these vacuoles are located in the neutrophils between the nerve cell bodies.6

Based on the etiopathogenesis, several different types of human TSEs have been recognized. The TSEs in humans include the following six types:7

1. Sporadic (classic) CJD – This is the most common type of CJD accounting for 85% of all CJD cases, occurring in middle or older age groups. The disease is characterized by progressive dementia, ataxia, myoclonus, cortical blindness, akinesia, and speech loss, followed by death within 4 months.

2. Iatrogenic CJD – This disease occurs following neurosurgery, dura mater transplantation, corneal grafting, and injection of pituitary hormones obtained from human cadavers. This type of prion disease is important to dentists due to the risk of cross-contamination after the use of infected dental instruments. The incubation period is variable, ranging from 2 to 35 years. The clinical features are similar to sporadic form, but cerebellar motor symptoms are predominant in this type.

3. Variant CJD (vCJD) – This type is associated with the intake of BSE-contaminated beef and beef products. The disease is characterized by depression, delirium, hallucinations, paresthesia, and dysesthesia in hands, feet, and mouth followed by dementia and akinesia. Deposition of amyloid plaques in the lymphatic tissues throughout the body is a prominent feature.

4. Kuru – This is endemic in Papua New Guinea and is transmitted by intake of infected nervous tissue in cannibalistic practices. The disease is characterized by ataxia, tremors, dysarthria, and death. Though cannibalism was banned in 1950, the incubation period is more than 40 years and the chance of appearance of new cases is still possible.

5. Fatal familial insomnia – It presents with progressive insomnia, dysautonomy in the form of hyperthermia, myosis, and loss of sphincter control, followed by dysarthria, tremors, motor dysfunction, and cognitive deterioration. Death occurs within 7–18 months.


**ORAL MANIFESTATIONS OF PRION DISEASES**

Oral manifestations are very rarely seen in prion diseases. Dysphagia (difficulty in swallowing) and dysarthria (poor articulation of speech) are noticed in all forms of human TSEs. Dysphagia and dysarthria could be early symptoms of the disease and occur as a consequence of pseudobulbar paralysis.8,9 In vCJD, paresthesia (tingling, pricking, or numbness), orofacial dysesthesia (abnormal sensations in the absence of stimulation), and one case of loss of taste and smell have been reported in the literature.1 The patient reported in Reuber et al had an unusual presentation: a 12-month history of loss of taste and smell, anxiety, low mood, and unusually short temper. He first became aware that something was wrong when he lost the ability to differentiate the taste of tea from that of beer. Loss of taste and personality change progressed gradually. He began to crave vanilla ice cream although he had never liked sweet foods in the past.1

Studies on human oral tissues for the presence of PrPSc showed positivity in a limited number of oral tissues.10 It seems likely that the oral tissues containing the highest infectivity will be located in the oral lymphoreticular region. Within the oral cavity, the largest collections of lymphoid tissues are located in the submucous tissue of the posterior third of the tongue, termed the lingual tonsil. Various human tissues like tonsil, tongue, submandibular and parotid salivary glands, trigeminal ganglia, inferior alveolar nerve, dental pulp, and gingiva taken from different postmortem cases of vCJD were analyzed for the presence of PrPSc.10 Majority of the cases showed positive PrPSc in tonsils and trigeminal ganglia, while the other human tissues were negative for PrPSc. Western blot, paraffin-embedded tissue blot, and immunohistochemical techniques were used for the study by Head et al10 in 2003 and the sensitivity of these assay indicated that PrPSc must have been at the level of less than 1% of that found in the brain tissue.

Presence of PrPSc in trigeminal ganglia may raise concerns about the extent of deposition of PrPSc along the cranial nerves and possible extension into oral and nasal
of transmission of prion infections during periodontal procedures. In the theoretical possibility of exposure to blood by needlestick injuries during treatment of a patient with preexisting prion disease, the World Health Organization (WHO) guidelines for decontamination with occupational exposure which recommends simple procedures like gently encouraging bleeding, washing with warm soapy water, covering with waterproof dressing, etc., should be followed.  

### Methods of Decontamination and Sterilization

The WHO has published the results of a detailed analysis of the risks of transmission of prion diseases during dental procedures. The WHO report concludes that oral tissues are of low infectivity, hence universal cross-infection control and generic decontamination procedures are sufficient for prevention of any iatrogenic transmission.  

**Steam sterilization:** Generic steam sterilization at 121 or 126°C for 15 minutes is only partially effective against most prion strains.  

**Chemical sterilization:** The Association for Professionals in Infection Control and Epidemiology (APIC) advocates use of both sodium hypochlorite (NaClO) and sodium hydroxide (NaOH) as the most effective disinfectants for reducing the transmission of prions. The APIC recommends concentrations of 5.2% for 1 hour to eradicate all infectivity.  

Finally, the WHO recommends that in case of patients with known prion disease, all instruments used in the treatment of such disease should be discarded after use or alternatively only single-use instruments are recommended for preexisting prion disease patients for preventing iatrogenic transmission.

### Prions in Periodontitis

To identify the relevant literature and published articles from the electronic databases PubMed and Medline, the search terms “Prions,” “Prion Diseases,” “Periodontitis,” “Periodontal Transmission,” and “Iatrogenic Transmission” were incorporated in the search parameters and returned a total citations of 1,198, with the keywords in either the titles or abstracts. After eliminating duplicate article listings, we discarded animal studies and selected only human studies and review articles written in English. Finally, we studied a total of 27 published reports and reviews from PubMed and Medline on the link between prions and oral transmission, manifestation and implications for treatment. Out of the total, there was nil mention in the literature about any reported incidence of cross-infection during periodontal surgical procedures.

The risk of transmission during regenerative periodontal procedures by using allogenic grafts infected with prion proteins is the primary concern of any periodontist, but is largely superseded by sourcing the grafts from accredited tissue banks which have stringent decontamination protocols and can guarantee the sterility of tissues provided as allogenic grafts for guided tissue or bone regeneration procedures.  

But the risk of iatrogenic transmission during periodontal surgeries with inadequately decontaminated surgical instruments does exist and is cause for concern in future. Hence, there is need for further research in this area to establish the susceptibility of periodontal tissues to prion infections and to determine the exact infectivity of prion-containing tissues. Especially given the long incubation periods of prion diseases (with asymptomatic patients) and transmission through blood and blood-related products, there is a clear theoretical but real risk of transmission of prion infections during periodontal procedures. In the theoretical possibility of exposure to blood by needlestick injuries during treatment of a patient with preexisting prion disease, the World Health Organization (WHO) guidelines for decontamination with occupational exposure which recommends simple procedures like gently encouraging bleeding, washing with warm soapy water, covering with waterproof dressing, etc., should be followed.

**CONCLUSION**

Prions are a unique form of pathogens which cause disease without initiating any of the traditional immune responses of the human body normally seen with other bodily invaders. They occur naturally, are transmissible...
both naturally and iatrogenically, and have long incubation periods with a fatal result, with the identifying feature of a nil host response and complete absence of any inflammatory process. Although previously considered as a rare neurodegenerative disease, prion diseases have exploded in importance in recent times with the discovery of the variant form of CJD which is primarily a human disease. Current epidemiological results based on open web search do not support human transmission iatrogenically, but given the long incubation periods and fatal outcomes, the need for developing foolproof sterilization and disinfection protocols to prevent cross-infection of prions during periodontal surgeries becomes the need of the hour. Also, education of periodontists and general dentists about the implications of prion disease transmission devolves on an increased need for research on prion diseases. Finally, in order to allay the fears of patients who express concerns about cross-infections in dental clinics, every dental surgeon should be aware of and practice the best sterilization procedures recommended by expert bodies like the WHO.

The oral cavity is a reservoir for a large number of microorganisms including bacteria and viruses. This ecological niche can be a pool for opportunistic and pathogenic microorganisms that can pose a risk for cross-contamination and infection and may even cause systemic infections. This is of particular importance in the case of routine dental practice, as the risk of exposure to microorganisms in the oral cavity is increased due to the open and invasive nature of the procedures.15

REFERENCES