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PRIONS IN DENTISTRY – A REVIEW

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ABSTRACT

Prion diseases are unique group of neurodegenerative diseases including the transmissible spongiform encephalopathies associated with a unique class of infectious proteins. Awareness about the transmission of these diseases during dental care is very low as the knowledge of such existence is indeed rare. Despite the extensive research in this field based on the proposed pathogenesis the diagnosis and management of the disease requires still further studies. The risk of transmission of prions through dental procedures draws our attention towards the need to maintain optimal standards of infection control and decontamination procedures for all infectious agents, especially prions. Hence this review is presented here to throw the light on this rare infection.

Keywords: Prions, Creutzfeldt-Jakob disease, Transmissible spongiform encephalopathies, Neurological disease, Prion protein.

INTRODUCTION

Prions are abnormal protein molecules that can spread and change the structure of their normal counterparts (cellular proteins) [1]. Prion diseases, also called spongiform encephalopathies, are fatal neurodegenerative disorders that have attracted enormous attention not only for their unique biological features but also for their impact on public health. This group of diseases includes kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Stra¨ussler syndrome (GSS), and fatal familial insomnia (FFI) in human beings, as well as scrapie in sheep and goats, bovine spongiform encephalopathy (BSE) in cattle, and encephalopathies in mink, cats, mule deer, elk, and several exotic ungulates.

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Prion Hypothesis

The unusual properties of the infectious agent became the focus of attention beginning in the 1960s, and in the early 1980s. Stanley Prusiner, building upon earlier suggestions, proposed the prion hypothesis. This stated that

the infectious agent in human and animal spongiform encephalopathies was composed exclusively of a single kind of protein molecule designated PrPSc without any encoding nucleic acid. Subsequent work has shown that PrPSc is, in fact, a conformationally altered form of normal, host-encoded membrane glycoprotein called PrPC. It was proposed that PrPSc impresses its abnormal conformation on PrPC, thereby generating additional molecules of PrPSc in an autocatalytic reaction. Prion diseases therefore exemplify a novel pathogenic mechanism based on a self-propagating change in protein conformation [2].

In prion diseases, the prion agent is primarily found in the lymphoreticular and nervous systems. In both natural and experimental prion infections, the prion agent is commonly amplified by replicating in the lymphoreticular system prior to entry into nerve cells and subsequent invasion of the brain. Spread within the nervous system can occur by transport along axons and between synaptically linked neurons. Experimental studies have demonstrated that the initial pattern of prion agent spread in the spinal cord and brain follows defined autonomic, sensory, and motor pathways modest levels of prion agent replication in skeletal muscle have been reported in a few studies following intracerebral or extraneural inoculation of the prion agent. Prion infectivity in skeletal muscle was first demonstrated in mink with transmissible mink encephalopathy (TME); the amount of infectious agent in skeletal muscle was 10,000 fold less than the amount found in brain [1] (See Table 1).

Transmissible Spongiform Encephalopathies (TSEs)

TSEs (also known as prion diseases) occur naturally in animals and humans (Prusiner, 2001). All have long incubation periods of months to years, leading to death over a short period after the onset of neurological disease. None evokes a host immune response, and all share a common noninflammatory pathologic process in the central nervous system, with vacuolation of the grey matter (hence "spongiform" encephalopathy) [4].

Summary of Different Types of Human TSEs

Types of CJD

Sporadic CJD (sCJD) -

The most common form of human TSE. Occurs worldwide with an incidence of approximately 1 case per million population per year. There is no convincing evidence of an environmental source of infection.

Familial CJD (fCJD) -

Between 10 and 15% of individuals with CJD have a family history consistent with autosomal-dominant inheritance. Over 20 different mutations in the PrP gene have now been described. On average, fCJD has an earlier age of onset and a more prolonged course than sCJD. Several mutations lead to phenotypes that have been regarded as different diseases—for example, Gerstman-Straussler-Scheinker disease.

Acquired CJD - Kuru

This disease reached epidemic proportions among the Fore ethnic group in Papua New Guinea. The disease was spread by ritualistic cannibalism. Since the practice ceased about 40 years ago, Kuru has declined, but occasional cases are still reported, indicating the lengthy incubation periods that can occur in this disease.

Iatrogenic (iCJD) - Surgical transmission

The first case was reported in 1974, when rapidly progressive neurological disease developed in a woman 18 months after a corneal transplant. Subsequently, 114 cases of CJD have been recognized 1.6 to 17 years after neurosurgical placement of grafts of human cadaver dura mater. Contaminated neurosurgical instruments have also been implicated in transmission of CJD.

Iatrogenic (iCJD) - Pituitary hormones

In 1985, CJD developed in four patients, all aged under 40 years, who had received human pituitary growth hormone 4 to 15 years before the onset of disease. In the UK, approximately 2% of recipients have been affected, with a mean incubation period of 12 years. Recombinant growth hormone was licensed in 1985 and is now used in many countries. Contaminated human pituitary gonadotrophin has also been linked with CJD.

Variant CJD (vCJD) -

First reported in the UK in 1996. Experimental data strongly link consumption of BSE-contaminated material with the vCJD agent. Differs from other types of human TSE by appearance of infectious agent outside the central nervous system [4].

Human TSEs present several significant challenges to those working in health care, including neurology, surgery, and dentistry. CJD in humans has been shown to be transmissible *via* several routes, including transplantation, contaminated medical products, and *via* neurosurgery. While the likelihood of transmission *via* dentistry is undoubtedly very low, this may be amplified considerably by unknown risk factors, such as disease prevalence (particularly in the UK), altered tissue distribution of vCJD, and the failure of decontamination processes to address the inactivation of prions adequately [5].

The biochemical marker of prion disease (PrPSc) is protease- and heatresistant, and binds strongly to stainless steel, and, therefore, is difficult to remove from surgical instruments by routine cleaning [6]. Endodontic files are used in dental procedures involved in the maintenance of dental pulp and the treatment of the pulp cavity, which includes blood and peripheral nerve tissue known to carry vCJD. Since endodontic files have an

intricate surface topography with a high 'surface area to volume' ratio, their intricate surfaces are able to trap protein, which is tenaciously attached to the surface through subsequent autoclaving cycles.

Despite many years of research, there is still no treatment or prophylaxis for this invariably fatal disease, and no diagnostic test to identify individuals with this disease. Additionally, the agent of the disease is a protein that is remarkably resistant to inactivation by conventional methods, raising concerns about transmission among healthcare professionals [5].

TSE agents are at best only partially inactivated using the sterilization techniques currently available in primary dental care as they are far more resistant to physical and chemical inactivation than conventional pathogens. WHO guidelines suggest the use of (a) immersion in sodium hypochlorite (20,000 ppm available chlorine) for one hour, (b) boiling in 1M sodium hydroxide for one hour, or (c) vacuum autoclaving at 121°C for 30-90 minutes in the presence of 2M sodium hydroxide for the inactivation of prions. Such procedures are inappropriate for surgical or dental instruments due to degradation and tarnishing of the metal surface, hazards to the user and issues with disposal [6].

The handpiece cannot be connected to the waterline. A separate, disposable method of suction, not the suction system of the dental unit, should be used on the patient. Whenever possible, disposable instruments should be employed [7]. Currently, there are three options to reduce instrument contamination with prions: disposal/incineration, chemical immersion, and physical processes (eg, autoclaving). (See Table 2).

Table 1. Etiological classification [3]

Sporadic	Sporadic Creutzfeldt – Jakob disease Sporadic fatal insomnia Variable protease – sensitive prionopathy
Hereditary	Familial creutzfeldt – Jakob disease Fatal familial insomnia Gerstmann – Sträussler – Scheinker disease
Acquired	Kuru Variant Creutzfeldt – Jakob disease Iatrogenic Creutzfeldt – Jakob disease

Table 2. Recommendations for inactivation of human infectious prions [8]

Incineration Use for all disposable instruments, materials, and wastes. Preferred method for all instruments exposed to highly infectious tissues.
Chemical methods (for surfaces, heat sensitive instruments, and histologic samples) Flood with 1N sodium hydroxide (NaOH) or 1N (20,000 ppm available) sodium hypochlorite (NaOCI)*; let stand for 1 hour; mop up and rinse with water. Where surfaces cannot tolerate NaOH or NaOCI, thorough cleaning will remove most infectivity by dilution. Some additional benefit may be derived from the use of another partially effective method, such as other chemical disinfectants. For histologic samples only, immersed in 96% formic acid tor 1 hour.
Physical process (autoclave/chemical methods for heat-resistant instruments) Thorough physical cleaning followed by immersion in NaOH or NaOCI (20,000 ppm available chlorine) for 1 hour; transfer instruments to water; autoclave in a porous load steam sterilizer at 134°C to 138°C for 18 minutes (or 6 successive cycles of 3 minutes each).ǂ
*NaOH is less harsh on instruments. ǂKnown not to be completely effective; eg, in the worst case scenarios, such as tissues bake-dried onto surfaces, infectivity will be largely but not completely removed.

CONCLUSION

There is a theoretical, yet real risk of prion disease transmission through dental treatment, although the magnitude of that risk has yet to be determined. Dental and other health care professionals need to understand these emerging diseases so that reasonable and practical changes to dental public health and infection control policies can be implemented [8]. It is difficult to inactivate prions, in particular, it is essential that all instruments are destroyed and not reused on any other patient [7].

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