Bahrain Medical Bulletin, Volume 18, Number 3, September 1996

Editorial

TO BEEF OR NOT TO BEEF

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In recent months, Bovine Spongiform Encephalopathy (BSE) or what is commonly known as "Mad Cow Disease" has made the headlines mainly as a consequence of the announcement by the British Spongiform Encephalopathy Advisory Committee on March 20, 1996 that 10 atypical cases of Creutzfeldt-Jacob disease (CJD), the human equivalent of BSE, were detected and their suspicion that these could have been caused by the consumption of beef or beef products from cattle affected by BSE[1].

BSE, a neurodegenerative disease of cattle, was first recognised in Britain in 1986. The disease was traced back to rendered sheep offal used as cattle feed supplement[2]. Sheep have a similar neurodegenerative disease, Scrapie, known to exist in the British Isles for several centuries[2]. Between 1986 and 1995 approximately 150,000 cases of BSE were confirmed in the United Kingdom. By May 1995, it had been reported from 10 countries outside the UK. Scrapie had not been documented to be naturally transmitted to any other animal species or man.

If the suspicions of the investigators concerning a relationship between BSE and the atypical CJD cases detected are substantiated, then the agent of the disease has managed to jump species yet another time1. To achieve this agent must have had to undergo some modification to break the species barrier, a change which may have also endowed it with increased transmissibility and pathogenicity. The transmissible nature of scrapie has been recognised for many years[2], but the agent, originally suspected of being a virus or viroid (transmissible circular double stranded RNA agent), defied isolation or identification.

Reports by scientists at the Hammersmith Hospital in London[3] that the agent might lack nucleic acids due to its resistance to ultraviolet and ionizing radiation stimulated further research into unraveling the nature of this unusual agent. Prusiner, in San Francisco, spearheaded research to identify the causative agent of the group of known spongiform diseases of man and animals, including Kuru, CJD

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Gerstmann-Sträussler-Scheinker disease (GSS), Fatal Familial Insomnia (FFI), and scrapie. He was able to isolate the proteinaceous substance causing scrapie and to produce enough data to support the original suspicion that the agent may not contain any nucleic acids[4,5]. This new proteinaceous infectious agent was dubbed "Prion"[4].

The concept of an infectious agent devoid of nucleic acids is difficult to reconcile with scientific dogma. However, further revelations of the origin and mode of action of Prions served to elucidate this dilemma.

In 1985 it was shown that Prion Protein (PrP) was coded for by a cellular gene[6,7]. Native cellular PrP (PrPc) was shown not to be disease-causing[8,9]. The difference between PrPc and disease-causing scrapie prion protein (PrPsc) appears to lie in differences in their secondary structure. A change in the

secondary structure of PrPc is induced either by extraneous PrPSc or a mutation in the PrPc gene resulting in an amino acid substitution influencing the folding of the native protein[10-12]. This explained the mystery of the inheritance of some Prion diseases, including 10 to 15 % of CJD cases, GSS and FFI.

In earlier studies investigators found it difficult to experimentally transmit scrapie from sheep to mice[13]. This transmission was characterised by prolonged incubation periods, and led to the concept of the species barrier. It was later shown that the species barrier is a reflection of the differences in PrP gene sequences between species[10,14]. Given that sheep and cattle prions differ only in seven positions, one may accept the possibility of species-jumping. However, as the difference between cattle and human prions is in more than 30 positions, one must be concerned about the possibility of unusual circumstances, which may have facilitated this species jump.

Phylogenetic analysis of prion proteins strikingly identified two pairs of amino acid substitutions uniquely shared by cattle and hominoids. These substitutions are in a part of the gene postulated to be involved in acquisition of prion diseases[15]. One can postulate then that cattle, by this shared similarity acted as an intermediate host which facilitated the infectious transmission of scrapie from sheep to humans.

It is noticeable in the last decades that new or unusual diseases, mostly viral, are on the rise, some of which, such as HIV, have reached pandemic proportions. Whether BSE/CJD will be added to this apparently growing list deserves serious consideration.

Evidence of oral transmission of prion diseases, is unquestionable as Kuru is known to be transmitted through cannibalistic rituals of the Fore tribes of Papua New Guinea[16]. In addition, CJD has been documented to be transmitted through the transplantation of organs or tissues from CJD-affected donors[2]. Community concern about the safety of beef and beef products is justified and shared by medical authorities. The absence of a reliable test to detect the presence of disease-causing prions in animal products or to detect cases of BSE before symptoms are apparent underlies this concern. Additionally whether prion diseases may be transmitted through medicinal or other products extracted from cattle including insulin, heparin, gelatin, lactose or serum proteins has not been satisfactorily resolved. In spite of assurances of treatments which eliminate or inactivate prions, the potential risk of contracting CJD through oral or parenteral contact with beef products will remain to be an unquantifiable risk. One should not confuse the lack of evidence with the absence of risk.

As the dismissals of politicians of the possible transmission of BSE to humans in the 1980s led to the identification of the new clinicopathological CJD variant in the 90s, one wonders what the 21st century may further reveal, particularly as six new suspicious cases of CJD are being investigated in the UK.

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