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A Pathological Review of Controversy Over U.S. Beef Imports and BSE Risk Perception in Korea

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Abstract

The Bovine Spongiform Encephalitis (BSE), also called as 'Mad Cow Disease', outbreaks created fear and social conflict in 2008 and 2012 in Korea, and their impacts still remain present. Therefore, the Korean government must raise public understanding of BSE issues by providing the accurate scientific data and implement reasonable and effective policies for socially acceptable solutions. We examined the pathological aspects of BSE by a review of the literature, including news articles. We focused on the five key controversies over BSE-infected beef from U.S. from a science communication perspective, such as (1) association between degenerative brain disease and vCJD, (2) prevalence of human vCJD, (3) risk of vCJD infection associated with beef from 30-month-old cattle, (4) establishment of SRM range, and (5) the review of claims that Koreans are genetically susceptible to CJD.

Key words: bovine spongiform encephalopathy, mad cow disease, U.S. beef controversy, vCJD, sCJD

Ⅰ. Introduction

In 2008, a controversy associated with US beef arose in Korea(Park, 2009), which has not yet been resolved. In July 2017, a resurgence of bovine spongiform encephalitis(BSE) was again reported in the US, which resulted in a renewed focus on BSE in Korea, leading to implementation of more stringent inspection and quarantine measures by the Korean government(Park, 2017). This phenomenon may reignite the conflict.

Ⅱ. Research Hypothesis & Methods

Thus, we here identified five key issues pertinent to the BSE crisis in Korea by reviewing the relevant media coverage and performing questionnaire surveys among Koreans, and analyzed the data obtained from veterinary, molecular biological and pathological perspectives. The present study analyzed 3,212 news articles on the BSE crisis publiched by seven Korean press companies(four daily newspapers and three

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broadcasting services) for 2007-2017, selected by three science reporters and expert in global trade. Then, based on a review of 200 relevant studies, we examined the five key issues pertaining to the possibility of BSE in Korea and the risk of infection. These five key points were 1) the association between degenerative brain disease and variant Creutzfeldt-Jakob disease(vCJD); 2) the prevalence of human vCJD; 3) the risk of vCJD infection inherent to consuming cattle aged 30 months or older, 4) the range of specified risk material(SRM); and 5) the vulnerability of Koreans to Creutzfeldt-Jakob disease (CJD). First, sporadic Creutzfeldt-Jakob disease(sCJD) can be differentiated from variant Creutzfeldt-Jakob disease(vCJD) which can be contracted from consuming BSE-infected beef and these two conditions were poorly associated. Second, vCJD is a rare disease with very low prevalence in humans; no case of human vCJD has been reported in Korea yet. Third, the risk of contracting vCJD from consuming beef from under 30-month-old cattle is thought to be very low. Fourth, the range of specified risk material(SRM) needs to consider more than the presence of the variant prion alone. Fifth, the methionine/methionine(M/M) genotype at codon 129 of PRNP in Korean may confer susceptibility to prion disease.

Ⅲ. Results

1. Association between degenerative brain disease and vCJD

vCJD is a degenerative brain disease involving nerve changes. Symptoms include loss of body control and severe mood swings. However, clinical differential diagnosis is difficult due to symptomatic overlap with other neurological diseases such as Alzheimer's disease(Kelleher, *et. al.*, 2004). Brain tissues from patients with Alzheimer's disease were injected into the brains of β-amyloid precursor protein-transgenic mice or primates, and facilitated abnormal protein accumulation. Thus, during the controversy surrounding US beef in Korea, there was a concern that relaxed inspection standards for US-imported beef would result in patients contracting vCJD by consuming BSE-infected beef, but that they would be misdiagnosed. The brain tissues of patients with sCJD show 5-20-μm vacuoles, while those of patients with vCJD characteristically show amyloid plaque deposits containing high levels of variant prion proteins(PRNP); these are absent in sCJD(Kane, *et. al.*, 2000). In western blotting- based strain classification, sCJD mostly shows prion types 1 and 2, whereas vCJD shows type 4(Yull, *et. al.*, 2006). Additionally, while sCJD involves hypertrophy of the caudate nuclei and putamen, bilaterally, vCJD shows high signal intensity in the posterior thalamus(Molloy, *et. al.*, 2000). Moreover, sCJD initially causes lesions in brain regions with densely populated nerve tissues, subsequently progressing to the central nervous system(CNS), and then to the peripheral nervous system(PNS). However, in vCJD, prions in tainted food enters the body through the intestines(PNS), and then moves through the PNS to the CNS, returning to the PNS again(Mabbott, 2006). Consequently, neurological symptoms appear earlier in sCJD than in vCJD, while vCJD progresses more rapidly. Detection of such PRNPs is relatively easy through tissue biopsy, decreasing the likelihood of confusing the two diseases. The association between the prevalence of sCJD and BSE should be examined as well(Donnelly & Ferguson, 1999).

2. Prevalence of human vCJD

Korea defines diseases with fewer than 20,000 domestic patients as rare. sCJD has a prevalence of 1 in 1,000,000(Will, *et. al.*, 1998). In 1999, when vCJD prevalence peaked in the UK, there were 29 patients with vCJD, equating to 1 in 2 million people. In 2006, the prevalence was roughly 1 in 20million people, while in 2007, there was no case of vCJD. Relative to a total population of 930 million in three regions comprising the EU(500million), the US(300million),and Japan(130million), the total number of new vCJD cases in 2006 was 9, indicating a vCJD prevalence of 1 in 100,000,000. The probability of vCJD occurring in Korea is even less likely. Modified prions develop into more toxic strains with transmission from different individuals, such as from cow to cow, sheep to sheep, and sheep to cow. Unlike in the UK, scrapie is not prevalent in Korea. While the EU implemented various regulations to prevent BSE, Korea did not implement regulation stop revent BSE; nevertheless, there have been no cases of BSE or vCJD in Korea. The species barrier is important in BSE transmission. There is a significant difference between human- to-human and cow-to-human transmission(Sikorska, *et. al.*, 2012). For kuru, which involves human- to-human transmission, 2,700 people in the Fore tribe, among a total population of less than 50,000, were infected between 1957 and 2004(Collinge, *et. al.*, 2006). In contrast, only 177 British victims of vCJD, a disease with cow-to-human transmission, were reported among over 50 million British people consuming BSE-infected beef. Despite involving the same prion, kuru and vCJD have different infectivities because Fore people consumed meat from the same species (other humans), whereas the British people consumed meat from a different species (cows). In humans, the PRNP open reading frame is 759 base pairs, from which 253-residue proteins are produced. About these numbers and amino acid sequences vary across species, but the differences are fewer among evolutionarily closely related species(WHO, 2006): cow and sheep PRNP are very similar (94%), and human and monkey PRNP are similar. As cow and human PRNP are somewhat dissimilar (88%)(Scott, *et. al.*, 2005), most individuals who unknowingly consuming BSE-infected beef were likely not infected due to this species barrier(〈Table 1〉).

The British government confirmed that BSE started in cattle, not sheep(Anderson, *et. al.*, 1996). BSE was first reported in the early 1980s, and by the mid-1980s, many cattle were infected. BSE may already have occurred during the 1970s and undergone several cycles over 10 years. Cows infected with naturally occurring BSE were slaughtered and the

Table 1. Similarities of the prion amino acid sequence across species (%)

	Number of amino acids	Human	Mouse	Hamster	Sheep	Cattle	Mink
Human	253	-	89	87	90	88	88
Mouse	254		-	93	87	84	84
Hamster	254			-	88	96	85
Sheep	256				-	94	94
Cattle	256/264					-	93
Mink	257						-

※ Source: Yoo(2008).

by products were used to make meat and bone meal(Brown, *et. al.*, 2001). A few cattle that consumed the tainted meat and bone meal would have been infected with BSE, and then byproducts from these newly infected cattle were reintroduced as feed, etc. The practice of feeding cattle with meat and bone meal from ruminants is now prohibited, preventing introduction of large amounts of tainted meat and bone meal, and markedly reducing the likelihood re-occurrence of a similar BSE outbreak in the UK. To confirm inactivation of prions by heating, a dry heat experiment, involving temperatures of 150℃-1,000℃ for 5-15 min, was conducted on scrapie tissues. When these tissues were directly injected into the brains of hamsters, 5 of 35 hamsters were infected, indicating that variant PRNPs could remain active and pathogenic even after high-temperature heating. Further experiments on changes in prion infectivity(263K strain) involved adjusting the heating time and temperature, and heating in the presence of water, fat, both water and fat, and glycerol(Appel, *et. al.*, 2001). Infectivity was reduced 5,000-10,000-fold with heating at 90℃ for 20-60 min in a solution of 90% fat and 10% water. Heating for longer than 180 min reduced infectivity 10,000-100,000-fold, while heating at temperatures above 100℃ reduced it further(〈Table 2〉). This may be due to changes in protein structure, which allowed fat to hinder dimerization(Garcia, *et. al.*, 2006).

Table 2. Reduced infectivity of pathogenic prion according to heating temperature

Condition	Temperature (℃)	Degree of reduction of infectivity
Heat for 20 minutes with 100% fat	110	40 thousand times
	140	20 thousand times
	170	〉100 thousand times
	200	〉100 thousand times
Heat for 20 minutes with 90% fat and 10% water	70	500 times
	80	400 times
	90	1 thousand times
	100	5 thousand times
	110	16 thousand times
	140	〉100 thousand times
	170	〉100 thousand times
	200	4 thousand times
Heat at 90 degrees with 90% fat and 10% water	60 minutes	5 thousand times
	180 minutes	10 thousand times
	540 minutes	1 thousand times
Heat for 20 minutes with 100% water	80	3 times
	90	50 times
	110	1000 times
	140	〉100 thousand times
	170	〉100 thousand times
Heat for 20 minutes with 90% water and 10% glycerol	80	10 times
	110	400 times
	140	6,000 times
	170	30 thousand times
Heat for 20 minutes with 100% glycerol	110	10 times
	140	250 times
	170	4,000 times
	200	〉100 thousand times

※ Source: Yoo(2008).

3. Risk of vCJD infection associated with beef from 30-month-old cattle

After the first vCJD-related death in the UK in 1996, the British government banned the slaughter of cattle aged 30months (equivalent to 8 years in humans) or older and incinerated all available stock(Gale, 2006). Cows with two permanent teeth at slaughtering were considered under, and those with three teeth were considered to be 30 months (Legname, *et. al.*, 2004). Approximately 4.5 million cows were slaughtered between 1996 and 2001. This age was chosen because most BSE-infected cattle showed clinical signs after this age. The average latent period in BSE-infected cattle is 48-60 months, while the infection period is 12 months; however, since the possibility of earlier infection

could not be excluded, 30 months was set as a conservative cut-off. To determine the route by which prions travel from the small intestines to the brain or spinal cord, and the duration of this process, a pathogenesis experiment was conducted on sheep(van Keulen, *et. al.*, 2008). Eleven sheep aged 4-5 months were fed the medulla-obex of BSE-infected cattle brain. Seven of the 11 sheep were autopsied; one each at 6, 9, 12, 13, 15, 17, and 19 months after starting this feeding. Variant prions were initially found in the tonsils and ileal Peyer's patches at 6 months after initial consumption. At 9 months, variant prions appeared in the gut-associated lymphoid tissue(GALT) and spleen. At 12-13 months, lesions spread to both sides in the brain and spinal cord. From 17 months after consumption, the variant prions moved up from the brain stem to the cerebrum, and from 19 months, the infection spread throughout the entire cerebrum and cerebellum. A similar experiment was conducted on 6-month-old calves(Espinosa, *et. al.*, 2007). After the animals were administered BSE-infected material, variant prions first appeared in the Peyer's patches after 6 months, while infection was confirmed in the tonsils after 10 months, and in the medulla oblongata after 27-30 months. Similar results were also found in a follow-up experiment on 230 cows(Arnold, *et. al.*, 2007). Therefore, even if asymptomatic BSE-infected cattle unknowingly entered the food chain, it would be highly unlikely that variant prions had accumulated in their nervous system by the age of 30 months.

BSE had occurred in some cattle younger than 30 months, for instance, in 84 cases in the UK, accounting for 0.05% of all BSE-infected cattle. However, no cases have been reported in the UK since June 1996. Twenty other cases were reported in European countries other than the UK, prior to the meat and bone meal ban. In Japan, two BSE-infected cows, a 21-month old and 23-month-old cow, were born after the cattle feed ban was enforced(Yamakawa, *et. al.*, 2003). The 23-month-old cow showed an atypical strain that differed from that found in cattle from the UK, while the other showed the UK cattle strain. Neither animal had variant prions in the medulla oblongata and the disease was unable to transmit to other animals. When we calculated the time of first detection of variant prion in the brain, the time of first infection is about 6 months + 27-30 months, that is, 33-36 months. Hence, cows aged 30 months or older plausible constitute the vCJD risk group, as tissues other than the tonsils, distal ileum, brain, and spinal cord, which are removed during slaughtering, were not infectious prior to the emergence of symptoms of BSE in a cow. Moreover, the spleen, muscles, and blood were not infectious, irrespective of symptom onset.

4. Establishment of SRM range

The SRM include cow organs showing an accumulation of variant prions, and thus, removal of SRM is considered the best method for preventing BSE(Balkema-Buschmann, *et. al.*, 2011). After demonstrations against the import of US beef in Korea in 2008, the permissible range of SRM was debated(Choi, 2011). The Korean government designated the tonsils and distal ileum as SRM, regardless of the age of the cattle, and later designated the brain, skull, eyes, spinal cord, and vertebral column from cattle 30-month-old as SRM. As the SRM range

expanded, some civic organizations and experts sharply criticized the government, protesting that such actions represented forfeiture of sovereignty over inspection and quarantine rights(Choe, 2008). The Korean government replied that these actions were taken in accordance with the Sanitary and Phytosanitary Measures Agreement established by the World Trade Organization, and the designation, by the International Organization for Animal Health(OIE) of the US as a "controlled BSE-risk country."(Korea Ministry of Agriculture, Food and Rural Affairs, 2008)

However, the OIE did not address regulations on SRM(OIE, 2007). Even if cattle parts or products were not subject to the trade ban, they may not have been scientifically proven to be safe. The OIE does not confirm the range of SRM based on experimental evidence, but by data from various sources, including the World Health Organization (WHO), and submits its findings to the general assembly. Each country's representatives use this data to establish the scope of their regulations according to mutual interests. The WHO does not specify regulations for defining SRM. It publishes BSE Tissue Infectivity Distribution reports, which only summarize the infectivity of tissues themselves (WHO, 2006), because it is difficult to establish the definition and range of SRM scientifically. The range of SRM is determined by applying the 50% lethal dose(LD50) based on titration. Accordingly, the OIE designated seven parts of over-30-month-old cattle as 'major SRM'(brain, skull, tongue, tonsils, eyes, spinal cord, and distal ileum), while the spine, mesentery, spleen, intestines, and feet were designated as 'other SRM.' However, specific regulations vary across countries. The US designated the transverse process, spinous process, and sacralis mediana of over-30-month-old cattle as SRM, while the EU lists the skull, eyes, and spinal cord of over-12-month-old cattle, and the back bone and dorsal root ganglia(DRG) of over-24-month-old cattle, as SRM.

In 2008, the Korean government argued that, because Korea and the US had no, or very few, instances of BSE, the SRM regulation could be much more relaxed than that of the EU, which had an incidence of nearly 200,000. However, this argument was unconvincing given the SRM regulation policy of Japan,which were more stringent than those of the EU, despite having only two instances of BSE(Tanaka, 2001). Britain designated intestines as SRM in 1994 because these serve as the main infection route and lymphatic tissues involved in the latent period of prion disease are distributed throughout the intestines. Accordingly, the EU also designated the intestines as SRM(Scientific Steering Committee, 1997). However, subsequent pathogenesis experiments did not detect pathogenic prions in the intestines, except in the distal ileum. An experiment on infectivity by tissue type showed that even the distal ileum did not have infectivity(Hoffmann, *et. al.*, 2011). The EU concluded that, during processing of intestines, parts other than the distal ileum may become tainted, and that the study that declared a lack of infectivity had an insufficient sample size; consequently, the intestines remained designated as SRM(European Food Safety Authority, 2007). In contrast, the US relaxed the SRM designation range to include only the distal ileum, rather than the entire intestine,based on these study results(US Department Of Health, 2005). Similarly, the US designated the brain and spinal cord of over-

30-month-old cattle as SRM, whereas the EU applied a cut-off of 20 months, as there had been incidences of BSE in 20-month-old cattle and the brain and spinal cord are tissues with the highest infectivity. Thus, it is difficult to establish the SRM range based on tissue infectivity and pathogenesis experiment results.

Ultimately, designation of the SRM range requires objective analysis and consideration of various political, cultural, and social factors, including the species of cattle raised, frequency of BSE, slaughter and meat processing, and government policies(Bickerstaff, *et. al.*, 2004). The amount of variant PRNP found in muscles was confirmed to be about 10,000-20,000 times less than that found in brain tissue(HERZOG, *et. al.*, 2005). If 5 g of brain tissue represents the LD50 of vCJD, then the LD50 of muscle tissues would be 50-100 kg of meat. Even if a person ate 1 kg of meat in a single sitting, that person would need to consume beef from BSE-infected cattle on at least 50 to 100 occasions to become infected with vCJD. Even if a person consumes BSE-infected meat from cattle and progressed to the point of showing clinical signs, it is extremely difficult to actually contract vCJD, otherwise, most people in the UK, excluding vegetarians and those with beef allergy, would have been infected with vCJD. In fact, atleast 150g of the brain of anasymptomatic BSE-infected cow must be consumed in order to be infected with vCJD, which is practically unlikely(Lasmezas, *et. al.*, 2005).

5. Review of claim that Koreans are genetically susceptible to CJD

Within the protein encoding region of PRNP, the amino acid sequence at codon 129 has three variants: M/M, M/V, and V/V. Analysis of PRNP in patients who died of vCJD in the UK showed that, without exception, all were M/M homozygotes at PRNP codon 129. Among the British population, the percentage of M/M, M/V, and V/V carriers is 36.79%, 50.94%, and 12.27%, respectively, and thus, M/M homozygosity in all vCJD patients is unlikely to be coincidental.

The percentage of Koreans carrying the M/M PRNP codon 129 variant is up to 94%(Jeong, *et. al.*, 2004), which is significantly higher than the 40-51% among Caucasians. During the BSE controversy in Korea in 2008, it was claimed that Koreans are genetically susceptible to vCJD,based on these findings. In addition to M/M, the G/L variant at this PRNP codon has also received attention, particularly in relation to its protective effect in suppressing the onset of vCJD(Shibuya, *et. al.*, 1998). An investigation of 85 Japanese patients with CJD showed complete absence of the G/L variant at PRNP codon 129. Statistically, this is unlikely given that 14% of the Japanese population have the G/L genotype. Thus, the G/L variant at PRNP codon 129 offers protection against the onset of sCJD. Interestingly, the G/L variant is more common among Koreans (7.94%) than Westerners (0%). Therefore, the potential effects of other genotypes at PRNP codon 129 should also be considered when focusing on genetic susceptibility(Lee, *et. al.*, 2001).

Age is also associated with vCJD infection (Ridley, *et. al.*, 1986). The average age of the 166 British patients who died of vCJD was 28 years. Considering a latent period of 13-16 years, these patients would first have been infected with variant prions at 10-12 years of age, or earlier, to show clinical signs at 28 years. The prevalence of vCJD

decreased sharply among those aged 40–59 years, while it was virtually absent among those aged 60 years or olde(Boelle, *et. al.*, 2004). Hence, considering the latent period, being exposed to BSE-infected beef from the age of 25–30 years does not always lead to disease onset, and being exposed at the age of 45–50 years led to almost no disease onset. The mathematical predication of vCJD latent periods and epidemiological scale was also investigated, by age(Rial, *et. al.*, 2009). The researchers predicted that the average vCJD latent period would be 16.7 years and the total number of patients would be approximately 205. There were no significant differences in the amount of beef consumed among those aged 20–59 years(Cooper & Bird, 2002). There may be an age class that is more susceptible to vCJD. The average age of vCJD onset was 28 years; latent period was 13–16 years; and the time of first infection was 10–20 years of age. The average age of vCJD onset at 28 years is a significant point. The onset of sheep scrapie is 2–3 years after birth and that of BSE is 5–7 years after birth. Considering their latent period (vCJD: 13–16 years, scrapie: 20 months, BSE: 4–6 years), these three diseases share the common feature of infection occurring in younger individuals. Variant prions can resist proteolytic enzymes and enter the body without degradation into amino acids, because variant PRNPs, which cannot be absorbed due to high molecular weight, are trapped by the M-cells in the Peyer's patches and drawn into the intestines (Hesketh, *et. al.*, 2008). Additionally, variant prions also infiltrate the body through dendritic cells and the submucosal plexus after passing through the Peyer's patch lymph nodes, or by binding with intestinal ferritin(Mabbot & MacPherson, 2006).

Consequently, infiltration of variant PRNP into the body is linked to development of Peyer's patches and GALT(Ryou, 2007). Thus, when Peyer's patches are immature, exposure to variant PRNP may not trigger a response to the infection. An experiment was conducted by reducing the Peyer's patches of rats through gene manipulation and feeding those rats variant PRNPs, in order to look for resistance (Prinz, *et. al.*, 2003). Rats with fewer Peyer's patches did not experience any difficulties after consuming variant PRNP. The relationship between the level of development of Peyer's patches and transmissible spongiform encephalopathy (TSE) susceptibility was investigated. The surface area of ileal Peyer's patches, lymphoid follicle density, and the weight and count of Peyer's patch tissue were investigated in 19 sheep, 94 cows, and 46 humans, and the correlation between the prevalent age of variant prion diseases and these factors was assessed(St Rose, *et. al.*, 2006).

The results indicated that, in sheep, the surface area of Peyer's patches and lymphoid follicle density peaked at about 12 months and decreased 12–24 months thereafter. The weight of Peyer's patch tissue in cows increase during the first 12 months, reached peak weight around 12–18 months, then decreases, and is maintained at a low level. This was also consistent with the pattern of BSE, in which infection peaks at 12 months. Humans show a pattern of increase in the number of Peyer's patches during childhood(Cornes, 1965), which reaches a peak during 10–20 years of age and decreases thereafter. This was also consistent with clinical signs of vCJD, which peak at around 15 years of age. With an immature immune system, intestinal permeability increases, and consequently, the risk of variant prion

absorption may also increase. From this perspective, it is surmised that 10–19 years represents a period when the immune system is being formed, and thus, age is a risk factor that increases intestinal permeability for variant prion infection.

Ⅳ. Recommendations and future directions

Taken together, we recommend the following. Since BSE outbreaks have previously caused fear and social conflict, it is necessary to identify the issues associated with BSE and respond reasonably. Therefore, the government must raise public understanding by providing accurate scientific facts, and implementing reasonable and effective policies that provide solutions that society can accept. Accordingly, we aim to continue our efforts in analyzing the state and contents of media reporting and identifying trends in the media, while conducting public awareness surveys to examine the associations between reported content and public awareness/attitude.

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한국의 미국산 쇠고기 논쟁 및 광우병 위험인식에 대한 병리학적 고찰

국문초록 한국에서는 2008년과 2012년, 미국산 쇠고기 수입에 반대하는 시위가 일어나 그 여파가 아직 이어지고 있다. 이런 혼란을 방지를 위해서는 광우병을 과학적 측면에서 접근해야 한다. 본 연구에서는 문헌조사를 통해 광우병의 병리학적 내용을 고찰한 뒤 광우병 파동의 5대 핵심쟁점에 대해 과학커뮤니케이션 측면에서 정리하였다. 그 결과는 다음과 같다. 첫째, 퇴행성 뇌 질병인 'sCJD'와 광우병 감염 소고기 섭취로 인해 발생하는 'sCJD'는 구분되며 연관성도 낮은 것으로 인정되었다. 둘째, 인간 대상 'vCJD'는 발병률이 매우 낮은 것으로 인정되는 희귀병이며 한국에서 발병한 적은 없다. 셋째, '30개월 이하 쇠고기로 인한 vCJD 발생 위험성'은 매우 낮은 것으로 인정된다. 넷째, 특정위험물질 'SRM' 범위는 변형 프리온 유무뿐 아니라 감염력 실험결과, 지역 내 광우병발병 빈도, 도축 과정 등을 복합적으로 고려해야 하는 '해석적 유연성'이 인정된다. 다섯째, 프리온 유전자(PRPN) 중 129번 아미노산의 'Methionine/Methionine형은 '프리온 질병에 대한 감수성'이 인정된다. 다만, 219번 아미노산의 Glutamic acid/Lysine형은 vCJD 발병에 저항성이 있는 것으로 확인됐는데, 이 'G/L형'은 서구인에 비해 한국인이 높아 '한국인의 vCJD에 취약성'을 언급할 때는 연령, 해부조직학적 구조 등 여러 요인을 종합적으로 고려해야 한다.

주제어 : 광우병, 광우병 감염소, 미국산 쇠고기, vCJD, sCJD, 산발성 크로이츠펠트-야콥병, 변형 크로이츠펠트-야콥병

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