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Committee on Sanitary and Phytosanitary Measures Original: English

VARIANT CREUTZFELDT-JAKOB DISEASE (VCJD)

Submission by the World Health Organization (WHO)[1]

1. Variant Creutzfeldt-Jakob disease (vCJD) is a rare and fatal human neuro-degenerative condition. Like Creutzfeldt-Jakob disease (CJD), vCJD is classified as a transmissible spongiform encephalopathy (TSE) because of characteristic spongy degeneration of the brain and its ability to be transmitted. vCJD is a new disease which was first described in March 1996.

2. Prior to the identification of vCJD, CJD was recognized to exist in only three forms: sporadic cases, which have an unknown cause; familial cases, associated with a gene mutation; and iatrogenic cases, which result from the accidental transmission of the causative agent via contaminated surgical equipment or as a result of cornea or dura mater transplants or human-derived pituitary growth hormones. 85-90 per cent of CJD cases are sporadic; 5-10 per cent are familial and less than 5 per cent are iatrogenic.

3. In contrast to the traditional forms of CJD, vCJD has affected younger patients (average age 29 years, as opposed to 65 years), has a relatively longer duration of illness (median of 14 months as opposed to 4.5 months) and is strongly linked to exposure, probably through food, to a TSE of cattle called Bovine Spongiform Encephalopathy (BSE).

Total cases

4. From October 1996 to early November 2000, 85 cases of vCJD have been reported in the United Kingdom, three in France and a single case in the Republic of Ireland. Insufficient information is available at present to make any well-founded prediction about the future number of vCJD cases.

Epidemiology

5. The first person to develop symptoms of what turned out to be vCJD became ill in January 1994. Most people who have developed vCJD have lived in the United Kingdom. Some of the patients had been long-standing residents in Wales, Scotland or Northern Ireland, and there was no preponderance of patients from any single part of the United Kingdom

6. As of early November 2000, the CJD surveillance unit for the United Kingdom reported 75 cases of vCJD, including 68 confirmed and seven probable cases. In addition, there are ten cases where vCJD is strongly suspected, but the diagnosis has not been definitively confirmed by post-mortem analysis. In addition, three people in France and one in Ireland have been diagnosed with vCJD.

[1] Fact Sheet N° 180, revised November 2000.

7. Some of these patients have donated blood. However, to date vCJD has never been known to have developed in a recipient of this blood; study of possible transmission through blood transfusion continues. The United Kingdom no longer sources plasma from its inhabitants, and as a further precautionary measure, has instituted leukocyte reduction (removal of white blood cells) from blood transfusions. Some countries have disallowed donations of blood from persons who have been resident of the United Kingdom for longer than six months.

Clinical features

8. Early in the illness, patients usually experience psychiatric symptoms, which most commonly take the form of depression or, less often, a schizophrenia-like psychosis. Unusual sensory symptoms, such as "stickiness" of the skin, have been experienced by half of the cases early in the illness. Neurological signs, including unsteadiness, difficulty walking and involuntary movements, develop as the illness progresses and, by the time of death, patients become completely immobile and mute.

Diagnosis

9. The clinical presentation, progressive nature of the disease and failure to find any other diagnosis are the hallmarks of vCJD.

10. There are no available, completely reliable diagnostic tests for use before the onset of clinical symptoms. However, magnetic resonance (MRI) scans and cerebrospinal fluid (CSF) tests may be useful diagnostic tests.

11. The brainwave pattern observed during an electroencephalogram (EEG) was abnormal in most of the vCJD patients, but the wave forms characteristic of sporadic CJD do not occur.

12. Currently the diagnosis of vCJD can only be confirmed following pathological examination of the brain. Characteristically, multiple microscopic and abnormal aggregates encircled by holes are seen, resulting in a daisy-like appearance described by the term "florid plaques".

Probable cause

13. vCJD is strongly linked with exposure to the BSE agent. BSE is a transmissible spongiform encephalopathy (TSE) affecting cattle and was first reported in the United Kingdom in 1986. Since that year, about 180,000 cases have been reported in the United Kingdom.

14. The most likely route of exposure was through food, although infectivity is mainly found in the brain and spinal cord of clinically ill animals over two years of age.

15. Since 1989 when the first BSE case was reported outside of the United Kingdom, relatively small numbers of BSE cases (in total approximately 1,500) have also been reported in native cattle in Belgium, Denmark, France, the Republic of Ireland, Liechtenstein, Luxembourg, Netherlands, Portugal and Switzerland. However, all but a couple of dozen cases have been reported in four countries – France, the Republic of Ireland, Portugal and Switzerland. Small numbers of cases have also been reported in Canada, the Falkland Islands (Islas Malvinas), Germany, Italy and Oman, but solely in animals imported from the United Kingdom. The International Office for Epizootic Diseases (OIE) reports these cases on their web site: www.OIE.int.

16. The nature of the TSE agent is being investigated and is still a matter of debate. According to the prion theory, the agent is composed largely, if not entirely, of a self-replicating protein, referred to as a prion. Another theory argues that the agent is virus-like and possesses nucleic acids which carry

genetic information. Although strong evidence collected over the past decade supports the prion theory, the ability of the TSE agent to form multiple strains is more easily explained by a virus-like agent.

Evidence of vCJD-BSE link

17. The hypothesis of a link between vCJD and BSE was first raised because of the association of these two TSEs in time and place. More recent evidence, supporting a link, includes identification of pathological features similar to vCJD in brains of macaque monkeys inoculated with BSE. A vCJD-BSE link is further supported by the demonstration that vCJD is associated with a molecular marker that distinguishes it from other forms of CJD and which resembles that seen in BSE transmitted to a number of other species. Studies of the behavior of the prion agent in mice artificially infected with tissues from humans with vCJD and cows with BSE showed nearly identical patterns.

18. The most recent and powerful evidence comes from studies showing that the transmission characteristics of BSE and vCJD in laboratory mice are almost identical, strongly indicating that they are due to the same causative agent.

19. Intensive surveillance in 17 European countries has confirmed the high incidence of vCJD in the United Kingdom, the country with the largest potential exposure to BSE. France (with three reported cases) imported relatively large quantities of cattle products from the United Kingdom. The one case in the Republic of Ireland lived in the United Kingdom. Australia, Canada and the United States of America (all with extremely low potential exposure) have no confirmed reports of vCJD.

20. In conclusion, the most likely cause of vCJD is exposure to the BSE agent, most plausibly due to dietary contamination by affected bovine central nervous system tissue.

Other human TSEs

21. Other human TSEs include kuru in Papua New Guinea, which is believed to be transmitted by funerary rituals involving brains of corpses; Gerstmann-Sträussler-Schenker (G.S.S.) syndrome (occurring in persons with an apparent hereditary predisposition) and fatal familial and sporadic insomnia. CJD is the most common of all the human TSEs and is the disease most commonly mistaken for vCJD.

Measures taken to protect public health

22. Due to strong suspicions of a linkage between vCJD and BSE, the British government made BSE a notifiable disease in June 1988. Shortly afterwards, a statutory ban on the feeding of protein derived from ruminants (e.g. cattle, sheep and goats) to any ruminant was introduced. The use in the food chain of bovine offals considered to pose a potential risk to humans was also banned in the United Kingdom in 1989, and the list was revised and expanded on several occasions as new information became available. In other countries, including Europe, measures taken, the date of implementation and the extent of enforcement vary from country to country.

World Health Organization (WHO) involvement

23. Since 1991, WHO has convened nine scientific consultations on issues related to animal and human TSEs. These meetings have made wide-ranging recommendations aimed at protecting human and animal health.

24. As exposure to the BSE agent may extend to populations outside Western Europe, it was recommended that to ascertain the number and distribution of any future cases, global surveillance of

CJD and its variants would be required.To protect human health, WHO has also recommended the following:

- No part or product of any animal which has shown signs of a TSE should enter any (human or animal) food chain;
- Countries should not permit tissues that are likely to contain the BSE agent to enter any (human or animal) food chain;
- All countries should ban the use of ruminant tissues in ruminant feed.

25. Human and veterinary vaccines prepared from bovine materials may carry the risk of transmission of animal TSE agents. The pharmaceutical industry should ideally avoid the use of bovine materials and materials from other animal species in which TSEs naturally occur. If absolutely necessary, bovine materials should be obtained from countries which have a surveillance system for BSE in place and which report either zero or only sporadic cases of BSE These precautions apply to the manufacture of cosmetics as well.

26. From 1997-2000, WHO held a series of training courses worldwide, particularly in developing countries, with the intention of helping individual countries establish national surveillance of CJD and its variants The first workshop, for West African countries, was held in Dakar, Senegal in June 1997 Similar workshops were held in Bangkok for Southeast Asian countries (October 1997), in Cairo for North African countries (February 1998) and in China for countries of the Western Pacific (July 1999) and for Eastern and Central European countries in May 2000 Another is planned for Mediterranean countries.

27. In 1999, consultants reviewed the known information about a number of animal TSEs to try to proactively determine if there are any new TSE threats Their principle recommendations were to eradicate BSE and to find out if BSE has infected sheep populations. The recommendations are available at http://www.who.int/emc-documents/ under the heading "TSE".

28. WHO published guidelines for infection control of TSEs in 2000. The full text is available at http://www.who.int/emc-documents/ under the heading "TSE".

Note: For further information, journalists can contact the Spokesperson's Office, WHO, Geneva Telephone (+41 22) 791 2599. Fax (+41 22) 791 4858. E-mail: inf@who.int. All WHO Press Releases, Fact Sheets and Features can be obtained on Internet on the WHO home page: www.who.int.