

Bovine Spongiform Encephalopathy in Israel: Implications for Human Health

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Abstract

Only one case of a cow infected with bovine spongiform encephalopathy has been reported in Israel. Its publication, in 2002, caused both public and professional concern. The inevitable health policy question raised was whether or not to recommend against consuming beef and what public health measures should be taken. In this article we describe the prion diseases among animals and humans, their interaction and the precautionary procedures that were carried out by the state Veterinary Services and the Ministry of Health since 1988. The BSE case (a 10 year old dairy cow) is believed to be the result of local consumption of infected mammalian meat and bone meal more than a decade earlier. The risk assessment took into consideration that no cases of vCJD (a new variant of Creutzfeldt-Jacob disease) have ever been diagnosed in Israel, as well as the low risk of contamination of the meat due to the religious method of slaughtering performed in the country. The policy decision was to implement a contingency plan prepared in advance. Israel was reclassified from the level II category of geographic risk where BSE is unlikely but not excluded in the herds, to level III where BSE is likely but not confirmed, or confirmed at a lower level. No undue damage to the meat industry has occurred. By the end of 2002, despite the examination of more than 3,800 brains from slaughtered cows older than 3 years, no other cases of BSE have been detected.

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On 28 May 2002, the first case of bovine spongiform encephalopathy in Israel was identified in a 10 year old cow on Kibbutz Ortal on the Golan Heights. The suspicion was raised after the cow exhibited neurologic symptoms resembling rabies several days before she died. Initial laboratory examination of brain tissue was carried out by the Department of Pathology at the Kimron Veterinary Institute, Beit Dagan. Results of the immunoblotting and immunohistochemistry tests were indicative of BSE. The brain tissue was sent to the World Organization for Animal Health (Office International des Epizooties) reference laboratory in the Institute of Animal Neurology, University of Bern, Switzerland, and was found positive on 4 June 2002.

This "breaking news" appeared in all the Israeli mass media, similar to what had occurred in the United Kingdom in 1995. It raised public concern and the inevitable question was whether to eat beef. Both the farmers and the meat and dairy industry felt the

approaching crisis might endanger their future in the local and export markets. Health professionals and the public expressed their fears regarding human health.

The European Economic Commission Scientific Steering Committee on BSE has identified four categories of geographic risk of bovine spongiform encephalopathy. In countries that are categorized in Level I, it is highly unlikely that cattle infected with the BSE agent are present in the domestic herds. For those in Level II, BSE is unlikely, but not excluded, in the herds. In Level III, BSE is likely but not confirmed, or confirmed at a lower level. Finally, in Level IV, BSE is confirmed at a higher level. Until recently Israel was regarded as being in the Level II category. In September 2002, as an outcome of the single BSE diagnosis, the EEC grouped Israel in Level III – i.e., BSE is confirmed at a lower level and the domestic cattle are likely, clinically or preclinically, infected with the BSE agent [1].

In this paper we review the information on BSE for health professionals, as well as the evidence for causation between BSE and variant Creutzfeldt-Jacob disease. We assess whether a diagnosis of BSE in one dairy cow is a risk to human health in Israel, and discuss the impact on the preventive policy measures that are being implemented.

Prion and the new entity of prion diseases

The pathologic feature of both BSE in cattle and vCJD in humans is a prominent vacuolation of the gray matter of the brain that produces a "sponge-like" appearance on light microscopy. Previously, the transmissible nature and the prolonged incubation period of diseases related to BSE were recognized in several animal hosts [2]. They include scrapie in sheep and goats, transmissible mink encephalopathy, a naturally occurring chronic wasting disease of deer and elk found in North America, exotic ungulate encephalopathy in zoo animals (like antelope), and feline spongiform encephalopathy [3]. These data led scientists to raise the possibility of the existence of a so-called transmissible spongiform encephalopathy etiologic agent, which was thought to be a "slow virus" [3].

Nevertheless, not a single strain of the "transmissible spongiform encephalopathy" or other infectious agent had ever been

BSE = bovine spongiform encephalopathy

EEC = European Economic Commission

vCJD = variant Creutzfeldt-Jacob disease

isolated from cattle with the natural disease. Experiments by Alper et al. [4] suggested that protein may be a critical component of the infectious agent. Prusiner [5] was the first to state that the agent is composed of protein, without nucleic acids. He coined it "prion" from "proteinaceous infectious," indicating that it is an infectious agent with protein-like properties. In 1997 Prusiner received the Nobel Prize in Medicine for this theory. Later on, it was demonstrated that the prion exists in two major isoforms of the cellular form of prion protein (PrP), the non-pathogenic or cellular form, designated PrP^C and the pathogenic or scrapie-inducing form, designated PrP^{Sc}. The PrP^{Sc} form was found in animals affected with "transmissible spongiform encephalopathy" and, surprisingly, was found to be one that is normally encoded by a chromosomal gene of the host [6]. In contrast to PrP^C, the pathogen PrP^{Sc} is very resistant to physical and chemical conditions [7]. It is insoluble in non-denaturing detergents and shows relative resistance to proteases [8]. Moreover, once an "infectious unit" has been generated, PrP^{Sc} appears to act as a conformational template by which PrP^C is converted to a new molecule of PrP^{Sc} through protein-protein interaction of PrP^{Sc} and PrP^C. These findings clearly illustrate that prions do not self-replicate but instead convert non-pathogenic PrP^C to pathogenic PrP^{Sc} [8]. It is worth noting that the current rapid postmortem tests detect PrP^{Sc} and not infectivity. In other words, detection of PrP^{Sc} is considered as evidence for the presence of infectivity.

Prion diseases are fatal neurodegenerative disorders represented in humans as a new variant of Creutzfeldt-Jakob disease (vCJD). Prion diseases include kuru, sporadic CJD, familial CJD, iatrogenic CJD, Gerstmann-Sträussler-Scheinker disease, and fatal familial insomnia. In 1936, Cuillé and Chelle [9] first showed the transmission of the prion disease scrapie to a healthy goat by the intraocular administration of scrapie-infected spinal cord. Thirty years later, kuru (a disease transmitted among the Fore people of New Guinea through cannibalism) was experimentally transmitted to chimpanzees by Gajdusek and colleagues [10]. Shortly thereafter, sporadic CJD was also transmitted to chimpanzees [11]. Jackson et al. [12] have proposed that the gene *DQ7* may protect people against vCJD.

The related etiology of BSE and vCJD

It is believed that the etiologic agent of BSE resulted from feeding cattle with mammalian meat and bone meal in the UK, almost 20 years ago. This was done in order to enhance the protein intake of the "vegetarian" cattle. The mammalian meat and bone meal allegedly contained offal from sheep and goats infected by scrapie.

Several factors are associated with the age at which the central nervous system of a cow becomes infected. These include the age at exposure, the strain of the agent, the dose, and the route of neuroinvasion. Based on epidemiologic and experimental evidence, it is possible to differentiate between three risk levels according to the age at exposure: from birth up to 12 months, from 1 year to 30 months, and over 30 months. Since the age of the youngest naturally occurring case of BSE is 20 months, it would be most unlikely that the central nervous system would be infected in cattle

under age 12 months [13]. Estimates provided in the EEC Scientific Steering Committee on BSE opinion of 12 January 2001 revealed that in the UK, the proportion of BSE cases aged 24 months or less at onset is less than 0.006%, for animals under 30 months of age 0.05%, and 0.17% for animals under age 35 months [14].

The limited available data from experimental oral infection of cattle suggest that infectivity would become detectable in the central nervous system only at a late stage of the incubation period, some months before clinical onset [13]. It is uncertain whether these data can be applied to the naturally occurring disease with its variations in doses and incubation periods. The mean incubation period is 60 months, with cases in animals aged 20 months to lifetime. To date, the first detection of infectivity in the central nervous system in these experiments (by conventional mouse bioassay) has been 32 months after exposure, with the onset of clinical signs 3 months later [13]. Therefore, it is assumed that the BSE incidence rate is very low in cattle less than 30 months of age, a fact that is important for health policy.

Although there is no direct proof, it is assumed that prion-contaminated meat and meat products, mainly central nervous system tissue from infected cattle or other products contaminated by such tissues, are the vehicles of transmission of vCJD to humans [3,8]. The main proof is ecological and is based on the finding that BSE in cattle and vCJD in humans are present in the same geographic regions and that patients diagnosed with vCJD had lived in areas where BSE in cattle was detected. Thus, from a health policy perspective, with the lack of adequate evidence fulfilling causality criteria, the "precautionary principle" has been applied. The policy measures introduced are based on the assumption that there is a cause and effect relationship between consuming meat infected by BSE and occurrence of vCJD. Therefore, BSE is regarded as a zoonosis with high risk to consumers of infected beef. This policy of precautionary principle [15] was adopted by the UK authorities, which in 1996 ordered the extermination of all the cows at risk. The cost of this policy was 27 billion dollars. As of 2001, more than 100 people have died from vCJD, mainly in the UK [8].

The Israeli perspective

There are three issues that should be considered when dealing with prion diseases in Israel. Firstly, several new patients are diagnosed each year with familial CJD in Jewish families originating from Libya and other North African countries. Secondly, there is a reduced risk of BSE infectivity due to the method used in religious slaughtering (Jewish and Moslem). Finally, since the late 1980s the government has implemented a number of preventive measures.

Familial CJD

The fact that familial CJD is relatively common in Israel requires increased sensitivity to the possibility that a new case of vCJD could be incorrectly classified as familial CJD. This emphasizes the need for an active surveillance system with a national registry. Since 1995, CJD has been included as a legally notifiable disease in Israel. Few autopsies are conducted in Israel, and thus increased use should be made of postmortem brain biopsies of suspicious cases.

The method of slaughtering animals

In the European Union a wide range of methods for slaughtering animals is practiced, including non-penetrative stunning, electro-narcosis and ritual slaughtering by Jews and Moslems. In the stunning method, cerebral emboli could enter the cerebral veins and sinuses and return to the right atrium. Some emboli might get trapped in the right atrium and some may exit the heart through the pulmonary arteries. Smaller emboli could traverse the capillary bed of the lungs and be distributed to any part of the body, including the liver [16,17]. The frequency with which CNS tissue enters the bloodstream depends on the method of stunning [18]. Irrespective of the type of penetrative stunning, the head, lungs, heart and blood collected 40 seconds after stunning are in decreasing order of risk of being contaminated with BSE.

In Europe, slaughtering without stunning is usually allowed under the law but only for religious reasons. In Israel, animal slaughtering is mainly performed according to the rituals of the two religions – Kosher in Judaism and Halal in Islam. In the Jewish ritual, the slaughterer (*shochet*), using a razor-sharp knife (about 46 cm long by 3.5 cm wide), makes a swift cut from side to side to sever both jugular veins and the two carotid arteries in a single stroke without burrowing, tearing or ripping the animal. The head is then raised further as the blood spurts out. For beef, the animal is cut horizontally across the throat, severing the trachea and the esophagus. The Moslem ritual consists of cutting simultaneously, with a sharp knife, the throat, trachea and the blood vessels in the neck, causing death without cutting the spinal cord. The blood has to be drained before the head is removed [19].

It is thus safe to state that the Kosher/Halal methods have negligible risk of the meat, excluding the brain, being contaminated with prions. It is possible that this could explain the absence of vCJD in Israel. Nevertheless, the literature still considers that the animal head has the potential of becoming contaminated even with Kosher/Halal methods [19].

Preventive measurements taken by the Israeli Veterinary Services

BSE is believed to have spread from Britain to the European continent at the beginning of the 1990s through feed-meal contaminated by the infectious agent. Early on, the Israeli Veterinary Services implemented rigorous measures even before BSE had been considered. This included a ban on the import of mammalian meat and bone meal for bovine feed from the UK since 1988, and from all other countries since 1990. Moreover, after the BSE and vCJD scandal surfaced in the UK, an active BSE surveillance program was introduced and has been operational since 1996. This includes testing of fallen adult bovines, randomly sampled healthy animals, and suspected animals. This could explain the fact that only a single infected cow with BSE has ever been diagnosed in Israel, 14 years after the reports on the first cases of BSE in the UK. This case was probably due to contaminated food that had been given to the infected cow more than a decade ago.

In comparison, since July 1994 the European Commission banned the feeding of mammalian meat and bone meal to cattle,

sheep and goats, and required higher processing standards for the treatment of mammalian waste (133°C and three bars of pressure for 20 minutes). From 1 May 1998, the EEC requires active BSE surveillance. On 1 October 2000 the requirement to remove specified high risk materials from cattle, sheep and goats from the human and animal food chains was ratified.

Preventive measurements taken by the Israeli Health Services

From the human health perspective, the health authorities in Israel have implemented certain measures. The Israeli national blood bank has published directives prohibiting people who have spent more than 6 months in the UK between 1985 and 1996 to donate blood, and vCJD has become a notifiable disease since 1995.

With the establishment of the diagnosis of BSE in the 10 year old cow in Israel, the Ministry of Agriculture's veterinary services implemented the emergency plan that was approved more than a year earlier by both the Ministries of Agriculture and Health and re-approved by the government. Accordingly, three cows of the same age group as the infected BSE animal and two of its offspring were culled and were later found to be free of prionic disease. Slaughtering of cows older than 30 months was temporarily banned. The ban was lifted when the infrastructure for the examination of brains of all cows over the age of 30 months was implemented. Internal organs, including brain, eyes, spleen, vertebral column and distal intestines of cows older than 12 months are destroyed. Intensifying control on animal movements is in place. Recently, Bartz et al. [20] reported that cattle tongue could contain high levels of the prion protein and suggest the need to reevaluate current guidelines on the meat allowed into the food chain.

The health policy chosen

The public has been encouraged by the Ministry of Health to buy meat only in licensed butchereries supervised by the Veterinary Services, and to dine only in licensed restaurants, which are under the supervision of the Ministry of Health. This policy was adopted by the Ministry of Health on the basis of control and surveillance measures taken by the veterinary services since 1988 and the comparative advantage of the religious slaughtering performed in Israel. The fact that there has not been a single incident case of vCJD in Israel since 1995, when vCJD became a notifiable disease, is an indicator of the success of the precautionary measures taken by the Israeli government.

The diagnosis of the first case of BSE in Israel was in the headlines for the first 24 hours following the diagnosis of the first case of BSE and disappeared from the media after a few days. This appears to be the result of sound risk management, which included a detailed risk communication plan by which the risk assessment was relayed to the media and the public.

Nevertheless, there is a need to monitor the situation continuously, both from veterinary and human perspectives, and in the light of new evidence in scientific publications. In addition, consensus statements by international organizations should be taken into consideration.

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