History and Neuropathology of Transmissible Disorders (Bovine Spongiform Encephalopathy)

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The group of disorders known as the spongiform encephalopathies is both pathologically fascinating and of immense practical importance. It affects several species and includes scrapie (in sheep and goats), kuru and Creutzfeldt Jakob disease (man), mink encephalopathy (mink) and chronic wasting disease (elk, mule deer). In all cases the diseases produced are characterised by a long incubation period and have a uniformly fatal outcome. They are transmissible disorders and are spread by means of a disease producing protein known as a prion. A spontaneously occurring form of this disease -bovine spongiform encephalopathy (BSE) - was first identified in England in 1986.

Epidemiological studies carried out in Great Britain in 1987 and 1988 indicate that bovine spongiform encephalopathy (BSE) was caused by the consumption of infected feed, probably due to the inclusion in cattle feed of protein derived from scrapie-infected sheep. A ban on the use of ruminant-derived protein in ruminant feedstuffs was therefore introduced in Great Britain in July 1988, as soon as the food-bome hypothesis had been established, to prevent further transmission of the infective agent by this route. Subsequent epidemiological analysis confirmed that ruminant protein in feed had been the source of infection and that recycling of infected cattle material from 1984 onwards had greatly increased the amount of infective agent in feed and so increased the number of cattle exposed to the risk of infection. It has recently been shown that the BSE agent can survive the times and temperatures reached in some systems used in the United Kingdom and elsewhere to process animal waste to produce tallow and animal proteins. The ruminant feed ban prevents infection from either cattle or sheep being transmitted in feed and remains the key measure which will bring an end to the BSE epidemic in the United Kingdom. The implementation of the feed ban in 1988 is conservatively estimated to have prevented at least 20,000 cases of BSE in 1992 and 30,000 cases in 1993. There has been a shift in the age profile of the disease with fewer young animals being effected. There has been a significant decline in the incidence of the disease in cattle less than five years old, this is considered to be related to the introduction of the feed ban.

Analysis of data in the United Kingdom re cattle to cattle transmission has indicated that the observed number of confirmed cases which occurred in the progeny of effected females with the number predicted if feed was the only source has revealed no excess of observed cases, on the basis of this data it has been concluded that if maternal transmission does occur it is undetected at present. Other recent studies have also suggested that there is no statistical

evidence to suggest that there is maternal transmission, with the present state of knowledge however it is not yet possible to exclude this route of transmission.

In the period of seven and a half years from November 1986 (when the disease was first identified) up to and including 15th April 1994 125,031 cases of BSE were confirmed on 30,136 farms. 30.9% of herds with adult breeding cattle have experienced at least one case of BSE. 49.8% of dairy herds but only 12.5% of beef suckler herds have been effected. Most of the beef suckler cases are in animals which were purchased as calves from dairy herds where they were exposed to infection through feed. From an adult cattle population in the United Kingdom of approximately 4.5 million the current annual incidence of confirmed cases of the disease is 7.5 cases per thousand. In recent years BSE has been confirmed in approximately 85% of the suspected cases slaughtered each year. In addition to the above recorded cases in Great Britain there have been 1,283 cases (913 farms) in Northern Ireland, 334 cases on the Isle of Man, 488 cases on the Island of Guernsey and 88 cases on the Island of Jersey.

Up to 20th April 1994 9.369 cases of BSE had been confirmed in Great Britain in animals born after the ruminant fed ban. The majority (including the 3% which were the offspring of dams in which BSE had been confirmed) had probably been exposed to ruminant protein in feed.

Current research programmes have demonstrated the transmission of disease from infected animals to susceptible mice. Transmission was only accomplished when the mice were exposed to brain mixed with cerebrospinal fluid, transmission did not occur when the mice were feed milk, mammary gland, placenta, lymph nodes or spleen from BSE effected animals. A recent study designed to investigate the assumption that BSE is not transmitted by embryos from BSE effected donor animals revealed that both cows and bulls suffering from BSE infection have produced gametes capable of fertilization and that their embryos have developed normally to calves. The study concluded that the reproductive performance of BSE positive cows did not seem to be impaired in comparison with BSE negative cows, the apparent normal viability of most of the embryos from BSE effected donors also supports the conclusion that BSE infection has little direct effect on reproduction. There was an observed decreased developmental potential of embryos derived from BSE positive bulls and BSE positive cows, the numbers involved however are statistically too small to allow valid conclusions re the significance of this finding.

Infected cattle show no signs of disease for several years, but once symptoms appear the course of the disease is rapid. "Sick" animals become edgy and irritable, they begin to lose the coordination of their limbs and they may eventually become very aggressive, hence "mad cow disease".

In pathological terms the spongiform encephalopathies are a unique group of diseases. Although once thought to be due to a viral infection they are now known to be transmissible by an abnormal protein particle (prion) resistant to heat and chemicals which would destroy all known bacteria and viruses.

Evidence of disease is seen only in the brain although the culprit protein is not confined to this organ and disease has been spread by transplantation/inoculation of other tissues eg corneas, pituitary extract, liver, kidney etc. In the nervous system the pathological findings are not those of a classical viral and bacterial infection but consist of widespread death of neurones, reactive changes in the supporting cells of the brain (gliosis) and formation of innumerable tiny "holes" in the brain tissue giving it a characteristic spongey appearance under the microscope, hence the term "spongiform encephalopathy". There are no inflammatory changes and effected animals do not show any antibody response as usually occurs with infective disease. The predominant focus of concern regarding BSE is whether or not the disease may be transmitted to the human population following the consumption of meat from infected cattle. National surveillance statistics re Creutzfeldt-Jacob disease in the United Kingdom which commenced in the form of a prospective study in May 1990 have revealed that during the past 25 years there has been an annual increase in the incidence of this condition. There is currently no data to suggest that there has been any significant increase in the incidence of Creutzfeldt-Jacob disease in the United Kingdom since the epidemic of BSE.

Australia's Disease status

Australia is free of bovine spongiform encephalopathy, scrapie and rabies.

In 1952 scrapie was diagnosed in two of 18 Suffolk sheep imported from the United Kingdom. The disease was eradicated by immediate slaughter of the effected flock and in-contact sheep and destocking of the property for 12 months. Surveillance was undertaken for 15 years.

In 1992 post-mortem examination revealed a spongiform encephalopathy in one of three cheetahs which had been imported two years earlier into a Western Australian zoo from a British zoo. Subsequently the British zoo was found to have cases of spongiform encephalopathy in other animals. The effected cheetah's two litter mates were subsequently destroyed. Post-mortem revealed no evidence of spongiform encephalopathy.

No case of BSE has been detected in Australia.

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