Chapter 3
The Problem of Bovine Spongiform Encephalopathy also Known as "Mad Cow Disease" in the United Kingdom

3.1 First Cases of Bovine Spongiform Encephalopathy in the United Kingdom

In 1984, an outbreak of disease in Pitsham Farm in West Sussex occurred in which several cows showed unusual clinical signs and then died.

Subsequently farms in Malmesbury, Wiltshire, reported cases of neurological diseases in dairy cows.

By 1986, it became apparent that histological examination of the brains from the affected cows from several farms in Kent and the Bristol area showed "spongiform changes" which resembled those previously observed in sheep affected by scrapie (Hope 1988).

The clinical features of the animal condition, together with the neurological examination suggested that a new disease had been discovered in British cattle and was given the name of "bovine spongiform encephalopathy" (BSE) (Wells et al. 1987).

The lay press quickly gave this condition the more expressive name of "Mad cow disease" which evoked some concern among the general public both in the U.K. and throughout the world.

The government then set up an exhaustive inquiry under the Chairmanship of Lord Phillips of Worth Matravers together with Mrs. June Bridgeman and Professor Malcolm Ferguson-Smith.

Their report ran to 16 volumes and was published under the aegis of the House of Commons in October 2000.

By late 1987, over 200 confirmed cases of bovine spongiform encephalopathy (BSE) had been identified in the U.K. (Wilesmith et al. 1988).

It was recognised that clinical symptoms of bovine spongiform encephalopathy had first appeared in Southern England (Sussex, Kent, Hampshire, Devon and Somerset) in 1985.

The disease then spread to the Midlands, Wales and Northern England, reaching Scotland in November 1987 and Northern Ireland in late 1988 (Wilesmith et al. 1991).

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3.2 Origin of the Disease

The origin of the disease evoked a great public interest lest consumption of the meat from the BSE affected animals entered the human food chain and caused similar diseases as observed in cattle. The possibility arose that Creutzfeldt-Jakob disease (CJD) which has similar histological features as bovine spongiform encephalopathy could have been transmitted to humans.

Several possible environmental factors were examined but no clear evidence emerged for their involvement in the onset of "bovine spongiform encephalopathy".

Although the use of toxic compounds was a possibility, it was found that 23 % of BSE farms had not used herbicides and 69 % of BSE farms had not used organophosphate pesticides (Lord Phillips of Worth Matravers et al. 2000).

The one factor common to all affected BSE farms was the use of commercial cattle feed. For many years, animal protein derived from abattoir material such as brain, spinal cord, intestines and spleen, had been incorporated in the form of "meat-and-bonemeal" (MBM) supplements into cattle feeds to provide a rich source of protein.

Further anecdotal evidence of "meat-and-bonemeal" (MBM) as the agent responsible for the appearance of "bovine spongiform encephalopathy" (BSE) were the reports of a similar disease in ruminant nyala and gembok in wildlife parks who also were fed MBM supplements.

Subsequently a scrapie like disease was reported in an Arabian oryx, greater kudu, eland, moufflon, scimitar horned oryx, ankole cow and bison (Lord Phillips of Worth Matravers et al. 2000).

Clearly the use of "meat-and-bonemeal" supplements in cattle farms also affected other animals kept in wildlife parks and zoological gardens.

The suspicion that the "meat-and-bonemeal" (MBM) supplements were somehow involved in the spread of the disease appeared to be gaining support.

A scrapie like disease was reported in carnivorous cats and then in exotic carnivorous animals kept in zoos such as cheetah, pumas, ocelots, tigers and lions. Post-mortem examinations of the brains in many of these animals showed "spongiform changes" similar to those found in sheep and goats affected by scrapie.

The use of the "meat-and-bonemal" (MBM) supplements was banned by the Government in June 1988 and since then the incidence of BSE has progressively declined in British cattle (Fig. 3.1).

3.3 Scrapie and Related Diseases

Scrapie is an endemic disease of sheep and goats which has been known in the U.K. for over 250 years. It first appeared in the USA in 1947.

It is also well known in Europe and is called "la Tremblante" in France.

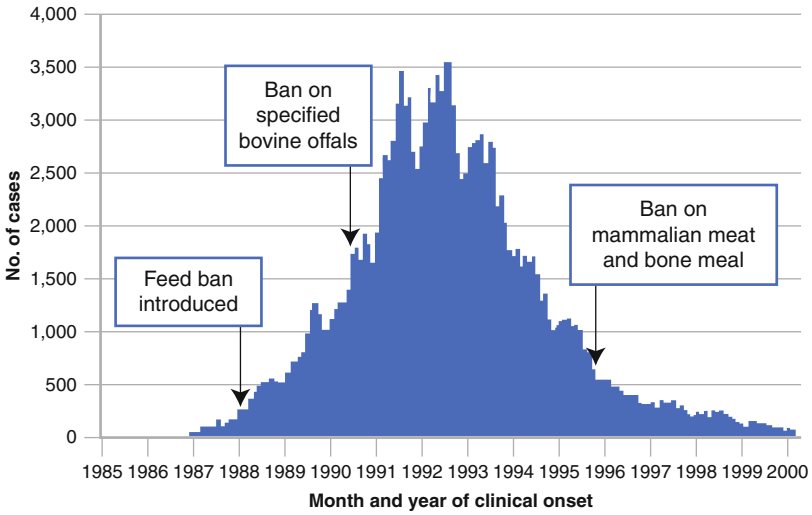

Fig. 3.1 Frequency of bovine spongiform encephalopathy in the UK

The first full description in England appeared just before the First World War (Stockman 1913).

The clinical signs include itching whereby the animal is scraping against garden posts or rocks, hence the term "scrapie".

It is characterised by incoordination, excitability of the animal and trotting movements. The disease is readily recognised by sheep farmers.

An interesting observation suggesting that a "virus" was involved was made when spinal cord homogenates from 80 animals affected by scrapie were inoculated into healthy sheep, leading to the development of the disease (Cuille and Chelle 1936). This was interpreted as the transmission of the disease by a "scrapie agent".

However injecting nervous tissue from the spinal cord, could also be explained by another mechanism, the production of a disease resembling "experimental allergic encephalomyelitis" (EAE).

Another possible suggestion that "scrapie" may have been caused by a virus, concerned the louping-ill vaccination program set up in 1937, in sheep. The vaccine was prepared as a saline solution of brain, spinal cord and spleen from sheep, which 5 days previously had been inoculated intra-cerebrally with formaldehyde inactivated louping-ill virus. The vaccine was given by subcutaneous injection and 2 years later the vaccinated sheep started developing "scrapie" (Greig 1950).

Again a homogenate of brain tissue was used but the possibility of an EAE-like autoimmune disease was not entertained as the concept of an allergic reaction to brain tissue had not yet made its entrance into medical and veterinary journals.

Louping-ill, also known as "ovine encephalomyelitis" is an acute viral disease caused by an RNA virus, belonging to the Flaviviridae. It is transmitted by the bite of the sheep tick, Ixodes ricinus.

The disease manifests itself by muscular tremors in the affected animal leading to paralysis, coma and then death.

Studies in Iceland indicated that the "scrapie" agent could be transmitted to sheep from scrapie-brain material that had been passed through filters designed to remove bacteria. It was suggested that the agent was a filterable virus (Sigurdsson 1954).

However it appeared that the transmissible agents were not viruses because no immune response could be demonstrated. The inability to demonstrate an immune response to scrapie infection was recognised in 1959 and this feature was found to be characteristic of other "transmissible infections" such as kuru, Creutzfeldt-Jakob disease and "transmissible mink encephalopathy" (Porter et al. 1973).

"Transmissible mink encephalopathy" was described in 1965 and documented several outbreaks of the disease on mink farms in Wisconsin.

Affected animals present with behavioural changes such as hyper-excitability, aggressiveness, followed by muscular incoordination and death.

A similar disease called "chronic wasting disease" of mules and elks occurs in the wildlife parks of Colorado and Wyoming (Williams and Young 1980).

The investigations on the pathogenesis of the "transmissible spongiform diseases" was based on the so-called "bio-assay", which is a method to quantify the amount of infective agent in animal tissue.

3.4 The "Bio-assay" is the Fundamental Flaw in "Transmissible Spongiform Diseases" Research

The investigation on the pathogenesis of "scrapie" like diseases is based on the "bio-assay".

For the bio-assay, tissues are ground up, usually in saline, to produce a suspension which is sequentially diluted.

A specified volume of each dilution is then injected into groups of experimental animals, usually mice, which are then observed for the development of the disease.

In this way the titre or concentration of infectivity per gram of particular tissue can then be calculated from the last dilution that was sufficient to cause disease in 50 % of a group of experimental animals.

The first assumption being made here is that the denatured tissue which contained the putative infectious agent, the "scrapie" agent will not evoke an immune response in the experimental animal.

The second assumption is being made here is that any pathological responses are due to the "scrapie" agent.

The first assumption is clearly wrong, since we know since the time of Pasteur that brain homogenates produce "experimental allergic encephalomyelitis" (EAE). Homogenates from any organ will evoke an auto-immune disease.

The second assumption is also wrong since the "scrapie" agent has not been identified.

The "prion" molecule is anyway a self-molecule encoded by the DNA of the original animal or patient, therefore it is a self-molecule.

It is certainly not "infectious" since infection implies replication of a bacterial or viral agent.

If denaturation of a self-molecule is described as "replication", then this occurs readily in patients with burns who make auto-antibodies against burnt skin.

Patients following a myocardial infarction will make antibodies against myocardial tissue and this is known as Dressler's syndrome.

3.5 Conclusions

The appearance of a neurological disease in British cattle in the 1980s has been called "bovine spongiform encephalopathy" (BSE) and was soon re-labelled by the press as "Mad cow disease".

Its clinical and histological features appeared to resemble the sheep and goat disease known as "scrapie", especially in that brain examination showed microsopic "evidence of spongiform changes".

Epidemiological studies indicated that the most likely causative factor was the exposure of cattle to "meat-and-bonemeal" supplementary feeds which were produced from offal material, including brain tissues, obtained from the abattoirs.

The use of "meat-and-bonemeal" feed supplements was banned in 1988 in the U.K. and since that time the number of cattle affected by "bovine spongiform encephalopathy" has progressively decreased.

The use of the "bio-assay" to provide a metric measurement of disease activity in "transmissible spongiform encephalopathies" is deeply flawed since it makes the unacceptable assumption that saline brain homogenates do not evoke an immune response in experimental animals which is contrary to extensive immunological evidence over the last 100 years.

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