Bovine Spongiform Encephalopathy (Mad Cow Disease) — Symptoms and Diagnosis

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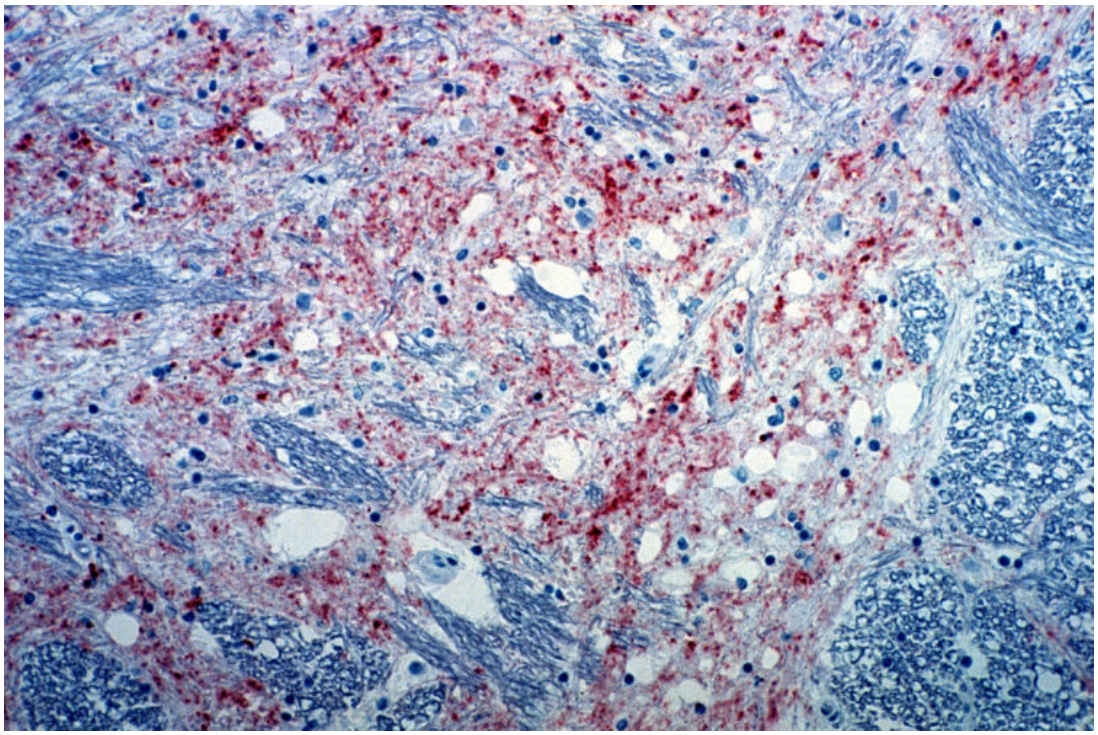
Bovine spongiform encephalopathy is also commonly known as mad cow disease. It causes spongy neurodegeneration in the brain and spinal cord of adult cattle. The main causative agent of bovine spongiform encephalopathy is a prion, which is a misfolded protein.



Etiology of Bovine Spongiform Encephalopathy

The postulated cause of the **spread** of mad cow disease is MBM (**meat and bone meal**), which is a concentrated, protein-rich supplement feed given to the **dairy cows**. Due to this reason, dairy cows are more prone to develop the disease as compared to beef cattle.

Image: “Cow with BSE.” License: Public Domain

The infectious agent, which is the prion protein, can survive in temperatures of more than 600 degrees Celsius. Some theories also state that the disease is caused by a **virus**. The animals carry an allele which converts the **normal alpha helical arrangement** of the protein into **beta pleated sheets**. This leads to the **formation and accumulation of plaques** causing degeneration and holes in the brain, leading to **mental impairment of the animal**.

Healthy animals can become infected by coming in contact with infected animals. Two leading hypotheses suggest that:

1. The disease might have come from other species, presumably sheep, or
2. It may have happened before as well, in the past centuries.

The incubation period varies from 2.5 to 5 years with the peak age of onset of 5 years.

Transmission to Humans

In humans, the disease variant is known as **Creutzfeldt-Jakob disease** (vCJD or nvCJD). It is said that the infectious agent is found in the brain and spinal cord, but it is also present in **every tissue of the body of the infected cattle**. The disease is likely to occur if a person consumes food that has been contaminated with the brain and spinal cord of the infected animal.

The disease is **not curable** and leads to a **fatal** end.

The classical clinical features of CJD include:

- Rapid cognitive decline,
- Ataxia,
- Myoclonus and the development of the akinetic mute state.
- Neurological symptoms need to be progressive in nature.

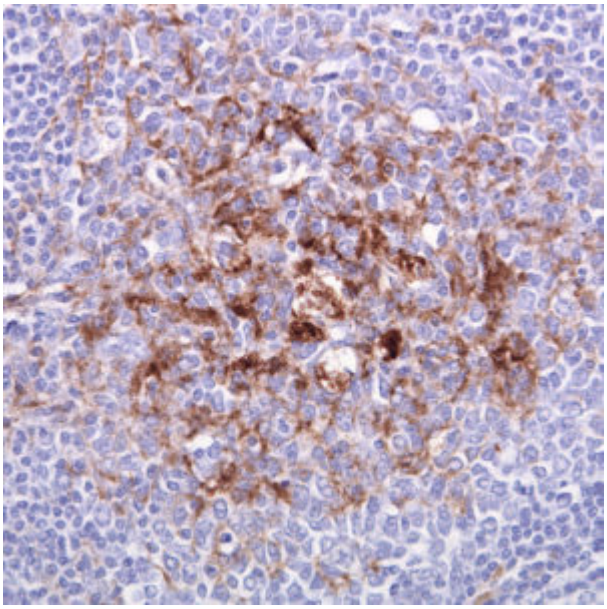


Image: “Tonsil biopsy in variant CJD. Prion protein immunostaining.” By Sbrandner – Own work. License: GFDL

The **diagnosis** of the disease can be done by the following methods:

- **Electroencephalography** demonstrates sharp wave pattern.
- **The cerebrospinal fluid analysis** shows misfolded proteins.
- **Magnetic resonance imaging of the brain** shows damage in the caudate nucleus and putamen.
- **Neuron-specific enolase**: this tumor marker is mostly raised in patients with Creutzfeldt-Jakob disease.

Signs and Symptoms of Bovine Spongiform Encephalopathy

As the disease has a **very long incubation period**, its symptoms and signs occur very late. The infected animal usually has an **abnormal gait,** and when muscles are affected, the animal **loses the ability to stand**. The animal might exhibit **changes in behavior**, **anxiety**, **aggression**, **persistent rubbing or teeth grinding due to pain**. The disease eventually leads to **coma** and **death**.

Diagnosis of Bovine Spongiform Encephalopathy

It is very difficult to diagnose the disease at an early stage due to its very long incubation period of months to years. So, a **presumptive diagnosis** can only be made by the developing signs and symptoms. At the time of development of signs and symptoms, however, the disease has virtually progressed into every body tissue and fluid.

Definitive diagnosis can only be made by examining the **postmortem brain and body tissues** by using neuropathological and immune-histochemical stains. The **toxic prion protein** is also present in the blood and urine of the infected animal, but the amount of the protein is very low. Thus, scientists are still working on developing methods to diagnose the disease via the blood and urine.

Pathogenesis of Bovine Spongiform Encephalopathy

Pathogenesis of bovine encephalopathy is still not well understood, and research is still under process. Although the disease affects the brain and spinal cord, pathogenesis occurs in other body parts as well.

One theory strongly suggests that there is a reason why the presence of the infectious **prion protein was demonstrable in the macrophages of the Peyer's patches of the ileum**. Months after inoculation, the protein was only found in the Peyer's patches which led the researches to think that the organism only replicates there.

Prevention of Bovine Spongiform Encephalopathy

Prevention can only be done by **regulating the constituents of the feed** given to dairy cows. In the UK and US, body parts like the brain, spinal cord, and eyes are considered to be high risk and proper methods are proposed for their disposal.

Diagnostic Criteria of CJD

The most important magnetic resonance imaging findings in sporadic CJD are high-intensity signals in the caudate, putamen, or cortex on diffusion-weighted imaging and FLAIR sequences.

Invariant CJD, symmetrical hyper-intensity of the posterior thalamus relative to the anterior putamen on T2 or FLAIR MRI images is the most common finding.

The most important finding on EEG in patients with CJD is periodic, triphasic sharp wave complexes.

The European Union has adapted new diagnostic criteria for the premortem diagnosis of sporadic and variant CJD in 2017:

Definite sCJD:

Progressive neurological syndrome and CJD confirmed via neuropathological, immunohistochemical, or biochemical testing.

Probable sCJD:

Rapidly progressive cognitive impairment plus two of the following (myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features, akinetic mutism) plus generalized periodic sharp-wave complexes on EEG.

OR

Rapidly progressive cognitive impairment plus two of the following (myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features, akinetic mutism) plus the typical MRI findings described above.

OR

Rapidly progressive cognitive impairment plus two of the following (myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features, akinetic mutism) plus positive cerebrospinal fluid results.

OR

Progressive neurological syndrome and positive real-time quaking-induced conversion in CSF or other tissues.

Possible sCJD:

Rapidly progressive cognitive impairment plus two of the following (myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features, akinetic mutism) for a duration less than 2 years.

Treatment of Bovine Spongiform Encephalopathy

There is **no treatment** of mad cow disease up to date.

References

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Bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease via bmj.com

Sporadic prion disease via prion.ucl.ac.uk

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Notes