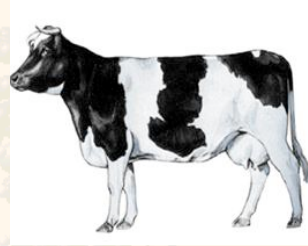


Mad Cow Disease

All known prion diseases are fatal. Since the immune system does not recognize prions as foreign, no natural protection develops. Scrapie in sheep was first described during the 18th century. It has been transmitted to other animals such as mink and cats, and more recently to cows (mad cow disease or bovine spongiform encephalopathy, BSE) through contaminated feedstuff.



In New Guinea, the Fore-people contracted kuru by eating the brains of deceased people. Creutzfeldt-Jakob Disease (CJD) frequently arises spontaneously, while fatal familial insomnia (FFI) Gerstmann-Sträussler-Scheinker (GSS) disease, and 10-15% of CJD are caused by mutations in the gene encoding the prion protein. A new variant CJD, diagnosed in some 20 patients, may have arisen through transmission of BSE to humans.



The Nobel Foundation

BSE - Mad Cow; A protein gone wrong

The prion protein exists in two forms. The normal, protein (PrP^c) can change its shape to a harmful, disease-causing form (PrP^{Sc}). The conversion from PrP^c to PrP^{Sc} then proceeds via a chain-reaction. When enough PrP^{Sc} proteins have been made they form long filamentous aggregates that gradually damage neuronal tissue. The harmful PrP^{Sc} form is very resistant to high temperatures, UV-irradiation and strong degradative enzymes.

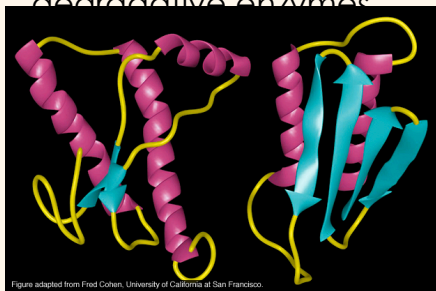
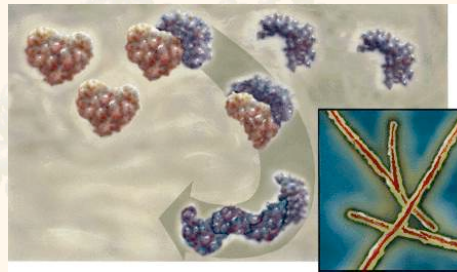
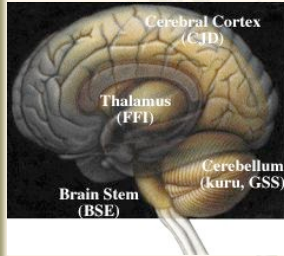


Figure adapted from Fred Cohen, University of California at San Francisco.



Prions and protein folding

Prions affect different regions of the brain. A sponge-like appearance results when nerve cells die. Symptoms depend on which region of the brain is affected.



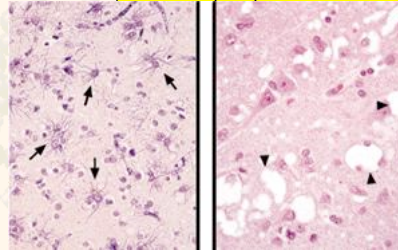
Cerebral cortex -loss of memory and mental acuity (CJD).

Thalamus Damage results in insomnia (FFI).

Cerebellum Damage results in problems to coordinate body movements and difficulties to walk (kuru, GSS).

Brain stem In the mad cow disease (BSE).

A precise diagnosis of a prion disease can only be made upon autopsy. The figures show thin sections of diseased brains. FFI, with typical proliferation of astrocytes, the support cells of the brain, is shown to the left (arrows). CJD, with the characteristic spongiform appearance with vacuoles (arrows) is shown to the right.



Prion diseases arise in three different ways

1. Through horizontal transmission from e.g. a sheep to a cow (BSE).
2. In inherited forms, mutations in the prion gene are transmitted from parent to child.
3. They can arise spontaneously.

Route of infection

When cows are fed with offals prepared from infected sheep, prions are taken up from the gut and transported along nerve fibers to the brain stem. Here prions accumulate and convert normal prion proteins to the disease-causing form, PrP^{Sc}. Years later, BSE results when a sufficient number of nerve cells have become damaged, affecting the behaviour of the cows.