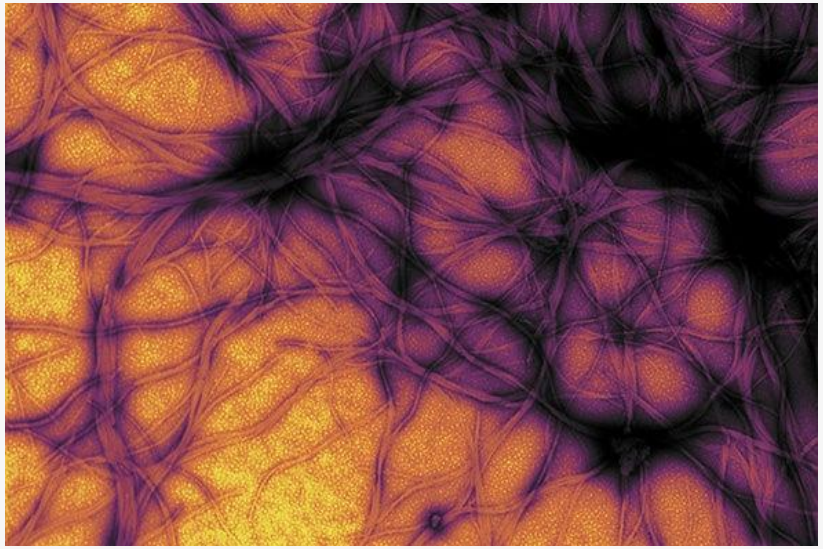
Prion:
A Puzzle Protein



Prion

Prion' term first used to describe the mysterious infectious agent responsible for several neurodegenerative diseases found in mammals, including Creutzfeldt-Jakob disease (CJD) in humans.

The word itself derives from 'proteinaceous infectious particle' which refers that the infectious agent causing those diseases consists only of protein, with no nucleic acid genome.

S"The term 'prion' was coined by Stanley B. Prusiner of the University of California School of Medicine at San Francisco in 1982 to distinguish the infectious agent that causes scrapie in sheep, Creutzfeldt-Jakob disease (CJD) in humans and bovine spongiform encephalopathy (BSE) in cattle from other, more typical infectious agents.

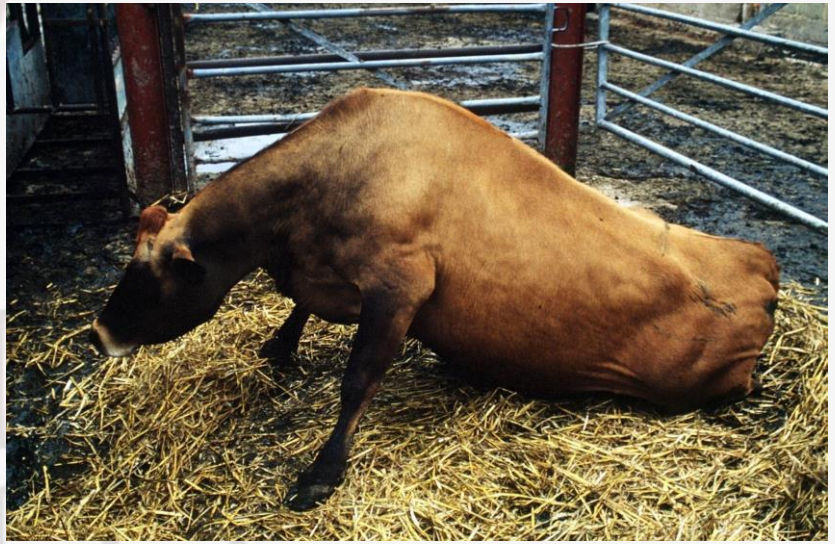
The prion hypothesis postulates that these diseases are caused not by a conventional virus or bacterium but by a protein that has adopted an abnormal form.

- A number of fatal neurodegenerative diseases in humans--such as Creutzfeldt-Jakob disease (CJD), kuru and Gerstmann-Strussler-Scheinker (GSS) disease--are thought to be caused by an infectious agent known as a prion.

- Prions also cause disease in a wide variety of other animals, including scrapie in sheep and bovine spongiform encephalopathy (BSE) in cows.

- Collectively these diseases are known as transmissible spongiform encephalopathies.

Scrapie disease in sheep



Bovine spongiform encephalopathy

- The cause of CJD was unknown for many years.
- In the 1950s an epidemic transmissible disease called kuru, similar to CJD, was identified in the Fore tribe of Papua New Guinea.
- Transmission of the disease occurred during a ritual funeral process in which the brain of a dead tribe member was removed from the skull, cooked and eaten.

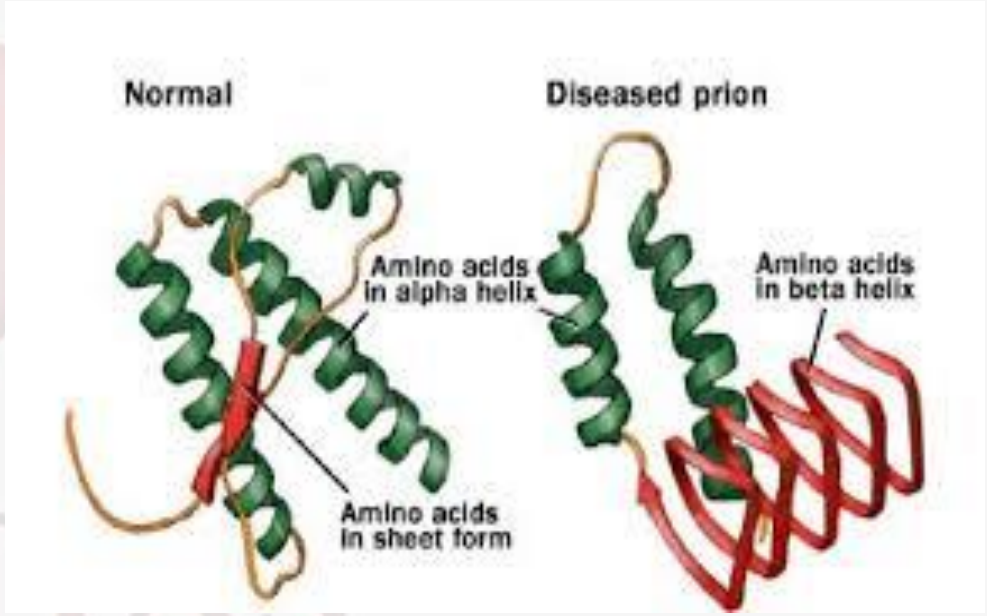
- Scientific analysis of the brains of people who had died from CJD or kuru showed that their brain tissue had a spongiform appearance,
- There were holes where cells ought to be, indicating an encephalopathy or reduction in the number of brain cells.

Kuru Disease

SD. Carleton Gajdusek, working at the U.S. National Institutes of Health, demonstrated that extracts of brain prepared from people who had died of CJD or kuru could cause a similar disease when inoculated into the brain of chimpanzees which showed the presence of an infectious agent.

We now know that a normal cellular protein, called PrP (for proteinaceous infectious particle) and which is found in all of us, is centrally involved in the spread of prion diseases.

This protein consists of about 250 amino acids.



- Some researchers believe that the prions are formed when PrP associates with a foreign pathogenic nucleic acid.
- This is called the virino hypothesis. (Viruses consist of proteins and nucleic acids that are specified by the virus genome.
- A virino would also consist of proteins and nucleic acids, but the protein component is specified by the host genome, not the pathogen genome).

- Scientists have not found any nucleic acid associated with a prion, however, despite intensive efforts in many laboratories.
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- Furthermore, prions appear to remain infectious even after being exposed to treatments that destroy nucleic acids.

- This evidence has led to the now widely accepted prion theory, which states that the cellular protein PrP is the sole causative agent of prion diseases; there is no nucleic acid involved.
- The theory holds that PrP is normally in a stable shape (pN) that does not cause disease.
- The protein can be folded, however, into an abnormal shape (pD) that cause disease.
- pD is infectious because it can associate with pN and convert it to pD, in an exponential process--each pD can convert more pN to pD.

- "Prions can be transmitted, possibly by eating and certainly by inoculation either directly into the brain or into skin and muscle tissue.

- Exponential amplification of the prion (converting pN into pD in the body) would then result in disease.

Types of prion diseases

Creutzfeldt-Jakob disease (CJD):

- A person can inherit this condition, called familial CJD.
- Sporadic CJD (occurring at irregular intervals or only in a few places), on the other hand.

- Most cases of CJD are sporadic around age of 60.

- Acquired CJD is caused by exposure to infected tissue during a medical procedure, such as a cornea transplant.
- Symptoms of CJD quickly lead to severe disability and death within a year.

Gerstmann-Sträussler-Scheinker disease (GSS):

•Extremely rare, but occurs at an earlier age, typically around age 40.

Kuru:

•This disease is seen in New Guinea. It's caused by eating human brain tissue contaminated with infectious prions. Because of increased awareness about the disease and how it is transmitted, kuru is now rare.

Fatal insomnia (FI).

•Rare hereditary disorder causing difficulty sleeping. There is also a sporadic form of the disease that is not inherited.

Cause of Prion disease

- Prion diseases occur when normal prion protein, found on the surface of many cells, becomes abnormal and clump in the brain, causing brain damage.

- This abnormal accumulation of protein in the brain can cause memory impairment, personality changes, and difficulties with movement.

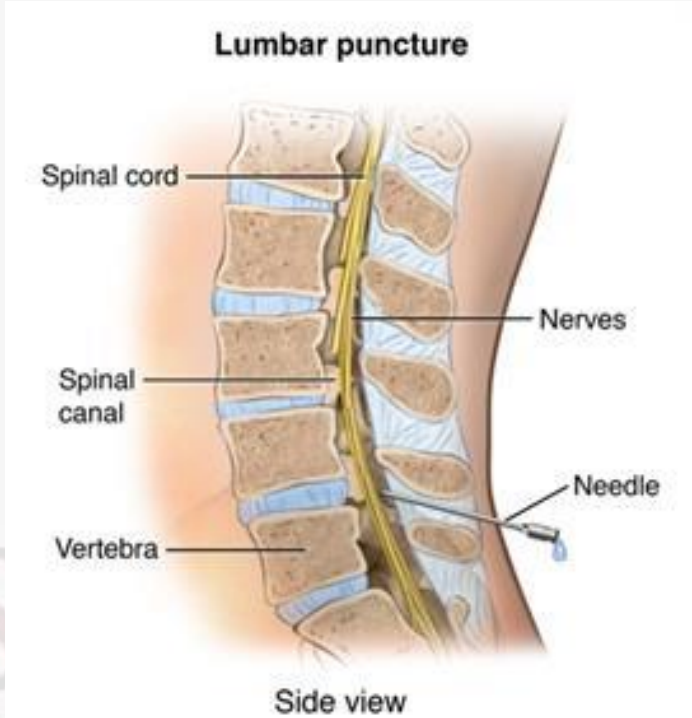
Symptoms of Prion disease

Symptoms of prion diseases include:

- Rapidly developing dementia
- Difficulty walking and changes in gait (a person's manner of walking)
- Hallucinations (an experience involving the apparent perception of something not present.)
- Muscle stiffness
- Confusion
- Fatigue
- Difficulty speaking

Diagnosis of Prion disease

- Prion diseases are confirmed by taking a sample of brain tissue during a biopsy or after death.
- Healthcare providers, however, can do a number of tests before to help diagnose prion diseases such as CJD, or to rule out other diseases with similar symptoms.
- Prion diseases should be considered in all people with rapidly progressive dementia.



Diagnosis of Prion disease

The tests include:

- MRI (magnetic resonance imaging) scans of the brain
- Samples of fluid from the spinal cord (spinal tap, also called lumbar puncture)
- Electroencephalogram, which analyzes brain waves; this painless test requires placing electrodes on the scalp
- Blood tests
- Neurologic and visual exams to check for nerve damage and vision loss.

Prevention of Prion disease

- Properly cleaning and sterilizing medical equipment may prevent the spread of the disease.
- If you have or may have CJD, do not donate organs or tissue, including corneal tissue.
- Newer regulations that govern the handling and feeding of cows may help prevent the spread of prion diseases.

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Thank you