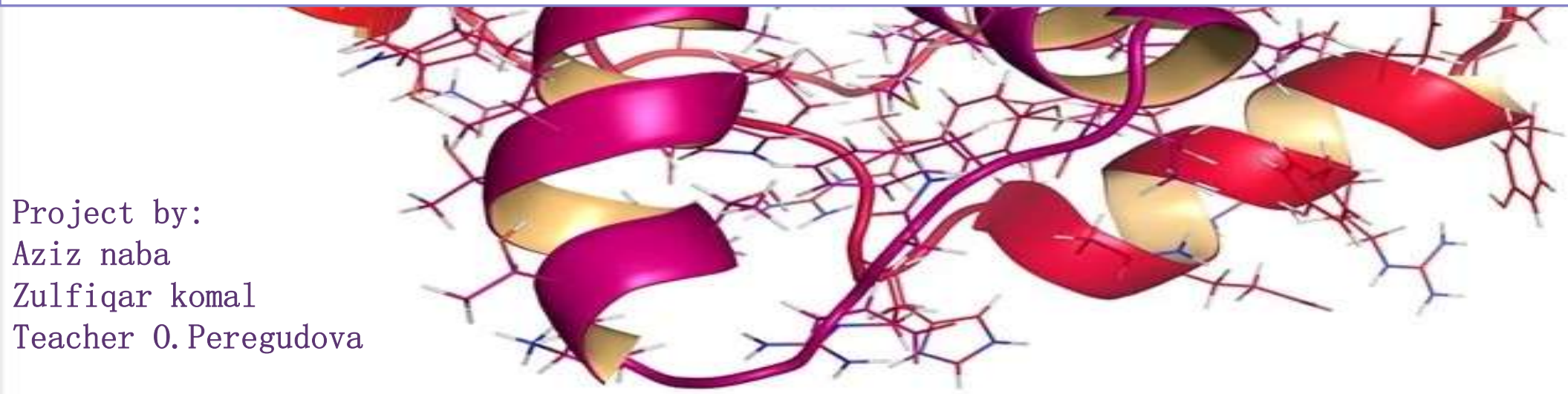
Prions role in The Pathogenesis of Neurodegenerative diseases



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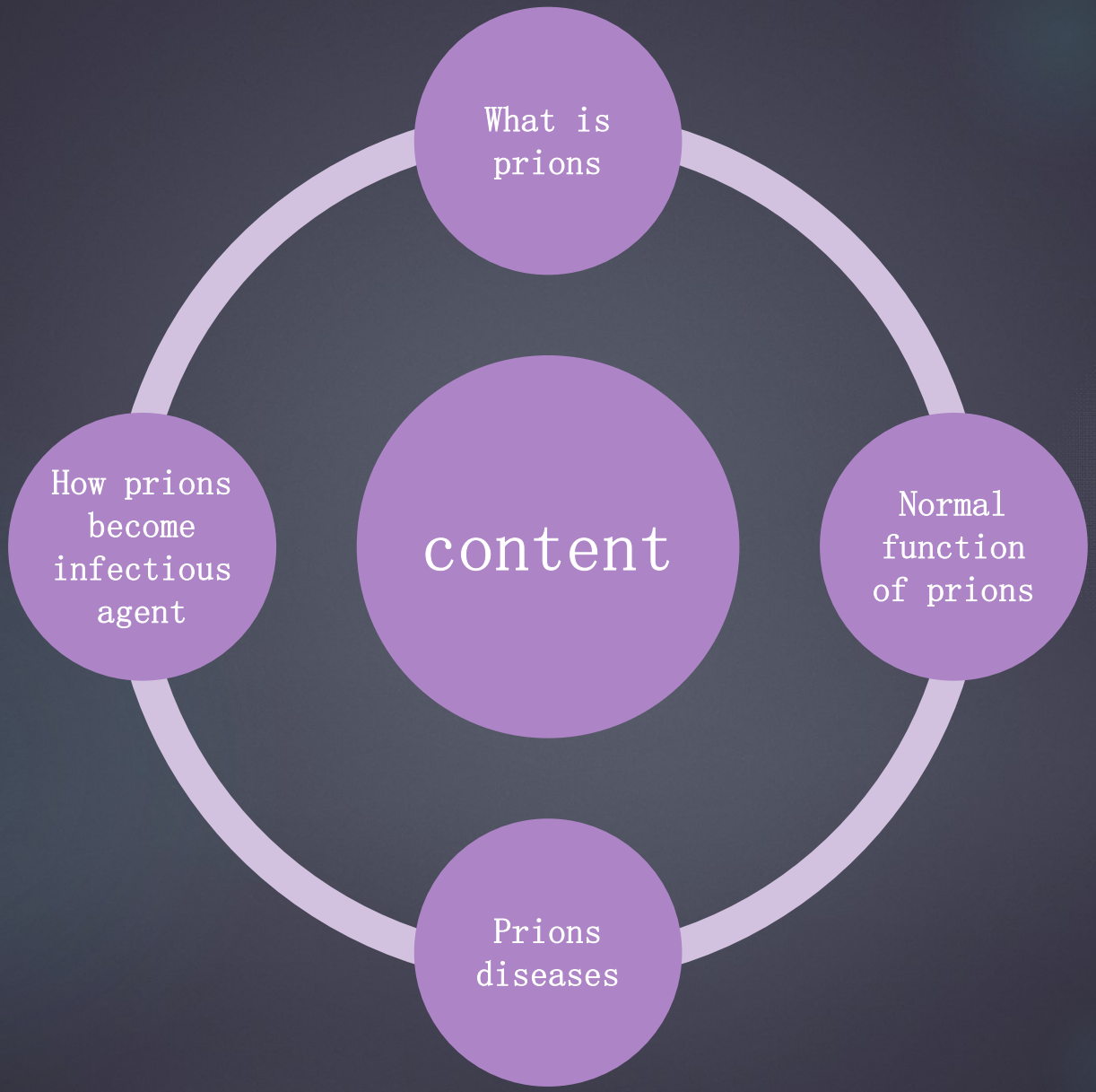
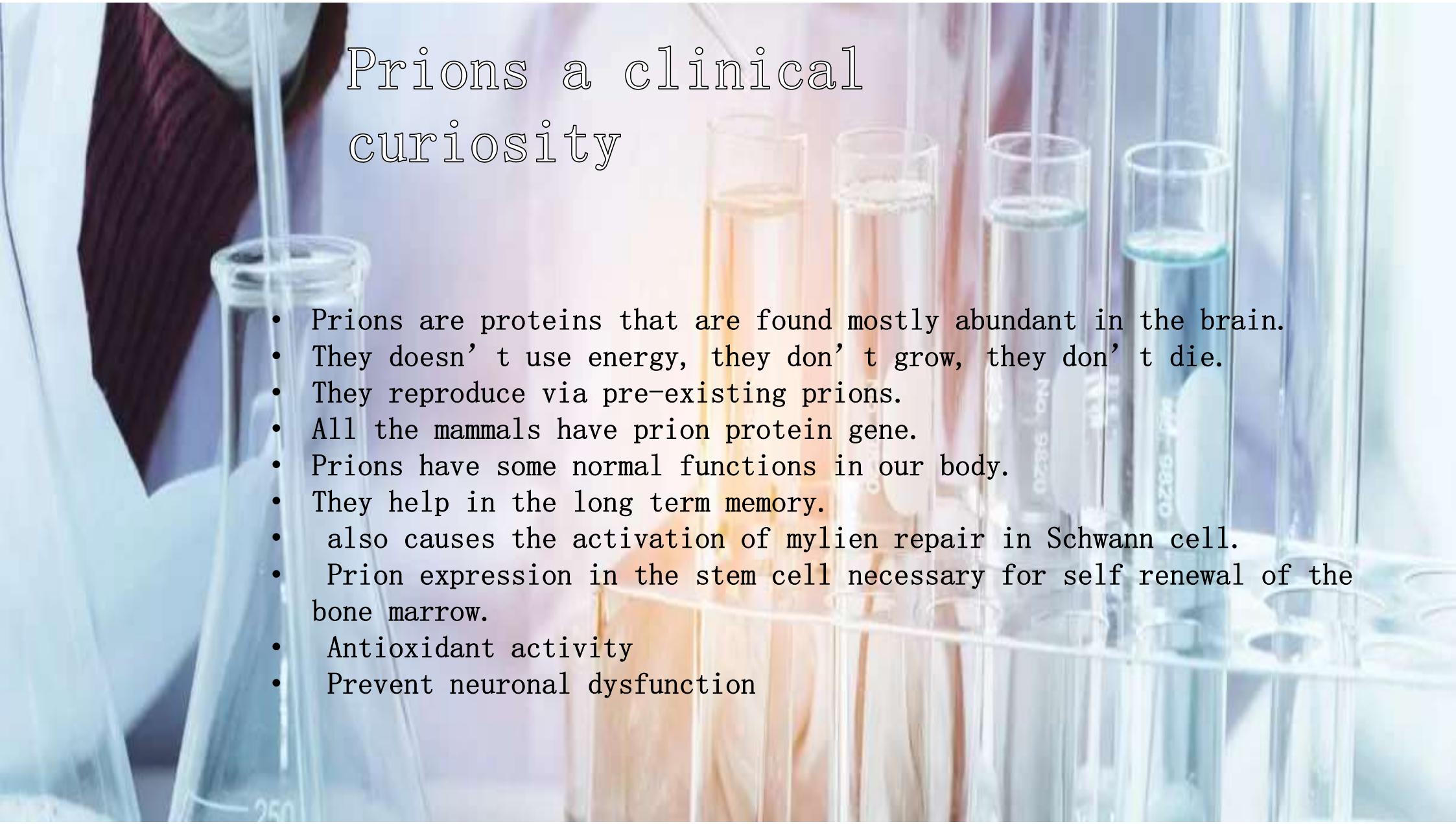
The main goal of the report – to show the important role of Prions in the pathogenesis of Neurodegenerative Diseases


What is prions
How prions become infectious agent
content
Normal function of prions
Prions diseases



Prions a clinical curiosity

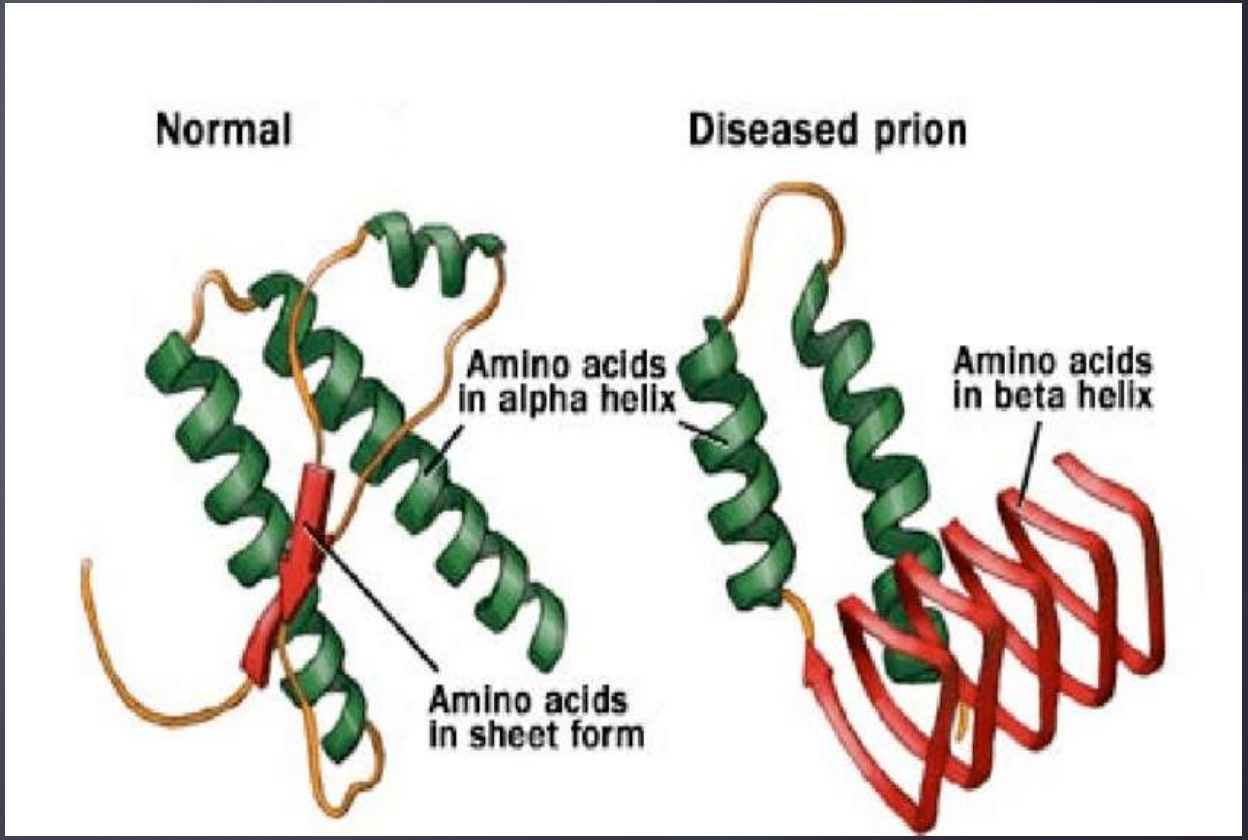
- Prions are proteins that are found mostly abundant in the brain.
- They doesn’t use energy, they don’t grow, they don’t die.
- They reproduce via pre-existing prions.
- All the mammals have prion protein gene.
- Prions have some normal functions in our body.
- They help in the long term memory.
- also causes the activation of mylien repair in Schwann cell.
- Prion expression in the stem cell necessary for self renewal of the bone marrow.
- Antioxidant activity
- Prevent neuronal dysfunction

PRIONS THE infective agent

Normally prions have the α-helical structure when their conformation changes it form β-sheets.

This occurs due to mutation in the prion gene or by infection of infective prion from other source.

Then its changes it nature , now it is an infective protein particle that are capable in producing diseases called prion diseases.



Stanley B Prusiner in 1982 coined the word Prion which is derived from the word protein and infection.

Prusiner got the Nobel prize in 1997 for his research into prions.

Normal prions are denoted as PrP and infective as PrPSc. This PrPSc can change normal prions to infective ones.

Abnormality of prion proteins can induce apoptosis of neurons.

Prion diseases

IN ANIMALS

- Scrapie
- Mad cow disease

IN HUMANS

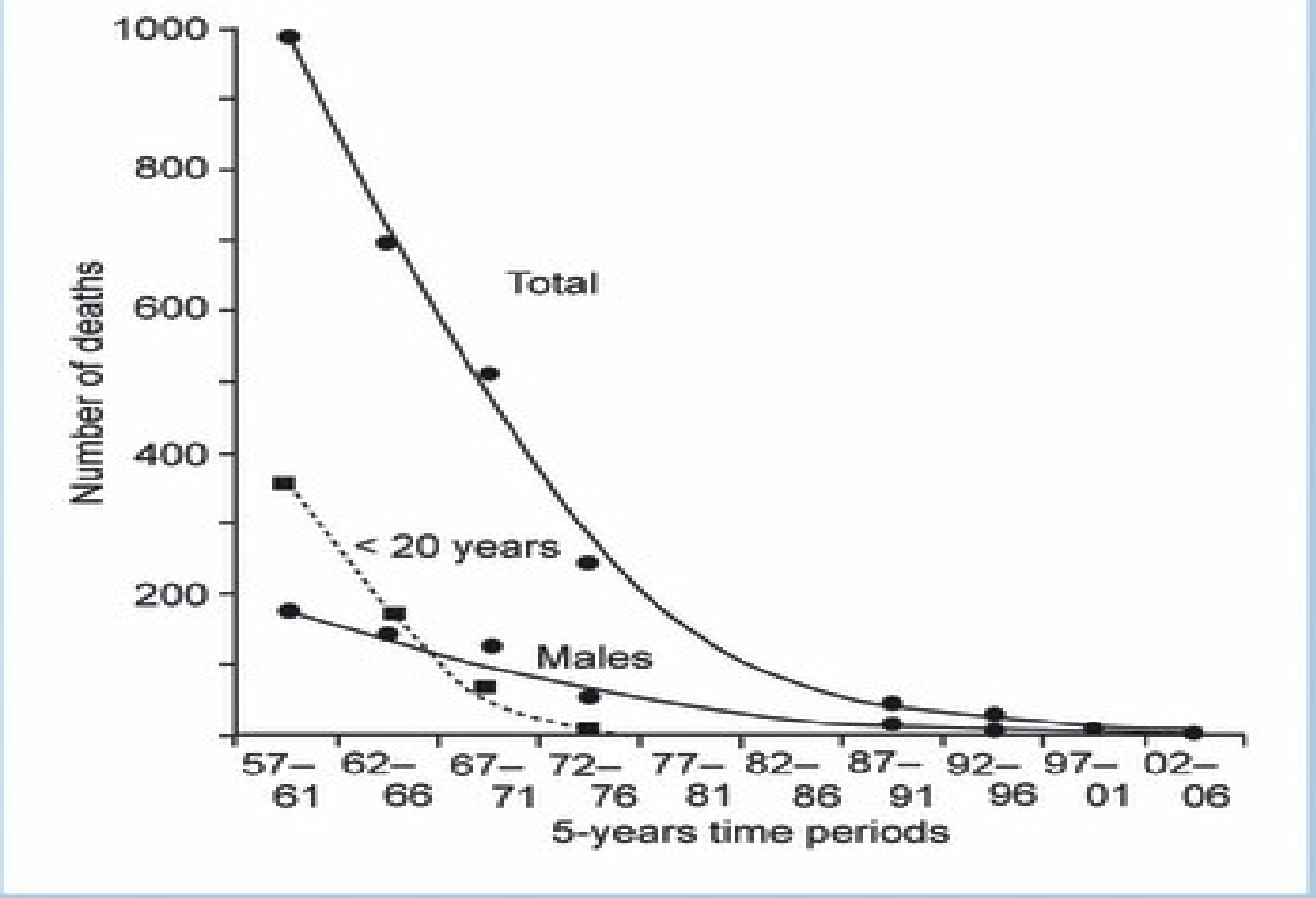
- Kuru
- Creutzfeldt Jacob disease
- Familial insomnia
- Gerstmann－Sträusler－Scheinker syndrome

Scrapie First diagnosed prion disease. Found in sheep which affect the nervous system of sheep and its is not transmissible to humans. Clinical signs are behavioral changes increased chewing movement ataxia and intense itching.

MAD COW DISEASE Neuro degenerative disease which caused by prions in cows and is also known as Bovine spongiform Encephalopathy and it infects the human beings by the consumption of the contaminated meat and also through its body fluids

KURU is an incurable degenerative disorder which found in the tribal region of Papua New Guinea is a type of transmissible spongiform encephalopathy caused by the prions.

it was the fatal neurological disease, amongst the stone-age Fore people in New Guinea, which provided the first insight into what came to be called prion diseases.
Studies of brain samples collected under primitive conditions from individuals who had died of kuru provided a principal link between the pathogenesis of two, until then considered, unrelated illnesses.

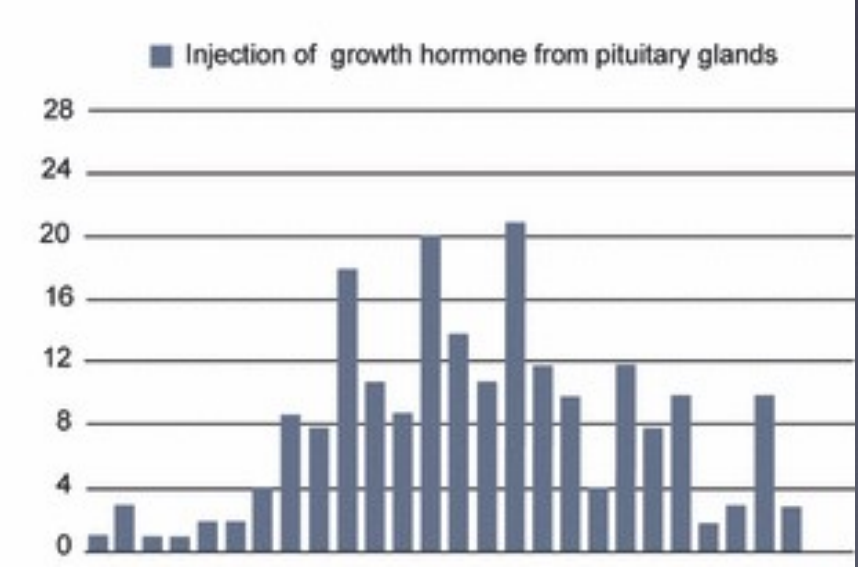


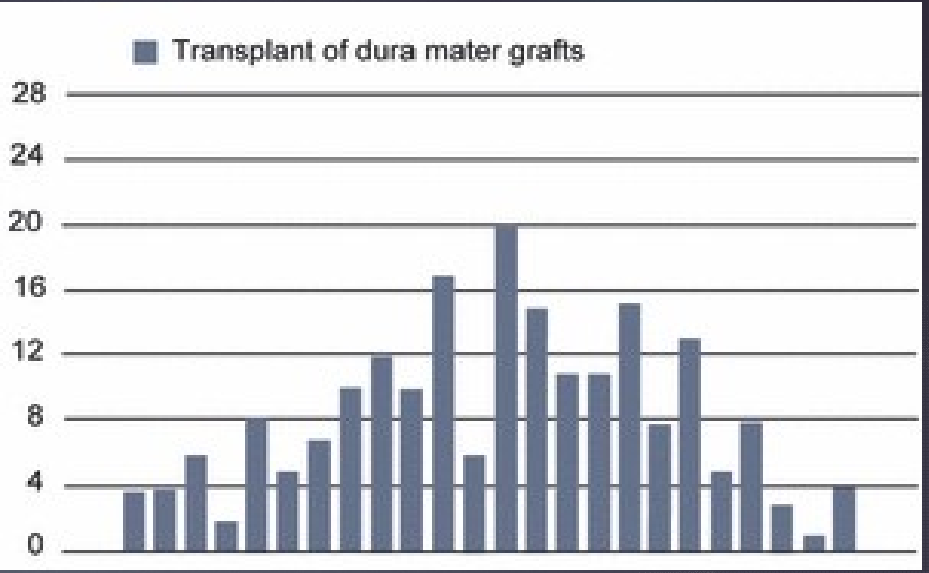
The epidemiology of kuru amongst the Fore people, which in 1960 had a total population of about 300 000 individuals. The number of cases in young individuals rapidly declined after 1960, the year in which the practice of ritual cannibalism ceased. The majority of victims were women. Single cases have appeared into the present century, implying an incubation time exceeding 40 years.

Creutzfeldt Jacob Disease

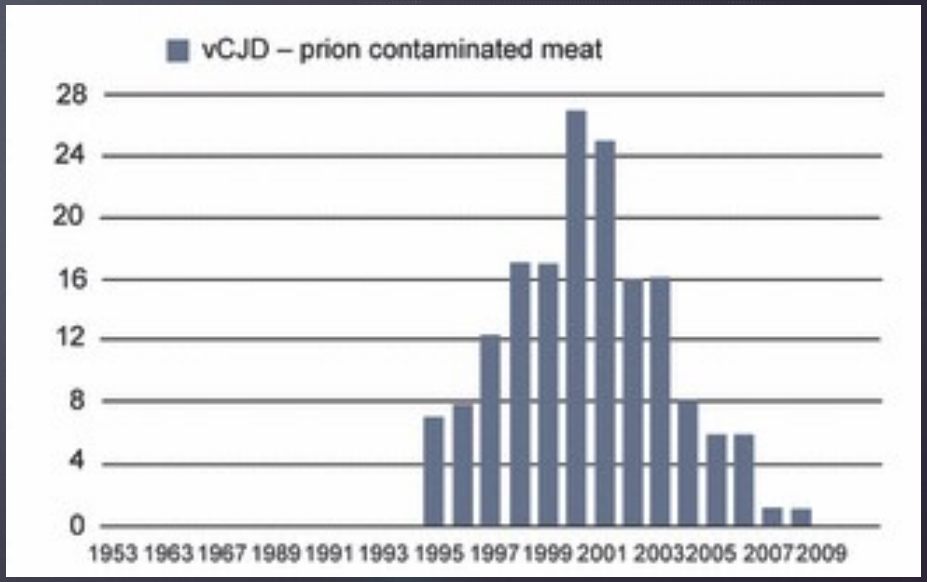
CJD is the most dangerous Prion disease with more death rates than the others.

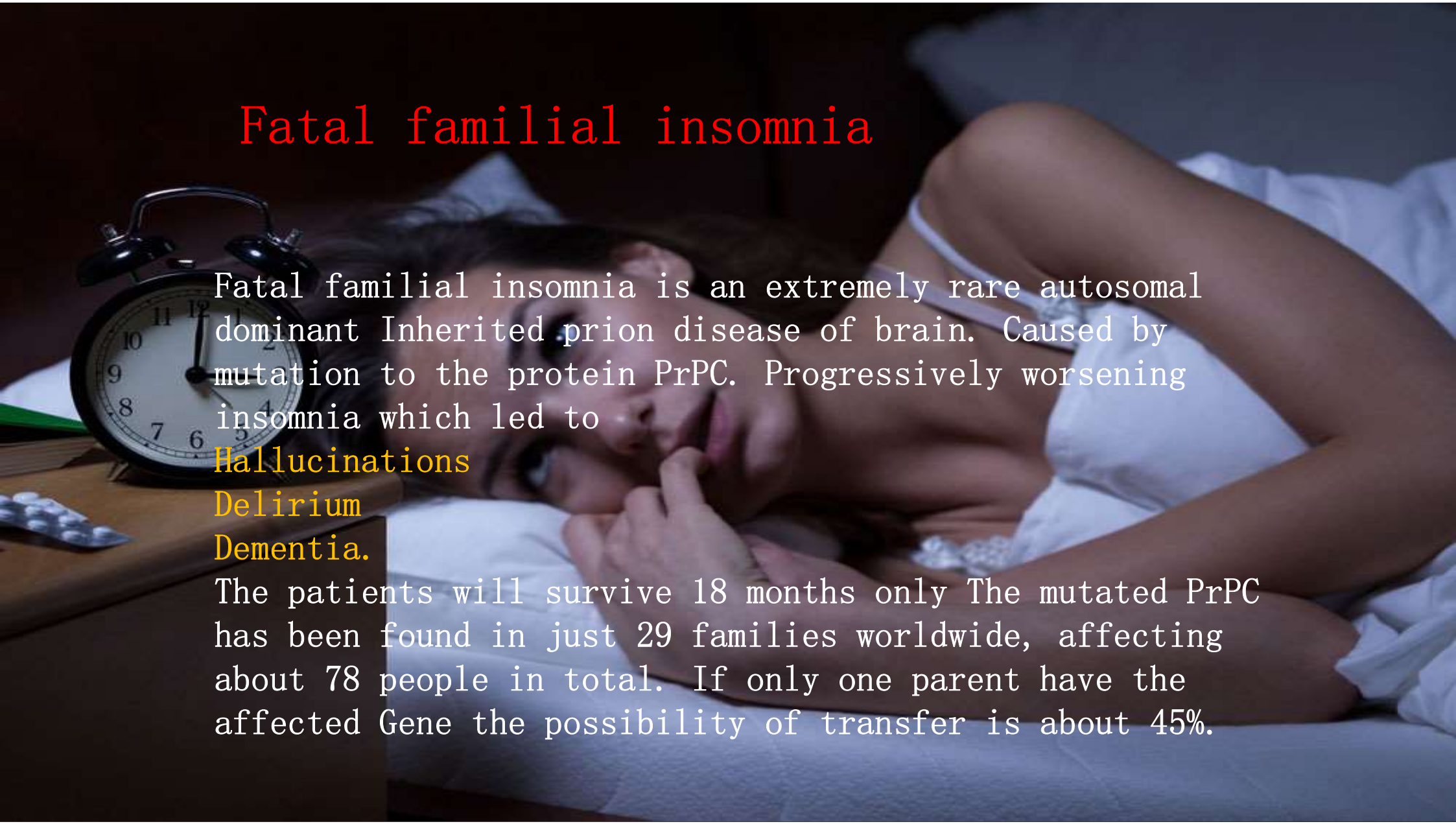
Creutzfeldt-Jakob disease was identified by two German neuropathologists in the 1920s. The disease is characterized by a progressive destruction of the brain, referred to as spongiform encephalopathy.





Comparison of three Creutzfeldt-Jakob disease (CJD) epidemics. Each of the epidemics involved about 200 patients and was caused by different human interventions: iatrogenic CJD by intra-muscular injection of pituitary gland-derived growth hormone; iatrogenic CJD as a result of Dura mater transplantation; and variant CJD because of ingestion of contaminated meat.
The average incubation time in the three epidemics was 15, 11 and about 11 - 12 years, respectively.





Fatal familial insomnia

Fatal familial insomnia is an extremely rare autosomal dominant Inherited prion disease of brain. Caused by mutation to the protein PrPC. Progressively worsening insomnia which led to

Hallucinations

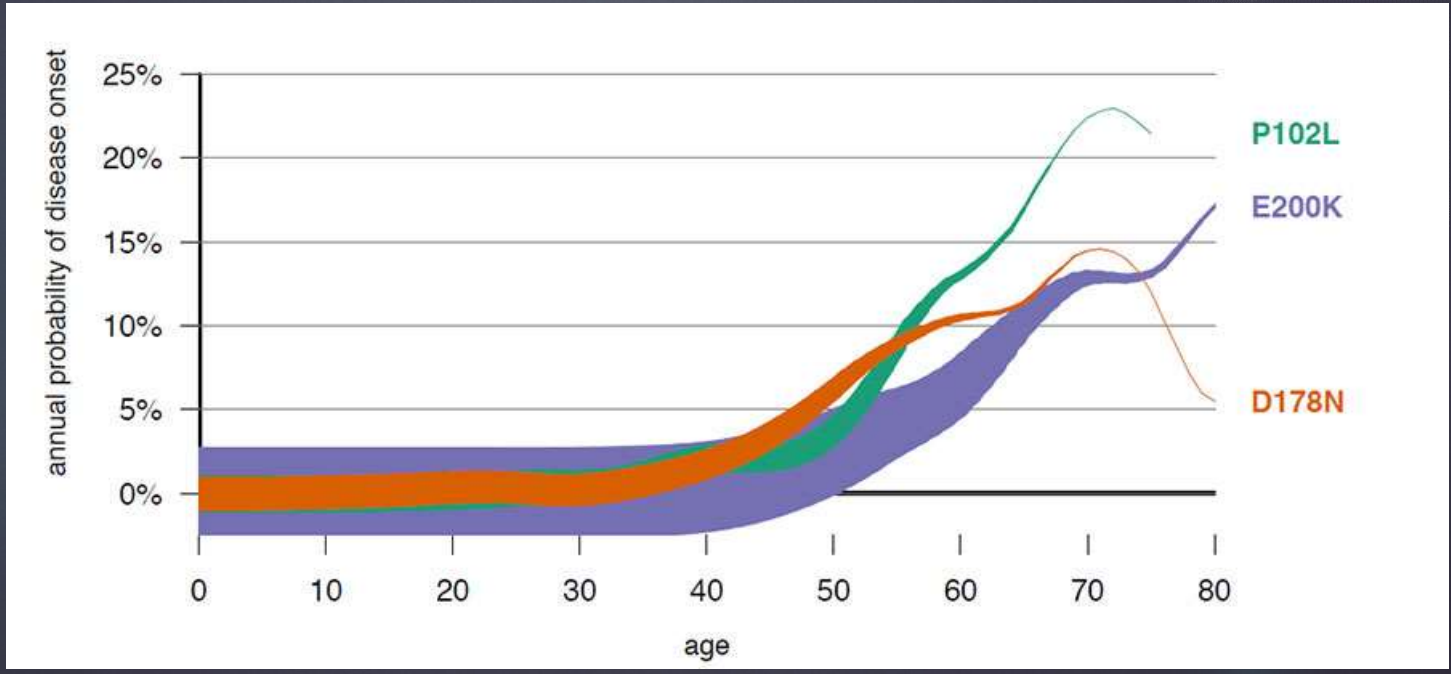
Delirium

Dementia.

The patients will survive 18 months only The mutated PrPC has been found in just 29 families worldwide, affecting about 78 people in total. If only one parent have the affected Gene the possibility of transfer is about 45%.

Gerstmann-Straussler-Scheinker disease (GSS)

(GSS) is an extremely rare, neurodegenerative brain disorder that is caused by an abnormal variant of the prion protein (PRPN) gene. The PRNP gene encodes the human prion protein (PrPc). Alterations in this gene lead to the generation of abnormally-shaped (misfolded) prion protein (PrPSc),



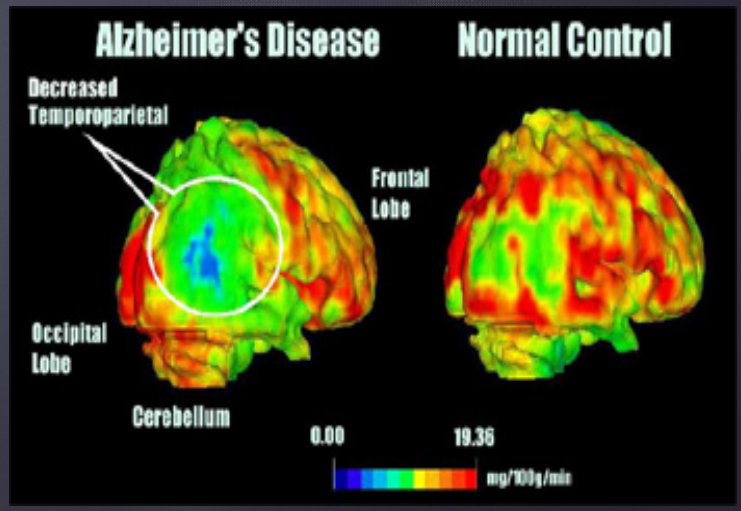

Alzheimer’s Disease is a
‘Double-Prion Disorder

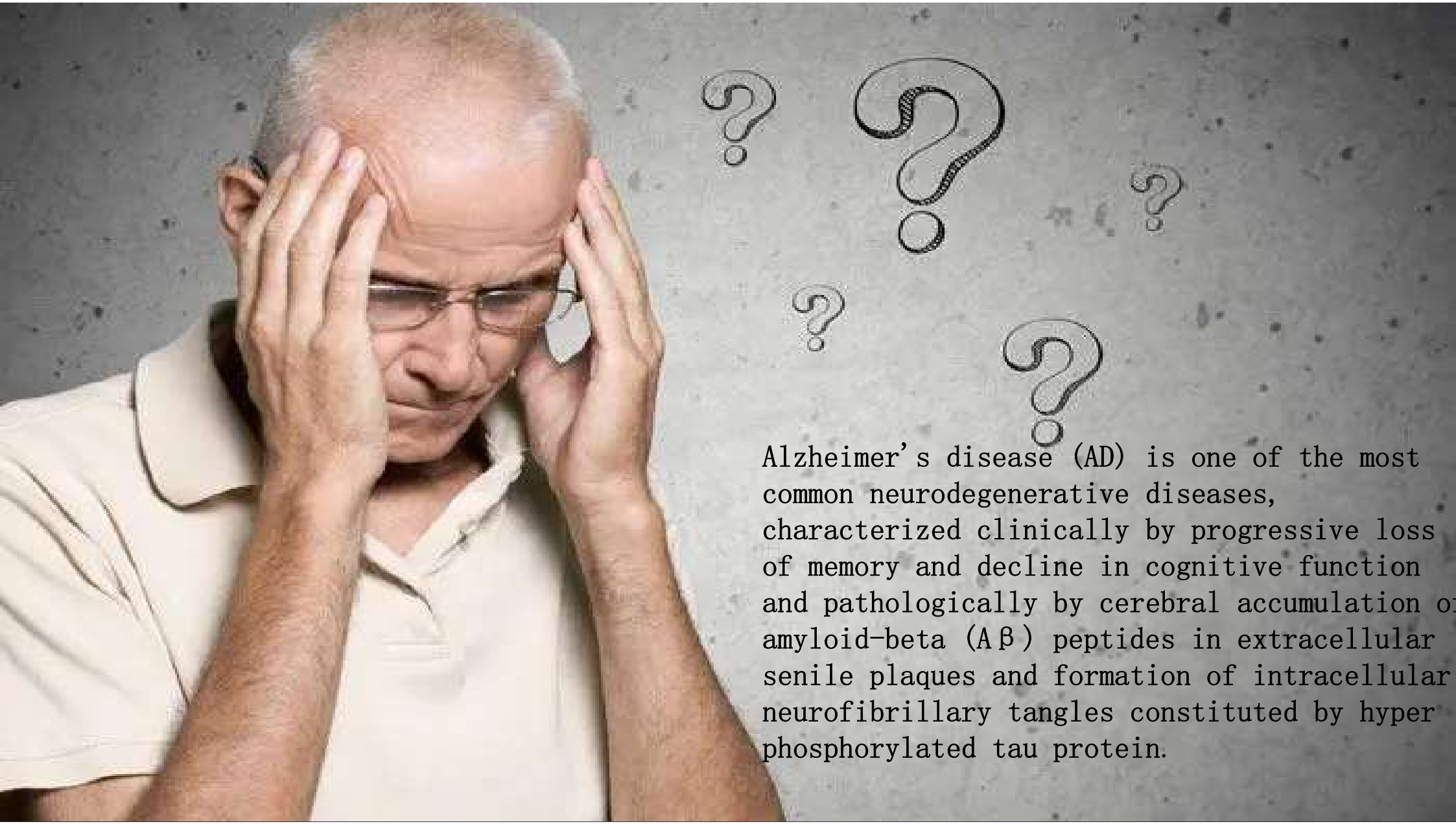
Alzheimer’s Disease

- The deterioration of intellectual capabilities, memory, judgment, and personality to the extent that daily functioning and quality of life are seriously impaired.
- Generally occurs in the elderly impairing brain function, which can lead to dementia.
- Named for German neurologist Alois Alzheimer in 1907.

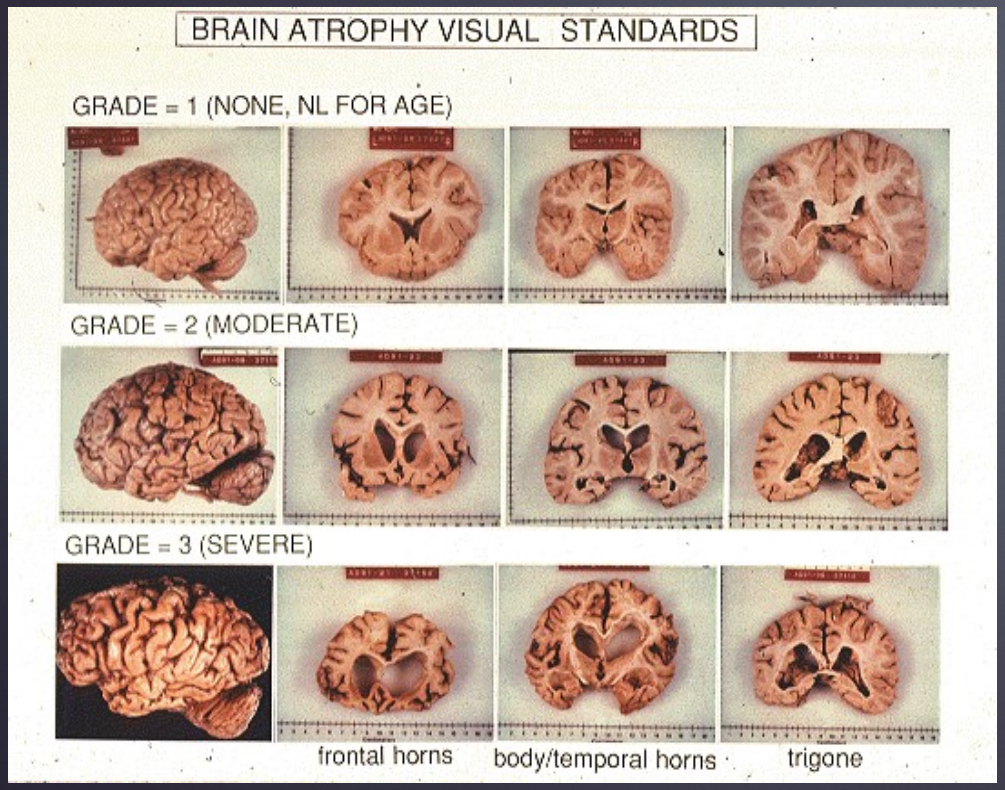
PREVALENCE

Approximately 5.8 million people in the United States age 65 and older live with Alzheimer's disease. 100,000 die each year.
Of those, 80% are 75 years old and older. Out of the approximately 50 million people worldwide with dementia, between 60% and 70% are estimated to have Alzheimer's disease.




Alzheimer's disease (AD) is one of the most common neurodegenerative diseases, characterized clinically by progressive loss of memory and decline in cognitive function and pathologically by cerebral accumulation of amyloid-beta (Aβ) peptides in extracellular senile plaques and formation of intracellular neurofibrillary tangles constituted by hyper phosphorylated tau protein.

Brain Degradation



Clinical Features

- Loss of short-term memory and ability to create memories
- Concentration on past
- Loss of time
- Communication diminishes
- Personality changes
- Delusions
- Become immobilized and uncomprehending
- Death due to respiratory failure
- 65 and up disease lasts 8-20 years
- 65 and down disease lasts 5-10 years disease more rapid

Many scientists have been reluctant to accept that Aß and tau are self-propagating prions — instead referring to their spread as "prion-like" — because unlike PrP prions, they were not thought to be infectious except in highly controlled laboratory studies

Stanley B. Prusiner
American neurologist

'' I believe this shows beyond a shadow of a doubt that amyloid beta and tau are both prions, and that Alzheimer' s disease is a double-prion disorder in which these two rogue proteins together destroy the brain."

CONCLUSION

There's currently no cure for Alzheimer’s and other neurodegenerative diseases, but medicines are available that can help relieve some of the symptoms.

Various other types of support are also available to help people with Alzheimer's and other neurodegenerative diseases live as independently as possible, such as making changes to home environment so it's easier to move around and remember daily tasks.

And we believe that knowledge about prions may help common humanity in treatment and management of Alzheimer’s and other neurodegenerative diseases

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THANK YOU