Prionoses (Transmissible Spongiform Encephalopathies)

Human Prionoses

- Creutzfeldt-Jacob Disease (CJD)
- Fatal Familial Insomnia (FFI)
- Gerstmann-Straussler-Scheinker *Syndrome* (GSS)
- Kuru
- Variant CJD (vCD)

Animal Prionoses

- Bovine Spongiform Encephalopathy (BSE) - *cows*
- Scrapie -*Sheep*
- Chronic Wasting Disease (CWD) – *Mules, deers*

Classification of Prionoses

- Familial/Hereditary
- Sporadic
- Infectious

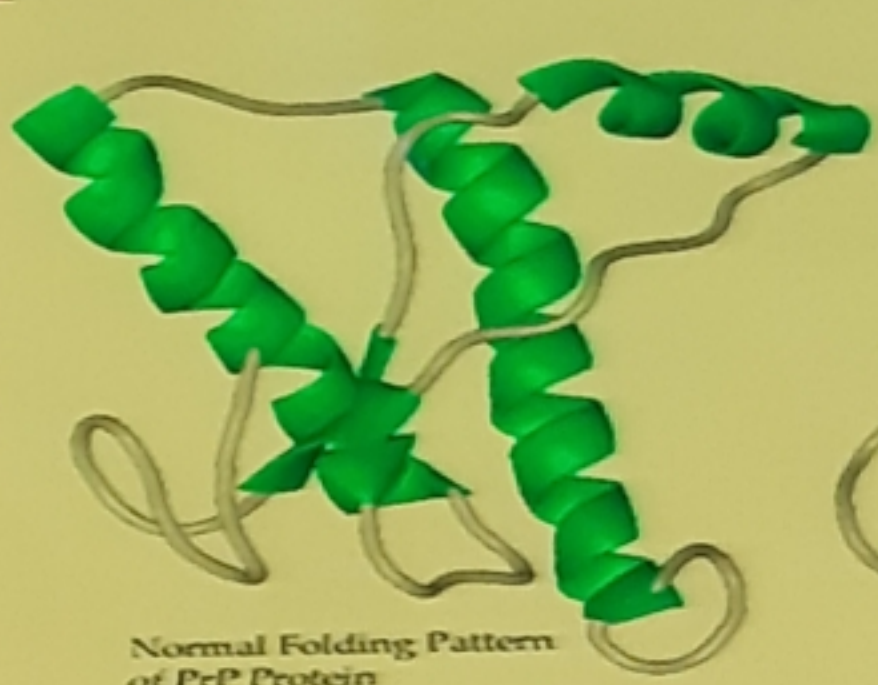
Prions: Definition

Small ***PRO****teinaceous* ***IN****fectious* particles that are *resistant to inactivation* by procedures that usually modify/denature proteins

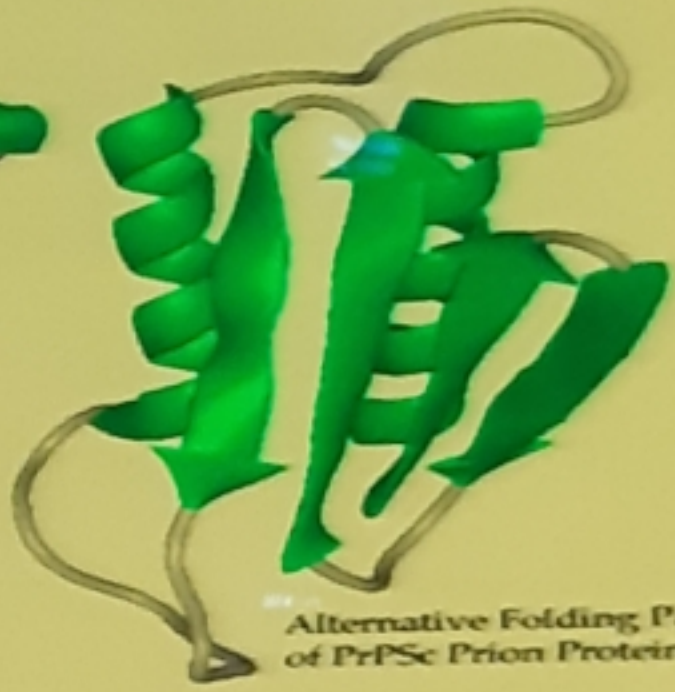
Prions: Characteristics

- Made of protein
- Resistant to inactivation
- Reproduce by converting normal protein to abnormal protein
- Do not induce the immune system
- Cause vacuolation of neurons >> spongiform appearance

Normal & Abnormal Prion protein

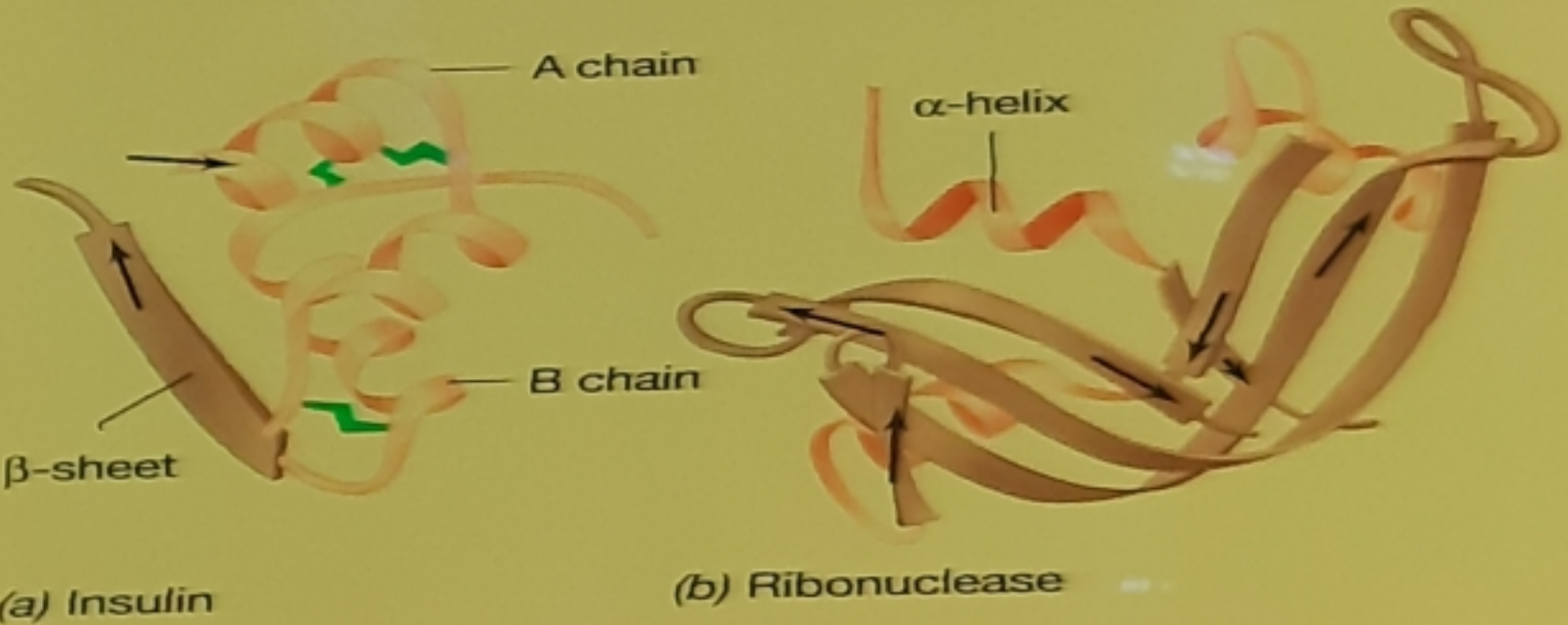


Normal Folding Pattern of PrP Protein



Alternative Folding Pattern of PrPSc Prion Protein

Protein structure: Examples



Cellular vs Scrapie Protein

Cellular (PrP^c)	Characteristic	Scrapie (PrP^{sc})
Predominantly Alpha-helical	**Structure**	Predominantly beta-sheets
Soluble	**Solubility**	Insoluble
Non-infectious	**Infectivity**	Infectious
Susceptible	**Resistance to Proteinase K**	Resistant

Transmission

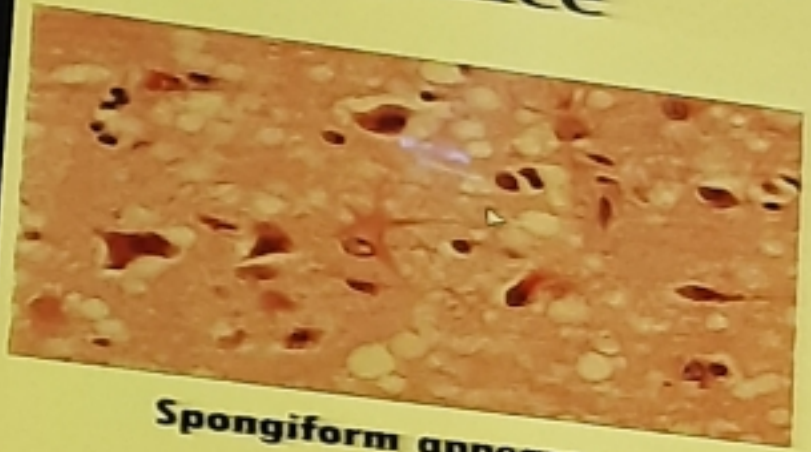
- Sporadic
- Iatrogenic: Blood transfusion, organ transplant
- Hereditary
- Ingestion
  - *Beef*
  - *Cannibalism*

Pathogenesis

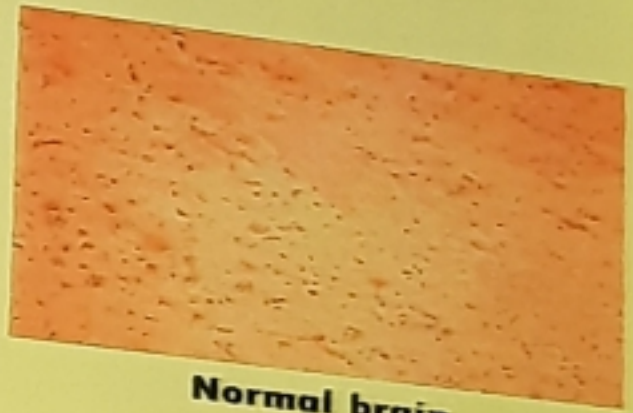
KEY FEATURE: Accumulation of abnormal prion protein PrP^{sc}

- Normal cellular protein (PrP^{c}) is found on the surface of brain cells & other cells
- Infection or Mutation of *PRNP* gene on c.20 can cause PrP^{c} to misfold into PrP^{sc}
- PrP^{sc} dissociates from the cell membrane
- PrP^{sc} causes more PrP^{c} to misfold and dissociate from the cell surface
- Accumulation of PrP^{sc} forms proteinaceous plaques between the brain cells
- Aggregated PrP^{sc} is then internalized into cells >> spongiform appearance

Vacuolation/spongiform appearance



Spongiform appearance



Normal brain

Clinical features

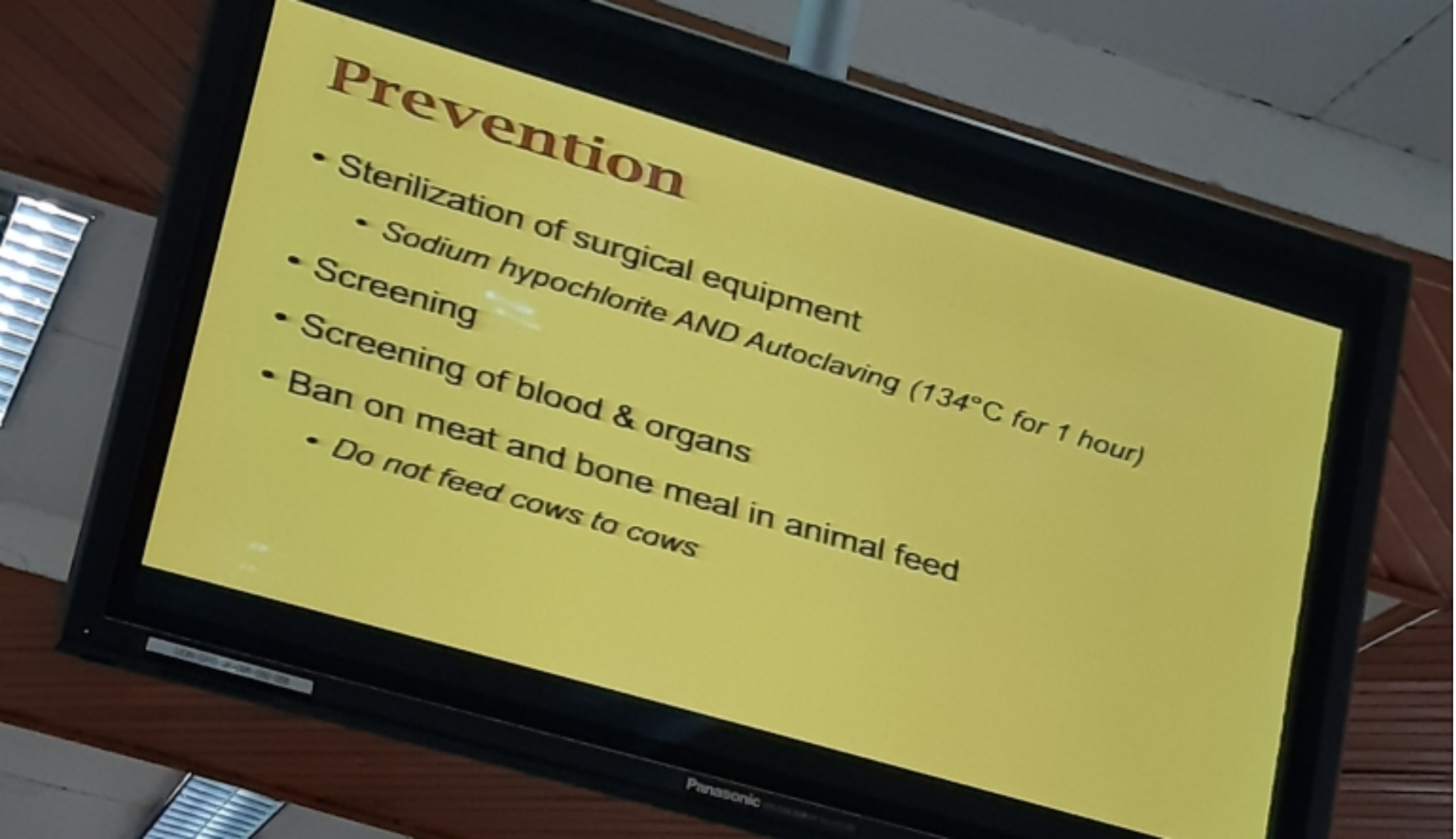
- Long incubation period, slow, progressive & fatal disease
- Cognitive impairment
- Ataxia
- Myoclonic jerks
- Mutism
- FFI: Insomnia, dysautonomia, motor paralysis

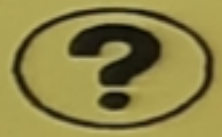
Diagnosis

- Clinical presentation
- Exclude Differentials
- CSF analysis (for 14-3-3 Protein and/or Tau protein)
- EEG
- MRI
- Brain biopsy (postmortem)

Treatment

- No treatment
- Prion diseases are invariably fatal (within months to years)
- Supportive treatment (Palliative care)


Prevention
• Sterilization of surgical equipment
• Sodium hypochlorite AND Autoclaving (134°C for 1 hour)
• Screening
• Screening of blood & organs
• Ban on meat and bone meal in animal feed
• Do not feed cows to cows
Panasonic



1. Describe the pathogenesis of prion diseases
2. What are the differences between PrP^{c} and PrP^{sc}
3. Outline 5 strategies for prevention of Prionoses