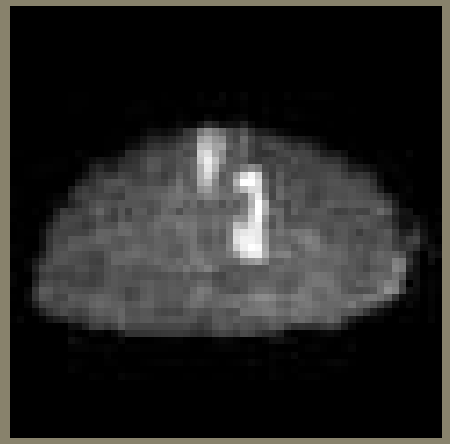
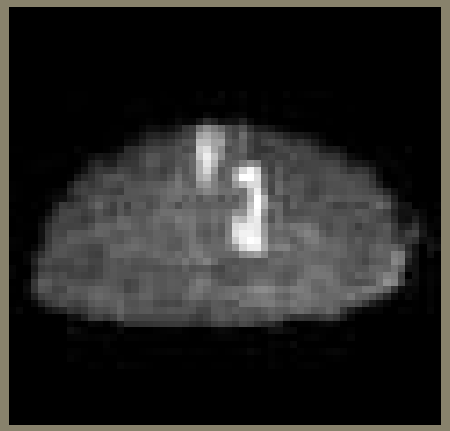
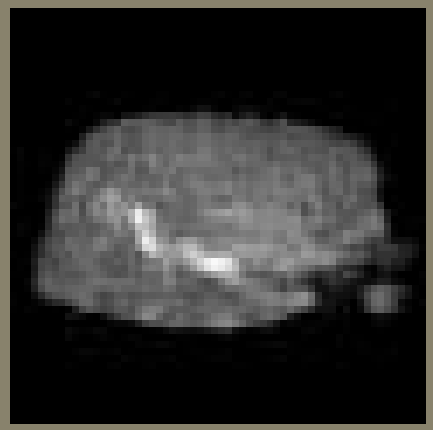
Fatal Familial Insomnia







The Human Genetic Prion Disease

Prion Diseases

- Fatal diseases affecting the Central Nervous System
- Causes spongiform degeneration of neurons (lesions) within the brain
- Characterized by a long incubation period
- Can be sporadic, inherited, or caused by ingestion of contaminated food

Prion: The Infectious Agent

- Prion: Proteinaceous Infectious Particle (PrP)
- Infectious prion is an aberrant isoform of the normal prion protein that every mammal possess
- PrP contains a protease-resistant fragment (leads to the build up of PrP within the brain)
- One PrP causes transformation of normal prion proteins; chain reaction accounts for the slow incubation period
- PrP causes apoptosis of neural cells

Fatal Familial Insomnia

- Affects people 30-60 yrs., progresses for 7-37 mos until death
- Genetically determined prion disease: dominant, autosomal gene
- Two families (pedigrees) in Italy, one in France, three in the U.S.
- Mutant allele for prion protein gene at position 129
- Mutant codon at position 178 is thought to activate the PrP gene.

General Symptoms

- Extreme reduction in sleep and acute restlessness
- Alteration of autonomic functions
- Motor signs include ataxia, disarthria, and myoclonus
- Dementia

Developing Stages of FFI

- Stage 1
  - Four months: progressive insomnia, panic attacks, bizarre phobias
- Stage 2
  - Five months: hallucinations, panic, agitation, intense perspiration
- Stage 3
  - Three months: complete insomnia, weight loss, incontinence
- Stage 4
  - Six months: muteness, sudden death

Sporadic Fatal Insomnia

- Non-genetic, hence, sporadic
- Possess same aberrant prion protein conformation
- Normal codon at positions 129 and 178
- Phenotypically identical to Fatal Familial Insomnia

Prevention and Treatment

- Pedigree histories, genetic screening for prevention
- No effective treatments

Scrapie Associated Prion Proteins

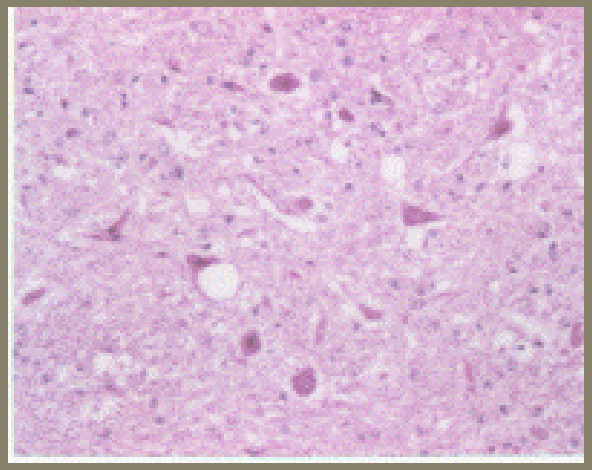
- All prion proteins are associated with the original scrapie protein found in sheep
- Two distinguishing characteristics between all prion diseases
  - Molecular mass of PrP
  - Glycoform ratio of PrP

Known Prion Diseases

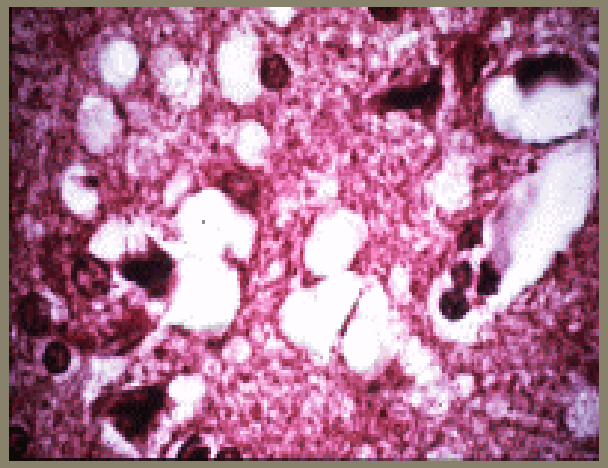
- Creutzfeldt-Jacob disease (human)
- Gerstmann-Straussler-Scheinker disease
- Mad Cow disease (bovine)
- Scrapie disease (sheep)
- Fatal Familial Insomnia (human genetic disease)

Kuru

Kuru: associated with cannibalism in New Guinea



Creutzfeldt-Jakob Lesions



Kuru Lesions

I’d rather eat beef !