Guess Who's Coming to Dinner-

"Mad Cow" Disease

Bree Murua-Cuney

History

- Description-

*** Transmissible Spongiform Encephalopathies (TSEs).**

***TSEs can be passed or spread from one to another.**

***TSEs are fatal neurodegenerative diseases affecting humans & animals**

*** Brain tissue contains microscopic vacuoles .**

Disturbing Nature

-Effects of the Disturbance-

- **Late 1970s- rendering industries changed their rendering process to eliminate processing step**
  - **British government banned ruminant-to-ruminant feeding in 1988**
  - **U.S. did not ban ruminant-to-ruminant feeding until ’97**
- **Mid and late 1990s, 21 cases of a new form of CJD identified in United Kingdom**
- **Suspicious products - gelatin, medication capsules, and cosmetics**

TSEs

-Animal TSEs-

- **Experimentally, the causative agent for CJD has been isolated from or transmitted to many animals- monkeys, mice, cats, raccoons**

*** Animal use:**

- **to determine sterilization and decontamination guidelines**
- **establish a definite diagnosis**
- **research the unknown factors of the disease**

PrP^C

-Causative Agent-

- **Suspected causative pathogen of CJD is the prion, a protein smaller than a virus and possibly devoid of nucleic acid**
- **Normal cellular prion protein (PrP^C)**

- **Tertiary structure of PrP^C-> 40% α-helix and little β-sheet**

TSEs Continued

Infectious particle composed largely of an abnormal disease-causing form (PrP^{SC}) of PrP^{C}

Normal prions fold into a stable configuration then partially unfold

Possibly unfold → pathogenic prion

PrP^{sc}

- Substitution of an amino acid within any of the α-helical segments:
  protein flips into the pathogenic β-sheet conformation
- Pathogenic PrP^{sc}: more β-sheet content and little α- helix
- Abnormal prion (PrP^{sc}) accumulates in brain, wreaking havoc

PrP^{sc}

- **Accumulation of PrP^{sc} follows an increase in infectiousness**

Ongoing process with no latency of the infectious agent during the asymptomatic period

Certain organs (brain, spinal cord, and retina) are very infectious long before clinical signs

Protein

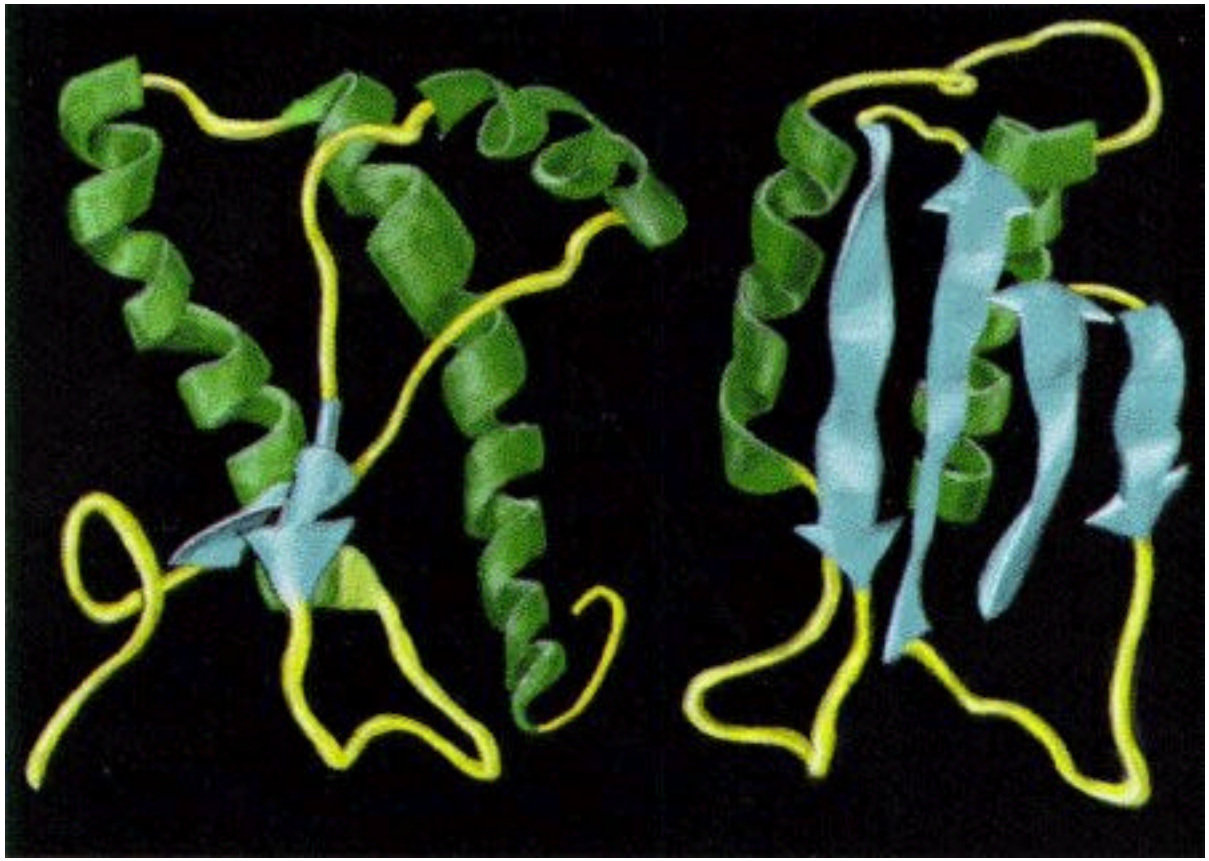

Fig. 4

Normal PrPc (left) & Prion (right)

Chaperones & Proteases

Quality Control

- Abnormal prion proteins stick together and form plaques

- Chaperones & proteases control

protein structure & function

Chaperones & Proteases

- **Chaperones- promote proper protein folding, prevent aggregation & dissolve aggregates**

- **Protect proteins by binding to them**

*** Proteases- eliminate irreversibly damaged proteins**

Aggregation

Failure of Quality Control

- Protein aggregates remove amino acids
- disrupt cellular functions
- tie up chaperones & proteases

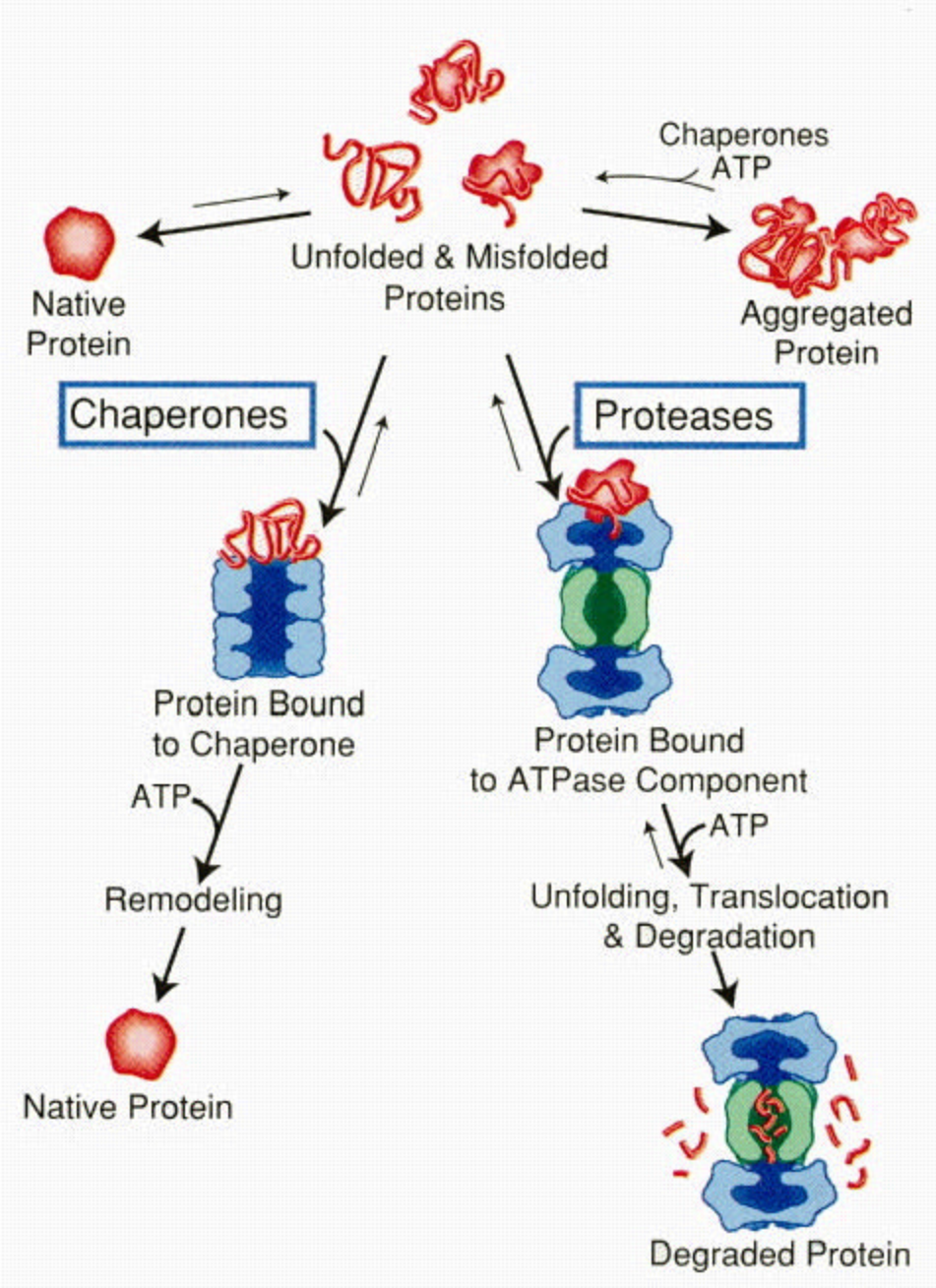

Fig. 3

Protein Model for Quality Control

Amyloid Plaque in new variant CJD

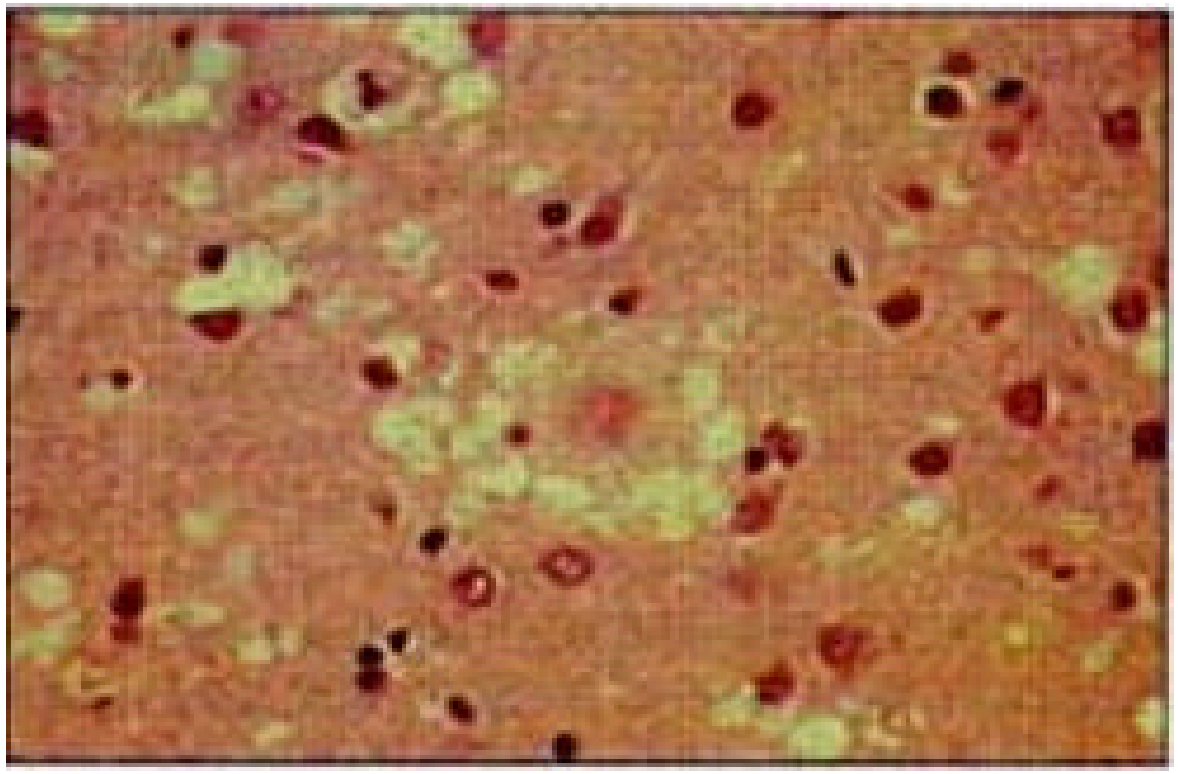

Fig. 4

Amyloid Plaques in sporadic CJD

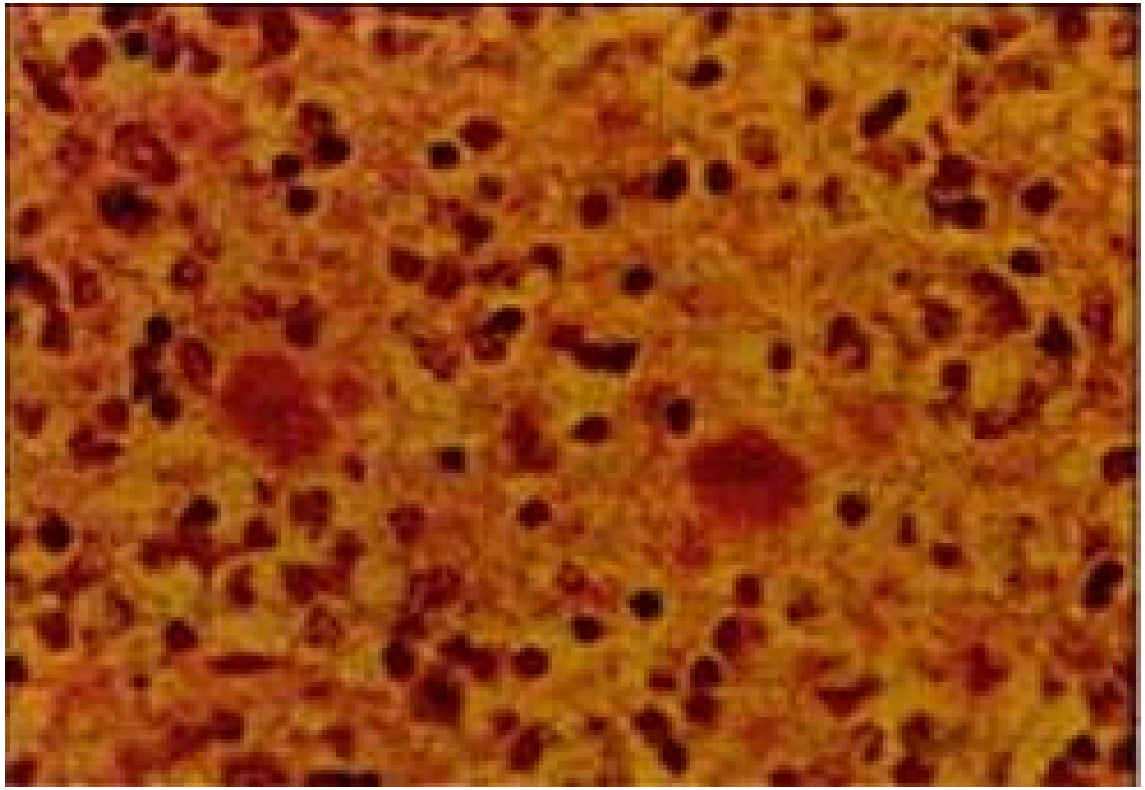

Fig. 6

Incidence of CJD

-Epidemiology

*** Sporadic- 90% of cases**

*** Genetic- 5%-10% of cases**

*** Iatrogenic -**

Rare disease fewer than 1% of human cases

*** ~ 1 case/million people worldwide**

- **No sex discrimination or socioeconomic differences.**

•Incidence in health care workers does not exceed what would be expected by chance alone.

Incidence of CJD in Health Care Workers

Type of Worker	Number with CJD
Neurosurgeon	2
Pathologist	1
Other physician	3
Nurse	9
Dentist	3
Nurse assistant	3
Dental surgeon	1
Histopathology technician	2

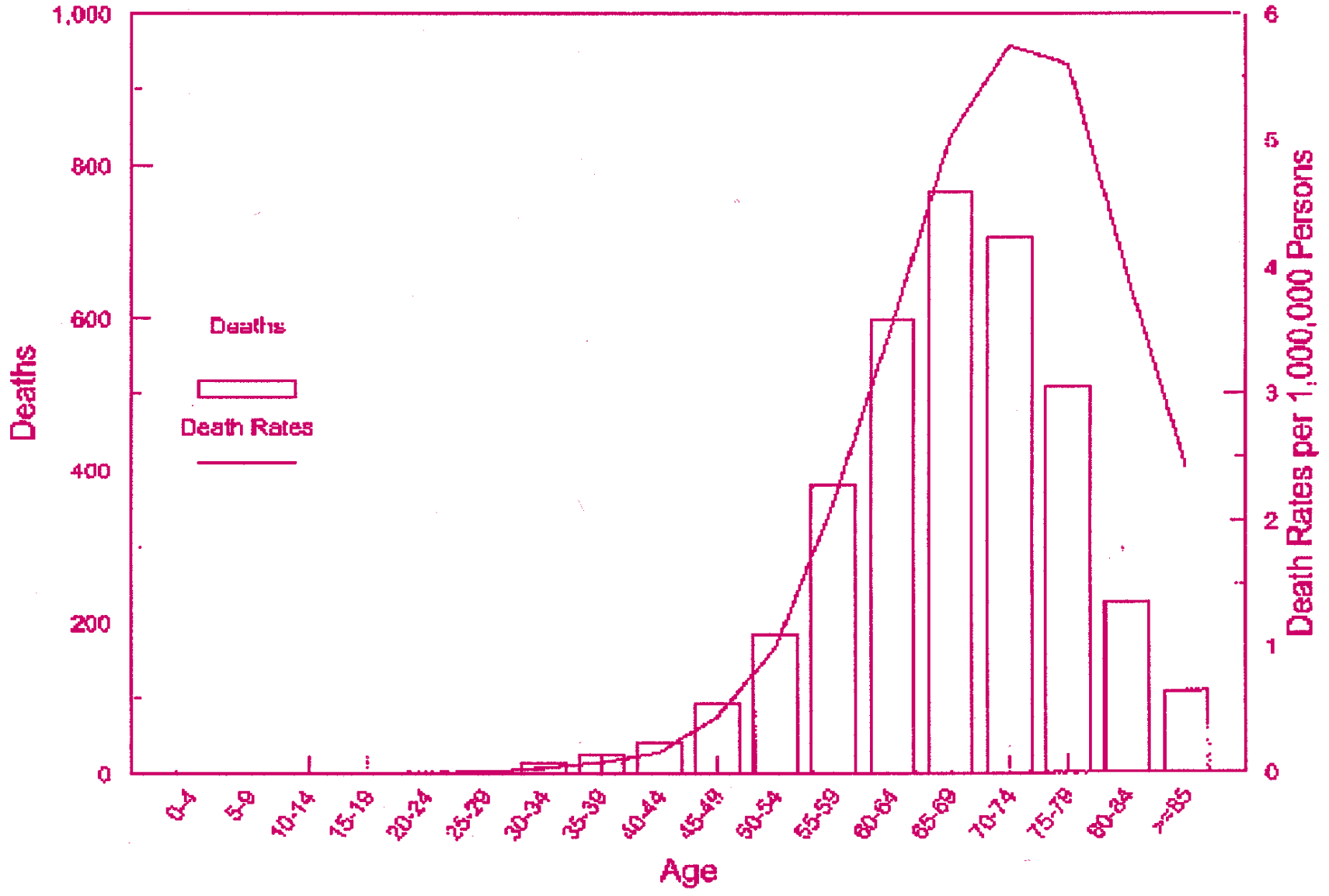

Figure 2. Creutzfeldt-Jakob disease deaths and death rates by age group, United States, 1979 through 1994.

Symptoms

-Clinical Features-

- **Cerebellar ataxia (defective muscular coordination)**

- **Cognitive and motor cerebral cortex most affected by prion aggregation**

Symptoms

* Develop involuntary muscle jerks, and may go blind or lose bladder control

* Lose ability to move and speak, enter a coma

* Pneumonia and other infections often occur, leading to death

* Mental changes→ Dementia→ Death

Symptoms

- **Behavior disturbances,**

  emotional instability, &

  impaired memory, judgment, &

  thinking

*** Insomnia, depression, or unusual sensations**

Development of CJD

Clinical Course

*** Mean age onset: 57-62 years**

*** Incubation stage: gradually develops over a period of 30+ years (no clinical symptoms)**

Development of CJD

- After appearance of symptoms, no remission

- Average duration of illness from onset of symptoms to death: 7-9 months

Diagnosing CJD

-Diagnosis-

*** Blood test**

- **Definite diagnosis- brain biopsy or autopsy**
- **Definite diagnosis- inoculate lab animal with diseased brain tissue & obtain a transmission**

Diagnosing CJD

- **MRI**

  nvCJD- vast number of amyloid plaques surrounded by daisy petal vacuoles

  *** Sporadic CJD- many large amyloid plaque deposits with vacuoles (no daisy config.)**

- **EEG**

- **Tonsil Biopsy**

Treating CJD

-Treatment-

- **Currently no treatment for CJD or any other TSE**

*** Only treatment to alleviate symptoms**

Opiate Drugs

Catheter

IV Fluids

Artificial Feeding