Prion Disease History and Transmission in a Medical Setting

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Objectives

1. Discuss History of Prion Related Diseases
2. Discuss Status of current Prion Diseases
3. Discuss Prion Transmission in a Medical Setting.

Nomenclature

- Prion – proteinaceous infectious particles
  - 1982 by Prusiner
- Slow virus or viroid
- Transmissible spongioform encephalopathies (TSE)
  - Long incubation period
  - Neurological signs and symptoms
  - Multifocal spongiform changes of brain
  - Neuronal loss
  - Absence of inflammatory reaction

Prion Proteins (PrP)

- PrP-C – normal product in mammals and birds.
  - Function is unknown
  - Mice bred without PrP-C resistant to scrapie
  - Essential for prion disease
  - 42% alpha helix, 3% beta helix
- PrP-res – abnormal present in disease
  - Cytoplasm of infected cells
  - 43% beta helix, 30% alpha helix
  - Resistant to heat, radiation, proteolytic enzymes and conventional disinfectants (alcohol, formalin, phenol)
  - Recruits PrP-C to configure as PrP-res possibly by acting as a template for new PrP-res.

Infectivity of Tissues

- High infectivity: Brain, spinal cord, eye
- Low infectivity: CSF, Kidney, Liver, Lung, Lymph nodes, Spleen, Placenta
- No infectivity: fat, adrenal, gingival tissue, heart muscle, intestine, peripheral nerves, prostate, skeletal muscle, testis, thyroid gland, tears, nasal mucosa, saliva, sweat, serous exudates, milk, semen, urine, feces.

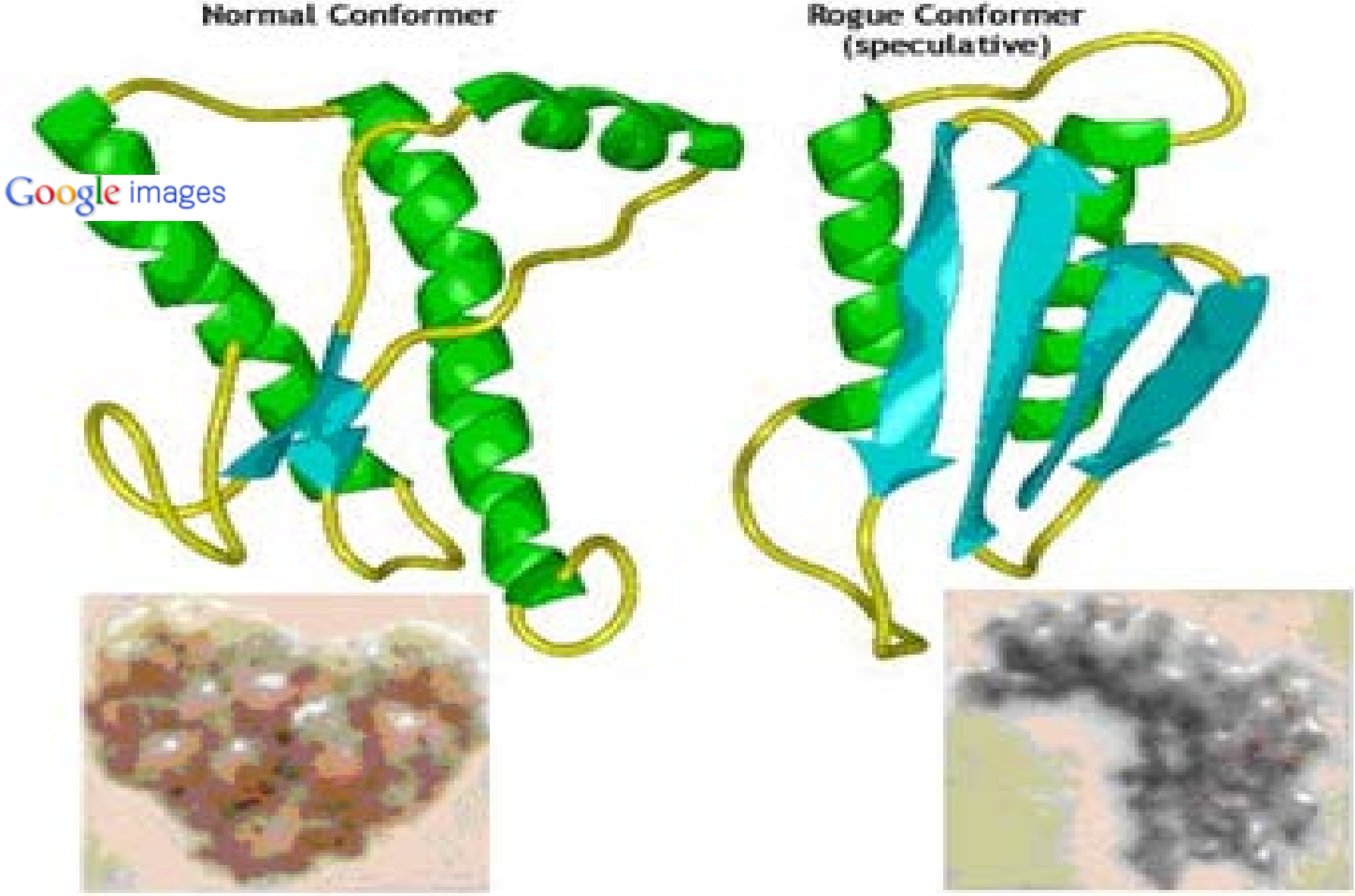
Scrapie – TSE of Sheep and Goats

- Found world wide
- Neurodegenerative disease
- Incubation time – 2-5 years
- Transmission –
- Ingesting fetal membranes and fluid
- Direct contact between sheep
- Host's genotype influences susceptibility and resistance.
- Food contaminated with infected PrPscr may have facilitated transmission across species

Properties of normal and scrapie-associated Prion protein isoforms

	PrPC	PrPsca
Encoded chromos 20	yes	yes
Present in normal brain	yes	no
Present in Scrapie brain	yes	yes
Soluble in detergent	yes	no
Effect of protease	hydrolyzed	resistant
Tertiary structure	40% alpha	30% beta
Quatenary structure	monomer	aggregated

Mandell, Inf. Disease, Table 178-1 page 2424



www.ecdc.europa.eu/en/healthtopics/Variant_Creutzfeldt-Jakob_diseasehealt.aspx

TSE's in Animals

- Sheep and Goats – Scrapie
- Deer and Elk – Chronic wasting disease
- Mink – transmissible mink encephalopathy
- Cows – bovine spongiform encephalopathy (BSE) mad cow disease
- Cat family – feline spongiform encephalopathy
- Exotic ungulate encepahlopathies
- Research settings – mice, guinea pigs

Bovine TSE (mad cow disease) vCJD

- UK 1986- 1998
- 173,952 cases in 34,500 herds
- Destruction of millions of cows

TSE's in Humans

- Creutzfeldt-Jakob Disease (CJD)
- Kuru
- Gerstmann-Straussler Syndrome (GSS)
- Fatal Familial Insomnia (FFI)
- New Variant CJD (vCJD)

Creutzfeldt-Jakob Disease -- CJD

- 1920's by Creutzfeldt – four cases with progressive dementia, tremors, spasticity, ataxia and myoclonus
- Found worldwide – spontaneous
- Almost equal sex ratio
- Peak onset – 55-75 (mean 61.5)
- Incidence 1 per million
- Rapid progression – mean time to death 7.6 months
- No treatment

Belay, TSE in Humans, Annu. Rev. Microbiol 1999, 53:283-314

CJD Diagnosis

- Clinical setting
- EEG – typical diagnostic pattern
- Immunoassay – 14-3-3 protein
  - 96% sens, 96-99% specificity
- MRI – suggestive pattern
- Brain biopsy – spongiform changes, gliosis, neuronal loss in the absence of inflammatory reaction

Belay, TSE in Humans, Annu. Rev. Microbiol., 1999, 53:283-314

Search for Risk Factors for CJD

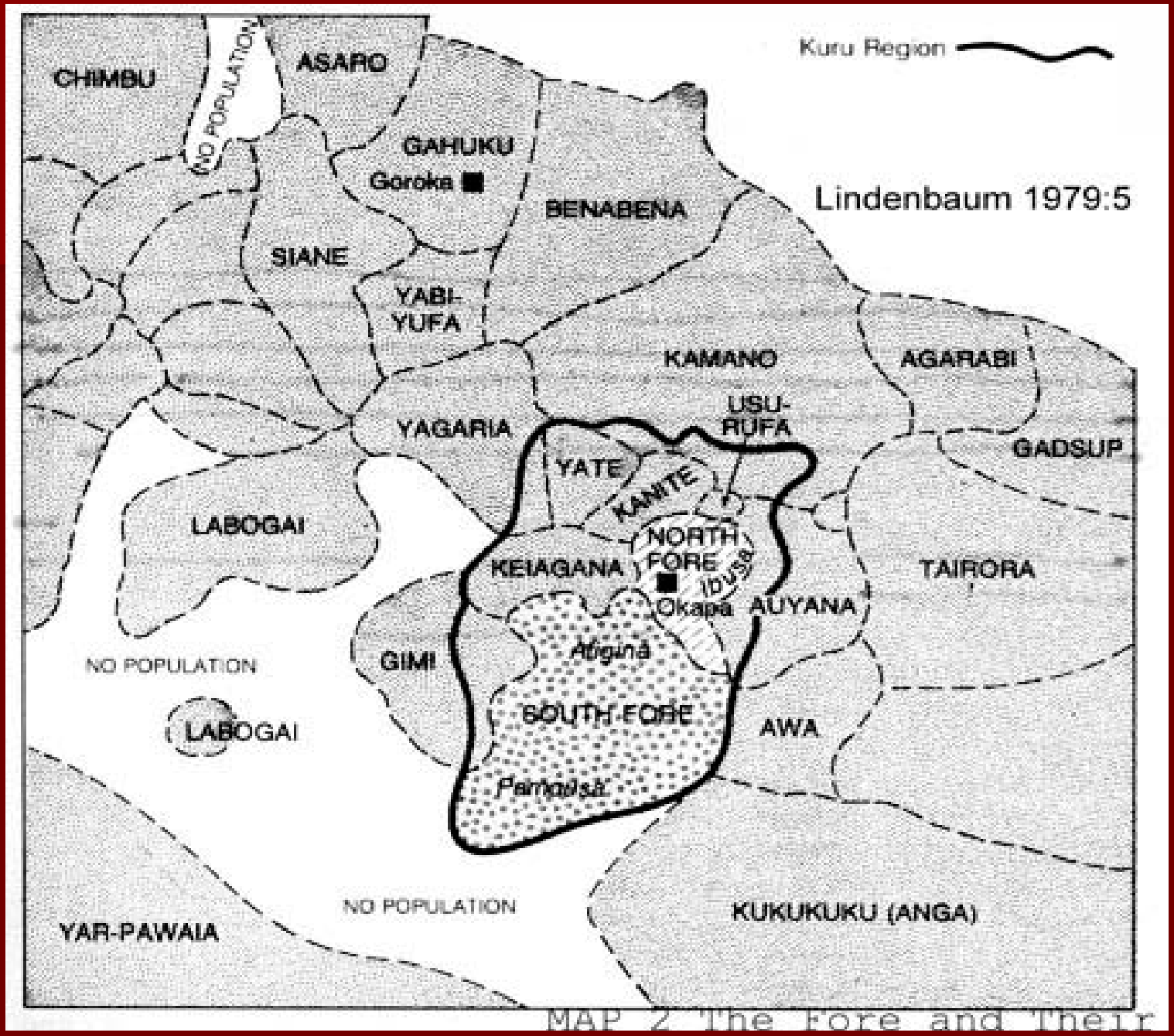
- No association:
- - MDs, Nurses, dentists laboratory workers, ambulance personnel
  - Head trauma, transfusions, hx of surgery, eating organ meat, brain, liver, and kidney
  - Exposure to animals of animal products
  - Not related to increased blood exposure

Belay, TSE in Humans, Annu. Rev. Microbiol., 1999, 53:283-314

Familial CJD

- Gerstmann-Straussler-Scheinker Syndrome, Fatal Familial Insomnia,
- Accounts for 5-15% of CJD
- Specific codon mutations – 102, 105, 129, 178, 208, 210, 180, 232, 200.
- Autosomal dominant
- Variable penetrance
- PrP may be more likely to form a beta helix.

Belay, TSE in Humans, Annu. Rev. Microbiol., 1999, 53:283-314



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Kuru in Papua New Guinea

- 1,100 plus of 8,000 died
- Male:Female 1:8
- Age: small children and elderly
- Incubation: 2 to 50 years
- Mortuary cannibalism
- Disappeared with end of cannibalism

National Prion Disease Pathology Surveillance Center 1996 - 2011

- Total Referrals 3952
- Prion Disease 2329
- Sporadic CJD 1965
- Familial 338
- Iatrogenic 5
- vCJD 3 (UK 2, Arabia 1)

www.cjdsurveillance.com

Iatrogenic 2005

- Human pituitary derived 180
- Human dura mater allografts 168
- Human gonadotrophin 4
- Neurosurgery instruments 4
- EEG electrodes 2
- Transfusions 3
- Variant CJD 192
  - UK 161, France 17, Ireland 4, US 2, Netherlands 2, 1 each in Canada, Italy, Japan, Portugal, Saudi Arabia and Spain.

Iatrogenic CJD -- 2006

- Human Growth Hormone 198
- Dura mater graft 196
- Neur. Surg. instruments or EEG electrodes 6
- Corneal Transplant 2

Mandell, Inf. Diseases, Chapter 178, page 2431

Occupational Exposure

- No Confirmed case due to occupational accident or injury
- Health care workers links have been suggested
- Contact with high or low infectivity tissues should be avoided: especially with contamination of broken skin or contact with mucus membranes.

Routes of Exposure

- Ingestion: Kuru
- Blood transfusion: vBSE
- Cutaneous exposure: negligible
- Mucus membrane: possible risk
- Transcutaneous exposure: potential risk

- Risk is increase if exposure to a high risk tissue or fluid

Patient Care Settings and TSE

- Isolation is not necessary
- Private room is not required
- Body fluids: no detectable risk except CSF
- No precautions for eating utensils, feeding tubes, suction tubes, bed linens, bed sore care
- Diagnostic procedures: use disposable equipment, strict decontamination of instruments.

Surgery of Known of Suspected TSE

- Surgery in operating theatre
- Minimum personnel
- Single use equipment
- Mask all non-disposable equipment
- Maintain one way flow of instruments
- Dispose of all clothing and covers
- Mark samples as Biohazard
- Clean all surfaces.

Cleaning Instruments and Environment

- Keep used instruments moist
- Cleaned soon after procedure
- Sort for level of tissue exposure
- Re-use only if adequately decontaminated
- Cover work surfaces with disposable material
- Be familiar with safe use of NaOH and Sodium Hypochlorite chemicals

Post-exposure Management

- Unbroken skin- wash with detergent and warm water. Brief exposure to 0.1N NaOH or a 1:10 dilution of bleach.
- Needle stick or laceration: encourage bleeding, wash with warm soapy water.
- Splashes of the eye: irrigate with saline or tap water.

Clinical Laboratory

- Blood and other body fluids: no transmission reported – can be considered none infectious.
- CSF: may be infectious, incinerated or decontaminated.

Laboratory for low and high infectivity tissues

- Experienced personnel
- Labeled Biohazard
- Single use protective clothing – liquid repellant gowns, gloves, mask, goggles
- Use disposable equipment – clean or incinerate
- Use non-permeable material to cover work space.
- Fixatives and waste fluids – decontamination
- Restrict number of personnel.

Identification of Persons at Risk for TSE

- Recipients of dura mater (110 cases)
- Recipients of human pituitary hormones (130 cases)
- Recipients of cornea transplants (3 cases)
- Persons who have undergone neurosurgery
- Members of families with hereditable TSE (5-10% of all TSE cases.)

Decontaminants Chemical

- Ineffective
  - Alcohol
  - Ammonia
  - B-propiolactone
  - Formalin
  - Hydrochloric acid
  - hydrogen peroxide
  - Peracetic acid
  - Phenolics
  - Sodium dodecyl sulfate
- Variably or partially effective
  - Chlorine dioxide
  - Glutaraldehyde
  - Guanidinium thiocyanate
  - Iodophores
  - Sodium dichloro-isocyanurate
  - Sodium metaperiodate
  - urea

Gaseous Disinfectants

- Ineffective:
  - Ethylene oxide
  - formaldehyde

Physical processes

- Ineffective:
  - Boiling
  - Dry heat
  - Ionizing UV or microwave radiation
- Variably or partially effective
  - Autoclaving at 121 C for 15 minutes
  - Boiling in 3% sodium dodecyl sulfate

General Protective Measures

- No Eating, drinking, smoking cosmetics
- Use disposable gowns or decontaminate non-disposable gowns
- Safety glasses or face shields
- Gloves – must be worn
- Avoid or minimize use of sharps
- Minimize formation of aerosols or droplets
- Decontaminate work surfaces
- Decontaminate or incinerate specimens
- Report exposures and/or accidents
- Ensure adequate training of safety procedures.

Decontamination

- Incineration – tissues and disposables
- Autoclave – NaOH soak and heat
- Immerse in Na Hypochlorite
- Benches and heat sensitive instruments – soak one hour in NaOH or Na hypochlorite

- ** 1 Normal NaOH – 40gm/liter
- ** 20,000 ppm available chlorine – undiluted 5.25% bleach contains 25,000 ppm

Prion Disease

- Unique disease that reconfigures a normal host protein into a disease causing protein
- Can be transferred from subject to subject within and among mammalian species
- Difficult to diagnose prior to symptoms
- No treatment available
- Infection control measures have been effective in limiting spread