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

<table>
<thead>
<tr>
<th></th>
<th>PrPC</th>
<th>PrPscA</th>
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<tbody>
<tr>
<td>Encoded chromos 20</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Present in normal brain</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Present in Scrapie brain</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Soluble in detergent</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Effect of protease</td>
<td>hydrolyzed</td>
<td>resistant</td>
</tr>
<tr>
<td>Tertiary structure</td>
<td>40% alpha</td>
<td>30% beta</td>
</tr>
<tr>
<td>Quaternary structure</td>
<td>monomer</td>
<td>aggregated</td>
</tr>
</tbody>
</table>

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

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

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

Familial CJD

- Gerstmann-Straussler-Scheinker Syndrome, Fatal Familial Insomnia,
- Accounts for 5-15% of CJD
- Autosomal dominant
- Variable penetrance
- PrP may be more likely to form a beta helix.

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 or 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 repellent 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