Epidemiology and Surveillance of Creutzfeldt-Jakob Disease in the United States

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Transmissible Spongiform Encephalopathies (TSEs)

- Subacute, transmissible neurodegenerative diseases
- Affect both animals and humans
- Distinctive clinical and pathologic features
- Due to unconventional, novel transmissible agent—prion hypothesis
Prion Hypothesis

- Prion—proteinaceous infectious particle
- Normal protein (PrP\textsuperscript{c}) encoded on short arm of chromosome 20; expressed in high concentrations in nervous tissue
  - Role of normal PrP\textsuperscript{c} unclear—cell signaling?
  - In normal state, non-pathogenic
- Abnormal form of prion protein (PrP\textsuperscript{TSE}) is pathogenic—may form by:
  - Spontaneous (stochastic) conversion
  - Genetic mutation
  - Conversion of normal PrP\textsuperscript{c}
PrPc – PrP^{TSE} “Conversion”
Prions as Transmissible Agents

- Protein as etiology of infection
- Unique characteristics for transmissible agent
  - Both transmissible and inherited
  - Extremely long incubation period (years)
  - Resistant to physical/chemical sterilization
  - Invariably fatal
TSEs: Pathology

• Unifying feature of all TSEs is underlying neuropathology
  – Predominantly gray matter
  – Neuronal loss
  – Gliosis
  – Spongiform changes
  – Absence of inflammatory reaction
Spongiform Changes

Normal Cortex  CJD Cortex
TSEs: Animals

- Scrapie—sheep, goats
- Bovine Spongiform Encephalopathy (BSE) –cattle
- Chronic Wasting Disease (CWD)—deer, elk
- Transmissible mink encephalopathy
- Feline spongiform encephalopathy
- Spongiform encephalopathy of captive ungulates
TSEs: Humans

• Sporadic
  – Creutzfeldt-Jakob disease (CJD)

• Acquired
  – Iatrogenic CJD (neurosurgical instruments, dura mater grafts)
  – Kuru
  – Variant CJD (vCJD)

• Familial (genetic)
  – Familial CJD
  – Gerstman-Straussler-Scheinker Syndrome (GSS)
  – Fatal Familial Insomnia (FFI)
“Classic” Creutzfeldt-Jakob Disease

- Prototypical TSE in humans
- Incidence of about 1 per million population per year worldwide
- Median age at onset 68 years
- Rapidly progressive dementia
  - Early dementing symptoms
  - Development of movement disorders, characteristic EEG changes
  - Progression to akinetic mutism, eventually death
  - Median interval between diagnosis and death 6 months; survival longer than a year unusual
Creutzfeldt-Jakob disease deaths and death rates by age group, United States, 1979-2001
Iatrogenic CJD

- Uncommon
- Contaminated neurosurgical instruments
- Dura mater grafts
- hGH recipients
- Specific recommendations for decontamination
Familial CJD

- Genetic mutation in gene encoding prion protein
- ~5% of cases
- Forms
  - Familial CJD
  - Gerstman-Straussler-Scheinker Syndrome (GSS)
  - Fatal familial insomnia
BSE and variant CJD

- Late 1985—cattle in disparate locations in UK dying of strange neurologic illness
  - Pathology appeared similar to scrapie
  - Identified as a novel TSE in cattle

- Explosive epidemic due to feeding practices
  - 1988 – 1989: Feed ban resulted in dramatic decrease

- 1990—heightened surveillance for CJD in the UK in light of BSE epidemic
  - 10 patients found to have features very different than “classic” CJD

- 1997: Epidemiology, neuropathology, animal studies suggested link between BSE and vCJD
Variant CJD

- Young age at onset
- Prominent early behavioral features—psychosis, depression
- Prominent early sensory abnormalities
- Movement disorders late
- Longer duration of illness
- Distinct neuropathology—presence of “florid plaques”, similar to that of BSE
Percent distribution of non-iatrogenic\# UK vCJD and US CJD deaths, by age group, 1995-2003

\# Excludes blood transfusion-associated vCJD and pituitary hormone- or dural graft-associated CJD

\* UK vCJD deaths, including UK-related nonresident cases, 1995-2003 (Will, RG; personal communication, 2004)

Deaths of Definite and Probable vCJD, UK, 1995 - 2004
CJD Surveillance

- Surveillance—detection of disease in population
  - Estimation of CJD disease rates
  - Detect changes over time
  - Gain better understanding of CJD in general
- Surveillance for CJD enhanced in 1996 in response to emerging threat of vCJD
CJD Surveillance Pitfalls

- No reliable antemortem diagnostic test
- Disease confirmed by pathology, but autopsy rates low
- Clinical diagnosis not always considered
- Long incubation period (years)—difficult to identify “common source” cases
How Does CDC Conduct CJD Surveillance?

- Periodic review of national cause-of-death data
- Active investigation of CJD decedents < 55 years of age
- Establishment and support of National Prion Disease Pathology Surveillance Center (NPDPSC)
- Active collaborative surveillance of special groups (hGH, blood transfusions)
- Spontaneous reporting by clinicians and public (iatrogenic cases, possible vCJD, etc.)
Review of Mortality Data

• Data for entire US at CDC’s National Center for Health Statistics (NCHS)

• Features of CJD amenable to mortality surveillance
  - 100% fatality rate
  - Diagnosis more accurate at terminal stages

• Rates, demographics essentially stable since 1979
  - 1.1/million population
  - Median age at death: 68 years
  - >98% of decedents >45 years
  - None <21 years
Creutzfeldt-Jakob disease age-specific and age-adjusted death rates, United States, 1979-2001
Investigation of Cases <55 Years

- Cases identified in cooperation with state health departments
- Clinical records obtained and reviewed
- Neuropathology reviewed if possible
- To date: no evidence of vCJD among 175 CJD deaths in patients <55 between 1994 – 2001
National Prion Disease Pathology Surveillance Center (NPDPSC)

- 1996-97: Collaboratively established by CDC and AANP
- Pathologists/neuropathologists requested to submit brain tissue specimens
- Free state-of-the-art diagnostic service
- Addressing need to increase autopsy rates in U.S.
Blood Transfusion, Iatrogenic CJD

• Longitudinal follow-up of blood transfusion recipients
  – 2003 – 04: 2 cases of probable transfusion-associated vCJD
  – Ongoing active collaborative monitoring of transfusion-associated sporadic CJD (sCJD) in US
  – No evidence of transmission of sCJD through blood to date
  – Continued surveillance; measures to protect U.S. blood supply

• Possible iatrogenic cases investigated and followed
  – Dura mater recipients
  – Human growth hormone recipients
  – Neurosurgical instruments
What Me Worry?

Going Hunting?
You should have your head examined

Test your heads maddeer.org
Chronic Wasting Disease

• TSE of deer, elk
• First identified among mule deer in late 1960s near Fort Collins, CO
  – Wasting, anorexia, listlessness, death
• Since 1960s—wider spread throughout states in West, Midwest, Canada
• Potential spread to humans consuming meat from animals unknown
  – No evidence to date
  – Surveillance ongoing
CJD Surveillance—The Role of the Healthcare Professional

• CJD surveillance can be improved by EDUCATION:
  – Considering CJD in the differential diagnosis of rapidly progressive dementia
  – Rapid referral to center with neurologic expertise
  – Notifying public health professionals of suspected cases of CJD antemortem
  – Approaching family members about the importance of autopsy in substantiating diagnosis
Questions?