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

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Prion Hypothesis

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

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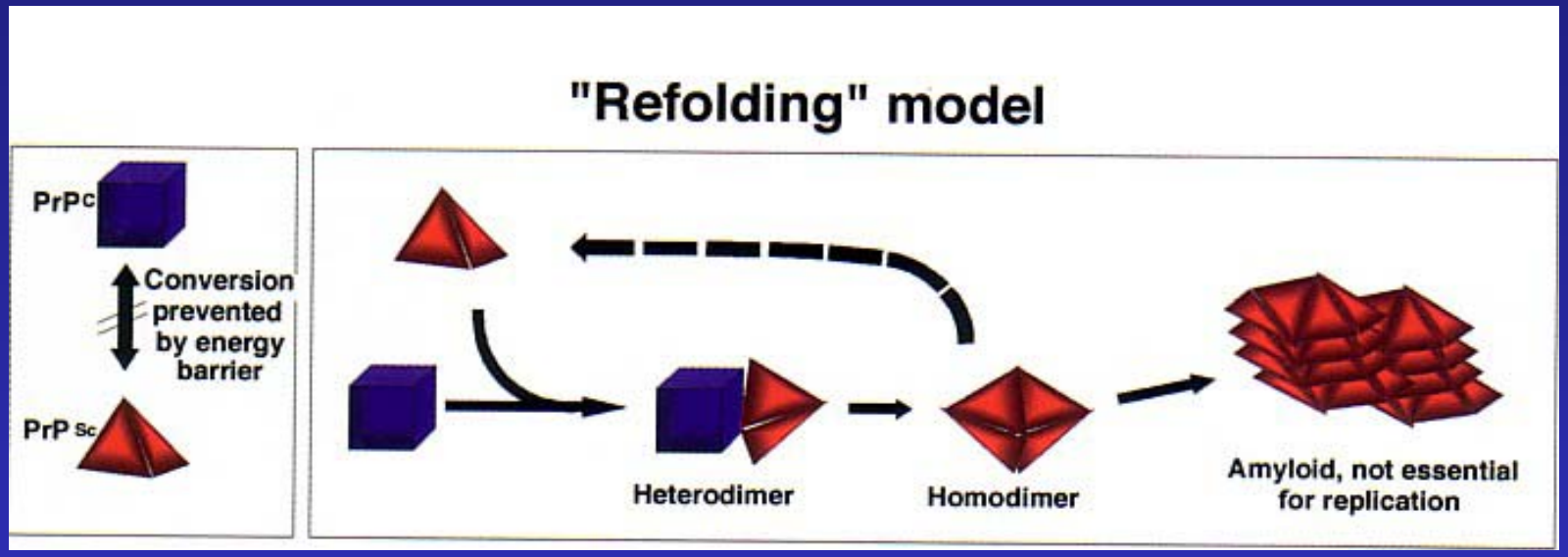
PrP^{c} – PrP^{TSE} "Conversion"



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**

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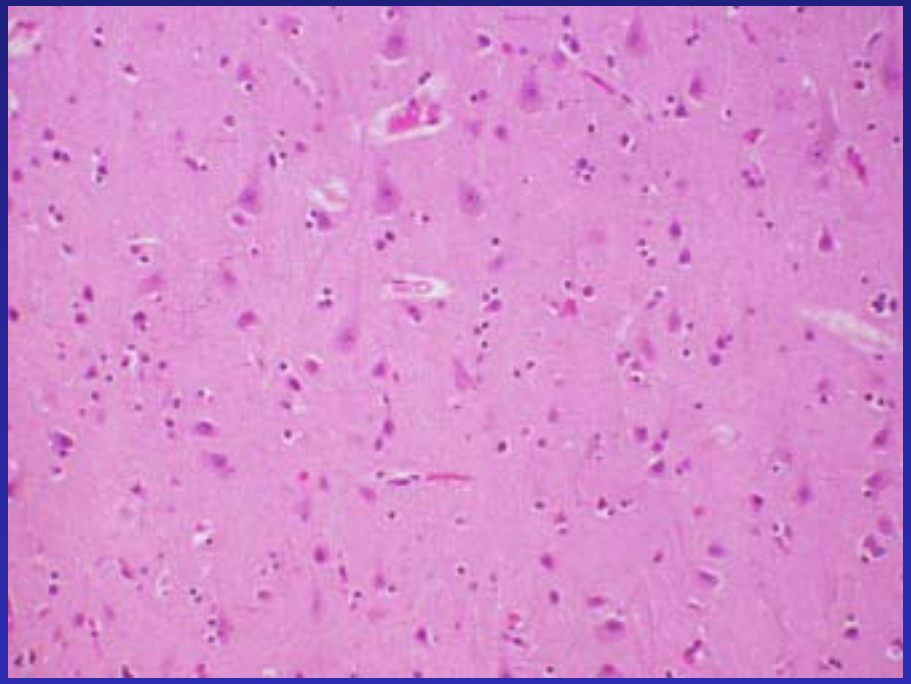
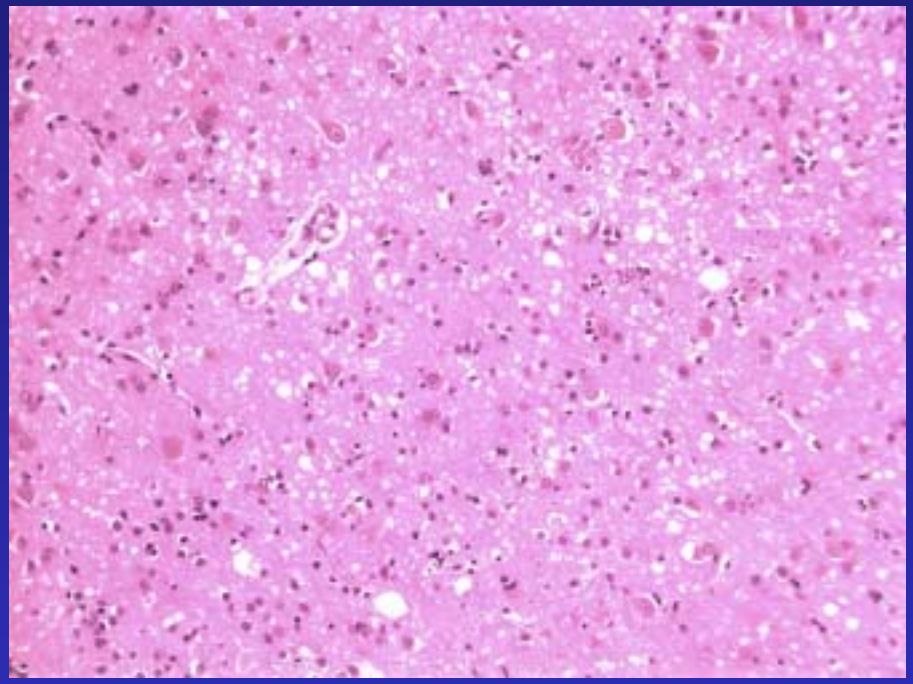
TSEs: Pathology

- **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

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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)**

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“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

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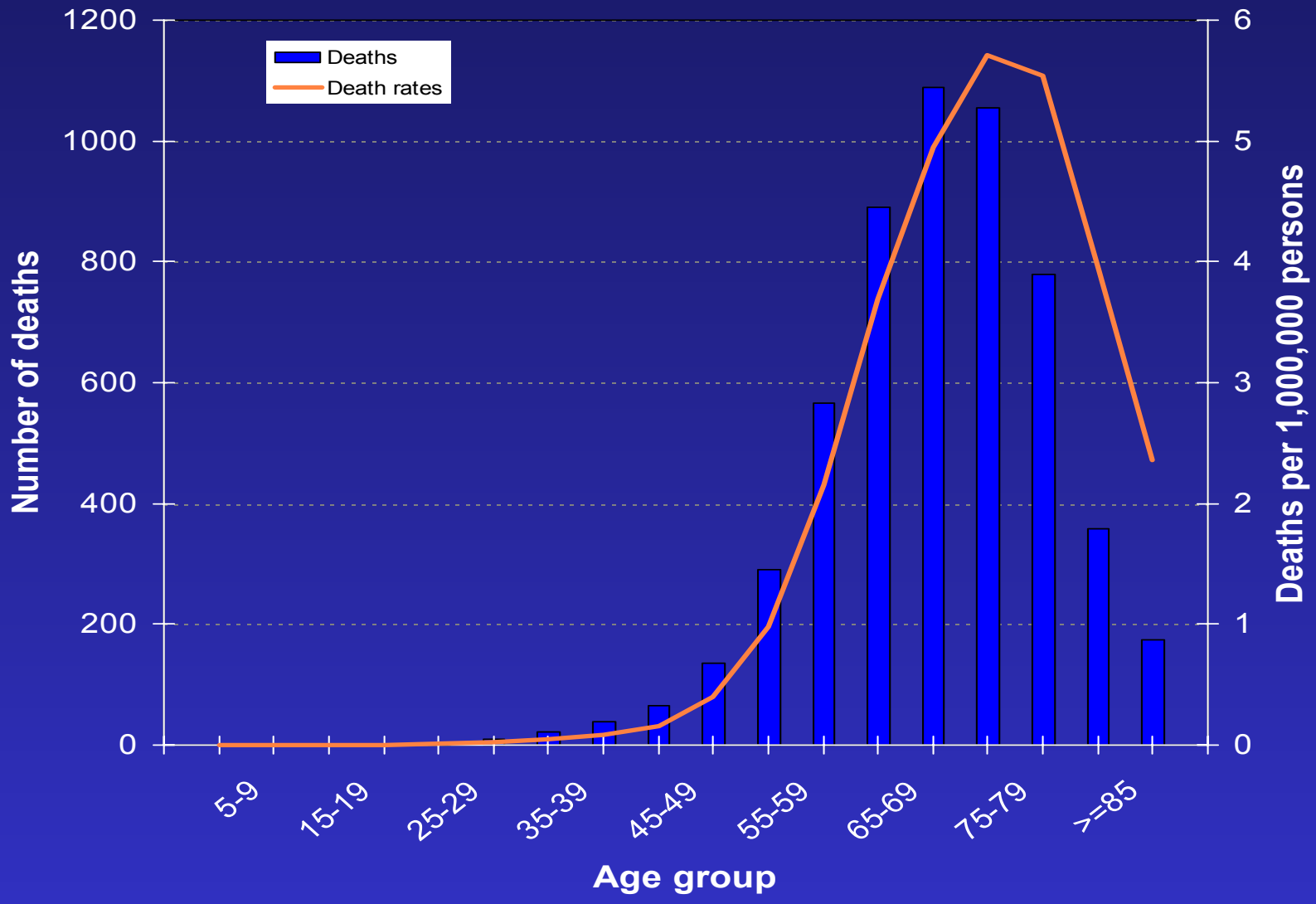
Creutzfeldt-Jakob disease deaths and death rates by age group, United States, 1979-2001



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**

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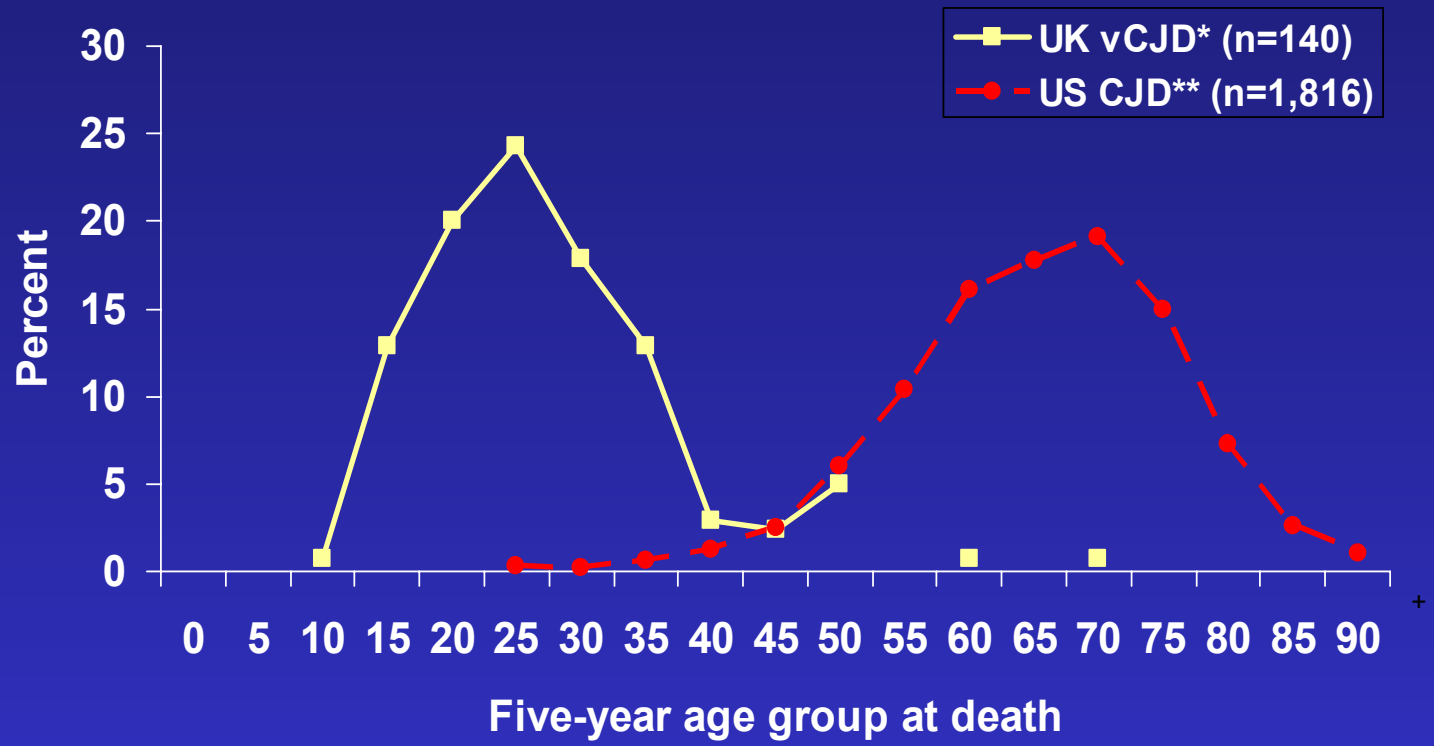
Variant CJD

- 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

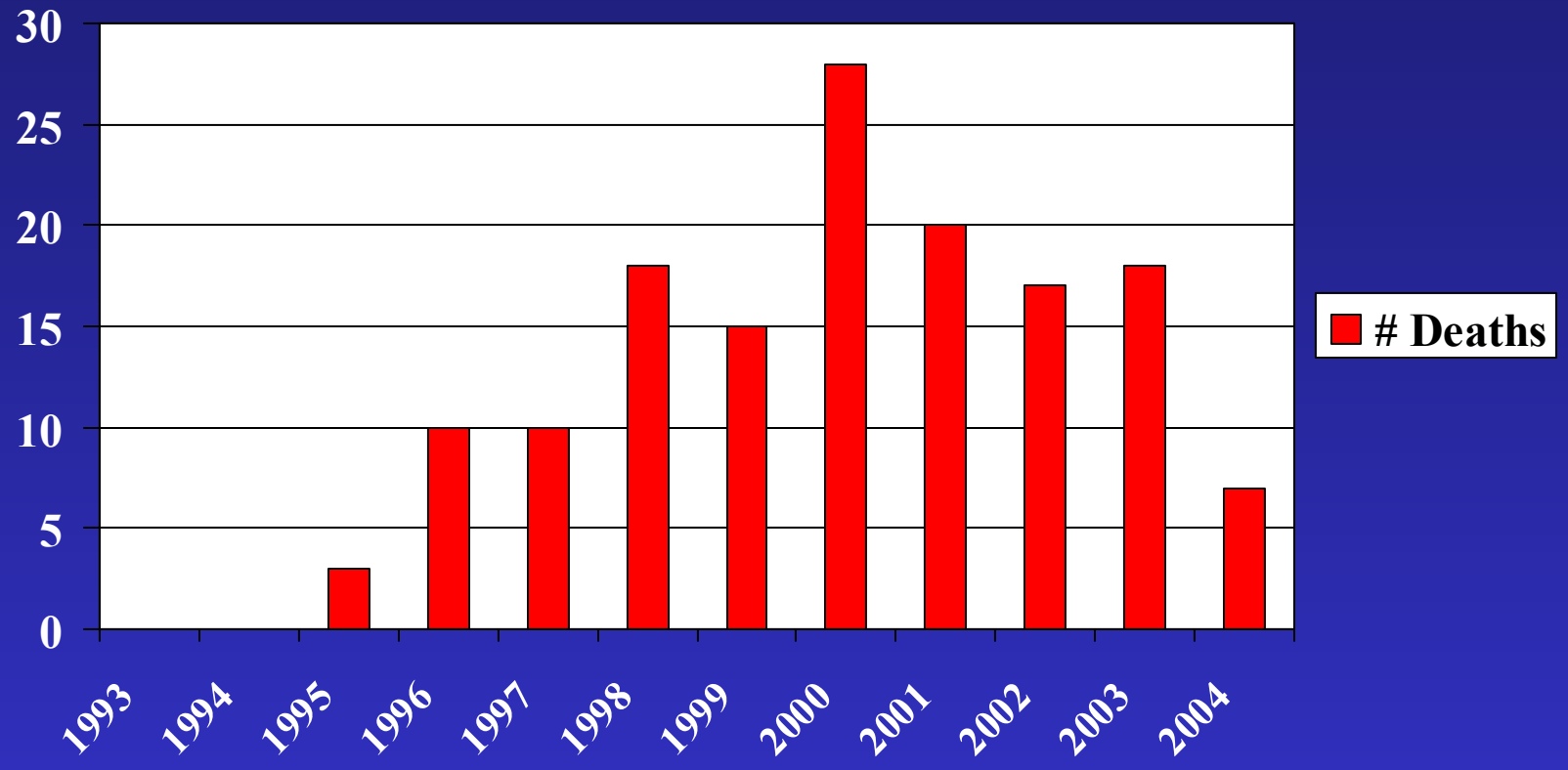


Excludes blood transfusion-associated vCJD and pituitary hormone- or dural graft-associated CJD

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

** US CJD deaths, 1995- 2001.

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

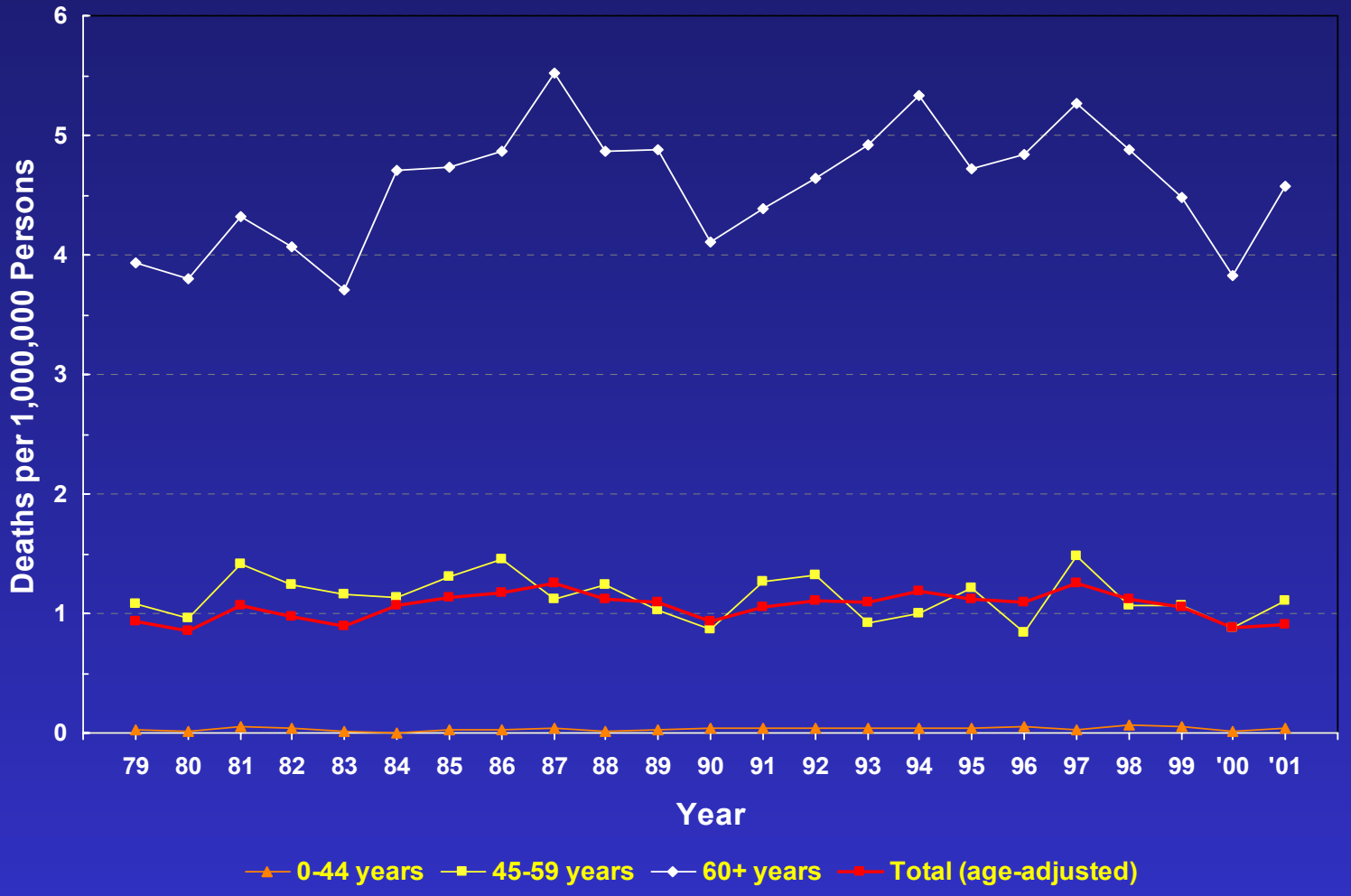
How Does CDC Conduct CJD Surveillance?

- 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**

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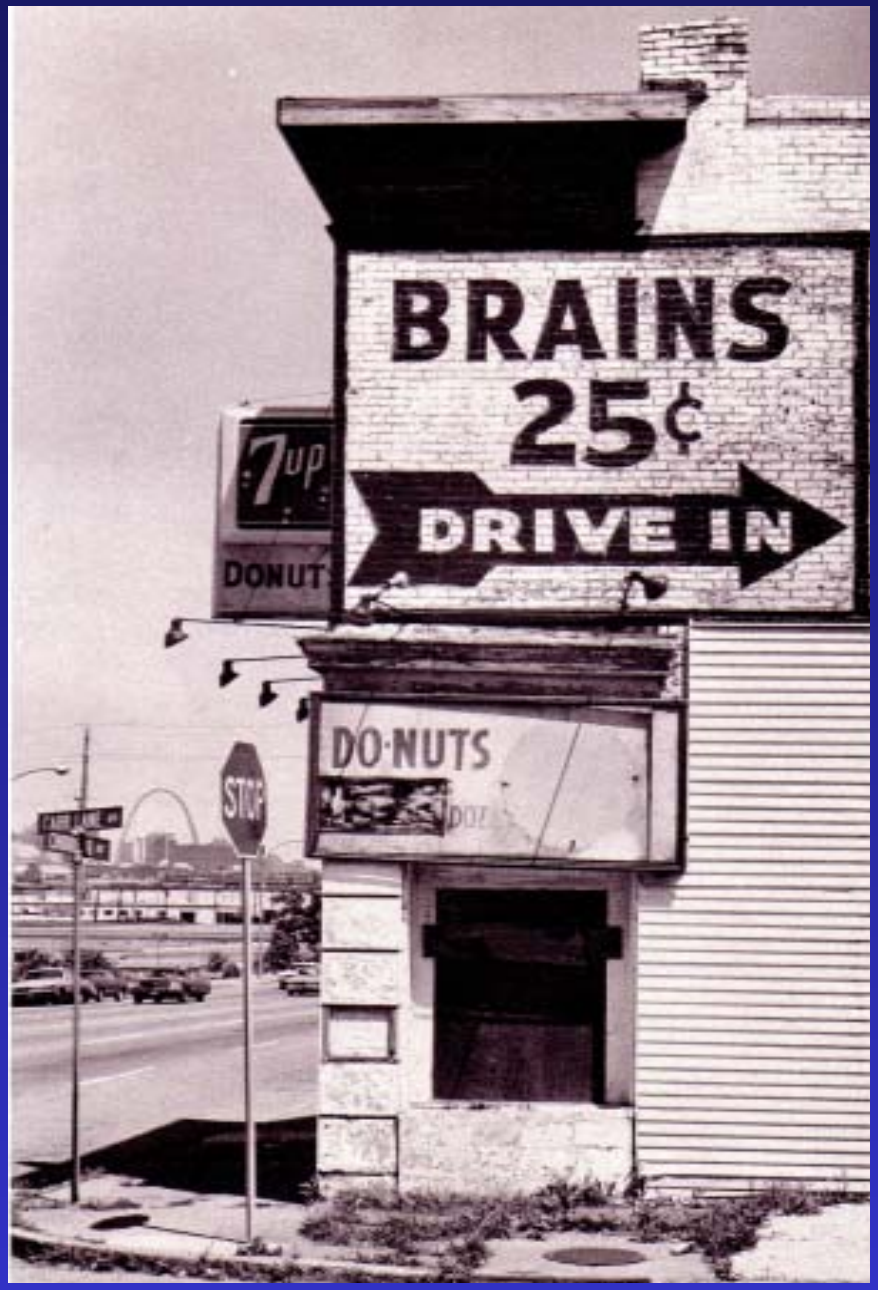
Chronic Wasting Disease

- 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?