Prions, CWD and human health: Cause for concern?

Ontario Federation of Anglers and Hunters
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Outline

• Prions and prion diseases
  > Nature of prions
  > Animal and human prion diseases
  > “Known” human health risks — Scrapie, BSE
  > Uncertain human health risk — CWD

• Scientific evidence
  > Human data
  > Animal models – nonhuman primates
  > Will not discuss mouse, “test tube” or computer models

• A perspective on human risk

• Personal and public health precautions

• Questions and discussion
What are prions and prion diseases?
Prions: A new kind of infectious agent

Transmissible agent = misfolded protein

Misfolded form: PrP^Sc
- Altered shape
- Reshapes normal PrP^C
- “Infectious” agent
- Physically resistant
- Biologically resistant
Prions are “high-consequence” pathogens

- Spontaneous origin → cannot eradicate
- Host protein → no protective immunity
- Resistance → environmentally persistent
- Low minimum dose → no known “safe exposure”
- Long latency → can spread undetected
- Variability → distinct “strains” within a species
- Adaptability → can overcome host resistance
- No treatment → always fatal once symptomatic
- No vaccine → prevention is costly and difficult
## Animal prion diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine Spongiform Encephalopathy (BSE)</td>
<td>• &gt; 180K cases 1986–2018, 26 countries</td>
</tr>
<tr>
<td>Cattle</td>
<td>• Canada: 19 cases 2003–2017</td>
</tr>
<tr>
<td></td>
<td>• <em>Human risk: known pathogen</em></td>
</tr>
<tr>
<td>Scrapie</td>
<td>• Found worldwide (since 1700s)</td>
</tr>
<tr>
<td>Sheep, Goats</td>
<td>• <em>Human risk: believed very low</em></td>
</tr>
<tr>
<td>Chronic wasting disease (CWD)</td>
<td>• 25 US states, 3 Canadian provinces</td>
</tr>
<tr>
<td>Deer, Elk, Moose, Reindeer/Caribou</td>
<td>• S. Korea 2000 – from Canada</td>
</tr>
<tr>
<td></td>
<td>• Norway 2016 – reindeer, moose, elk</td>
</tr>
<tr>
<td></td>
<td>• <em>Human risk: poorly understood</em></td>
</tr>
</tbody>
</table>

Q: Is CWD more like scrapie or BSE?
Human prion diseases:
Creutzfeldt-Jakob disease (CJD)

Hans Gerhard Creutzfeldt
(1885-1964)
German neuropathologist

Alfons Maria Jakob
(1884-1931)
German neuropathologist

Microscopic “spongiform” change in CJD brain tissue

Source: Emerging Infectious Diseases 2017;23(6): 956
# Major types of CJD

<table>
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</tr>
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</table>
| Classic Creutzfeldt-Jakob disease (*CJD*) | • Death rate: 1–2 /million people /year  
• Canada: 60–80 cases /year (> 1 /week)  
• Sporadic, genetic and acquired forms  
• May incubate silently for 30 years  
• No known link to animal prion diseases |
| Variant Creutzfeldt-Jakob disease (*vCJD*) | • 231 deaths, 12 countries (1995-2016)  
• Canada: 2 cases (2002, 2011) – imported  
• Can be transmitted by blood transfusion  
• UK: thousands of silent carriers  
• Linked to BSE exposure |
How can we address the risk of CWD to human health?
CWD continues to spread in North American cervid populations (February 2019)


Map created by Dr. Bryan Richards, USGS
CJD surveillance: Canada and USA

• Canada: Jan 1, 1998 – Feb 28, 2019
  > Classic CJD – 972 cases (sporadic, genetic, acquired)
  > Variant CJD – 2 cases (imported)
  > No other forms of CJD observed

• USA: Jan 1, 1999 – Dec 31, 2018
  > Classic CJD – 3976 cases (sporadic, genetic, acquired)
  > Variant CJD – 4 cases (imported)
  > No other forms of CJD observed

• Surveillance covers period of highest concern
• Intensive approach – negative findings meaningful
• No direct evidence of human CWD to date
Targeted studies of CJD and CWD

• 5 studies published to date (others ongoing)
• All from USA
• Total of 72 CJD cases included
• Samples collected 1979 – 2011
• No associations found between CJD and CWD
• Note: Such studies are very difficult to conduct
  > Long-term follow-up required
  > Assessment of CWD exposure is challenging
Primates used for CWD transmission studies

Cynomolgus macaque
("Old World" monkey)
Credit: André Ueberbach

Squirrel monkey
("New World" monkey)
Credit: Luc Viatour

Sources
http://commons.wikimedia.org/w/index.php?curid=2087907
https://commons.wikimedia.org/w/index.php?curid=2136833
Evolutionary tree of primates

- Lemurs
- New World monkeys
- Old World monkeys
- Apes
- Humans

Time:

- 39-48 Million yr
- 26-38 Million yr
- 6-18 Million yr

Present
## Primate studies: Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Species</th>
<th>Infected</th>
<th>Material</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Marsh 2005 (U. Wisconsin)</td>
<td>Squirrel monkey</td>
<td>2/2</td>
<td>Brain</td>
<td>Intracranial</td>
</tr>
<tr>
<td></td>
<td>Macaque</td>
<td>11/12</td>
<td>Brain</td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0/6</td>
<td>Brain</td>
<td>Intracranial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0/8</td>
<td>Brain</td>
<td>Oral</td>
</tr>
<tr>
<td>3. Czub 2017, 2018, ongoing (APRI)</td>
<td>Macaque</td>
<td>1/1</td>
<td>Brain</td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2/3</td>
<td>Muscle</td>
<td>Oral</td>
</tr>
</tbody>
</table>
Primate studies: Interpretation

- Squirrel monkeys
  > highly susceptible by oral route – first reported in 2009
- Macaques
  > NIH results negative; APRI results positive
  > Several differences in design – both studies valid
  > NIH: “.. (a) barrier protects humans from CWD infection”
  > APRI findings suggest this barrier is not absolute
  > CWD muscle may not be “safe” – unlike BSE
- “Macaques are clos(er) to humans”
  > But: Both primate species are distantly related to humans
- Some nonhuman primates are susceptible to CWD
- Caution is required to apply findings to human risk
A perspective on human risk

• No direct evidence of human CWD (so far), **But:**
  > Human exposure to CWD is likely widespread
  > Recent scientific evidence questions some assumptions
    – No scientific basis for human “immunity” to CWD
  > Additional factors to consider
    – Some people may be more susceptible
    – CWD prions may adapt to humans
    – There may be silently infected human CWD “carriers”
    – Etc.

• **Risk of human CWD infection cannot be dismissed**
• **Human CWD could have very serious consequences**
• **“Precautionary principle” is relevant**
Personal and public health precautions

• Be aware that CWD could be transmissible to humans
• Carefully consider testing
  > especially in CWD-endemic areas
• Do not consume CWD-positive animals
• Do not consume cervid brain
  > especially in CWD-endemic areas
• Continue surveillance for CWD and CJD
• Continue research on CWD and CJD
• Contribute to reducing the spread of CWD
Questions? Comments?

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