Chronic Wasting Disease (CWD) 101

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Transmissible Spongiforme Encephalopathy (TSE)

IN HUMANS – Creutzfeldt-Jokab Disease (CJD), Variant CJD (vCJD), and Kuru

• Cattle – BSE, (in Humans vCJD)
• Sheep – Scrapie (not in Humans)
• CWD – some Cervid (deer) species, (not in Humans)
• Other TSE’s in other animals such as mink, cats; none transmissible to humans
BSE

- Remains a significant “driving force” behind TSE panic
- Only TSE proven to be Zoonotic
  - Still only small fraction of exposed humans
    > vCJD
- vCJD-Long Incubation Period
- Age -> Protective Effect
Introduction to Prion Protein

- **PrP^C**: soluble glycoprotein found at the cell surface
- Expressed in most tissues (especially CNS)
- Secondary structure dominated by alpha helices (3)
- Capable of being digested by proteases
Proposed functions of PrP<sup>C</sup>

- Copper binding and transport
- Superoxide dismutase activity
- Synaptic homeostasis; neuronal survival
- Cell surface receptor for signal transduction
Infectious Prion Proteins

- \( \text{PrP}^\text{Sc} \) (Scrapie Protein), \( \text{PrP}^\text{Res} \); Largely beta sheets

- Conformational change in \( \text{PrP}^\text{C} \) gives rise to \( \text{PrP}^\text{Sc} \) or \( \text{PrP}^\text{cwd} \)

- \( \text{PrP}^\text{Sc} \) highly insoluble and protease resistant
CWD: Biochemical Model

Synthesis of Normal Endogenous Cervid PrP^C

Exposure to PrP_{cwd}^{C}

Conversion of Normal PrP^C to PrP_{cwd}^{C}
Spongiform
History of CWD

• First identified in elk of wild origin in the mid 1960’s at Colorado State University
• The origin of CWD is unknown
• Hypotheses:
  1. a natural disease of elk and deer
  2. from scrapie infected sheep
  3. deer/elk fed pelleted feed with TSE in it
  4. spontaneous genetic mutation deer prion
Host Distribution
Host Distribution
Host Distribution
Sika Deer
Red Deer
Clinical Signs of CWD

- Reduced appetite, polydipsia/polyuria
- Loss of body weight (Resultant poor condition)
- May carry head and ears lowered
- Increased salivation → slobbering/drooling
- Incoordination, ataxia, head tremors
- Wide body stance
Typical Elk With CWD

E. S. Williams
Typical Elk with CWD
Typical Mule Deer With CWD
How is CWD transmitted

- Close contact with infected animals and/or infected food; contaminated environment
- CWD prions are shed in saliva, urine and feces
- Above, plus infected carcasses (esp CNS) may contaminate environment.
- Once contaminated, the environment stays contaminated for years-decades.
Diagnostic Tests for CWD

- Postmortem: “Gold Standard” is IHC test performed on Obex of brain or “Retro LNs”

- IHC test is an antibody-based staining procedure (presence/absence PrP\(^{Sc}\)) which is evaluated using light microscopy

- Other tests: ELISA-based tests (enzyme linked immunosorbent assay)

- Antemortem Test: Tonsillar and rectal biopsy test using IHC technology

- Others in development
Spongiform
Immunohistochemistry (IHC)
Prevention of CWD

• No Approved Vaccines Available; disease is inevitably fatal to infected cervids

• Preventing exposure prevents disease (Importation of cervids from CWD endemic areas)
  – Live or dead (CNS)

• Can’t stop natural migration
Genetic Component: Heritable Resistance to CWD

- Naturally occurring genetic variation (PRNP) exists within deer and elk populations that either enhances susceptibility or resistance to CWD

- Natural resistance does not appear to be complete.
Transmissibility of CWD

• NO evidence of natural transmission to domestic animals or other non-cervid species

• CWD can be experimentally transmitted to cattle via intracranial inoculation*

• CWD can be transmitted to transgenic mice expressing a cervid PRNP gene, but NOT to mice expressing the human PRNP gene
Transmissibility of CWD to Humans

- **ABSOLUTELY NO EVIDENCE** that CWD is transmissible to humans despite the frequent and long term (50+ years) consumption of venison

- Transgenic mice “humanized” by insertion and expression of the human prion gene (PRNP) show no evidence of disease following experimental challenge with CWD
CWD conflict

• WL agencies: meat from harvested game be consumed
• Advise against consuming meat from any “diseased” animal
• -> conflicting message re CWD
Levels of Prions

- Brain > Spinal Cord & some LN > organs > Heart > Skeletal Muscle

- “Reasonable Precaution”: don’t eat brain, spinal cord or lymph nodes of the head
Should we be concerned about CWD?

• Yes! But don’t panic!
• No evidence yet that it has widespread impact
• Some local populations -> declines
• Long-term impacts on megapopulations unknown
  – May impact different areas differently
How CWD kills

• Direct mortality

• Indirect mortality
  – Hunters
  – Predators
  – Trauma (HBC)
CWD transmission

- Direct: (animal to animal)
- Indirect: (animal to environment to animal)
- Direct probably more important early, indirect late
- Role of dose
Studies in WY & CO

• Cautionary Tale
• CO & WY probably have had CWD for 20+ years before anywhere else
• MAY indicate what might happen with other populations
• Notably, some populations in CO/WY doing fine w/ CWD
• NOT predictive
Table Mesa, CO Study

- Non-hunted Mule Deer population
- Abundant habitat
- High prevalence (41% males; 20% females)
- 1988-2006 declined 45%
- Due to CWD?
Table Mesa, CO Study

- Used Tonsil Biopsies and Radio Collars to look at Survival
- CWD dramatically reduced Life Expectancy
  - Negative Deer-5.2 years
  - Positive Deer-1.8 years
- Mt. Lion Predation 4 times higher for CWD
Glenrock, WY study

- Hunted WTD population
- High prevalence (29% males; 42% females)
  - Prevalence increasing
- Well established herd, known for trophy bucks
- Also used tonsil biopsies and radiocollars
  - Only fawns brought into study
Glenrock, WY results

- $\lambda = 0.8960$
- 10.4% annual population decline
- **If** nothing changes will go extinct in 48 years
  - Things can change
- Results indicate this is due to CWD
Other interesting Findings

• CWD has biggest impact on 2 year old age class

• Age Structure shifted to younger deer
  – May explain reduction in Trophy Bucks

• No new infections in deer after 6
  – Does age offer a protective effect?
Will CWD impact all cervid populations?

- No evidence of large-scale impacts
- Many variables
  - Animal density
  - Genotypes
  - Species
  - Soil
- No way to predict
How should we manage CWD?

- Don’t panic
- Common-sense: control/contain it
- Recognize it may have population impacts
- Recognize the above will take decades
- Realize more options will become available
- Try to prevent environmental contamination
How to minimize environmental contamination

• No CNS from endemic areas
  – Bone out- or remove brain/spinal cord

• Remove live sources of CWD prion
  – Sacrifice known positives
  – Sacrifice high-risk animals
  – Require sequential live-animal tests on potentially-exposed cervids
I support trying a new approach!

- Let me know how I can assist!
- I recognize that TPWD & TAHC will lead response and I fully support their efforts
- I applaud the TX deer industry for supporting a novel approach, recognizing the risks involved
Questions

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