Chronic Wasting Disease: Diagnosis & Surveillance
CWD Research Collaborators

Colorado Division of Wildlife
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Colorado State University (multiple departments)
Wyoming Game & Fish Department
USDA/ARS Animal Disease Research Unit
NIH/NIAID Rocky Mountain Laboratories
USDA/ARS National Animal Disease Center
Canadian Food Inspection Agency
USDA/APHIS Veterinary Services
New York State Institute for Basic Research
Neuropathogenesis Unit, Edinburgh, UK
Imperial College, London, UK
Institut fur Neuropathologie, Zurich, Switzerland
Other universities, private institutes & corporations
Diagnosing CWD

Clinical diagnosis:

• abnormal behavior
• emaciation
• CNS signs
• other signs
CWD Diagnostics: An Overview

Histopathology

- “spongiform” lesions in brain
- cannot detect early cases (misses ~50%)
- original “gold standard”; replaced by IHC

Immunohistochemistry (IHC)

- PrP<sup>CWD</sup> accumulations in select tissues
- detects “most” infected animals
- current “gold standard”: lymphoid IHC*

ELISAs, immunoblots, & other “rapid” tests

- tests in various stages of development & evaluation
Diagnosis of CWD in deer & elk

- Immunohistochemistry (MAb 99/97.6.1)
- Retropharyngeal lymph node (± obex, tonsil)
Tonsil biopsy as a live-animal CWD test in deer

**Rationale:**

- CWD pathogenesis ~ scrapie
- \( \text{PrP}^{\text{CWD}} \) abundant in tonsil
- early \( \text{PrP}^{\text{CWD}} \) accumulation
CWD diagnostics:

Immunohistochemistry (IHC)*

- **Deer**
  - brain (sensitivity ~0.9; specificity ~1.0)
  - lymphoid (sensitivity ~0.99; specificity ~1.0)
    - retropharyngeal LN ~ tonsil
    - tonsillar biopsy ~ postmortem tonsil IHC

- **Elk**
  - brain (sensitivity ~0.93; specificity ~1.0)
  - lymphoid (sensitivity ≥0.95; specificity ~1.0)
Immunohistochemical diagnosis of CWD in free-ranging elk & deer

Elk

Deer

(Hibler et al. 2003) (Miller & Williams 2002)
CWD diagnostics:
ELISAs, immunoblots, & other “rapid” tests

- brain or lymphoid
- use “fresh” (unfixed) tissue
- sensitivity >? IHC (“sampling”)
- specificity < IHC (adjustable interpretation)
- more useful in screening than in “diagnosis”

Many tests under development & evaluation
Performance of brELISA on RLN (vs. IHC; OD cutoff = 0.1)

- sensitivity ≥ 98%
- specificity ≥ 99.7%
- agreement ≥ 96%

CWD diagnostics: A “consumer’s” comparison

<table>
<thead>
<tr>
<th>Immunohistochemistry</th>
<th>“Screening tests”</th>
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<tbody>
<tr>
<td>fixed tissues</td>
<td>fresh tissues</td>
</tr>
<tr>
<td>longer processing</td>
<td>short processing</td>
</tr>
<tr>
<td>complex process</td>
<td>simpler process</td>
</tr>
<tr>
<td>relatively inflexible</td>
<td>somewhat flexible</td>
</tr>
<tr>
<td>assess sample quality</td>
<td>no assessment</td>
</tr>
<tr>
<td>high confidence</td>
<td>less confidence*</td>
</tr>
<tr>
<td>subjective</td>
<td>quantifiable</td>
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</tbody>
</table>
Diagnosing CWD: Deer vs. Elk

**Deer**
- early lymphoid involvement
- heavy PrP$^{\text{CWD}}$ deposition

**Elk**
- later lymphoid involvement
- lighter PrP$^{\text{CWD}}$ deposition
Diagnosing CWD: Deer vs. Elk

Tissue sampling advice:

• RLN preferred

• add obex where feasible
CWD Surveillance Goals

- Detect cases (estimate distribution)
- Estimate prevalence
- Monitor trends & detect changes
  - natural
  - response to management
CWD Surveillance Approaches

• Detect cases (estimate distribution)
  – clinical suspect surveillance
  – mortality-based surveillance

• Estimate prevalence & monitor trends
  – harvest-based (random) surveys
Clinical Suspect Surveillance

all clinical suspects sampled

brainstem & RLN (or tonsil)

IHC (± H&E) to confirm

biased toward clinical disease

useful in detecting infected herds

analogous to US scrapie program
Mortality-based Surveillance

all natural deaths sampled

brainstem & RLN (or tonsil)

IHC (± H&E) to confirm

biased toward later stages

useful in detecting infected herds

only practical in captive settings
Population-based Surveys

geographically-targeted
random sampling
(via harvest or road-kill)
RLN ± brainstem (obex) ± tonsil
ELISA or IHC screening
IHC to confirm
all disease stages (except very early)
prevalence estimates & trends
analogous to BSE slaughter surveys
CWD Surveillance Strategies: Relative Strengths & Weaknesses

- Few samples → Lower probability of detection
- High probability of detection → Many samples

**BIASED**
- Symptomatic targeting
- Natural mortalities
- Roadkills
- Primitive weapons hunts

**UNBIASED**
- Random sampling (harvest)
References on CWD Surveillance:


CWD Surveillance: Design Complications

• multiple host species
• uncertain population sizes & boundaries
• mobile populations
• heterogenous disease distribution
• variable ( & ill-defined) risk
CWD Surveillance Strategies

- Collect & examine suspects statewide
- Annual random surveys of endemic herds
- Systematic surveys of other herds (detect 1%)
  - high-risk areas (geographic or epidemiological)
  - economically-important herds
- Other opportunistic sampling
CWD Surveillance Methods

- Clinically-targeted (distribution)
- Roadkills (distribution)
- Random sampling (prevalence)
  - harvest
  - geographic culling
  - antemortem
- Epidemiological culling (local prevalence)
Efficient Mass Testing

Screening test (negative or “suspect”)

Confirmation test (“suspect” = ? positive)
CWD surveillance issues

- Surveillance objectives (Detection? Estimation?)
- “National” vs. state/provincial/local needs
- Disease monitoring vs. carcass testing
- Strategies for assessing exposure risk
- Funding & human resources support
Chronic wasting disease: Distribution & occurrence
Chronic Wasting Disease in Farmed Elk and Deer (1996-2003)

(+ South Korea)

captive elk

captive white-tailed deer
Adaptive Management of Chronic Wasting Disease

Design & Planning
Terrestrial Management
Region
Wildlife Health

Analysis & Evaluation
Wildlife Health
Terrestrial Management
Region

Field Operations
Region
Terrestrial Management
Wildlife Health

Surveillance data
Chronic wasting disease: implications for wildlife management

- Uncertainty & fear may erode public support
- Addressing CWD may usurp resources
- Technology may limit management options
- Unrecognized factors may impede success
- Impacts on wildlife resources unknown