

Y Chronic Wasting Disease Resource Center

December 11, 2019 Webinar: Chronic Wasting Disease (CWD) Strains



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cidrap.umn.edu/cwd



Y Chronic Wasting Disease Resource Center

CWD Response, Research, and Policy Program

The Chronic Wasting Disease (CWD) Response, Research, and Policy Program addresses the transmission of CWD in cervids and its potential for spread to humans and other animal species. The program supports current and reliable information on CWD for the public, including hunters; the medical, veterinary and public health communities; wildlife scientists and managers; and public policymakers.

About CIDRAP's CWD Program

About CWD

CWD Advisory Group



CWD confirmed in Wyoming deer near elk feeding area

Stephanie Soucheray | News Reporter | CIDRAP News | Oct 07, 2019

"Seeing a deer test positive for CWD west of the continental divide again is concerning."

cidrap.umn.edu/cwd

Expert Advisory Group

The program includes 54 national and international world-renowned and distinguished leaders in public health, medicine, science, wildlife, and agriculture.

CWD Strains

Debbie McKenzie

Ctr for Prions and Protein Folding Diseases Biological Sciences,

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Judd Aiken, PhD Professor



Ted Allison, PhD Professor



Satya Kar, PhD Professor



Debbie McKenzie, PhD Professor





David Westaway, PhD Professor/Director



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Valerie Sim, MD Associate Professor



Holger Wille, PhD Associate Professor

Omics	Environ- mental	Risk	CWD strains	GE ³ LS	Partners
David Wishart	Judd Aiken	Evelyn Merrill	Debbie McKenzie	Ellen Goddard	<u>Margo Pybus</u> Alberta Environment and Parks
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		Ellen Goddard	David Westaway	Brenda Parlee	<u>Glenn Telling</u> Colorado State Univ.
Genome	e Canada: Biology &	Trent			<u>Han Sang Yoo</u> Seoul National Univ.
Molecule of (ar Ecology CWD	Bollinger	Valerie Sim	Kim Tallbear	<u>Qingzhong</u> <u>Kong</u> Case Western Univ.

Overview

- What is a prion?
- What is CWD?
- Where is CWD found?
- What is a prion strain?
- History of prion strains
- Identification of CWD strains
- Characterization of CWD strains
- How do CWD strains affect transmission, management?
- Environmental contamination by CWD

Glossary

- PrP—the prion protein
- PrP^C---normal cellular form of the prion protein
- PrP^{Sc}—the abnormal form of the prion protein
 - Aka PrP^{CWD}, PrP^{TSE}, PrP^{CJD}, PrP^{BSE}
 - Associated with infectivity
- PrP-res—the proteinase resistant form of the prion protein
 - May or may not be infectious
- Prions—the infectious agent---comprised of PrP^{Sc}

Prion Diseases













From J Aiken

Characteristics of Prion Diseases

Spongiform Degeneration

Transmissible

Accumulation of PrP^{Sc}

Long Incubation Period

Extended Preclinical Stage

Extreme Resistance to Degradation

Always fatal

No treatment



Prions (<u>pro</u>teinaceous <u>in</u>fectious particles) are unprecedented pathogens that seem to be composed of protein only (PrP^{sc}) and are devoid of nucleic acid.

(Stanley Prusiner, 1982, Science, 216:136-144)



From H. Wille

Normal protein movements e.g. in an enzyme Conversion into a dangerous conformation

From H. Wille



Cellular Prion protein (PrP^C)

Mainly α-helix structure Proteinase K susceptible



https://prionsfactorfiction.files.wordpress.com/2013/11/photo4157-ursinus-edu.jpg?w=474&h=242&zoom=2

Chronic Wasting Disease







Scandinavia's wild cervids



Rangifer tarandus tarandus

Alces alces sp.



Transmission in captive cervids- South Korea



Cervus nipon sp.



One confirmed case in wild Korean water deer Prion 2016

Hydropotes inermis



CWD in North America



CWD in Alberta







From Alberta Environment and Parks



2018









In 2016/2017 (corrected)

-32,000 deer shot in 4 counties (Richland, Sauk, Iowa and Dane)

-1 in 8 tested

-50% prevalence in bucks



Strains

- Sheep
- Cattle
- Mice
- Hamsters
- Humans
- Cervids



Citation:

Wemheuer WM, Wrede A and Schulz-Schaeffer WJ (2017) Types and Strains: Their Essential Role in Understanding Protein Aggregation in Neurodegenerative Diseases. Front. Aging Neurosci. 9:187. doi: 10.3389/fnagi.2017.00187

Science MAAAS



John Collinge, and Anthony R. Clarke Science 2007;318:930-936

What makes a "strain" a strain?

Stable characteristics
 Incubation period
 Clinical symptoms
 Neuropathology
 Biochemical properties of PrP^{Sc}
 Host range

Transmission of TME into hamsters: selection of two new strains

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Adaptation and Selection of Prion Protein Strain Conformations following Interspecies Transmission of Transmissible Mink Encephalopathy

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TME transmission -> Hamsters



Hamster-Adapted TME Strains

HYPER (HY) 65 day incubation period clinical stage: excitable



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DROWSY (DY) 165 day incubation period clinical stage: sleepy **PrPHY PrPDY**

Strains and CWD

CWD1 and CWD2 Strains

Angers et al. Science 2010

- Elk, mule deer and white-tailed deer agent passaged into "elk" mice
 - 2 "strains" identified
 - Long vs short incubation period

Different neuropathology

Cervid PrP gene coding polymorphisms



Figure adapted from David Westaway

White-tailed deer PrP^C















Incubation periods



Johnson et al. 2011 PLoS ONE

H95/S96 polymorphisms modified the structure of PK-res PrP^{CWD}



Camilo Duque Velasquez

Strain Differentiation in tg mice



Are there additional strains?

Confirmed:

- **•** 116G
- Elk agent
- Potential:
 - Elk agents with different Prnp alleles
 - WTD 020

WTD-06(G116+) & Elk agents cause disease in S96 mice





Brain homogenates were treated with 150µg/ml of proteinase K at 37°C during 1 hour.

Open symbols represent tg60 mice with no evident disease signs at the time when the experiment was terminated.

Camilo Duque Velasquez

How do strains arise?

Cloud hypothesis
 Prnp genotypes

 Heterologous conversion

 Interspecies transmission
 Other host factors

 Scrapie in different sheep breeds

Science MAAAS



John Collinge, and Anthony R. Clarke Science 2007;318:930-936

Generation of novel CWD strains

- several major foci of CWD in North America
 - Colorado/Wyoming
 - Wisconsin/Illinois
 - Saskatchewan/Alberta
 - Pennsylvania
- Different populations of free-ranging cervids infected
 - Colorado/Wyoming—white-tailed deer, mule deer, elk and moose
 - Wisconsin/Illinois/Pennsylvania—white-tailed deer
 - Saskatchewan/Alberta—primarily mule deer (white-tailed deer, elk and moose)
- Different PRNP polymorphisms

Why are strains important?

Surveillance
Different tissue distribution
Different PK-resistance
Host range

Differential susceptibility of hamsters and mice to CWD strains

Hamsters						C57BL/6			
CWD	Ν	Clinical PrP-res +	Subclinical PrP-res +	Incubation Period (dpi)		Ν	Clinical PrP-res +	Subclinic PrP-res	cal Incubation + Period (dpi)
Deer wt/wt	8	3	5	652,653, 653		6	0	0	
Deer wt/S96	8	1	4	634		6	0	0	
Deer H95/wt	8	1	6	652		7	5	2	669, 671, 706, 706, 706
Deer H95/S96	8	0	1		1	7	7	0	306, 593, 593, 593, 593, 673, 675
Alberta Elk Pool(CWD2 (4)	8 (2	1	673, 719		4	0	0	
Uninfected deer	8	0	0			2	0	0	

Herbst et al., (2017) EID

Species Barrier Effect

Extension of incubation period observed when prion transmitted from one species to another

not necessarily a complete block

Incubation period decreases with each passage in the new host species

Species Barrier Effect: Mink and Ferret





Photos courtesy of Mike Samuel

Does CWD transmit to humans?

- NO known cases of human disease linked to CWDBUT:
 - As number of infected deer increases, probability increases
 - Different strains may have differential ability to infect
 - Peripheral distribution increases potential risk
- DO NOT EAT untested animals from areas where CWD is high or if your animal tests positive





Chronic Wasting Disease in Cervids: Implications for Prion Transmission to Humans and Other Animal Species

Michael T. Osterholm, Cory J. Anderson, Mark D. Zabel, Joni M. Scheftel, Kristine A. Moore, Brian S. Appleby

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ABSTRACT

Chronic wasting disease (CWD) is a prion-related transmissible spongiform encephalopathy of cervids, including deer, elk, reindeer, sika deer, and moose. CWD has been confirmed in at least 26 U.S. states, three Canadian provinces, South Korea, Finland, Norway, and Sweden, with a notable increase in the past 5 years. The continued geographic spread of this disease increases the frequency of exposure to CWD prions among cervids, humans, and other animal species. Since CWD is now an established wildlife disease in North America, proactive steps, where possible, should be taken to limit transmission of CWD among animals and reduce the potential for human exposure.

Prions are difficult to "kill"

- Chemically Resistant to Inactivation
 - Acids
 - Base
 - Detergent
 - Extreme conditions (1 N NaOH) will inactivate
- Resistant to Standard Sterilization Methods
 - Autoclaving---medical sterilization (120 ° C 20 min)
 - Extreme conditions (autoclaving at 134 C for 1 hour) will inactivate
- UV and gamma irradiation levels that inactivate most bacteria and viruses





Transmission: Direct vs Indirect



Shed CWD Prions can interact with:

SoilsVegetation



Prion-vegetation-soil interactions

Boreal Region



Prions bind to licher



Prairie region



Prions bind to upper soil horizons.

Bioavailable

From Alsu Kuznetsova

Take home messages

- Transmission of CWD through cervid species expressing different Prnp genotypes results in the selection/generation of new CWD strains
- CWD strains have different biochemical and biological properties (expanded host range)
- CWD can bind to soil and other environmental components---no easy means of decontamination
- All CWD is not the same!

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Questions?