

Chronic Wasting Disease (CWD)

Disease Agent:

- Chronic Wasting Disease (CWD) prions

Disease Agent Characteristics:

- Current evidence supports the theory that the infectious agent is a prion. However, the existence of accessory factors has not been excluded.
- Prions are proteinacious infectious agents causing transmissible spongiform encephalopathies (TSEs): a group of neurodegenerative diseases that includes in humans kuru, Creutzfeldt–Jakob Disease (CJD) and variant CJD (vCJD) and in animals scrapie of sheep and goats, bovine spongiform encephalopathy (BSE) of cattle, CWD of deer, elk and moose, a spongiform encephalopathy of felines and zoo ungulates and spongiform mink encephalopathy. (vCJD and human prion diseases other than vCJD, are discussed in separate fact sheets).
- Prions differ from other infectious agents in that they are formed mostly of an abnormally folded prion protein and devoid of detectable nucleic acid.
- Mammalian prions replicate by recruiting the normal cellular prion protein PrP^C to form a disease-causing isoform designated PrP^{Sc} (Sc is an abbreviation for scrapie). PrP^{Sc} or PrP^{Res} (abbreviation for misfolded core PrP protein resistant to proteinase K) or PrP^{TSE} (a wider definition accepted by WHO) are the designations for the pathogenic forms and are used interchangeably in the literature. Prion diseases represent disorders of protein conformation in which the tertiary structure of the native protein is profoundly altered. The transition occurs when the α -helical PrP^C changes into a β -sheet-rich molecule of PrP^{TSE} that is resistant to proteases (proteinase K, lysosomal enzymes).
- Prions are nonimmunogenic as a result of the sharing of epitopes with the normal cellular isoform.
- PrP^C is a glycosylated protein attached to the outer-layer of plasma membrane through a glycosylphosphatidylinositol anchor. It is present on a variety of cells but also circulates in plasma and has a molecular weight of about 33-35 kDa.
- PrP^{TSE} has a more restricted tissue range than does PrP^C.
- PrP^{TSE} forms aggregates that precipitate as diffuse accumulations or as amyloid plaques in the central nervous system; these are a histopathological hallmark of the TSEs. Generally, PrP^{TSE} is identified in a form of PrP^{Res} using immunohistological techniques or by immunoblotting after the treatment of tissues by proteinase K.
- At least two strains, type 1 and type 2, of elk CWD prions exist as shown by experimental disease transmission into transgenic mice carrying a mule deer transgene array.
- Physicochemical properties: Resistance of prions to commonly used disinfectants (formaldehyde, glutaraldehyde, ethanol, and iodine [partially]) and other treatments that damage nucleic acids is well recognized. Prions are resistant

to ultraviolet light and ionizing radiation, ultrasonication, nucleases, boiling, and heat. Immersion in undiluted bleach (60,000 ppm or mg/L of available chlorine) for 1 hour can be partially effective. High concentrations of NaOH (1-2N) or heat in a gravity displacement autoclave at 121°C or higher or in a porous load autoclave at 134°C for 1 hour are advocated for disinfection.

Disease Name:

- Chronic wasting disease (CWD), a TSE/prion disease of deer, elk and moose.

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Very low
- Public concern regarding disease agent: Low/Moderate

Background:

- CWD was identified in US in late 1960 in captive mule deer in a Colorado wildlife research facility but was recognized as a TSE in 1978. It has spread in the wild and has been recorded in 14 states in the US, with the highest incidence in Colorado and Wyoming, and in 2 provinces in Canada. It was also reported in South Korea due to the export of farmed animals infected with CWD from North America. To date, CWD has not been reported in Europe.
- The origin of CWD is unclear. CWD occurs in both captive and wild-ranging cervids, mule deer, white-tail deer, Rocky Mountain elk and moose.
 - Efficient natural transmission of CWD in cervids may occur through saliva, urine and feces.
 - The PrP^{TSE} of cervids has been found in water sampled from a CWD endemic area.
 - Cattle and sheep apparently do not develop the disease when challenged orally with CWD.
- CWD can be transmitted in some but not all experimental animal models:
 - The disease has been transmitted by the most efficient intracerebral route to cattle, sheep, ferrets, mink, goats and hamsters. It has also been transmitted to genetically manipulated mice expressing hamster prion protein gene, transgenic mice overexpressing mouse prion protein gene, and transgenic mice expressing elk or deer prion protein gene, but not to conventional mice.
 - Transgenic mice carrying human *PRNP* transgene arrays with either the codon 129 methionine or valine allele have been resistant to direct intracerebral inoculation with CWD-infected brain homogenate.
 - CWD has been transmitted by direct intracerebral inoculation and by oral feeding to squirrel monkeys but not to cynomolgus macaques. Both monkeys are also susceptible to human TSEs and BSE.

- Recently, the human cellular prion protein was converted to abnormal PrP^{TSE} in the presence of CWD-infected brain homogenate from a genetically manipulated mouse expressing the prion protein gene of cervids. This artificial cell-free reaction, utilizing cycles of sonication and incubation, produced a new strain of human TSE as demonstrated by comparison of biochemical profiles to other strains of human TSEs.
- Blood of experimentally infected deer contains infectivity residing in B-cells and platelets but not in plasma. The blood contains infectivity as early as after one third of the incubation period.

Common Human Exposure Routes:

- No known transmission to humans. A recent study found that the CWD prion might be present in skeletal muscle from infected animals. Spleen, lymph nodes, tonsils, blood, fat, saliva and “antler velvet” contain animal infectivity. Recent investigation of cases of CJD in deer hunters showed no epidemiologic link with CWD.

Likelihood of Secondary Transmission:

- Unknown, not reported; however, in the absence of any human infection, a theoretical concern exists if human-adapted strains were to appear.

At-Risk Populations:

- In theory only: hunters, meat processors, taxidermists, and those who consume deer or elk products (according to one report 40% of US blood donors have consumed venison obtained from the wild).
- A CDC survey that inquired about hunting for deer and elk by US residents found that 18.5% had done so, with 1.2% having hunted in areas considered endemic for CWD at the time of the survey. Wild venison was consumed by over 60% of the respondents.

Vector and Reservoir Involved:

- Reservoir is infected cervids.

Blood Phase:

- Unknown, but blood of CWD-infected cervids is infectious in animal studies.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- Unknown

Cases/Frequency in Population:

- No human case of the disease has ever been confirmed.
- The incidence of CWD in wild cervids is estimated to be 15% in affected areas; up to 50% in hyperendemic areas have evidence of CWD.

Incubation Period:

- Difficult to determine in natural infection; experimentally, 1-2 years after peripheral routes of exposure.

Likelihood of Clinical Disease:

- Unknown in humans

Primary Disease Symptoms:

- Not applicable in humans.
- Wasting, behavioral changes, excess salivation, difficulty swallowing, polydipsia, polyuria, and ataxia occurs in infected animals.

Severity of Clinical Disease:

- High among cervids (progressive, invariably fatal)

Mortality:

- 100% for symptomatic disease in cervids

Chronic Carriage:

- Unknown

Treatment Available/Efficacious:

- Not applicable

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because of the absence of recognized human infection.
- No sensitive or specific question is feasible. If risk to humans is confirmed and route of transmission is identified, exposure to cervids (e.g., hunting, meat consumption) could be evaluated as a screening question.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- No presymptomatic test is available.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.

Impact on Blood Availability:

- Agent-specific screening question(s): Not applicable; would be significant if required given the popularity of hunting in the population
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:

- Unknown, but probably limited by analogy with other TSEs

Pathogen Reduction Efficacy for Plasma Derivatives:

- Inactivation data not available. Highly significant dilution and/or partitioning of infectivity away from final derivatives by fractionation process suggested in animal models using other prion agents.

Suggested Reading:

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