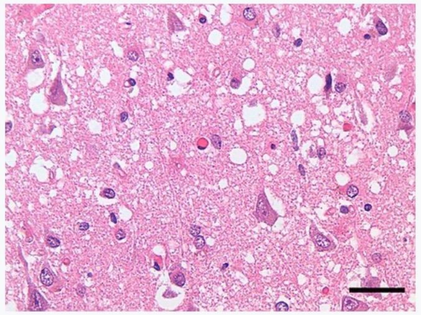
Transmissible spongiform encephalopathies (**TSEs**), also known as **prion diseases**,[1] are a group of progressive, incurable, and fatal conditions that are associated with prions and affect the brain and nervous system of many animals, including humans, cattle, and sheep. According to the most widespread hypothesis, they are transmitted by prions, though some other data suggest an involvement of a *Spiroplasma* infection.[2] Mental and physical abilities deteriorate and many tiny holes appear in the cortex causing it to appear like a sponge when brain tissue obtained at autopsy is examined under a microscope. The disorders cause impairment of brain function which may result in memory loss, personality changes, and abnormal or impaired movement which worsen over time.[3]

Transmissible spongiform encephalopathy (TSE)	
Other names	Prion disease
	

TSE: Transmissible Spongiform Encephalopathies

Group of neurodegenerative diseases

Also called: Spongy brain, holes in the brain

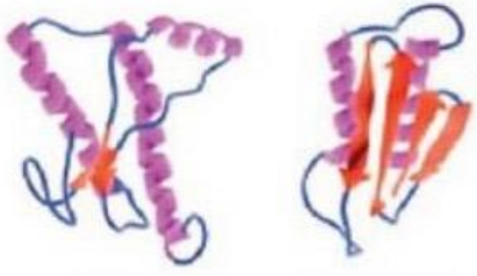
Autopsy is required to examine the brain tissue

NOTICE: According to the most widespread HYPOTHESIS

How Creutzfeldt-Jakob disease works

CAUSE

Creutzfeldt-Jakob disease is caused by abnormal proteins called prions that are not killed by standard methods for sterilizing surgical equipment.



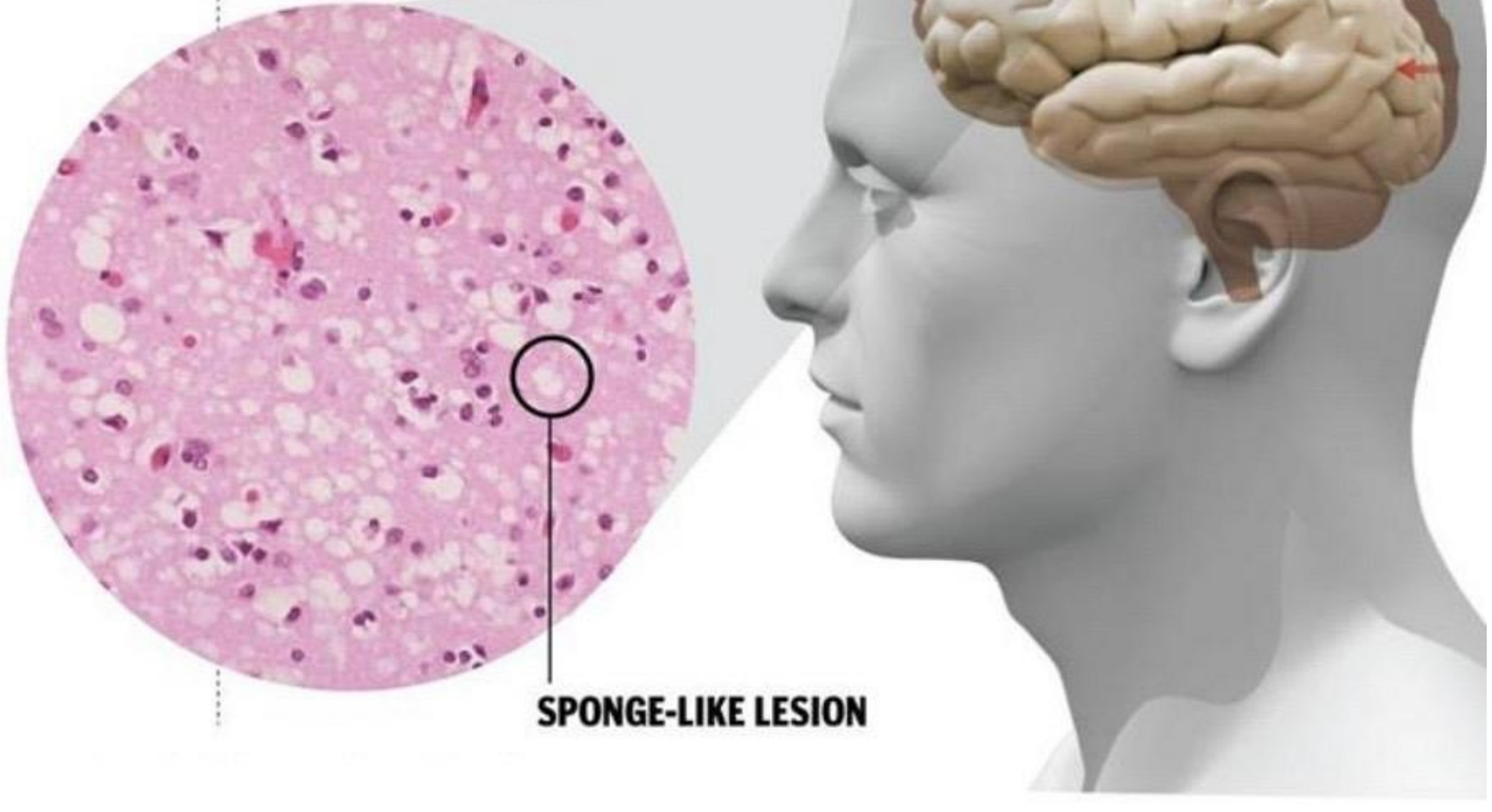
NORMAL HUMAN PROTEIN

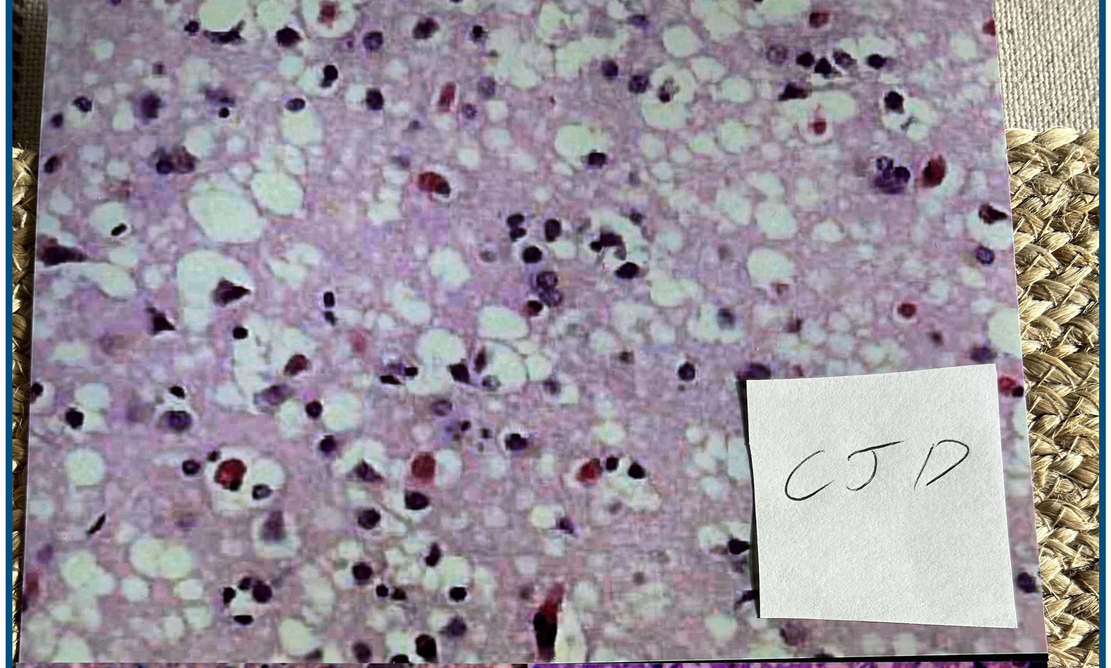
DISEASE-CAUSING PRION

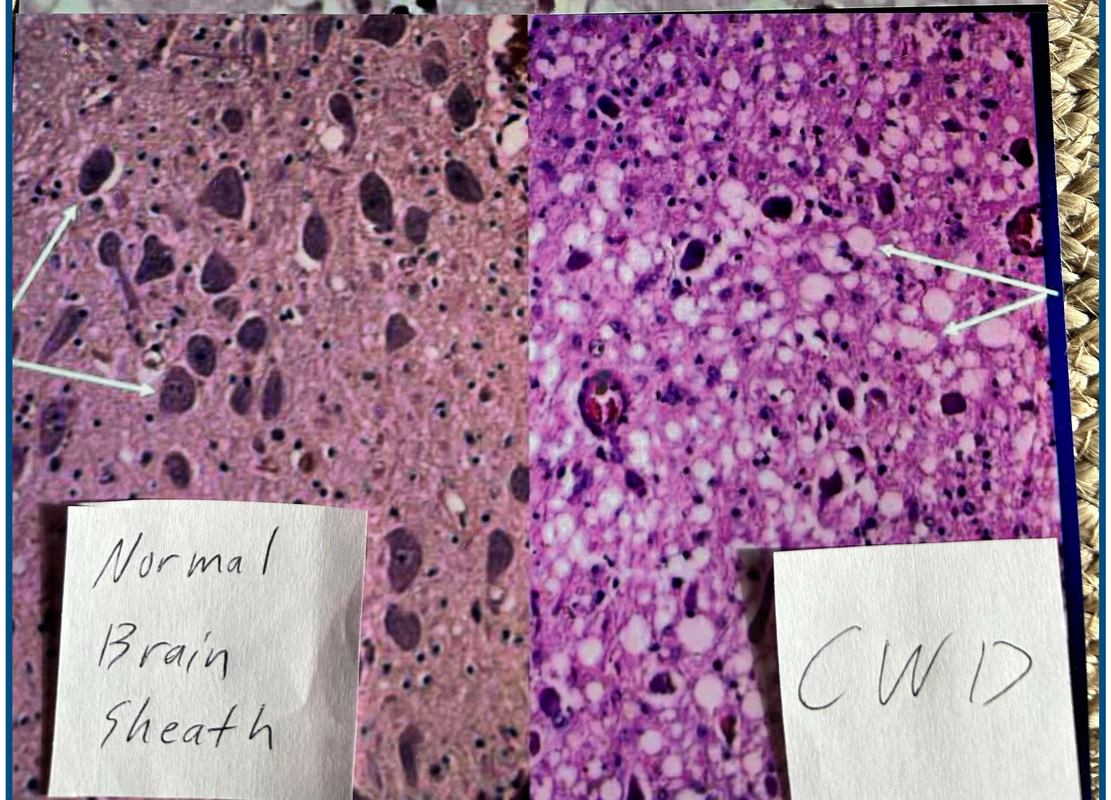
As prions build up in cells, the brain slowly shrinks and the tissue fills with holes until it resembles a sponge.

CONSEQUENCES

Those affected lose the ability to think and to move properly and suffer from memory loss. It is always fatal, usually within one year of onset of illness.







CJD

- pathology is identical to CWD
- is considered a prion disease
- not contagious through bodily fluids

CASE WESTERN RESERVE UNIVERSITY

School of Medicine
Pathology

Navigation + Search

HOME › DIVISIONS › NATIONAL PRION DISEASE PATHOLOGY SURVEILLANCE CENTER › HUMAN PRION DISEASES

Human Prion Disease

Prion diseases are a group of rare, invariably fatal brain diseases that occur both in humans and animals. They are caused by the presence of an abnormal protein in the brain tissue, called scrapie prion protein (**PrPSc**), and is believed to result from a change in the shape, of a normal protein which is present in the brain. As the amount of abnormal prion protein grows, it becomes hard to break down, causing brain degeneration and neurologic disease

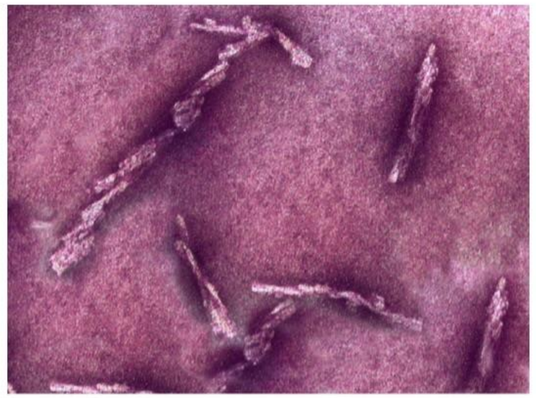
Case Western Reserve University
Cleveland, OH

Considered the highest level Prion Institute in the nation, for the human side.

Requested a micro-scopic slide of a prion.
- spoke top pathology administrator

Provided was a 2021 research paper filled with graphics and pink stained cover page with no label.

Requested confirmation that the cover picture was a prion and she would not confirm.

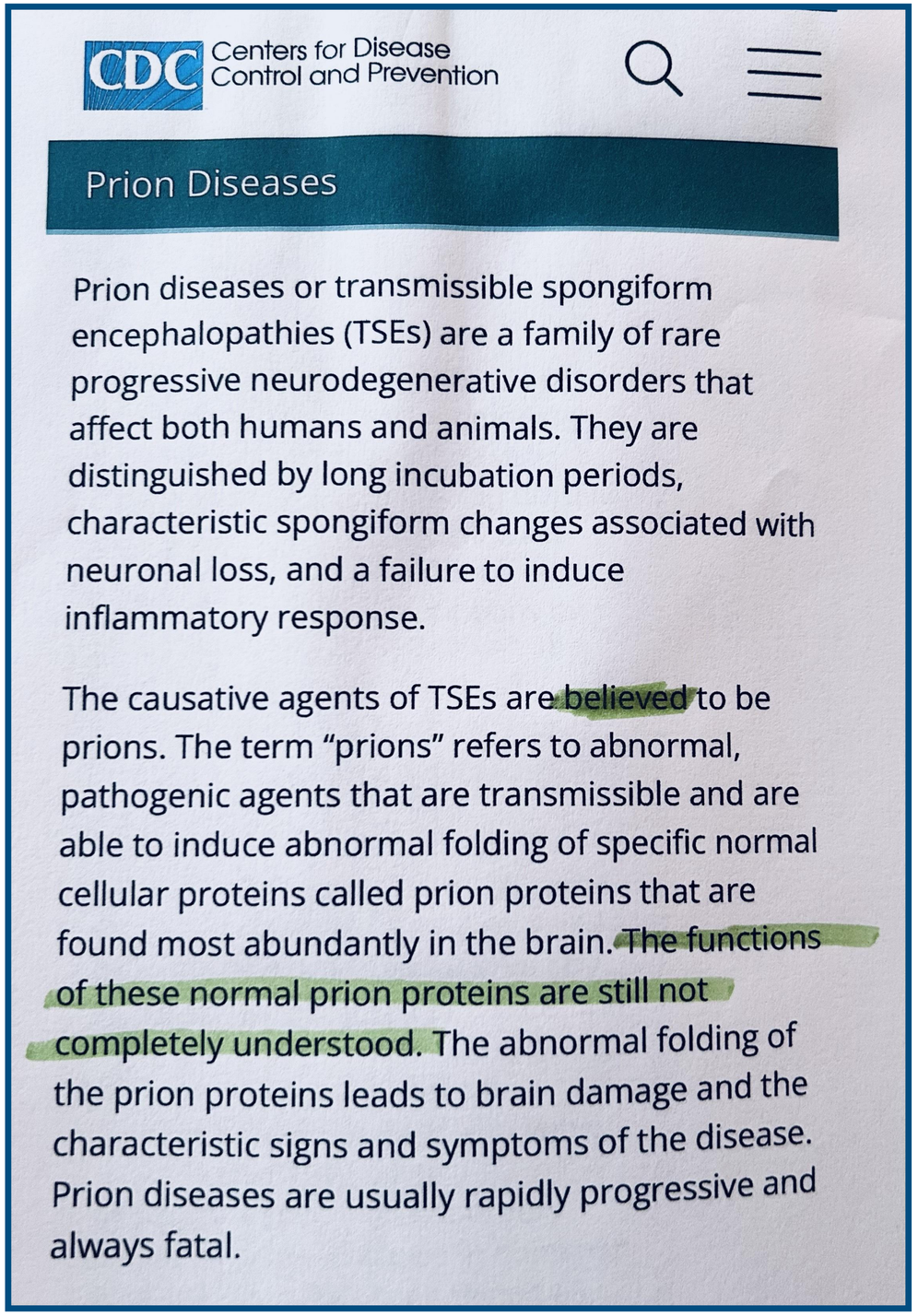


First atomic-level imaging of lethal prions provides sharpened focus for potential treatments

AUGUST 30, 2021

The causative agents of TSEs are *believed* to be prions.

The Functions of these normal prion proteins are still *not completely understood*



CDC Centers for Disease Control and Prevention

Prion Diseases

Prion diseases or transmissible spongiform encephalopathies (TSEs) are a family of rare progressive neurodegenerative disorders that affect both humans and animals. They are distinguished by long incubation periods, characteristic spongiform changes associated with neuronal loss, and a failure to induce inflammatory response.

The causative agents of TSEs are believed to be prions. The term "prions" refers to abnormal, pathogenic agents that are transmissible and are able to induce abnormal folding of specific normal cellular proteins called prion proteins that are found most abundantly in the brain. The functions of these normal prion proteins are still not completely understood. The abnormal folding of the prion proteins leads to brain damage and the characteristic signs and symptoms of the disease. Prion diseases are usually rapidly progressive and always fatal.

USDA APHIS | Cervids: Chronic Wasting Disease

Cervids: Chronic Wasting Disease

Chronic Wasting Disease (CWD) is an infectious, degenerative disease of animals in the family cervidae (elk, deer, and moose, etc.) that causes brain cells to die, ultimately leading to the death of the affected animal. First recognized in Colorado in 1967, CWD was described as a clinical 'wasting' syndrome of unknown cause. It later became clear that CWD was a member of a group of diseases known as transmissible spongiform encephalopathies or TSEs. TSEs include a number of different diseases that affect animals or humans, including bovine spongiform encephalopathy (BSE or "mad cow") in cattle, scrapie in sheep and goats, and Creutzfeldt-Jacob disease (CJD), variant CJD, Kuru, fatal familial insomnia, and Gerstmann-Straussler-Scheinker syndrome in humans. Unlike other infectious diseases, TSEs are not caused by bacteria or viruses, but rather by a naturally occurring protein, that when folded incorrectly, becomes both infectious and deadly. The prion protein in its normal state is thought to have a role in functions such as cell signaling and neuroprotection. It is still unclear what initially causes the normal shaped protein to misfold into the infectious form. Once misfolded, the infectious prion proteins continue to convert more and more normal prion proteins to the misfolded form. Misfolding of prion proteins in the brain leads to the death of neurons (brain cells) resulting in dysfunction in the body, ultimately causing death. The incubation period can be long (several months to years) depending on species and genetic factors, and infected animals are in good body condition until the end stages of the disease, making them difficult to distinguish from healthy animals.

The prion protein in its normal state is *THOUGHT* to have a role in functions such as cell signaling and neuroprotections. It is *STILL UNCLEAR* what initially causes the normal shaped protein to misfold into the infectious form.

USDA APHIS

North Dakota Game and Fish Department Informational Video

- 2020 Advisory Board Meeting CWD Presentation

Reports/Studies:

- Association of Fish and Wildlife Agencies - AFWA Technical Report on Best Management Practices for Prevention, Surveillance, and Management of Chronic Wasting Disease
- Association of Fish and Wildlife Agencies - Statement on Chronic Wasting Disease Etiology
- Cornell Wildlife Health Lab - Prion Hypothesis for CWD: An Examination of the Evidence

The Department maintains an extensive archive of over 200 peer reviewed scientific journal articles. For technical questions about CWD, contact Dr. Charlie Bahnson, Wildlife Veterinarian.

Links provided on gf.nd.gov

Robust Science

- AFWA Document
- AFWA Statement
- Prion Hypothesis

AFWA Document

30 contributors and reviewers

Could potentially	Generally	Have been shown	Have the potential	
Implicated	Indicates	Likely	Likelihood	May	May be
May not	Might	Most	Most likely	Possibly	
Potentially	Probably	Reasonable to infer	Suggests	
Suggesting	Typically	Unlikely	Widely considered	

AFWA (Associations of Fish and Wildlife) Document

Page 34

There is currently no evidence that baiting and feeding of free range cervids can be conducted to mitigate increases in the opportunity for disease transmission.

(Rudolph et al. 2006)

162 of these terms are in the AFWA document

(The AFWA document is what the Agencies use to make decisions about CWD)

Where is the ***SCIENCE*** in these terms???

Association of Fish and Wildlife Agencies

Statement on Chronic Wasting Disease Etiology

Transmissible spongiform encephalopathies (TSEs) are a family of diseases that have been documented in numerous mammalian species, including cattle, sheep, humans, and members of the deer family (Cervidae or cervids), among others. Decades of scientific research have been dedicated to understanding the cause and treatment of TSEs, including chronic wasting disease (CWD) of cervids. The consensus that has emerged from this research indicates that prions (misfolded proteins) are the causative agents of TSEs, including CWD.

However, alternate theories regarding the cause of CWD have been postulated and continue to be examined by some in the scientific community. These theories, which explore possible etiologies including viruses, bacteria, trace mineral imbalances, and others, have been advanced for many years and often are supported by peer-reviewed, scientific publications. While our understanding of CWD epidemiology can benefit from diverse research perspectives and investigations, the preponderance of scientific information currently available strongly supports prions as the causative agent of all TSEs, and this is accepted by the vast majority of scientists working in this field.

There currently are no vaccines, no treatments, no cures, and no practical live animal, 'carcass-side,' nor food safety tests for CWD, despite extensive efforts and research to develop them. Consequently, CWD must be managed with available science-based tools that include, but are not limited to, regulation of live cervid and carcass movements, prohibition of activities that congregate susceptible species, targeted removal, hunting, surveillance and monitoring, and public education.

The Association of Fish and Wildlife Agencies (AFWA) supports the scientific consensus regarding prions as the causative agent of CWD and endorses use of the above and other available management strategies by state, federal, provincial, and territorial wildlife agencies as well as research that further elucidates the epidemiology of CWD and identifies effective management practices. Additional information on CWD management can be found in the *AFWA Best Management Practices for Prevention, Surveillance, and Management of Chronic Wasting Disease* that are available online at: https://www.fishwildlife.org/application/files/5215/3729/1805/AFWA_CWD_BMPS_12_September_2018_FINAL.pdf .

Approved March 8, 2019.

gf.nd.gov

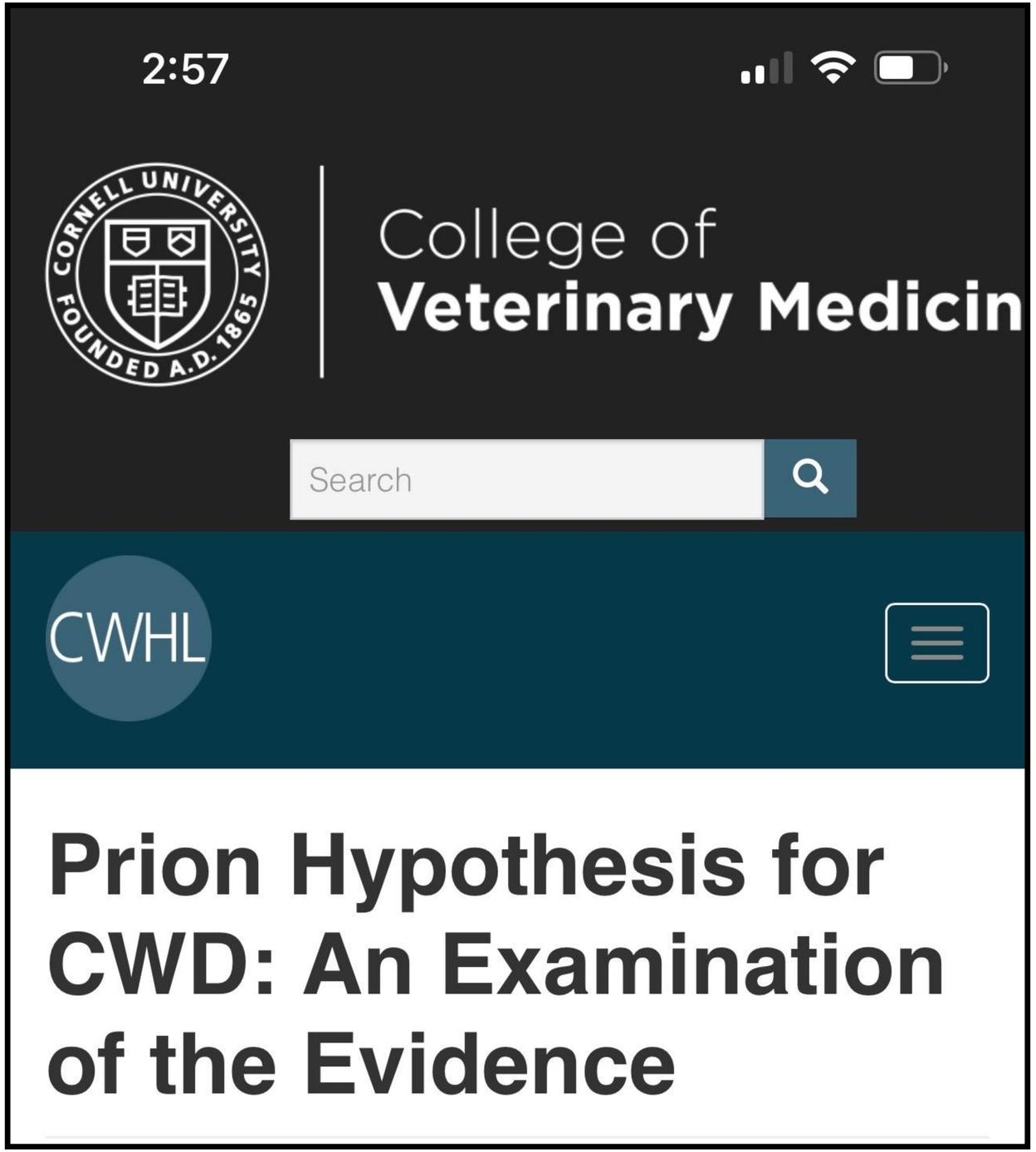
In summary, the Associations of Fish and Wildlife (AFWA) *supports* the consensus that prions are the causative agent for CWD and at this time, is accepted by the majority of scientists in the field.

Notice, they do not say "prion" **ARE** the causative agent.

There are alternate theories including virus, bacterial, trace mineral imbalances and others.

The AFWA **chose** to follow the **"Prion Hypothesis"**

gf.nd.gov



Synthetic “artificial” prions??
How with no pictures?

5. Synthetic “artificial” prions have been created and they cause TSE-like disease.

Most studies use brain material as the source of prions for infection trials, which could potentially transfer other disease agents. However, researchers created prions in E. coli bacteria and produced disease in mice, which is compelling evidence that prions are infectious proteins[8].

February 21, 2019

Contagious?

No neurodegenerative disease is contagious

-Degrading of the myelin cannot be contagious

CJD has SAME pathology and not contagious

Irrefutable evidence that CWD is contagious through bodily fluids was requested in November 2023. (no response).

Innoculation Studies

- deer were put under light anesthesia every week and awaken just enough to drink saliva. Continued for 3 months. After 3 months, there were detections by test.

- no necrospy and no control groups used.

- jamming brain material

NONE of the studies demonstrate natural transmission

Inflammation can cause cells to die and disease.

Chronic wasting disease (CWD) is an emerging infectious disease that is fatal to free-ranging and captive animals in Cervidae, the deer family. CWD is one member of a family of diseases called transmissible spongiform encephalopathies (TSEs), and is thought to be caused by prions. CWD is the only TSE known to affect free-ranging wildlife.

Deer that have been detected at 3-4 years old are still alive at 9-10 years

gf.nd.gov

animal or pet. Many animals, including pigs (including wild pigs), cattle, dogs, moose, hares and birds, can carry the bacteria in their intestines.

Most infected animals will not show signs of disease, but they can develop diarrhea.

American Veterinary Medical Association

Chronic Wasting Disease (CWD)

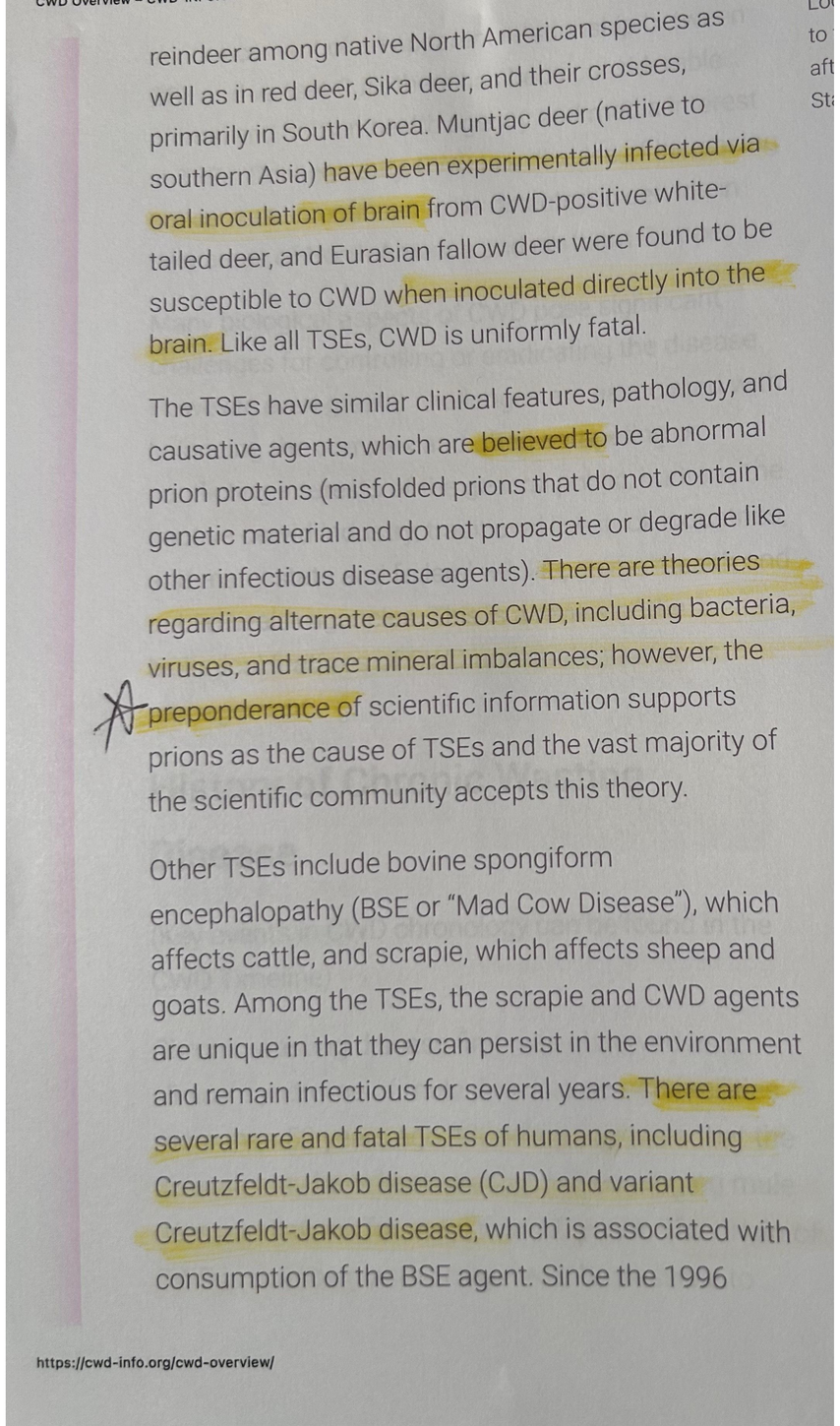
CWD is a transmissible spongiform encephalopathy, in the same class of diseases as bovine spongiform encephalopathy (BSE – more commonly known as "mad cow disease"). These diseases are caused by prions, which are infectious proteins. The diseases affect the brain and spinal cord, causing signs such as weakness, incoordination and abnormal behavior. How CWD is spread from animal to animal is not fully understood, but it is believed to be transmitted through direct animal-to-animal contact or when an animal eats soil contaminated by saliva or manure from an infected animal. CWD prions have been found in elk antler velvet, suggesting a possible route of transmission from elk to elk.

Believed

gf.nd.gov

CWD or Pneumonia

may occur; this may be more common in the wild than in the relative security of captivity. Aspiration pneumonia is a common finding at postmortem examination of terminal CWD cases and may confuse the diagnosis if the brain is not examined. Aspiration pneumonia likely is due to difficulty swallowing,



reindeer among native North American species as well as in red deer, Sika deer, and their crosses, primarily in South Korea. Muntjac deer (native to southern Asia) have been experimentally infected via oral inoculation of brain from CWD-positive white-tailed deer, and Eurasian fallow deer were found to be susceptible to CWD when inoculated directly into the brain. Like all TSEs, CWD is uniformly fatal.

The TSEs have similar clinical features, pathology, and causative agents, which are believed to be abnormal prion proteins (misfolded prions that do not contain genetic material and do not propagate or degrade like other infectious disease agents). There are theories regarding alternate causes of CWD, including bacteria, viruses, and trace mineral imbalances; however, the preponderance of scientific information supports prions as the cause of TSEs and the vast majority of the scientific community accepts this theory.

Other TSEs include bovine spongiform encephalopathy (BSE or "Mad Cow Disease"), which affects cattle, and scrapie, which affects sheep and goats. Among the TSEs, the scrapie and CWD agents are unique in that they can persist in the environment and remain infectious for several years. There are several rare and fatal TSEs of humans, including Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease, which is associated with consumption of the BSE agent. Since the 1996

https://cwd-info.org/cwd-overview/

- Experimentally infected via oral inoculation of brain
- inoculated directly into the brain
- There are theories regarding alternate causes of CWD, including bacteria, viruses, and trace mineral inbalances (nutrition), however the preponderance…..
- There are several rare and fatal TSEs of humans including CJD

Diagnosis

Clinical signs of CWD alone are not diagnostic as several other diseases cause similar symptoms. Diagnosis can be confirmed upon postmortem examination of the brain for spongiform lesions and/or accumulation of the CWD-associated prion in brain and/or lymphoid tissues. The correct portion of the brain must be examined for a meaningful test.

From: Bahnson, Charlie cbahnson@nd.gov
Subject: request for information
Date: Nov 16, 2023 at 2:25:15 PM
To: Dusty and Pat Backer backerbees@hotmail.com

Hi Dusty. I got a note that you had requested images of a prion at a recent advisory board meeting. In the attached article, published in the journal *Molecular Cell,* cryo-electron microscopy was used to produce images of prions at 81,000X magnification.

Feel free to give me a call if you'd like to discuss more.

81,000 magnification

Charlie Bahnson
Wildlife Veterinarian

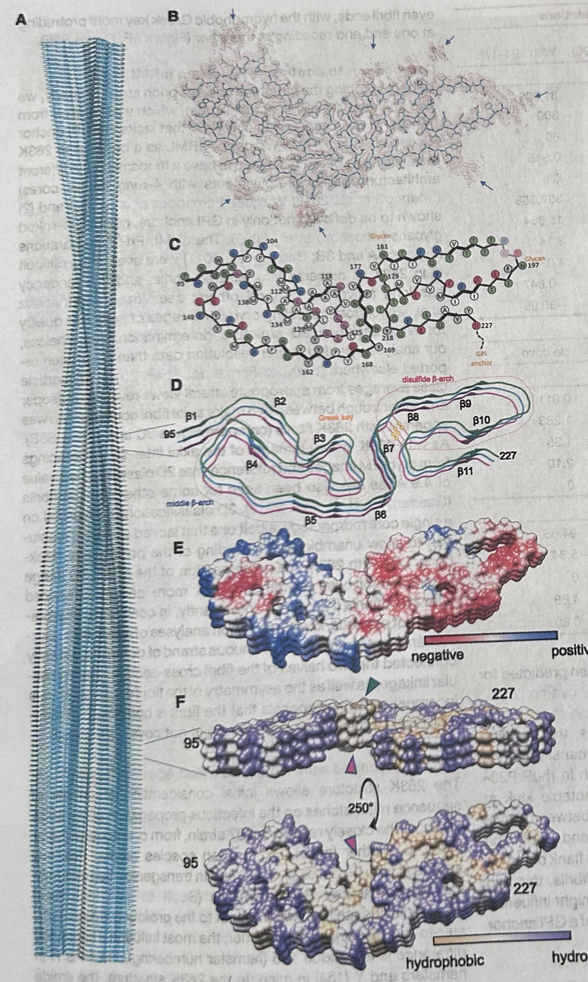


Figure 2. 263K prion model based on cryo-EM density map

(A) Extended fibril model as a ribbon diagram.

(B) PrP residues 95–227 threaded through a cross-sectional density map (mesh). Blue arrows indicate peripheral densities outside of the core polypeptide, some of which are likely attributable to glycans and GPI anchors attached at sites labeled in (C).

(C) Schematic depiction of fibril core showing side-chain orientations relative to the polypeptide backbone. Residues assigned to β sheets in Chimera are marked by thicker backbones with arrowheads. Side chains of residues 194–196 (faded) were poorly resolved. Green, polar; blue, basic; red, acidic; white,aliphatic; gray, aromatic; pink - glycine.

(D) β sheets in a stacked trimeric segment of the fibril. Structural elements are as labeled, and disulfide bond is indicated by a pair of yellow spheres.

(E) Coulombic charge representation.

(F) Kyte-Doolittle hydrophobicity surface of fibril ends (templates) showing the protruding (green arrowhead) and receding (magenta arrowheads) hydrophobic Greek key motif at opposite ends.

led to adjustments of both the adjacent Y157 side chains and the polypeptide backbone to eliminate steric clashes (Figures S8G and S8H). This modeling suggests that incorporation of a PrP^C molecule with a differently shaped and bulkier Y side chain at that residue might stall due to local steric clashes, alterations in hydrogen bonding, or longer-range allosteric effects on templated conversion.

In contrast to the profound effects of the N155Y mutation, substitutions of mouse residues at 12 other positions in the hamster sequence have little effect on the efficiency of 263K-induced PrP^C conversion (Priola et al., 2001; Scott et al., 1993). Four of those substitutions are outside of the ordered 263K prion core and therefore would not be expected to influence its stability. The remaining seven substitutions may be tolerated because (1) they are more isosteric and, except for the T-to-V substitution at 215, conservative of side-chain polarity (or nonpolarity) and lack of charge (Figure S8A); and/or (2) they would be incorporated into less tightly packed locations within the prion structure (Figures S8A and S8B).

DISCUSSION

Infectious versus non-infectious PrP fibrils

From the cryo-EM-based density map of the highly infectious 263K prion, the serpentine threading of the polypeptide backbone of residues 95–227 and orientations of almost all of the side chains relative to the backbone were clear. Further atomistic details of side-chain conformations and backbone hydrogen bonding were approximated by molecular modeling and best fit with the density map. The span of 134 residues packed into the ordered 263K core is more than double the residue span included in the protofilament cores of previously

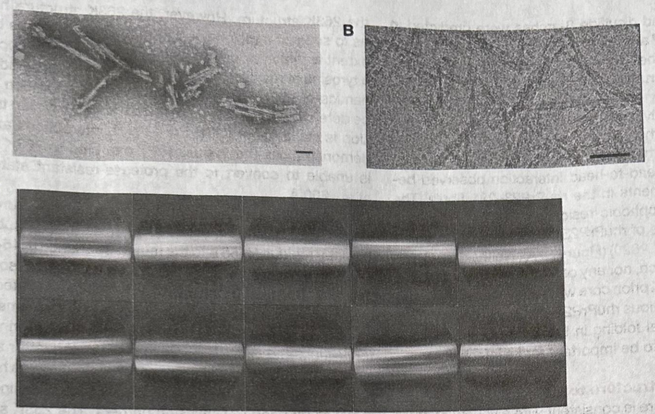


Figure 3. Anchorless RML (aRML) prions have distinct fibril morphology and cross-section

(A) Negative-stain electron micrograph of aRML fibril preparations. Scale bar, 50 nm.

(B) Representative micrograph of cryo fibril preparations. Scale bar, 50 nm.

(C) Select 2D classes show features of aRML fibrils.

(D) Projections of the aRML and 263K fibril cross-sections, with 263K low-pass filtered at 10 Å to match the resolution of aRML. Scale bar, 5 nm.

(E) Projections of aRML and 10-Å-filtered 263K fibrils from a lateral view showing overall topologies. aRML projection indicates the overall fibril topology; the cross-over distance scale may not be identical to that of 263K.

studied recombinant PrP fibrils (Glynn et al., 2020; Theint et al., 2017; Wang et al., 2020). The asymmetric cross-sections of both 263K and aRML fibrils in our current study are also starkly different from what had been surmised for aRML fibrils based on lower-resolution cryo-EM and X-ray fiber diffraction studies (Spagnolli et al., 2019; Vázquez-Fernández et al., 2016). In both the 263K and aRML structures, the halves of the cross-section are connected by continuous electron density and show no evidence of the previously postulated independent, equivalent protofilaments or intertwined β-solenoids. In the 263K structure,

All slides are labeled fibril

Nov 2021

Tests Used to "Detect" CWD

IHC
(Immunohistochemistry)

The IHC detects and grabs **antigens** (which are foreign substances)

ANTIBODIES are protective proteins produced by the immune system.

Antibodies attach to antigens (foreign substances) such as bacteria, fungi, viruses and toxins --and remove them from the body.

ELISA
(Enzyme-Linked Immunosorbent Assay)

Used to diagnose bacteria and virus.

Home pregnancy tests are based on the ELISA technique.

ELISA detect: Bacteria infections (Lyme disease, brucellosis, syphilis)

Viral infections: HIV, Hepatitis A, B, C

Fungal infections: Yeast infections

Detects antibodies in the *blood*, *urine* or other *bodily fluid*.

What are Antigens and Antibodies?

Antibodies are substances in the immune system that bind to unwanted substances in order to eliminate them from the body.

Antigens are usually proteins or sugars found on the surfaces of cells or viruses.

Antigens exist on several types of Cells:

viruses, bacteria, allergens, parasites, proteins, tumor cells and normal cells

Contact to ELISA technique Manufacturer

- client must state what is to be detected to create a test
- ELISA techinique does not detect prion
- only universities, research labs, Agencies have access.
- no one can purchase.
- testing only done at universities State and federal agencies (32)
- information is confidential as to what is being detected (Iowa)


CWD
THEY MISSED IT BY A MILLION MILES
DR. JOEL WALLACH, BS, DVM, POST DOC (PATH) ND