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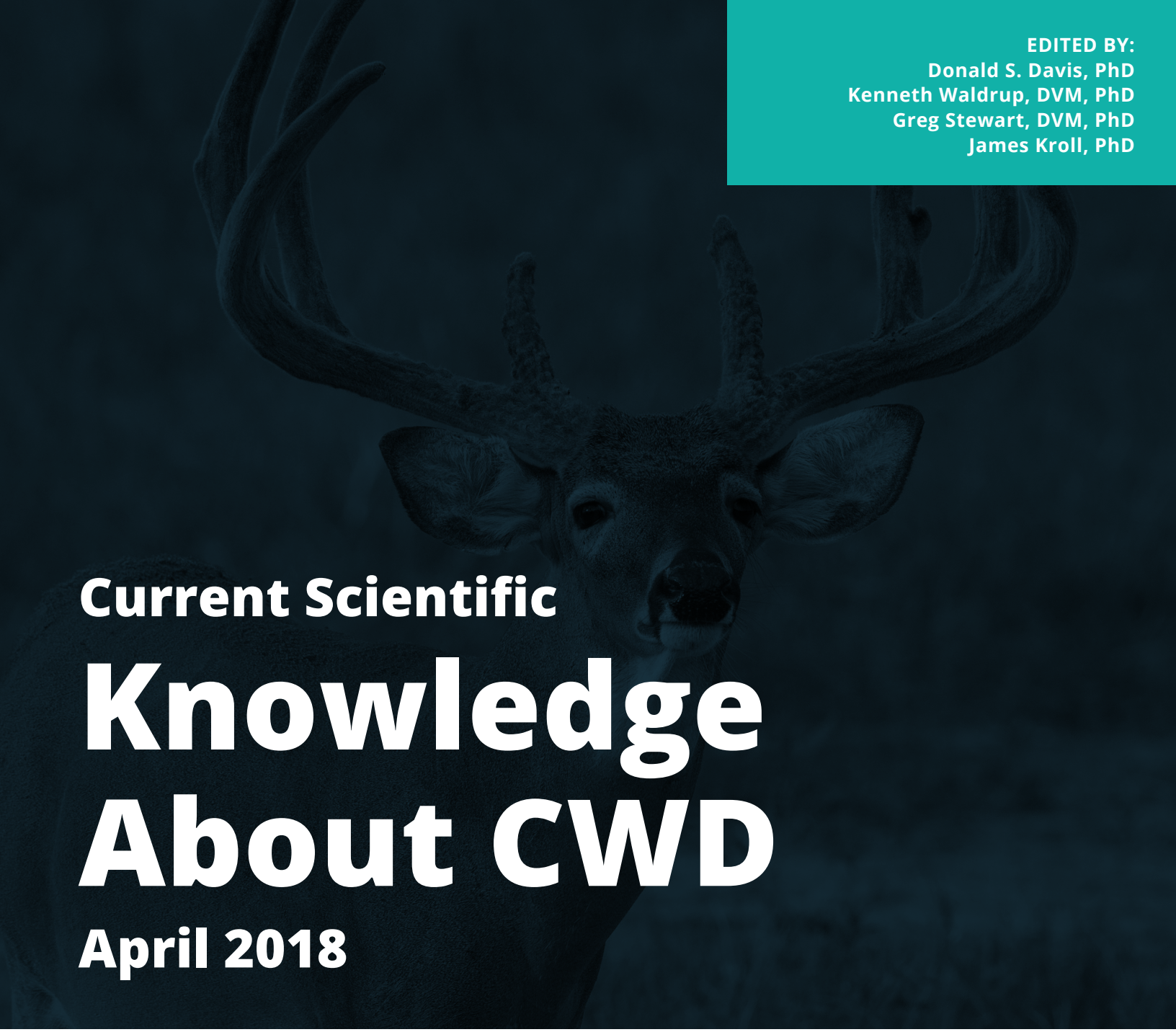

Current Scientific Knowledge About CWD

April 2018

American Cervid Alliance Introduction

American Cervid Alliance Introduction

In an ongoing effort to keep the public apprised of the latest in scientific facts as they relate to Chronic Wasting Disease, the American Cervid Alliance is endorsing the following scientific paper prepared by Dr.'s Don Davis, James Kroll, Greg Stewart, and Ken Waldrup, which dispels much of the mythology surrounding CWD.

This well-prepared paper, sponsored by the ACA, uses science-based facts, giving the reader a clear view of what is known and not known about the disease in contrast to what some are merely theorizing about CWD by using non-scientific opinions, theories, and beliefs to further a biased agenda.

We welcome you to share this document with your legislators and wildlife or animal health officials, as well as members of the media and the public to give a more accurate perspective about a disease that is affecting all segments of deer and elk populations.

Basic Facts Surrounding CWD

Basic Facts Surrounding CWD

A

If an individual deer of a species susceptible to CWD is exposed to a sufficient number of infectious CWD prions, morbidity and mortality may be induced after a prolonged incubation period of 17 months to more than 4 years. After the onset of clinical signs caused by spongiform encephalopathy (holes in the brain) the disease is usually fatal and rapidly so.

B

CWD is a fairly rare disease with a prevalence less than 1% in the over million deer tested nationally over the last 20 years, and a prevalence of 11.2% in the 196 CWD positive counties in the 23 CWD positive States. After 30 years, the CWD test positive prevalence rates in a few states have been reported to be 35-40%. Actual data shows much less. CWD test positive prevalence is an indication of infection and exposure, but CWD test positive prevalence is not a measure of and does not equal mortality from CWD.

C

CWD has continued to be found in new areas since the 1960's. This is a function of increased surveillance testing, natural animal movement, commercial transportation of animals, and the occasional spontaneous genetic mutation of the CWD prion.

D

In spite of the expenditure of over $100,000,000 of public funding, and thousands of animals killed, none of prevention, control, or eradication methods employed by the various States since 1998 have been shown to be effective in either preventing increased prevalence of CWD or the increased geographic distribution.

EDITED BY:

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Basic Facts Surrounding CWD

E

CWD is neither a “wild deer” disease nor a “captive deer” disease but can be found in both. There are 3 States with CWD only in captive deer herds and 8 States with CWD only in wild free-ranging populations. Based on USDA positive test prevalence numbers, CWD is more common in wild cervids than in captive cervids.

F

In small populations in localized areas of Wyoming, CWD may possibly be a factor along with many other factors in causing population declines. Deer populations in the Western States have been declining at 18-20% for over a decade in both states with CWD and those without CWD. Wildlife agencies report that habitat fragmentation, habitat loss, severe weather (droughts and bad winters), human disruption (oil exploration, real estate development), malnutrition, and predation are thought by biologists to have more influence on populations than disease (all disease including EHD, parasites, and CWD).

G

Predictive computer simulation models are just predictions not known facts. They are based on currently available information or assumed information on many variables. If either new scientific data becomes known or conditions such as climate change in the future, then the predictions generated by the model become invalid.

H

Since CWD primarily is a frequency dependent disease in wild deer instead of a density dependent disease, and the benefits of supplemental feeding in most cases far outweigh any possible problems associated with crowding. There is no published scientific data regarding the risk of CWD transmission associated with supplemental feed.

I

The exact modes of CWD transmission in wild deer are unknown. The numbers of CWD prions shed by infected deer in natural conditions is unknown. The length and timing of CWD shedding by infected deer is unknown. The genetic effects on CWD susceptibility and resistance to infection are unknown in susceptible species. All the above unknowns should be given an increased research priority.

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I. General Concepts And Definitions

Chronic Wasting Disease (CWD) is well-known Transmissible Encephalopathy (TSE) of several species of Cervidae or the Deer Family primarily found in North America. Centers for Disease Control (CDC) defines CWD as follows:

"Chronic wasting disease (CWD) is a prion disease that affects deer, elk, reindeer, sika deer and moose. It has been found in some areas of North America, including Canada and the United States, Norway and South Korea. It may take over a year before an infected animal develops symptoms, which can include drastic weight loss (wasting), stumbling, listlessness and other neurologic symptoms." CDC Aug 2017

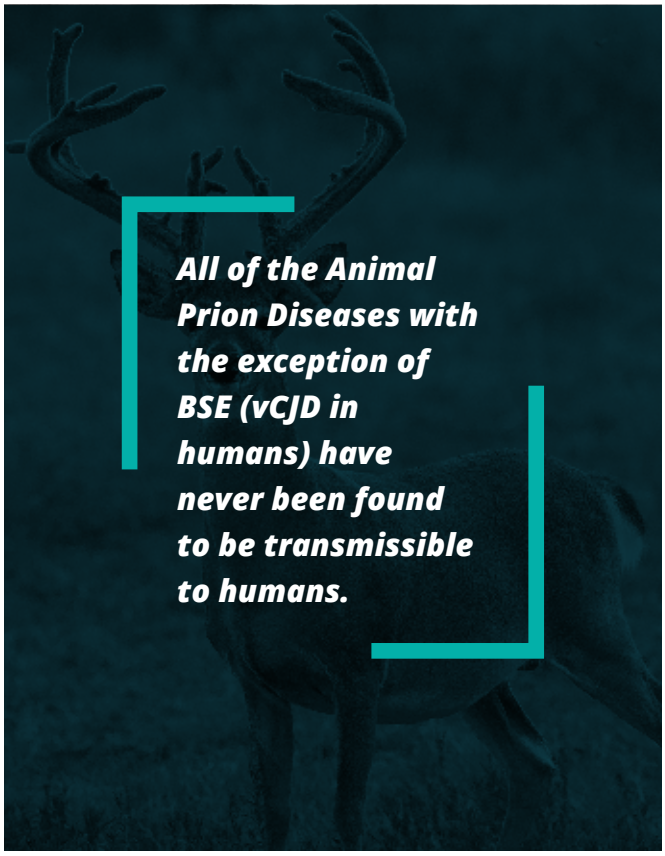
Note: CWD has very recently been diagnosed in the remains of a 15 year old European Elk (moose) in Finland. https://yle.fi/uutiset/osas/news/first_case_in_finland_elk_dies_due_to_chronic_wasting_disease/10108115

The etiologic agent of CWD and other TSEs based on available data is thought to be prions. Prions are self-replicating proteins and are found in their natural structure in normal animals and humans. An atypical structured prion causes pathologic changes in the susceptible host.

"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." CDC Aug 2017

"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." CDC Aug 2017

There are a number of TSEs that occur in humans and animals.



Human Prion Diseases

- Creutzfeldt-Jakob Disease (CJD) (found in 1 per million worldwide, WHO)
- Variant Creutzfeldt-Jakob Disease (vCJD) (Total worldwide 229 cases)
- Gerstmann-Straussler-Scheinker Syndrome
- Fatal Familial Insomnia
- Kuru

Animal Prion Diseases

- Bovine Spongiform Encephalopathy (BSE)
- Chronic Wasting Disease (CWD)
- Scrapie (sheep)
- Transmissible mink encephalopathy
- Feline spongiform encephalopathy
- Ungulate spongiform encephalopathy

Note; All of the Animal Prion Diseases with the exception of BSE (vCJD in humans) have never been found to be transmissible to humans. This is discussed in detail below in other sections.

II. Host Distribution

Naturally Occurring in Free-Ranging

Mule Deer (*Odocoileus hemionus*)

Rocky Mountain Elk (*Cervus elaphus nelsoni*)

White-tailed Deer (*Odocoileus viginianus*)

Shiras Moose (*Alces alces shiras*)

NOTE: More recently in Reindeer (Rangifer spp) and European Elk (Alces spp) in Norway and European elk remains in Finland.

Other Susceptible Cervidae (Deer Family)

Sika Deer (*Cervus nippon*) one in Korea in captive situation with other imported animals.

Red Deer (*Cervus elaphus*) – in captive and experimental infections

Muntjac deer (*Elaphodus muntiacus*) – experimental infection

NOTE: Fallow deer (Dama dama) resisted attempts to infect them for 7 years by USDA. Axis deer (Axis axis) have been tested in surveillance programs without finding any positives.

NOTE: There has been speculation since the 1980's about possible transmission to humans. To date, there has NOT been a single case of CWD in humans. This is discussed in detail in later sections.

III. Ocurrence And Geographic Distribution

CWD was first observed as an unnamed clinical syndrome in 4 captive mule deer and elk groups of wild origin at Colorado State University (CSU) in the 1960's. (Spraker). That fact does not imply or in any fashion confirm that CWD originated in captive deer at CSU. There are several theories about the possible origins of CWD and all are not proven and never will be. The same may be said about the origins of BSE, scrapie, CJD, or any of the other naturally occurring TSEs.

The best review of the early cases of CWD at CSU and the Early History of CWD can be found in the "Chronic Wasting Disease: A Review for Health Canada' 105 pages by Dr. Terry Spraker from CSU.
The first published article on CWD was by Williams and Young in 1980 in the Journal of Wildlife Disease titled "Chronic Wasting Disease of Captive Mule Deer: A Spongiform Encephalopathy."

In 1981, CWD was found in a free-ranging 18 month old male elk in the Rocky Mountain Park. Then CWD was found in a 4-5 year old mule deer buck near CSU in 1984. The first case of CWD in a white-tailed deer was found in 1985 in a wild adult male near Loveland Colorado.

Now after more than 40 years, the rest, as they say, "is history". Presently as of Feb 2018, CWD has been found in 23 States and 2 Canadian Provinces, in Korea, Norway, and Finland. Uninformed and misinformed pundits often characterize CWD as a "common", "widespread" and/or "rapidly expanding" disease. A closer examination and even casual glance at the available scientific data refutes those claims.

According to CDC in 2012, "More than1,060,000 cervids have been reportedly tested for CWD, and ~6,000 cases have been identified." (Prevalence of positives = 0.56% which is 5 test positives per 1000 tested). USDA Records from 1998-2012. Dr. Patrice Klein USDA/APHIS on April 2012.

Total Farmed Surveillance
170,120 403 positives (0.2%)

Total Wild Cervid Surveillance
848,706 3,600+ positives (0.4%)

Total Tested
1,018,826 4,003 positive (0.39%)

Data from the Texas Veterinary Diagnostic Laboratory (TVMDL)

From 2013-2018 98,524 deer tested for CWD, with 87 positives (0.88%)

CWD Distribution By Counties

In the US, there are 3,144 Counties. As of February 2018 there are 196 Counties with CWD Positive Deer (CDC Jan 2018). That equals to 6.2% of the Counties in the US with CWD. That also means 93.8% of the US is free of CWD.

In the 23 States (counting Mississippi) that have CWD, there are 1,714 Counties. So according to CDC in January 2018, there

Ocurrence And Geographic Distribution cont.

are 196 counties with CWD positive animals in the 1,714 total counties in the 23 CWD positive States. That equals 11.4%. Which means that even in the 23 CWD Positive States 88.6% of the counties are free of CWD as on February 2018, and some only have one positive.

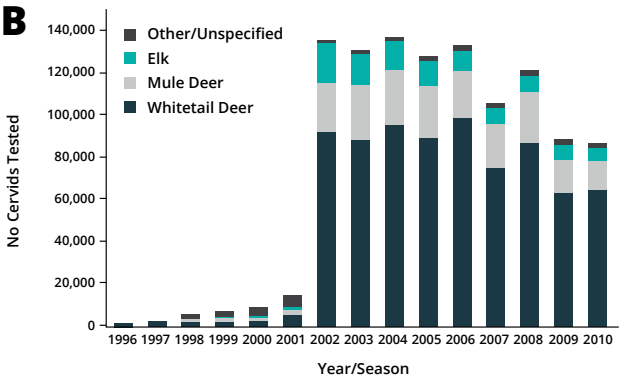
CWD Test Positive Prevalence – SCWDS Briefs. January 2018. Michigan since 2015, 1.9 % (57/30,000); Missouri 2016-2017, 0.24% (58/323,456); Nebraska since 1997, 0.99% (499/51,000); Wisconsin, since 1999, 1.99% (4174/209,700). Wyoming Game and Fish, January 2018, in 2017, 8.8%, 342/3883).

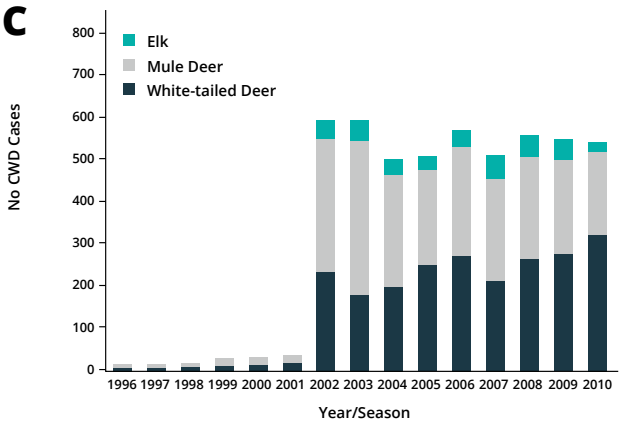
NOTE: The numbers above from SCWDS do not even approach the exaggerated prevalence numbers frequently and widely reported in the popular media sources.

It must be pointed out that the entire US and Texas do not entirely represent the CWD situation in all of the individual States. Wyoming, for example, has been reported to have a 35% prevalence of CWD in tested animals, there are CWD test positive animals in 16 of the 23 Counties in Wyoming, and the disease has been there for about 40 years. Wisconsin has recorded CWD in 20 of the 72 counties from 2002-2018. But the CWD situation in Wyoming and similar States should not be extrapolated to or used to make policy decisions in other States.

The five states of Wyoming (16/23), Colorado (20/64), Wisconsin (20/72), Nebraska (35/93) and Kansas (22/105 have 113 of the 196 or 58% of the CWD infected counties. There are 15 States that have less than 10 Counties each with CWD.

DATA from CDC that clearly shows that CWD is NOT Increasing in Prevalence Since 2002 When Surveillance Drastically Increased





Bottom Line on Occurrence and Distribution

Prevalence rates of less than 1% for CWD, like all the other TSE, shows that CWD is a fairly rare disease on a national scale. "Widespread" also depends on the scale by which it is measured. By total State is 44%, by Counties in the US it is 6.2%, by positive counties in the 23 positive states it is 11.2%.

Even with the dramatic increase in surveillance and the number of deer tested since 2002, the prevalence has not increased nationally, however the increase in the number of States with CWD can be attributed to: 1) the natural movement of deer, 2) the transportation/translocation involved in deer commerce, and 3) the increase in required CWD testing.

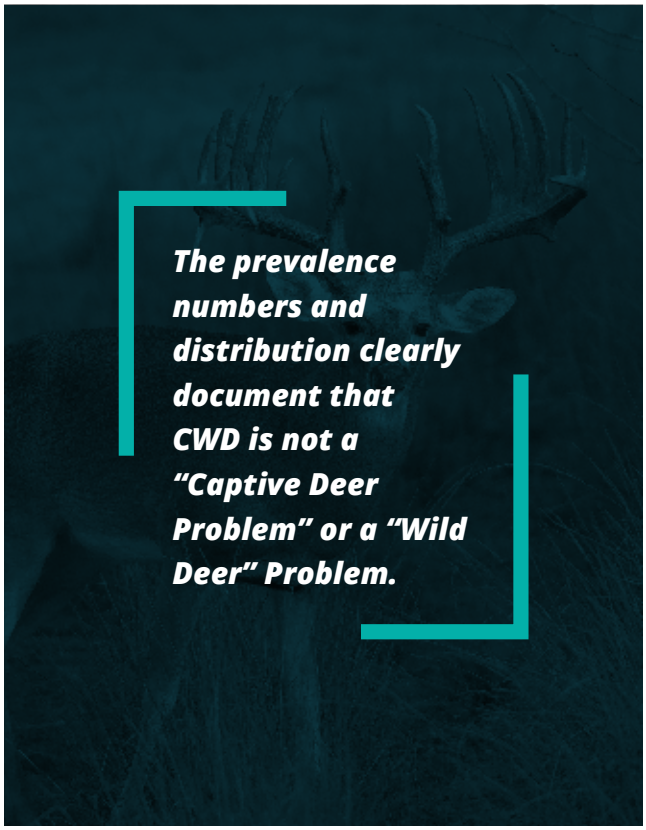
It should also be noted that some of the "spread" of CWD could be cases due to spontaneous mutations. All TSEs have spontaneous cases of atypical forms of prions. Diagnostic testing for Spontaneous CWD is rarely done. This will be discussed at length in TRANSMISSION.

NOTE: The prevalence numbers and distribution also clearly document that CWD is not a "Captive Deer Problem" or a "Wild Deer" Problem.

According to USDSA/APHIS, "since 2001, CWD has been identified in free-ranging cervid populations in 23 States: Colorado, Illinois, Kansas, Maryland, Minnesota, Mississippi, Montana, North Dakota, Nebraska, New York, New Mexico, South Dakota, Utah, Virginia, Wisconsin, West Virginia, Iowa, Michigan, Missouri, Pennsylvania, Arkansas, Texas, and Wyoming.

Since 1997, CWD has been found in farmed cervids in 16 States: Colorado, Kansas, Michigan, Minnesota, Missouri, Montana, New York, Oklahoma, South Dakota, Iowa, Nebraska, Ohio, Pennsylvania, Texas, Utah and Wisconsin."

NOTE: There are 3 States (Oklahoma, Ohio, and Utah) with CWD only in captive herds. There are 8 States (Arkansas, Illinois, Maryland, Mississippi, New Mexico, West Virginia, Virginia, and Wyoming) with CWD only in wild populations.



IV. Diagnosis

Testing by USDA/APHIS, 2018.

"Currently, definitive diagnosis is based on immunohistochemistry (IHC) testing of the obex area of the brain stem or the medial retropharyngeal lymph nodes. Gross lesions seen at necropsy reflect the clinical signs of CWD, primarily emaciation and sometimes aspiration pneumonia, which may be the primary (acute?) cause of death. On microscopic examination, lesions of CWD in the central nervous system resemble those of other spongiform encephalopathies."

At this time, abnormal prion proteins can be detected using immunohistochemistry (IHC), Western blotting, enzyme-linked immunosorbent assay (ELISA), prion misfolding cyclic amplification (PMCA), and real-time quaking induced conversion (RT-QuIC), however, approved diagnostic assays are limited to IHC and ELISA.

Research is being conducted to develop live-animal diagnostic tests for CWD. The rectal biopsy test, while not yet approved for routine regulatory testing, appears promising but may have limited applicability due the number of positive animals in the early stages of the disease that may not be detected.

Ante-mortem rectal and tonsil biopsy tests are presently being utilized and evaluated by the Texas Animal Health Commission in captive cervids.

Official CWD tests are performed only at APHIS-approved University, State, or Federal veterinary diagnostic laboratories. If the animal to be tested is a farmed deer or elk, accredited veterinarians should check with Federal or State regulatory veterinarians for information on sample collection and appropriate sample submission. If the animal to be sampled is a wild deer or elk that is suspected of having CWD, accredited veterinarians should inform State and Federal authorities and work with their State wildlife management agency to find out how officials would like the sample collected and submitted."

"If the animal to be sampled is a clinically normal wild animal that an individual hunter would like tested, accredited veterinarians should also work with their State wildlife management agency or department of agriculture to find out how best to proceed. Several approved laboratories exist with sufficient capacity to provide fee-for-service testing for samples collected by individual hunters. Accredited veterinarians should always check with the diagnostic laboratory to make sure samples are properly collected, packaged, and shipped." USDA

NOTE: All the Official IHC tests are post-mortem tests and are done on tissues collected from dead animals.

The vast majority of the samples from free-ranging animals and submitted by wildlife agencies were either hunter harvested or road kills. Therefore at the time of death the animals were mobile and not exhibiting the advanced clinical signs compatible with CWD.

The majority of postmortem IHC tests on captive cervids are from animals euthanized during depopulation of CWD exposed herds and by mandatory mortality testing requirements imposed by the States. Again at the time of death, clinical signs compatible with CWD are extremely rare.

A clinical case of CWD in Texas with over 4.5 million deer and over 100,000 captive cervids has never been observed.

NOTE: At even a 1% CWD mortality rate, there should be 45,000 dead wild deer and a 1,000 captive deer annually available to be found in Texas. This obviously has not been observed.

A positive IHC test does not document spongiform encephalopathy, nor does it document CWD as the cause of death.

Much of what is known about CWD in free-ranging cervids is based on prevalence based on the results of IHC testing. Prevalence is an indication of exposure rates and infection rates. Prevalence for diseases including prevalence for CWD does not equal morbidity or mortality from that disease.

V. Transmission

Modes Of Disease Transmission In Regard To Cwd

Most epidemiologists that are familiar with the scientific literature about TSEs in general and CWD specifically hypothesize that CWD is mainly transmitted in the wild by:

1. Frequency dependent direct contact.

2. Indirect through environmental contamination.

The most comprehensive publication on the subject is by Jenelle et. al, 2014. PLOS. "Transmission of Chronic Wasting Disease in Wisconsin White-tailed Deer: Implications for Disease Spread and Management", which is a retrospective study of 10 years of CWD data. It clearly shows that in wild deer CWD transmission is frequency dependent rather than density dependent.

The other view, "The mode of transmission of CWD is unknown."(USGS National Wildlife Health Center).

USDA –"The routes of transmission are still unknown. Epidemiologic evidence suggests that this disease is transmitted laterally, from animal to animal. It is thought that CWD can be transmitted through nose-to-nose contact. It also appears that CWD also can be spread indirectly through the environment; contaminated pastures seem to be the source of exposure in some outbreaks. Vertical transmission may occur, but does not seem to be important in maintaining epidemics and cannot explain many cases."

Currently the scientific evidence about the modes of transmission of CWD in wild, free-ranging cervids is extremely limited. Most of the known data are entirely based on artificial experimental infections of captive deer in pens as evidenced below. (The highlights below are those of the editor's).

From CDC 2017. "Scientists ***believe*** CWD proteins (prions) ***likely*** spread between animals through body fluids like feces, saliva, blood, or urine, either through direct contact or indirectly through environmental contamination of soil, food or water. Once introduced into an area or farm, the CWD protein is contagious within deer and elk populations and can spread ***quickly***. Experts ***believe*** CWD prions can remain in the environment for a ***long time***, so other animals can contract CWD from the environment even after an infected deer or elk has died."

There is a serious problem in objective science when terms such as "believe", "likely", or even "suggest", and "perhaps" are used. Subjective terms like "quickly" and "long time" should be avoided.

Science is, or should be, based on demonstrable data. When those highlighted terms above are used, they are a euphemism for "we are not sure" and "we don't really know".

There is also a serious issue when data from very small numbers of experimental captive animals in one location are extrapolated

to free-ranging populations everywhere. Experiments may show what is possible in laboratory conditions but may not reflect what is probable in the real world.

Let's examine some examples in detail. First is in regard to "spread between animals by body fluids like feces, saliva, blood, or urine".

Blood – A single white-tailed fawn experimentally injected intravenously ***(IV) with 250 ml*** of blood from CWD positive deer, and 2 other fawns injected intraperitoneally (IP) with 250 ml of blood from CWD positive deer. All 3 fawns became CWD positive by 18 months post injection.

NOTE: Where in nature in free-ranging deer receive 250 ml of blood in a IV transfusion, or 250 ml of blood injected IP?

Urine and Feces– 3 fawns (one died) orally inoculated with a total 50 ml each of urine and feces over 3 days from CWD infected deer. The 2 remaining fawns were CWD negative at 180 days.

Saliva – 3 fawns were orally exposed to ***50 ml of saliva*** from CWD infected deer. By 180 days post-oral exposure, all 3 fawns were CWD Positive.

NOTE: Where in nature are free-ranging deer exposed to 50 ml of saliva in 3 days?

The above results were published in a very prestigious journal- Science 2006: Mathiason et al., "Infectious prions in the saliva and blood of deer with chronic wasting disease."

The big problem is that scientific results like the above are misunderstood, misquoted, and extrapolated by others. It is a fact that CWD prions can be found in saliva, blood, urine and feces in experiments, but perhaps only the numbers of prions in saliva in large doses are capable of transmitting CWD by normal routes of infection in nature.

Another excellent CWD researcher Dr. Nicholas j. Haley (et al.) published an article in the Journal of Virology 2011. "Detection of Chronic Wasting Disease Prions in Salivary, Urinary, and Intestinal Tissues of Deer: Potential Mechanisms of Prion Shedding and Transmission." That investigation showed

V. Transmission cont.

that prions are shed in very low numbers in feces and urine and could only be detected by special amplification methods (serial protein misfolding cyclic amplification or sPMCA) which result in a million fold concentration of the prions to allow detention.

More recently Dr. Haley ranked the infectively of various bodily fluids in relation to potential CWD transmission. They are ranked as follows from highest to lowest in terms of CWD prions present.

Brain
Carcass
Lymphoid Tissue
Deboned Meat
Digestive Tissue
Blood
Saliva
Feces
Urine – takes 33.000 gallons of infected urine to equal 1gm of infected brain

Unfortunately public policy often is made even in the face of published science. Urine lure bans commonly are imposed by State wildlife agencies, but a quote from Dr. Haley (who did the research) is "The Chance of Bottled Urine Transmitting CWD Is Virtually Zero" and that puts things into prospective.

TRANSMISSION BY CLOSE CONTACT

Miller et al., 2004. Experimentally placed 9 CWD naïve mule deer in 3 pens of 3 with that contained mule deer carcasses that died of CWD. 19% of the CWD naïve mule deer became infected.

TRANSMISSION BY ENVIRONMENTAL CONTAMINATION

Miller et al., 2004. Experimentally 3 groups of 3 deer each of CWD naïve mule deer were placed in pens at Colorado State University. One set of 3 pens that had been occupied by CWD infected animals 2 years ago, another set of 3 pens with a CWD carcass, and a third set of 3 pens with a CWD infected animal. A total of 16% of the CWD naïve deer in the 3 experimental conditions in 9 pens became infected, and 84% did not become infected.

OTHER POSSIBLE MODES OF CWD TRANSMISSION

1. More recently evidence of in utero transmission of CWD has been reported by:

A. Selariu et. al., 2015. Journal of General Virology, "In utero transmission and tissue distribution of chronic wasting disease-associated prions in free-raging Rocky Mountain elk".

B. Nalls, et al., 2013. PLOS, "Mother to Offspring Transmission of Chronic Wasting Disease in Reeve's Muntjac Deer."

2. By Predators and Scavengers

A. Nuwer, 2012. Smithsonium.com. "Brain-Eating Crows May Help Spread Prion Diseases'.
B. Nichols et. al., 2015. Prion. "CWD prions

remain infective after passage through the digestive system of coyotes (Canis latrans)'"

POSSIBLE CWD TRANSMISSION BY PLANTS

A. Pritzkow et al., 2015. Plants were exposed to prion (not solely CWD prions) positive Hamster Brain Homogenates, then plant material injected back into hamsters.

NOTE: Hamsters are not deer, the prions used were not all CWD, and injection is not a normal route of CWD transmission.

B. Rasmussen et al., 2014 found that plants were unable to transport sufficient amounts of CWD prions from roots to wheat stems to be infectious

NOTE: Never in nature or under experimental conditions have CWD prions in plants been documented to be infectious to deer.

TRANSMISSION BY SEMEN

NOTE: No prions of any TSE have ever been isolated from semen from any species.

CWD TRANSMISSION TO OTHER SPECIES INCLUDING HUMANS

FROM CDC – "The CWD prion has been shown to experimentally infect squirrel monkeys, and also laboratory mice that carry some human genes. In addition, a study begun in 2009 by Canadian and German scientists is evaluating whether CWD can be transmitted to macaques, a type of monkey that is genetically closer to people than any other animal that has been infected with CWD previously. On July 10, 2017, the scientists presented a summary of the study's progress in recorded presentation in which they showed that CWD was transmitted to monkeys that were fed infected meat (muscle tissue) or brain tissue from CWD-infected deer and elk. Some of the meat came from asymptomatic deer that had CWD (i.e., deer that appeared healthy and had not begun to show signs of the illness yet). Meat from these asymptomatic deer was also able to infect the monkeys with CWD. CWD was also able to infect the macaques that had the infectious material placed directly into their brains.

Data reported from this unpublished Canadian presentation showed different results than a previous published study, which had not shown successful transmission of CWD to macaques. The reasons for the different experimental results from the Canadian study and other studies are unknown.

More recently it was shown definitively that "Chronic wasting disease (CWD) did not cross the species barrier to infect Cynomolgus macaque monkeys during a lengthy investigation by National Institutes of Health scientists" exploring possible risks to humans.

In the NIH study, titled "Lack of Transmission of Chronic Wasting Disease to Cynomolgus Macaques" which was published in 2018 in the Journal of Virology, "14 macaques

V. Transmission cont.

were cerebrally and orally exposed to brain matter from CWD-infected deer and elk, and then monitored for up to 13 years."

Researchers screened tissues for prion disease using several tests--including the highly sensitive Real-Time Quaking-Induced Conversion (RT-QuIC) assay--and found "no clinical, pathological or biochemical evidence suggesting that CWD was transmitted" to the macaques.

To date, there is no strong evidence for the occurrence of CWD in people, and it is not known if people can get infected with CWD prions. Nevertheless, these experimental studies raise the concern that CWD may pose a risk to people and suggest that it is important to prevent human exposures to CWD.

Additional studies are under way to identify if any prion diseases could be occurring at a higher rate in people who are at increased risk for contact with potentially CWD-infected deer or elk meat. Because of the long time it takes before any symptoms of disease appear, scientists expect the study to take many years before they will determine what the risk, if any, of CWD is to people.

From CWD Alliance – No cases of human prion disease have been associated with CWD. In fact, current research from Colorado confirms that the incidence of Creutzfeldt-Jakob disease in humans living within 7 CWD endemic counties has not significantly increased between the years of 1970-2001 and no case of a human prion disease resulting from CWD exposure has ever been documented (McWhinney et al., 2006). The tendency toward a natural "species barrier" reducing human susceptibility to CWD and other prion diseases has been demonstrated by in vitro studies; in those studies, PrPCWD inefficiently converted human PrPC to the abnormal isoform as compared to homologous PrPCWD to cervid PrPC conversions. Cervid PrPCWD to human PrPC conversions were essentially equivalent to conversions of human PrPC by scrapie and BSE PrPres. However, lingering uncertainty about interpreting these data and assessing any potential risk that CWD may pose to humans is fostered by differing experiences with two more common animal TSEs. Although there is a long history of human exposure to scrapie through handling and consuming sheep tissues, including brain, there is no evidence that this presents a risk to human health. In contrast, massive exposure of British and perhaps other European citizens to the BSE agent resulted in approximately 106 deaths due to variant Creutzfeldt-Jakob disease as of February 2002.

In the absence of complete information on risk, and in light of similarities of animal and human TSEs, public health officials and wildlife management professionals recommend that hunters harvesting deer and elk in the endemic area, as well as meat processors and taxidermists handling cervid carcasses, should take some common sense measures to avoid exposure to the CWD agent and to other known zoonotic pathogens. Because TSE agents have never

been demonstrated in skeletal muscle, boning game meat is recommended as an effective way to further reduce the potential for exposure. Raw velvet antler, a product unique to the farmed cervid industry, may deserve further evaluation for presence of PrPCWD in order to preserve markets for this commodity.

NOTE: Many of the experiments in other species used intracranial injection (IC) of CWD infected brain homogenates containing millions of CWD prions through a hole in the skull. This is both a huge dose of prions and a completely abnormal route of infection. Results from studies using IC injections should be viewed with some skepticism.

NOTE: Cattle, sheep, goats, and fallow deer resisted experimental infections.

NOTE: Some corrections of the above statements are needed. Transgenic mice with humanized immune systems resisted CWD infections while transgenic mice with elk immune systems became infected.

NOTE: To date NOT one single case of CWD has been found in humans in spite tens of thousands of CWD test positive deer and elk being ingested by people.

NOTE: the macaque study was not a published study. The total number of prions contained in the meat, and the total amount of meat fed are unknown. The time interval of feeding, and or number of feedings of infected material is also unknown. The chimpanzee is more closely related to humans than macaques. Completely extrapolating results from one species to another is scientifically inappropriate. As an example, in 2 related species, CWD in elk is known to be a different disease from CWD in white-tailed deer.

VI. CWD And Deer Population Declines

"The total U.S. deer population in 2014 was about 32.2 million; 28.6 million whitetails and 3.6 million mule deer, blacktails, and other. That's down from 33.5 million in 2013; 29.9 million whitetails and 3.6 million mule deer, blacktails, and other. Recent peak U.S. deer population is estimated to have occurred around the year 2000 at 38.1 million, 33.5 million whitetails and 4.6 mule, blacktails, and other. The estimate is based on population information from state agencies and other groups collected on this website, discussed on each state page that can be accessed by clicking on the drop-down menus above. The estimate also relies on harvest data for each state, available using the links at the top of the column at right. As illustrated in the figure below, the U.S. deer harvest has fallen by 18.8 percent since 2000, a few state numbers are unavailable and estimated."
Deer Friendly 2018

Over the past decade, there has been a steady decline of 18-20% in deer populations in the Western US in States both with and without CWD .

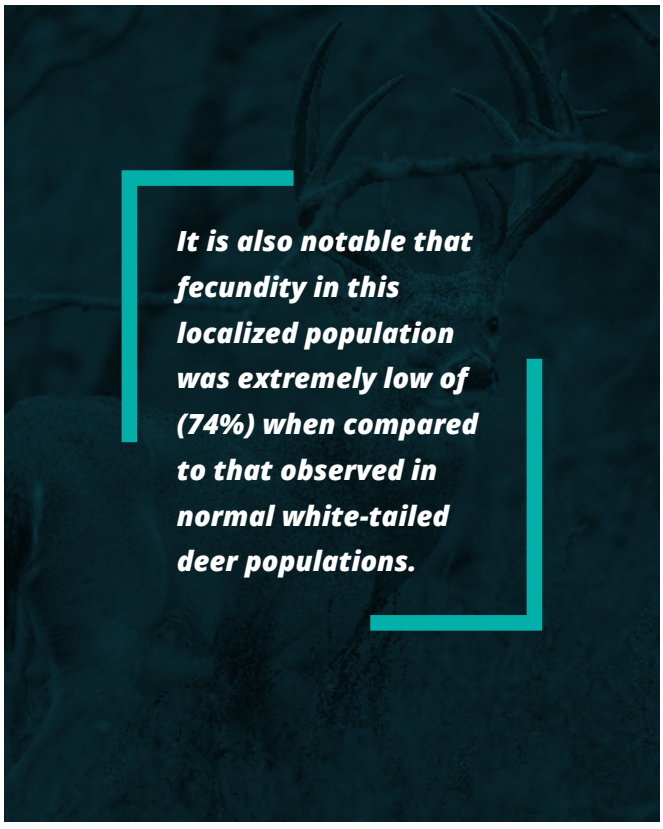
Two of the most recent published and most frequently quoted articles on deer population declines are:

A. "Chronic Wasting Disease Drives Population Decline of White-tailed Deer" Edmunds, et al., PLOS 2016.

B. "Endemic chronic wasting disease causes mule deer population decline in Wyoming" DeVivo, et al., PLOS 2017

Both are well-designed studies for Doctor of Philosophy Degrees to gather data from radio-collared deer. There is a great deal of helpful information generated by the two investigations.

They do, however, have several understandable limitations in scope. First of all, they both were conducted on small populations in a localized area. DeVivo captured and radio-collared 143 mule deer (118 females and 25 males) in Converse County, Wyoming for 4 years. Edmunds captured and radio-collared 175 deer (112 fawns, 57 females -55 males; 63 adults (27 female-55 male) on the VR Ranch and surrounding area. Did the sex-ratio and age



class of the research deer represent and reflect deer populations across Wyoming? Did the localized study areas represent the habitat fragmentation, plants, soils, stocking rates, predation levels, human disruption, weather conditions, and concomitant disease of deer as the rest of Wyoming?

DeVivo 2017 documented 97 mortalities in the 143 radio-collared deer. The causes were determined (in some cases subjectively) to be as follows: 20 mountain lion predation; 14 'clinical" CWD (which were CWD test positives with no other overt signs of trauma, etc); 4 hunter harvest; 2 poaching; and 37 undetermined cause of death. One wonders why the title of the paper is "CWD causes Decline", instead of "Mountain Lions cause Decline", or better yet "Undetermined Causes are Responsible for the Majority of Population Decline".

Edmunds 2016 – similar criticisms can be made on the data collected from the 175 white-tailed deer in a localized geographic area. Also the variable of possible immigration into the population was not considered. It is also notable that fecundity in this localized population was extremely low of (74%) when compared to that observed in normal white-tailed deer populations.

NOTE: Edmunds in his dissertation in 2013 wrote on page 14, ".... further few deer and no elk populations are considered in danger of decline due to CWD." On page 18 Edmunds wrote "However, no population of mule deer or white-tailed deer in either Colorado or Wyoming where endemic CWD have occurred for greater than 50 years have been lost."

NOTE: In the Wyoming studies, there was a brief mention of the relationships between apparent susceptibility to CWD and genetics. Apparent resistance was explained by saying that a deer with resistant genetics may also have negative behavioral traits, negating the positive effect of resistance.

NOTE: Both the results of the 2 Wyoming studies have been misinterpreted, misrepresented, and misreported by others not familiar with statistical procedures. An example – 'Survival of CWD-negative deer in these studies was 30-40% greater than survival of CWD-positive deer" was erroneously used to show a "cause and effect" relationship between CWD and population declines. CWD and Survival is a correlation not a cause and effect statistical relationship. There are many other factors that can be correlated with survival, but a correlation value (R) does not equal cause in statistics.

NOTE: The most serious problems associated with the two above studies are the erroneous extrapolations of these investigations to white-tailed deer and mule deer in other locations with notable differences in population dynamics, climate, topography, plant communities, habitat fragmentation, soil composition, minerals, domestic animal stocking rates, predation, and other sympatric wildlife.

Both the 2 above, and all other CWD computer simulation models that are utilized to predict the possible population effects for 25-40 years have inherent limitations. Simulation models are designed to incorporate the interactions of multiple independent and dependent variables that control how a dynamic process works. Data both past and

VI. CWD And Deer Population Declines cont.

present are required to design the simulation model as well as knowledge of the process.

If the fundamental assumptions that are used to design the model are not reflective of the actual process simulated, then model will not be valid. If the fundamental assumptions of the model are valid but the required data inputs are erroneous or missing, the model will make inaccurate and erroneous predictions.

The most common misunderstanding and false assumptions concerning predictive computer simulation models are associated with the validity of their predictive value. Predictions or projections of such models ***are not absolute facts.*** They are ***simply predictions*** and their predictive outcomes are made based on current knowledge about the condition of variables and the interactions of these variables. If those variables and their interactions change in the future, the model will be invalid. In plain English, if a model is constructed about the effects of CWD on a deer population in a location for the next 25-40 years, and there is a drought, a very hard winter, another disease, or an increase of human disruption (i.e. the conditions change) during the next 25-40 years, then the model is and will be invalid.

Bottom Line on Models of CWD Causing Population Declines

Over the last 20 years, there have been many computer simulation models generated predictions of the long-term population effects of CWD. They all have been uniformly wrong. Schauber and Woolf, 2003 wrote an article "Chronic Wasting Disease in Deer and Elk: a Critique of Current Models and Their Applications. The authors stated "CWD will remain at a relatively low prevalence indefinitely". Obviously there interpretation of the available data does not support "population decimation'. They were well ahead of their time. Predictive models on CWD have not been either accurate or reliable.

NOTE: Wyoming Deer Population – "An estimated population of 423,000 deer in 2015, up from 400,000 in 2014. The population was trending higher after three mild winters into 2016, but a very harsh winter for 2016-17 west of the continental divide resulted in very low fawn survival. Also an EHD die-off. A total population of about 578,000 in 1991. "Deer Friendly, 2018.

NOTE: Colorado Deer Population – "An estimated population of 419,000 in 2017, 436,000 deer in 2016, a decline in part as a result of a harsh winter. In 2015, about 445,000 deer. The mild 2014-15 winter allowed for better survival, especially in the northwest. The 2014 post-hunt population was estimated at 424,190 compared to 391,000 in 2013. " Deer Friendly, 2018.

Deer populations in Colorado and Wyoming (as well as in other States) have historically increased and decreased over time because of several reasons previously discussed, but disease is rarely listed as a major cause of these variations with the exception of epizootic hemorrhagic disease (EHD).

VII. Prevention And Control

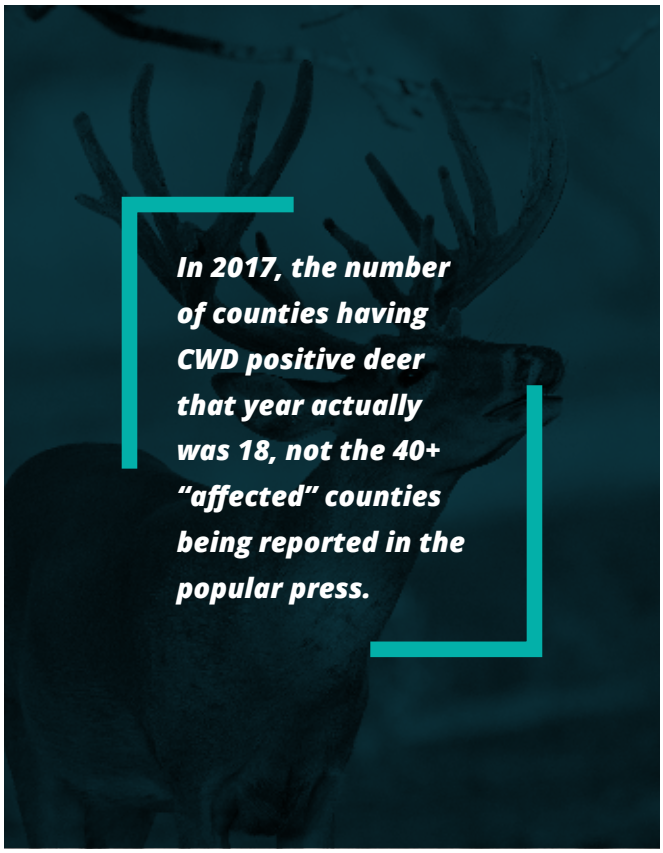
Control Strategies

CDC 2018 – "No treatment is available for animals affected with CWD. Once clinical signs develop, CWD is invariably fatal. Affected animals that develop pneumonia may respond temporarily to treatment with antibiotics, but ultimately the outcome is still fatal. Similarly, no vaccine is available to prevent CWD infection in deer or elk. It follows that controlling CWD is problematic. Long incubation periods, subtle early clinical signs, absence of a reliable ante-mortem diagnostic tests, extremely resistant infectious agent, possible environmental contamination, and incomplete understanding of transmission all constrain options for controlling or eradicating CWD."

CDC 2018 – "In captive facilities, management options currently are limited to quarantine or depopulation of CWD-affected herds. Two attempts to eradicate CWD from cervid research facilities failed; the causes of these failures were not determined, but residual environmental contamination following depopulation and/or facility clean-up was likely in both cases. Attempts to eliminate CWD from farmed elk populations are more recent, and consequently the efficacy of these attempts remains uncertain. Whether contaminated environments can ever be completely disinfected remains questionable. Until effective cleaning and disinfection procedures are identified, captive cervids should not be reintroduced into commercial facilities where CWD has occurred; moreover, free-ranging cervids also should be excluded from previously-infected premises. Establishment of free-ranging reservoirs of infection in the vicinity of infected game farms, as exemplified by probable cases in Saskatchewan and Nebraska, could severely impair attempts at eradication from captive facilities. Inherent difficulties in managing infected herds and premises underscore the need for aggressive surveillance to prevent movements of infected animals in commerce."

Wisconsin has had the most experience with CWD prevention and control. Since the appearance of CWD in southwestern Wisconsin in 2002, that state has become somewhat of a "testing laboratory" for reducing or eradicating CWD. The Wisconsin Department of Natural Resources (WDNR) instituted a host of strategies to eradicate CWD from the "CWD Eradication Zone," including sharp-shooting and a confusing array of hunting seasons and bag limits. The response plan included depopulation of a 287 square mile zone, containing an estimated 15,000 deer. During 2004-2005, hunters killed a total of 27,032 deer in the "Zone," and sharp shooters shot 1,383 and trapped 102 (total 1,484), at a cost of approximately $478 per deer. By 2006, about $35+ million was expended on these efforts, the result of which was loss of public confidence and failure to eradicate CWD. In 2006, the Wisconsin Legislature conducted an audit of the program, concluding, the efforts had not been effective, and the approach should be re-evaluated. By 2012, some 172,000 deer had been removed from the Eradication Zone, where the initial population estimate was 15,000. In 2011, Governor Scott Walker appointed a White-tailed Deer Trustee to evaluate these and other issues of deer

VII. Prevention And Control cont.



management in Wisconsin. The June 10, 2012 report confirmed the program had not been successful and recommended a drastically different approach of containment and intensified monitoring to detect "spark outs." Since, there has been little spread of CWD, in spite of what has been published in popular outlets. In addition, the DTR report found sampling bias had greatly inflated infection rate estimates. In 2015-16, for example, the vast majority of the 3,156 CWD samples came either from the original four county area or the immediate zone around these counties.

There have been many popular articles published in the last five years asserting that CWD in Wisconsin has "exploded," and there now are over 40 "affected counties." Distribution of CWD sampling by the WDNR in 2015-16. – showed that the vast majority of samples came either from the four original "Zone" counties or counties immediately surrounding these counties. (Source: WDNR CWD monitoring database.)

In 2017, the number of counties having CWD positive deer that year actually was 18, not the 40+ "affected" counties being reported in the popular press. Of the 9,766 deer tested in 2017, a total of 595 testing positive (6.1%); however, 534 (89.7%) of these positives came from the original four counties (Dane, Iowa, Richland, and Sauk). One hardly can accept that CWD has "exploded" in Wisconsin.

There also have been claims that the approach Illinois has used (sharp-shooting, increased bag limits) has been effective. From 2003 to 2017, the number of counties with CWD positive animals has increased from 7 counties to 17 counties.

(www.dnr.illinois.gov/programs/CWD/Documents/CWDAnnualReport20162017.pdf); Again, not successful by any analysis. Hence, eradication or even control of CWD does not seem to be possible using the most common approach to this time.

CDC 2018- "Managing CWD in free-ranging animals presents even greater challenges. Long-term, active surveillance programs to monitor CWD distribution and prevalence have been instituted in the endemic area to determine the extent of the endemic area and to assist in evaluating both temporal changes

and effects of management intervention. Management programs established to date focus on containing CWD and reducing its prevalence in localized areas. Ultimate management goals vary among affected states and provinces. In areas where CWD may not yet be endemic, eradication could be considered as an ultimate goal for CWD management. In endemic states like Colorado and Wyoming however, managers have refrained from committing to eradication because it appears unattainable in their situations.

A variety of specific strategies for managing CWD in free-ranging wildlife have been adopted in affected jurisdictions. Translocating and artificially feeding cervids in endemic areas have been banned in attempts to limit range expansion and decrease transmission. Selective culling of clinical suspects has been practiced throughout the endemic area of Colorado and Wyoming for a number of years, but this approach alone has proven insufficient to reduce prevalence in affected populations. Localized population reduction in an area of high CWD prevalence has been undertaken in Colorado as a management experiment, but efficacy remains to be determined. Although it seems intuitive that lowered herd densities should reduce both transmission and likelihood of emigration by affected animals to adjacent areas, historic migration patterns and social behaviors characteristic of some deer and elk populations may diminish the effectiveness of wholesale density reduction in controlling CWD. Models of CWD epidemic dynamics suggest early, aggressive intervention via selective culling or more generalized population reduction show the greatest promise of preventing new endemic foci from being established; unfortunately, surveillance limitations (both cost and sensitivity) may delay detection of newly infected free-ranging populations for a decade or more after CWD has been introduced or spontaneously occurred. In both Nebraska and Saskatchewan, for example, aggressive reductions of deer numbers in newly identified endemic foci have been undertaken in attempts to eliminate CWD from these areas. Although the development of tonsil biopsy as an ante-mortem test for CWD in deer might aid control efforts under some conditions, large-scale applications to free-ranging populations seem impractical."

NOTE: On Feeding Bans - Many States have instituted ban on supplemental feeding and/or baiting in an attempt to reduce the risk of transmission of CWD. There is not a single published article based on hard scientific data that addresses either the positive or negative effects of a feeding ban in regard to CWD transmission.

There are many articles on feeding bans in regard to the transmission of bovine tuberculosis (TB) in deer in Michigan and Minnesota. Michigan initiated feeding bans in 1998 and now in 2018 (twenty years later), the geographic distribution of TB in deer dramatically, TB has been found in other wildlife species, TB has been found in many cattle herds. One must conclude from the data that the feeding ban has been ineffective.

NOTE: Over the last 20+ years and to date, all

VII. Prevention And Control cont.

control and prevention strategies including population reduction, supplemental feeding bans, baiting bans, importation of live cervids (even species not susceptible to CWD), importation of deer carcasses from CWD areas, bans on importation of trophies, restrictions on taxidermists, and bans on the use of urine based lures have not been effective.

NOTE: Population Management Programs. Zebal 2016, PLOS. "Chronic Wasting Disease: Transmission Mechanisms and the Possibility of Harvest Management." In an evaluation of 4 different harvest strategies and their effects on disease prevalence Zebel found that harvest strategies were not effective and were not well accepted by the public. Uehlinger et al., 2016. BioMed Central. 'Systematic review of management strategies to control chronic wasting disease in wild deer populations in North America" wrote " After a review of 9 individual studies (3 of which were based on observational data, and 9 were predictive models), evaluating *four unique techniques they concluded that "Control efforts to date have been largely unsuccessful, resulting in continuing spread and increasing prevalence."*

NOTE: The history of CWD in New York State often is quoted as an example of a successful CWD eradication program. New York Department of Environmental Conservation (NYDEC) "Status of CWD" in 2017 does not even mention the term "eradication". They instead state, "No new Chronic Wasting Disease (CWD) cases have been identified in New York since 2005". "No new cases have been identified" does not equal eradication. NYDEC also states more than 31,000 wild deer were tested from 2002 through 2010, and "no new cases were detected." Again that does not mean New York State is free of CWD in wild deer. From 2011 to 2017, 13,992 deer have been tested which is an average of 1,749 deer tested per year. Hunter Harvest in NY in 2017 was over 219,000 from a deer population in excess of 1.5 million. So in summary, testing less than 0.79% of the Hunter Harvest and less than 0.1% of the population is not a very aggressive surveillance and monitoring program for a disease with a prevalence rate of less 0.02% (7 pos/35,000 tested) in NY. It would be very easy to miss a disease at that prevalence and at that testing rate.

CWD VACCINES

Pilon et al., 2013. Journal of Wildlife Diseases "Immunization with a Synthetic Peptide Vaccine Fails to Protect Mule Deer (Odocoileus hemionus) from Chronic Wasting Disease. All the vaccinated deer produced antibodies but all the vaccinated animals eventually became infected (CWD test positive).
Taschuk et al, 2017. Prion. "Induction of PrPsc-specific systematic and mucosal immune responses in white-tailed deer with an oral vaccine for chronic wasting disease." Was done in 10 deer and they developed antibodies. No exposure to CWD prions was done so no evaluation of protection was established.

NOTE: A vaccine that confers a significant level of protection against CWD infection potentially might be a boon to the captive deer industry if it did not interfere with diagnostic testing, but without an effective vaccine delivery system suitable for free-ranging animals, the vaccine would have no application for wild deer and elk.

BOTTOM LINE ON CWD PREVENTION AND CONTROL EFFORTS

A review of the literature based on actual data (not predictive models) clearly shows that that any past combination of quarantines, containment zones, surveillance zones, depopulation, elective harvest, increased harvest limits, supplemental feeding bans, baiting bans, bans on the importation of live cervid species, bans on the importation, of carcasses, bans on the importation of trophies, and bans on urine based lures, HAVE NOT been effective in preventing, controlling, or eradicating CWD in any State. These programs have cost in excess of $100,000,000 of public funding and the killing of thousands of deer without any measurable positive results.