Chronic Wasting Disease

Introduction

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) that infects mule deer, white-tailed deer and elk. The term encephalopathy refers a disease in which the functioning of the brain is affected by some agent or condition. Spongiform refers to the porous structure resembling that of a sponge that results from disease. Other TSE's include Creutzfeldt-Jakob disease in humans, scrapie in sheep, and bovine spongiform encephalopathy (BSE) in bovines, also referred to as "mad cow disease". These diseases are always fatal. CWD was first recognized in the late 1960's but not confirmed as a prion disease until 1980. Currently, CWD has been confirmed to be present in free-ranging deer, elk and/or moose in at least 25 continental United States, as well as two provinces in Canada. The disease has also been found in farmed deer and elk with the infection rates among some captive deer can be as high as 79%.

The transmissible agent in these diseases is a misfolded protein, a prion protein. The normal form of the prion protein is found on the surface of nerve cells, but when it changes into its misfolded form (Image 1), it aggregates into long fibrils that clog up the normal functioning of the brain. All proteins are made of amino acid molecules, each with a positive or negative charge that combine to form a complex protein. The positive and negative charges are also what cause the protein to fold into its functioning form. It is when prion proteins are misfolded that they can cause problems. The misfolded prion protein interacts with other prion proteins in a way that causes the normal proteins to change and misfold in the same way. These misfolded prion proteins clump together leaving empty spaces within the brain tissue giving it the sponge-like appearance (image 2).

The name chronic wasting disease refers to the condition of the infected deer as the disease progresses. They become confused with dementia, don't behave normally and eventually functions such as foraging, eating and chewing diminish causing them to waste away (image 3).

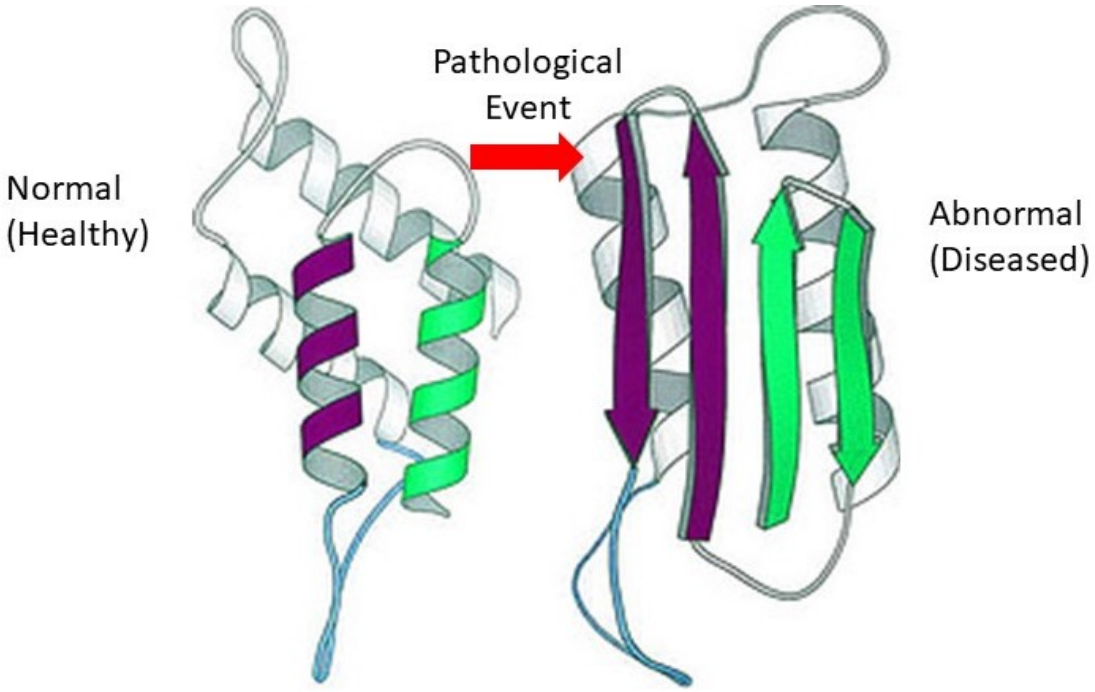

Image 1. The normal form of the prion protein is found on the surface of nerve cells, but when it changes into its misfolded, prone to clumping form.

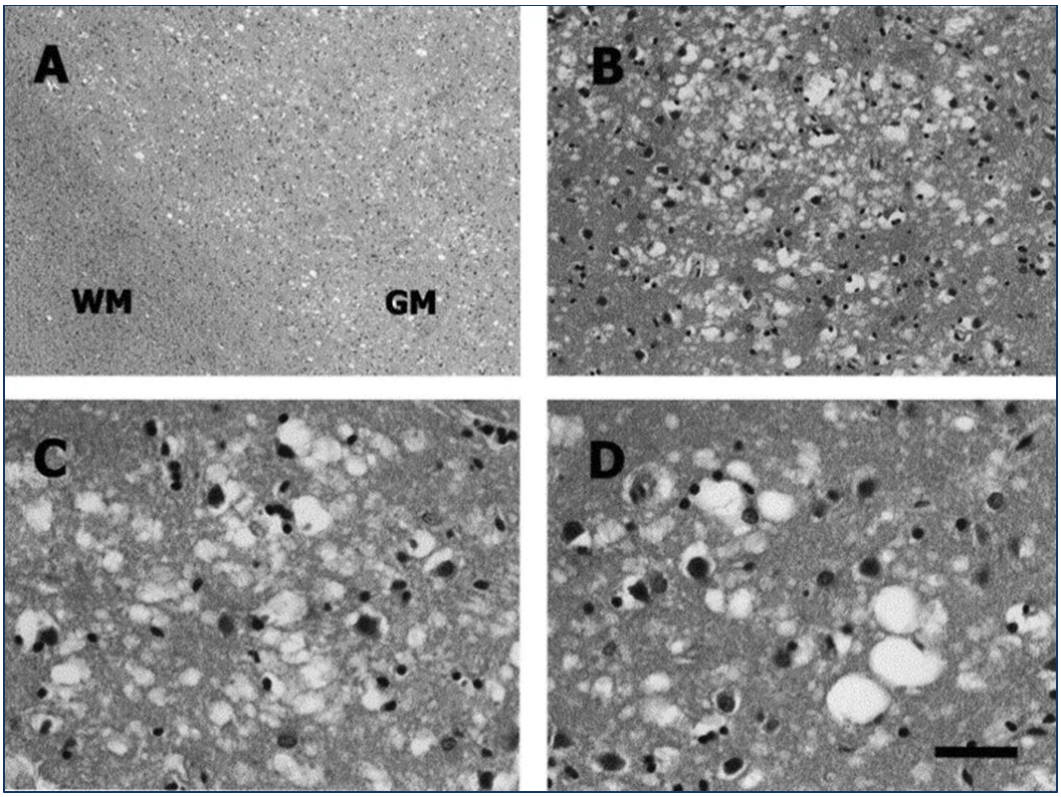

Image 2. Diseased proteins have a high propensity for clumping together resulting in vacuoles in the brain. A – D shows the progression of the disease from a healthy brain to a brain filled with vacuoles. Thus, the name Spongiform Encephalopathy.


Image 3. CWD positive deer, McHenry, Illinois, May 3, 2015

CWD Transmissibility in White-tailed Deer

Horizontal transmission of CWD within species readily occurs via oral and nasal secretions. Direct contact between white-tailed deer is the primary mode of transmission. Saliva left on shared food sources is also a common mode of transmission. Mineral licks in particular can serve as reservoirs of CWD prions and facilitate disease transmission. In addition, mineral licks provide potential for cross – species transmission to wildlife and domestic animals. Transmission of CWD can also occur through environmental routes. CWD positive animals may contribute to environmental prion contamination via decomposing carcasses and biological materials including saliva, blood, urine and feces.

Soil and surface water contaminated with urine, feces, saliva, blood and decomposing carcasses from prion infected animals have been implicated as possible transmission vehicles for CWD prions. Studies have been done to evaluate the persistence of CWD prions in both soil and water. Several studies have shown the persistence of prions in soil with clay soil absorbing higher concentrations than sandy soil. One study examined samples of water and showed that CWD prions were detected in environmental water samples from runoff from melting snow and in water samples obtained from the flocculation stage of water processed by municipal water treatment facility. Although the levels found were low, the results suggest persistence and accumulation of prions in water may promote CWD transmission. It should be noted that increased water runoff also increases the concentration of inorganic environmental components, including minerals, clay and other soil components to which prions have been demonstrated to absorb and may carry prions into water sources.

There has been considerable speculation on whether plants uptake CWD prions found in contaminated soil. One study with wheat plants found that if prions are transported from the roots to the stems, they were at levels that are below those detectable with the conventional methods of western blot (Rasmussen et al, 2014). However, another study showed that plants can efficiently bind prions contained in brain extracts from diverse prion infected animals, including CWD-affected cervid (Pritzkow, 2015). In addition, leaves were contaminated by spraying them with a prion containing extract and remained detectable in living plants for as long as the study was performed (several weeks). The prion contaminated plants transmitted prion disease to animals upon ingestion, producing a 100% attack rate and similar incubation periods as direct oral administration of sick brain homogenates (mixtures of infected brain cells and tissue). Finally, an unexpected, result was that plants were able to uptake prions from contaminated soil and transport them to aerial parts of the plant tissue. The high resistance of prions to degradation and their ability to efficiently cross biological barriers may play a role in this process. The mechanism by which plants bind, retain, uptake and transport prions is unknown.

Transmissibility of Chronis Wasting Disease to Humans

There has been no evidence that CWD has crossed the species barrier to humans. To date, only BSE prions have shown zoonotic potential, transmitted to humans from ingestion of infected cattle, to cause a variation of Creutzfeldt-Jakob disease, a human prion disease. Research is ongoing regarding the transmissibility of CWD to non-cervid species. Studies have been done in vivo with nonhuman primates and transgenic mice (genetically humanized mice) and in vitro with human prion protein.

Studies with transgenic mice with one or more active copies of the human prion protein inserted into their genome have provided no evidence to date that support the possibility of transmission of CWD to humans. The negative transmission results reported in seven studies support the conclusion that the transmission barrier associated with the interaction of human prions and CWD prions is stronger than the

species barrier between human prions and the BSE prion. Studies with non-human primates may better mimic human transmission than the transgenic mice experiments.

In research with macaques, the primates were challenged by intracerebral, oral and intradermal inoculations with CWD prions and then observed for periods ranging from 1.5 to over 10 years with no indication of prion disease. However it is possible that it may take more than 10 years for macaques to develop CWD as it takes more than five years for macaques to develop a prion disease post-inoculation with BSE prions. These studies are ongoing.

However, there have been studies that provided evidence that CWD prions can be transmitted to another non-human primate, squirrel monkeys. Two studies that challenged squirrel monkeys with intracerebral inoculation and oral intake both caused prion disease. The incubation period averaged 41 months after intracerebral inoculations with approximately 85% verified as having CWD. Squirrel monkeys were also challenged with other prion diseases including variant CJD and scrapie. The incubation period with these prion diseases averaged 24 months with 100% transmission rates. The extended periods and lower attack rates for squirrel monkeys with CWD inoculation may suggest a partial species barrier to CWD.

Several in-vitro experiments provided evidence that CWD prions can convert human prion protein to a misfolded state. These studies offer an indirect assessment of the transmissibility of CWD prions to humans. These in-vitro studies may suggest that oral transmission of CWD prions to humans is possible but there may be intestinal barriers and pathways that were not included in the studies.

The future discovery that CWD transmission to humans cannot be ruled out. It is difficult to diagnose prion disease in humans and the incubation period my last decades. In addition to continued research on CWD and epidemiologic surveillance in humans and animals, emphasis should be place on improving the understanding of how humans are exposed to CWD prions and prevention strategies to minimize exposure. Given that CWD prions are present throughout the host, muscle, fat, organs, the central nervous system, and many bodily fluids, it is critical to understand the extent of risk for human exposure to CWD prions.

Is CWD Positive Meat Safe to Eat?

CWD prions are present throughout the host, muscle, fat, organs, the central nervous system, and many bodily fluids. As stated in the previous section, the current research does not conclusively show that CWD is transmissible to humans but it can't be ruled out either. If CWD could spread to people, it would most likely be through eating of infected deer and elk.

The Center for Disease Control (CDC) does not recommend consuming meat that has tested positive for any prion disease, "Since 1997, the World Health Organization has recommended that it is important to keep the agents of all known prion diseases from entering the human food chain." In areas where CWD is known to be present, CDC recommends that hunters strongly consider having those animals tested before eating the meat. The CDC states unequivocally, "If your animal tests positive for CWD, do not eat meat from that animal."

What Can a Recreational Hunter Do to Avoid CWD Contamination?

Personally processing harvested deer instead taking it to a processing site is recommended to prevent possible contamination of meat from improperly cleaned utensils. Prions are invisible to the eye, very

stable and can be difficult to inactivate. Although corrosive, household bleach has been shown to inactivate prion agents. Bleach (sodium hypochlorite) concentrations with 40% dilution and direct contact to stainless steel utensils for five minutes has been shown to eliminate prion activity from stainless steel surfaces.

General precautions to avoid CWD contamination:

• Do not eat any part of a deer that appears sick.

• Do not eat the eyes, brain, spinal cord, spleen, tonsils or lymph nodes of any deer.

• Wear rubber or latex gloves when field dressing.

• Minimize contact with the brain, spinal cord, spleen and lymph nodes as you work.

• Remove all internal organs.

• Clean knives and equipment of residue and disinfect by soaking in a 60/40 solution of household chlorine bleach and water for at least five minutes.

•Use only knives or utensils selected for the purpose of field dressing that have properly cleaned.

Cutting and processing harvested deer:

• Wear rubber or latex gloves.

• Minimize handling brain or spinal tissues.

• Do not cut through the spinal column except to remove the head. Use a knife designated only for this purpose.

• Bone out the meat from the deer and remove all fat and connective tissue. This will also remove lymph nodes.

• Dispose of brain and spinal cord, eyes, spleen, tonsils, bones, and head as instructed by the State you are hunting in.

• Thoroughly clean and sanitize equipment and work areas with bleach/water solution after processing.

Fawns and CWD

Data has shown the probability of infection of CWD in deer increases with age. Fawns have tested positive for CWD but in lower numbers than adult deer. A relatively early study with mule deer fawns (1999) indicated that CWD can be detected in lymphoid tissues within a few weeks after oral exposure to infectious prions. The rapid infection of deer fawns following exposure by the most plausible natural route is consistent with horizontal transmission of CWD in nature.

A study in Wisconsin with white-tailed deer fawns in 2002 involved approximately 4,200 fawns (deer under 1 year of age) were sampled for CWD. The majority of fawns sampled were between the ages of

5 to 9 months, some were as young as 1 month. Only six were found to be CWD positive, 0.14%. Because of the generally low prevalence rate of CWD in fawns, IDNR does not recommend testing harvested fawns for CWD. As an added precaution, however, hunters are advised to remove all lymph nodes when processing harvested fawns and not including them in edible portions targeted for consumption and removing them from further processing such as grinding meat for sausage.

Research conducted in Wisconsin (Blanchong et al., 2012) showed that preclinical stages of CWD infection did not prohibit white-tailed deer from successfully reproducing. This same study showed that while CWD infection may not negatively affect a deer's ability to reproduce, it may interfere with the ability of a female to provide parental care, and thus ensure the survival of her fawns to adulthood. They found a higher harvest vulnerability of male fawns with CWD-positive mothers.

Strategies for Controlling CWD

CWD isn't caused by a virus or bacteria. The infective agent is an abnormal form of a harmless protein found in the brain, a prion. Once prions are present in the brain, they multiply by causing normal proteins to refold into an abnormal shape. Because of this the immune system of the animal doesn't detect prions as an enemy, so there's no immune response against the disease and so traditional vaccine immunization does not work to prevent the disease. However, recent research at the University of Calgary has discovered a vaccine that was effective in trials involving mice. But the vaccine didn't prevent the disease, it only delayed its onset. The work to see if it is effective in deer is ongoing.
The dangers with only delaying the onset of the symptoms of the disease without preventing it is that the animal would still be carrying and potentially spreading the disease to other animals until it finally succumbs to and dies from the prion disease. Therefore, it may be more dangerous to have a vaccinated animal come in contact with other animals than the unvaccinated animal that has a prion disease. The vaccinated animal with delayed onset may come in contact with more animals over time than the unvaccinated animal with the normal disease onset that would succumb sooner than the vaccinated animal. However, this is all hypothetical as no vaccination as yet has been found to be successful in deer for prevention or delaying the onset of chronic wasting disease.

Currently, nonselective deer harvest is the most feasible and effective approach available for managing CWD in wild populations. Despite the unpopularity of localized culling, it is the only method currently known that can maintain low disease prevalence while minimizing impacts on recreational deer harvest.

McHenry County CWD Trends

The District closely monitors deer densities, deer mortality and disease. Figure 1 and 2 show CWD prevalence (Figure 1), deer mortality, number of samples, and CWD positives (figure 2). The distribution of CWD in Illinois is shown in image four. Illinois Department of Natural Resources puts out detailed annual reports on CWD that can be found on their website: https://www2.illinois.gov/dnr/programs/CWD/Pages/default.aspx . The CWD statistics were taken directly from Illinois Department of Resources (IDNR) reports.

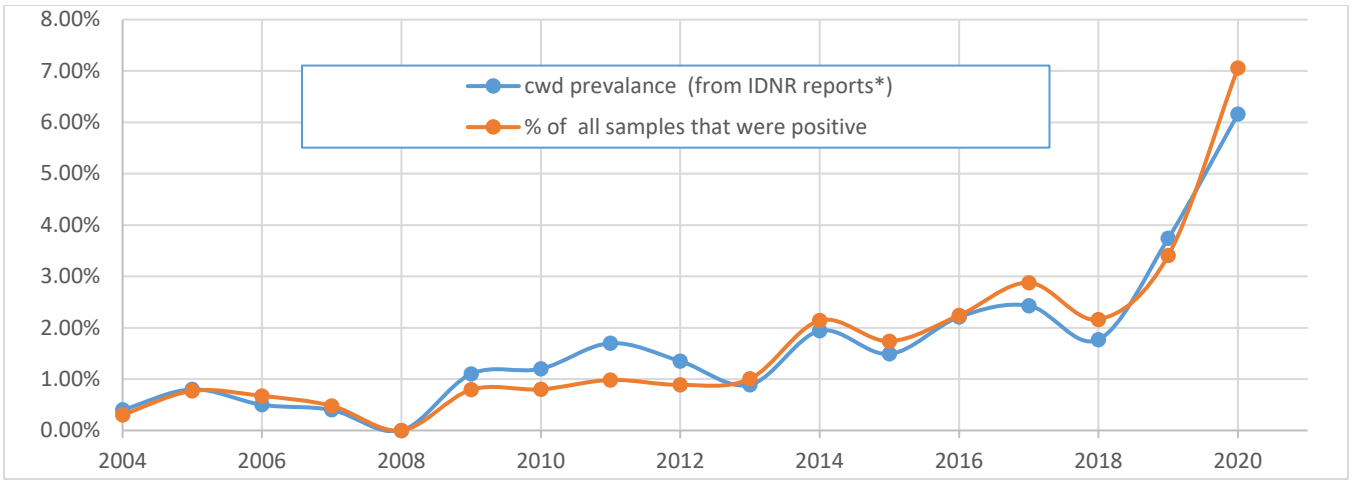

Figure 1. CWD prevalence in McHenry County, taken from IDNR reports. County prevalence rates were calculated using only hunter-harvested adult deer (both sexes).

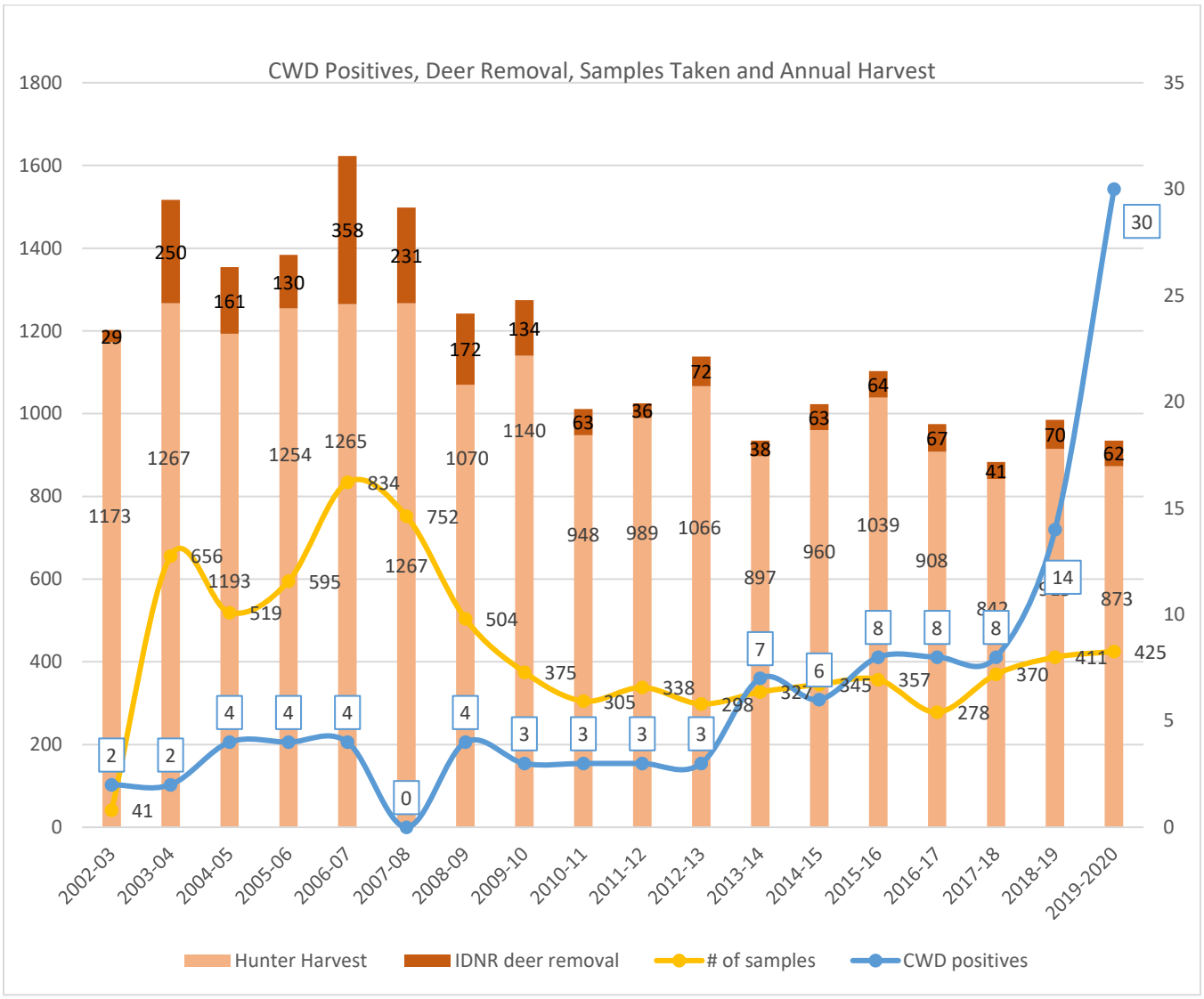

Figure 2. Deer mortality, number of samples, and CWD positives in McHenry County

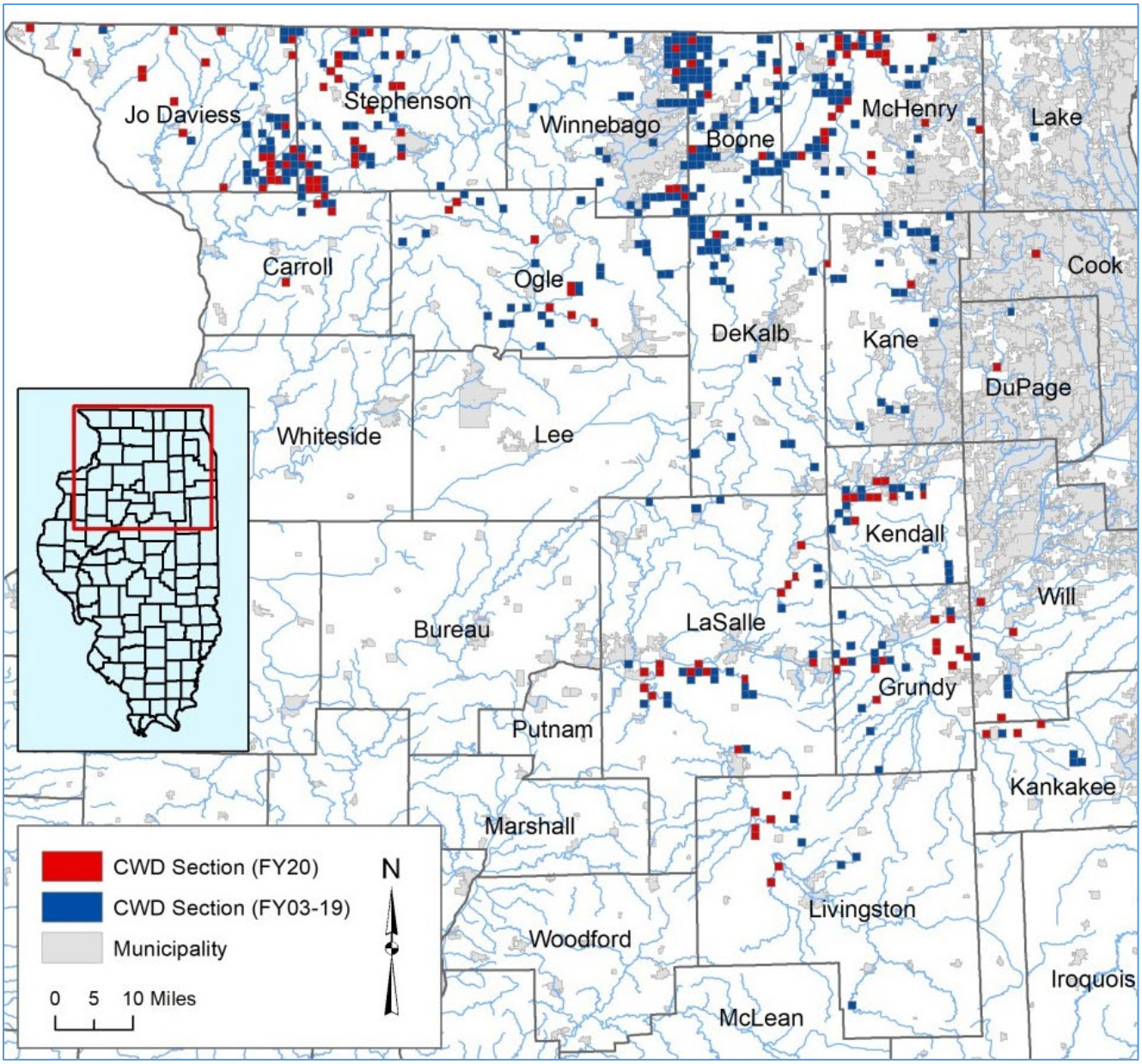

Image 4. Distribution of all known CWD-infected deer identified in Illinois through June 30, 2020 (IDNR)

Literature Reviewed

Abdelaziz, D.H., Thapa, S., Brandon, J., Maybee, J., Vankuppeveld, L., McCorkell, R., Schätzl, H.M. 2018. Recombinant prion protein vaccination of transgenic elk PrP mice and reindeer overcomes self-tolerance and protects mice against chronic wasting disease, Journal of Biological Chemistry, Vol. 293, Issue 51,2018,Pp. 19812-19822, ISSN 0021-9258, https://doi.org/10.1074/jbc.RA118.004810.

Blanchong, J.A., Grear, D.A., Weckworth, B.V., Keane, D.P., Scribner, K.T., Samue,l M.D. 2012. Effects of chronic wasting disease on reproduction and fawn harvest vulnerability in Wisconsin white-tailed deer. Journal of Wildlife Dis. 2012 Apr; 48(2):361-70. doi: 10.7589/0090-3558-48.2.361. PMID: 22493111.

Edmunds, D.R., Kauffman, M.J., Schumaker, B.A., Lindzey, F.G., Cook W.E., et al. 2016. Chronic Wasting Disease Drives Population Decline of White-Tailed Deer. PLOS ONE 11(8): e0161127. https://doi.org/10.1371/journal.pone.0161127

Grear, D.A., Samuel, M.D., Langenberg, J.A., Keane, D. 2006. Demographic patterns and harvest vulnerability of chronic wasting disease iInfected white-tailed deer in Wisconsin. The Journal of Wildlife Management. Vol. 70(2), 546-553, (1 April 2006). https://doi.org/10.2193/0022-541X(2006)70[546:DPAHVO]2.0.CO;2

Green, M. L., Manjerovic, M.B., Mateus-Pinilla, N. & Novakofski, J. (2014) Genetic assignment tests reveal dispersal of white-tailed deer: implications for chronic wasting disease. Journal of Mammalogy, 95(3):646-654.

Goñi, F., Mathiason, C.K., Yim, L., Wong, K., Hayes-Klug, J., Nalls, A., Peyser, D., Estevez V., Denkers, N., Xu, J., Osborn, D.A., Miller, K.V., Warren, R.J., Brown, D.R., Chabalgoity, J.A., Hoover, E.A. and T. Wisniewski. 2015. Mucosal Immunization with an Attenuated *Salmonella* Vaccine Partially Protects White-Tailed Deer from Chronic Wasting Disease. Vaccine. 2015 January 29; 33(5): 726–733. doi:10.1016/j.vaccine.2014.11.035.

Haley N.J., Mathiason C.K., Zabel M.D., Telling G.C., Hoover E.A. (2009) Detection of sub-clinical CWD infection in conventional test-negative deer long after oral exposure to urine and feces from CWD+ deer. PLoS ONE 4(11): e7990. https://doi.org/10.1371/journal.pone.0007990

Henderson DM, Manca M, Haley NJ, Denkers ND, Nalls AV, Mathiason CK, et al. (2013) Rapid Antemortem, Detection of CWD Prions in Deer Saliva. PLoS ONE 8(9): e74377. https://doi.org/10.1371/journal.pone.0074377

Kurt, T.D. and Sigurdson, C.J. (2016) Cross-species transmission of CWD prions, Prion, 10:1, 83-91

Marsh, R.F., Kincaid, A.E., Bessen, R.A. & Bartz, J.C. (2005) Interspecies transmission of chronic wasting disease prions to squirrel monkeys (*Saimiri sciureus*). Journal of Virology, Nov. 2005, p. 13794-13796

Mathiason, C. K., Powers, J. G., Dahmes, S. J., Osborn D. A., Miller, K.V., Warren, R.J., Mason, G. L., Hays, S. A., Hayes-Klug,J., Seelig, D. M., Wild, M.A., Wolfe, L. L., Spraker, T. R., Miller, M. W., Sigurdson, C.J., Telling, G. C., Hoover, E. A. (2006) Infectious prions in the saliva and blood of deer with chronic wasting disease. *Science* 314, 133.

Nichols, T.A., Pulford, B., Wyckoff, C., Meyerett, C., Michel, C., Gertig, K., Hoover, E. A., Jewell, J. E., Telling, G. C. & Zabel, M. D. (2009) Detection of protease-resistant cervid prion protein in water from a CWD-endemic area, Prion, 3:3.

North Carolina Wildlife Resources Commission. Processing deer and handling precautions. NC Wildlife Resources Commission, 1751 Varsity Drive, Raleigh, N.C. https://www.ncwildlife.org/Portals/0/Learning/documents/Chronic%20Waste_CommonSensev5%20(003).pdf

Pilon, J.L., Rhyan, J.C., Wolfe, L.L., Davis, T.R., McCollum, M.P., O'Rourke, K.I., Spraker, T.R., VerCauteren, K.C., Miller, M.W., Gidlewski, T., Nichols, T.A., Miller, L.A., Nol, P. 2013. Immunization with a synthetic peptide vaccine fails to protect mule deer (Odocoileus hemionus) from chronic wasting disease. J Wildl Dis. 2013 Jul;49(3):694-8. doi: 10.7589/2012-07-200. PMID: 23778624.

Plummer I.H., Johnson C.J., Chesney A.R., Pedersen J.A., Samuel M.D. (2018) Mineral licks as environmental reservoirs of chronic wasting disease prions. PLoS ONE 13(5): e0196745. https://doi.org/10.1371/journal.pone.0196745

Potapov A, Merrill E, Pybus M, Lewis MA (2016) Chronic wasting disease: transmission mechanisms and the possibility of harvest management. PLoS ONE 11(3): e0151039. https://doi.org/10.1371/journal.pone.0151039

Pritzkow, S., Morales, R., Moda, F., & Khan, U., Telling, G., Hoover, E., & Soto, C. (2015). Grass Plants Bind, Retain, Uptake, and Transport Infectious Prions. Cell reports. 11. 10.1016/j.celrep.2015.04.036.

Race, B., Meade-White,K.D., Phillips, K., Striebel, J., Race, R. & Chesebro, B. (2014) Chronic wasting disease agents in nonhuman primates. Emerging Infectious Diseases Vol. 20, No. 5, May 2014

Race,B., Williams,K., Orrú, C.D., Hughson, A.G., Lubke,L., & Chesebroa, B. (2018) Lack of transmission of chronic wasting disease to Cynomolgus Macaques. Journal of Virology. Vol. 92 Issue 14

Rasmussen, J., Gilroyed, B.H., Reuter, T., Dudas, S., Neumann, N.F., Balachandran, A., Kav, N., Graham, C., CZub, S., McAllister, T.A. (2014) Can plants serve as a vector for prions causing chronic wasting disease? Prion, 8:1, 136-142, DOI: 10.4161/pri.27963

Seidel B, Thomzig A, Buschmann A, Groschup MH, Peters R, Beekes M, et al. (2007) Scrapie Agent (Strain 263K) Can Transmit Disease via the Oral Route after Persistence in Soil over Years. PLoS ONE 2(5): e435. https://doi.org/10.1371/journal.pone.0000435

Sigurdson, C. J., Williams, Elizabeth, S., Miller, M. W., Spraker, T. R., O'Rourke, K. I., and Hoover, E. A., 1999. Oral transmission and early lymphoid tropism of chronic wasting disease PrPres in mule deer fawns (Odocoileus hemionus). Other Publications in Zoonotics and Wildlife Disease. 121.

Thompson, A. K., Samuel, M. D. & Van Deelen, T. R. (2008) Alternative Feeding Strategies and Potential Disease Transmission in Wisconsin White-Tailed Deer. Journal of Wildlife Management, 72(2):416-421.

Waddell L, Greig J, Mascarenhas M, Otten A, Corrin T, & Hierlihy K. (2016) Current evidence on the transmissibility of chronic wasting disease prions to humans—A systematic review. Transbound Emerg Dis. 2018; 65:37–49.

Williams, E.S., (2005) Review Article, Chronic wasting disease. Vet Pathology 42:530-549

Williams, K., Hughson, A.G., Chesebro, B., Race, B. 2019. Inactivation of chronic wasting disease prions using sodium hypochlorite. PLOS ONE 14(10): e0223659. https://doi.org/10.1371/journal.pone.0223659

Wisniewski, T. & Goñi, F. (2012)Could immunomodulation be used to prevent prion diseases? Expert Review of Anti-infective Therapy, 2012 March ; 10(3): 307–317.