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Could avian scavengers translocate infectious prions to disease-free areas initiating new foci of chronic wasting disease?

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Mechanisms for the spread of transmissible spongiform encephalopathy diseases, including chronic wasting disease (CWD) in North American cervids, are incompletely understood, but primary routes include horizontal and environmental transmission. Birds have been identified as potential vectors for a number of diseases, where they ingest or are exposed to infected material and later shed the disease agent in new areas after flying substantial distances. We recently identified American crows (*Corvus brachyrhynchos*) as having the potential to translocate infectious prions in their feces. Our results suggest that this common, migratory North American scavenger is capable of translocating infectious prions to disease-free areas, potentially seeding CWD infection where no other initial source of pathogen establishment is forthcoming. Here we speculate on the role avian scavengers, like American crows, might play in the spatial dissemination of CWD. We also consider the role mammalian scavengers may play in dispersing prions.

Keywords: American crows, *Corvus brachyrhynchos*, CWD, disease transmission, transmissible spongiform encephalopathy, TSE

Abbreviations: CWD, chronic wasting disease; PrP^{Res}, abnormal isoform of prion protein; TSE, transmissible spongiform encephalopathy

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From the first observations of chronic wasting disease (CWD) in mule deer (*Odocoileus hemionus*)[1] and Rocky Mountain elk (*Cervus elaphus nelsoni*)[2] in Northern Colorado, USA, the disease has been identified in an increasing geographic area. In the 1980s and early 1990s, CWD was documented in wild elk, mule deer, and white-tailed deer (*Odocoileus virginianus*) in southeastern Wyoming and northeastern Colorado.[3,4] Not until 1999 was CWD found outside the Colorado-Wyoming endemic area, in wild deer in western Nebraska, at which point the contiguous portions of these 3 states were deemed the core CWD endemic area.[5] Thereafter, surveillance and testing has revealed that CWD is spreading sporadically across much of North America.

Currently, CWD is found in 21 states and two Canadian provinces (http://www.cwd-info.org/index.php/fuseaction/about.map). Unlike pathways in which a disease spreads animal-to-animal within host populations, the geographic spread of CWD has not always proceeded contiguously from the core endemic area, with new cases sometimes being separated from previous positives by large distances. It is postulated that movement of farmed cervids has unwittingly amplified the dramatic discontinuous spread of CWD across North America,[6,7] though not all isolated CWD foci can be attributed to that cause. It is also likely that hunters unknowingly harvest CWD-positive cervids in the core endemic area and return to their homes, maybe several states away, with the carcass. Once the meat is removed, waste tissue (i.e., head, neck, vertebral column) may be disposed of by dumping in cervid habitat, inadvertently contaminating the environment, infecting naive cervids, and potentially establishing a new foci of CWD.

The exact mechanisms of transmission of CWD are poorly understood, but research suggests that transmission occurs directly, animal-to-animal[4,8] as well as indirectly, from environmental sources.[6,9,10] Environmental sources may be the most difficult to quantify, but

epidemiologic modeling suggests these indirect routes may play a major role in CWD transmission.[11] Point sources for prion accumulation in the environment, such as mineral licks,[12] water sources,[13] farmed cervid pens, and decomposed carcasses[9] may promote CWD transmission for years. Once in the soil, prion infectivity is influenced by soil type[14] and long-term (i.e., >2 y) survival of prions has been documented.[9] North American predators and scavengers, such as wolves (*Canis lupus*), mountain lions (*Puma concolor*), coyotes (*Canis latrans*), raccoons (*Procyon lotor*), opossums (*Didelphis virginiana*), vultures (*Cathartes aura* and *Coragyps atratus*), and crows (*Corvus brachyrhynchos*) may also participate in the spread of CWD. Jennelle et al., (2009) documented a host of mammals and birds that scavenged on white-tailed deer carcasses in central Wisconsin, with crows being a primary scavenger.[15] These species could consume and transport infectious material through feces deposition,[16,17] or simply transport of material through food-caching, young-provisioning, and other natural behaviors.

It seems logical that crows could ingest infectious prion material while scavenging on CWD-contaminated carrion and translocate infectious material in their feces to CWD-free areas. A host of other pathogenic agents, such as *Mycobacterium avium, Mycobacterium bovis*, and avian influenza virus, have been shown to be transported considerable distances, via feces, by birds.[17-19] Relatedly, migration and dispersal patterns of birds have been implicated with the rapid spread of West Nile virus across North America from east to west, with avian hosts transporting the virus to naive areas.[20] Our recent work established that abnormal isoform prion proteins (PrP^{Res}) remain infectious after passage through the digestive tract of crows.[21] These results confirmed passage of PrP^{Res} material through crows gavaged with infected material and suggested that crows can excrete infectious prions; bringing to light a new and potentially important transmission route.

Scavenging is a key ecological process in the flow of energy through food webs and the mechanisms and behaviors of scavengers at carrion sites could partially explain disease transmission dynamics. Crows have been documented to be one of the first species to discover carcasses.[22] Once at a carcass, crows begin feeding on the eyes, nose, navel, and anal areas. Scavenging birds may also attack live animals in certain instances, initially pecking out the eyes or feeding on open wounds.[23] Hooded crows (*Corvus corone*) in Scotland were either unable or reluctant to tear open the skin of salmon carcasses, resulting in removal of exposed soft tissue on salmon carcasses; eyes and gills.[24] Similar scavenging tactics of lamb carcasses by birds in west Scotland resulted in eye and tongue removal.[25] As PrP^{Res} has been found in eyeballs and optic pathways of Rocky Mountain elk,[26] consumption of infectious material by crows during the scavenging process is both possible and probable. Also, once other scavengers have removed the easily obtainable flesh crows may be negated to scavenge less preferred or harder to access tissue (i.e., tissue between vertebrae or in the skull cavity) which may also contain higher densities of prions.

Crows have an extensive geographic range in North America, are migratory, and communally roost in the fall and winter;[27] all of which could contribute to the spread of CWD. The migratory nature of many crows in North America ensures that individual birds traverse extensive distances during annual movements and spend long portions of the annual cycle in distinctly different geographical areas. For example, of 65 crows banded in central Oklahoma during winter 1935–1936 and later recovered during the breeding season, 49 were recovered in Alberta, Manitoba, and Saskatchewan.[28] The remaining crows were recovered in Montana, North and South Dakota, Nebraska, and Kansas—none were recovered in Oklahoma during the breeding season. Thus, crows wintering in central Oklahoma are likely representative of crows distributed broadly across central North America during breeding and migratory periods.

We feel though that exposure risk for naive cervids posed by random deposition of PrP^{Res}-infected crow feces would likely be low. However, communal roosting by crows could provide a plausible mechanism for concentrating crow feces, regurgitated castings of indigestible material, and pathogens included in these egesta. Crows can exist at high densities (0.7–1.1 birds/m^2, 5 birds/m^2 of ground covered by roost trees) at rural roosts and estimates of crow numbers at rural roosts in central Oklahoma ranged from a few thousand up to 394 000 crows/roost.[29-31] At urban roosts, numbers ranged from 18–1941 crows/roost in Davis and Woodland, California (n = 4 roosts);[32] 4000–33 000 crows/roost in Lancaster, Pennsylvania (n = 6 roosts),[33] and 5000–63 800 crows in 5 cities in New York (n = 5 roosts).[34] In addition to noise, pronounced quantities of crow feces and castings are primary public complaints and have been used to identify locations of urban crow roosts.[32] Feces deposition estimates at a winter roost site in Oklahoma ranged from 2576–3941 kg/day.[29] Communal roosting of crows in this area begins in October and ends late March or early April. Assuming similar estimates per day, feces deposition for one winter season (n = 152 d) at this roost site would conservatively range from 391 552–599 032 kg. Given that roosts may be used for many years,[27] there is strong potential for concentration of crow feces and environmentally resistant pathogens below them.

In contrast to concentrating infective PrP^{Res} material, crows and other scavengers might actually be diluting source material at the landscape level. Through the scavenging process, PrP^{Res} material is consumed and spatially redistributed via feces deposition. This could lessen the PrP^{Res} environmental reservoir at the carcass site and perhaps reduce the potential for naive individuals to encounter infectious material.

Although prion disease is not known to occur in avian species,[35] repeated exposure via consumption of contaminated tissues may increase infection risk for individuals across the full suite of mammalian scavenger species; with potential consequences for human health. In laboratory settings, felids and mustelids have been shown to be susceptible to prion diseases.[36] Existence of multiple natural strains of PrP^{Res} in the environment,[37] variation in normal cellular PrP within and among scavenger species, and demonstration of strain adaptation between

species[38] suggests the potential transmission to novel hosts. Interspecies transmission of prion diseases often modifies PrP^{Res} strains through adaptation and selection, potentially broadening the range of susceptible species and altering virulence of infectivity.[39] Thus, new strains of PrP^{Res}, more likely to breach "species barriers," could result from scavenging; particularly for CWD as it expands across North America and prevalence rates increase. New strains of CWD could increase risk of transmission to humans and other noncervid hosts.[37,39,40]

In conclusion, our study showed that the digestive system of crows did not eliminate PrP^{Res} infectivity prior to excretion of feces,[21] which suggests that avian scavengers may play a role in the transmission and translocation of prion diseases. Relatedly, crows often forage and defecate on feed at farmed cervid facilities, providing an opportunity for farmed cervids to ingest crow feces and crows to ingest feed with elk saliva, and other potentially PrP^{Res}-infected material. Further experiments involving other avian, as well as mammalian, scavengers are needed to evaluate PrP^{Res} infectivity after passage of natural transmissible spongiform encephalopathies through their digestive systems. We are currently conducting a study to evaluate CWD passage through the digestive system of coyotes. It would be prudent to evaluate other mammalian scavengers for their ability to act as intermediate CWD hosts between cervids and humans.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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