Health Products and Food Branch (HPFB) Risk Advisory Opinion: Potential Human Health Risks from Chronic Wasting Disease

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Issue:

Chronic Wasting Disease (CWD) is a progressive, fatal, transmissible neurological disease that naturally infects cervids, and has been identified in deer, elk, moose, and reindeer. To date there is no direct evidence that CWD has been or can be transmitted from animals to humans. However, initial findings from a laboratory research project funded by the Alberta Prion Research Institute (APRI) and Alberta Livestock Meat Agency (ALMA), and led by a Canadian Food Inspection Agency (CFIA) scientist indicate that CWD has been transmitted to cynomolgus macaques (the non-human primate species most closely related to humans that may be used in research), through both the intracranial and oral routes of exposure. Both infected brain and muscle tissues were found to transmit disease.

Health Canada's Health Products and Food Branch (HPFB) was asked to consider the impact of these findings on the Branch's current position on CWD in health products and foods.

Summary and Recommendation:

Health Canada's Health Products and Food Branch (HPFB) is responsible for assessing risks to human health from diseases of animal origin that may be transmitted through health products and food, and for developing regulations and policies to mitigate risks from products regulated under the *Food and Drug Act* as well as various associated regulations. While extensive disease surveillance in Canada and elsewhere has not provided any direct evidence that CWD has infected humans, the potential for CWD to be transmitted to humans cannot be excluded. In exercising precaution, HPFB continues to advocate that the most prudent approach is to consider that CWD has the potential to infect humans. This position has been aligned with that of the World Health Organization (WHO) since the late 1990s, and remains consistent with the WHO's 2012 position that "No tissue that is likely to contain the bovine spongiform encephalopathy (BSE) agent, nor part or product of any animal which has shown signs of a TSE should enter the (human or animal) food chain." This precautionary position on TSEs is also consistent with the conclusions documented by the Transmissible Spongiform Encephalopathy (TSE) Secretariat in 2003, and a systematic literature review conducted by the Public Health Agency of Canada (PHAC) in 2017. The findings of the macaque experiment do not change HPFB's current position with respect to the safety of food and health products and CWD, which considers that a precautionary approach to the management of the potential risks of exposure through food and health products is warranted.

Background:

Chronic Wasting Disease (CWD) is a fatal disease that has been detected in cervids. To date, the disease has been identified in deer, elk, moose, and reindeer. CWD belongs to a class of diseases called transmissible spongiform encephalopathies (TSEs). Along with other well-known TSEs, such as bovine spongiform encephalopathy (BSE) in cattle, scrapie in sheep and goats and Creutzfeldt–Jakob disease (CJD) and variant CJD (vCJD) in humans, CWD is characterized by the accumulation of abnormal misfolded proteins (called prions) in multiple organs and tissues, including lymphatic, muscle and neural tissues. CWD was first recognized as a fatal wasting disease of captive deer in the United States in the late 1960s, and was later identified as a TSE in 1980. In Canada, CWD was first detected in the Toronto Zoo in the 1970s and diagnosed in farmed elk in 1996. The first Canadian case in a wild cervid was confirmed in a mule deer in Saskatchewan in November 2000. The disease has now been detected in cervids in 24 US states and two Canadian provinces (Alberta and Saskatchewan).

The exact routes and mechanisms of CWD transmission between animals remain unclear. There is evidence that infection is transmitted directly from animal to animal during close contact with saliva, urine and feces, and indirectly through the environment. While incubation periods may be variable, once the disease is contracted, the time to presentation of clinical symptoms is about 16 to 36 months. It is only in the later, clinical stages that CWD is typified by the chronic weight loss and behavioral changes that eventually lead to death.

In 2003, Health Canada's TSE secretariat assessed the potential for CWD to pose a hazard to human health. It was noted at that time that there was no evidence to indicate that CWD had ever infected a human. Given the lack of scientific evidence of the potential for CWD to become a human pathogen, it was stated that the most prudent course of action was to consider that CWD could have the potential to infect humans, and thus take a precautionary approach to its management, which was consistent with the position taken by the World Health Organization (WHO).

The Public Health Agency of Canada (PHAC) recently published a systematic review summarizing the evidence in the scientific literature on the transmissibility of CWD prions to humans (2017). This review summarized available epidemiological evidence, as well as evidence on CWD infectivity using experimental models, including non-human primates, transgenic mice, and *in vitro* experiments. The review showed that animal models using humanized transgenic mice did not demonstrate transmission. Two transmission experiments using squirrel monkeys have been able to show prion disease after intracerebral and oral inoculation with CWD prions. The systematic review also summarized two transmission experiments using macaques (a non-human primate species considered genetically closer to humans than squirrel monkeys) which, at the time of review, had not caused prion disease after inoculation with CWD prions by several modes (e.g., intracerebral, oral) up to 10 years of observation since exposure to CWD prions.

Health Portfolio partners were recently made aware of initial findings from a research project led by a CFIA scientist that have demonstrated that cynomolgus macaques can be infected via intracranial exposure and oral gavage with CWD infected muscle. These findings suggest that CWD, under specific experimental conditions, has the potential to cross the human species barrier, including by enteral feeding of CWD infected muscle. While the study is ongoing, and findings have yet to be subjected to formal peer review, the initial results will be presented at PRION 2017, an annual international conference on TSE diseases (Edinburgh May 23-26, 2017).

In advance of this conference, a multi-departmental working group (including CFIA, PHAC, HC (HPFB and FNIHB), INAC, Parks Canada, ECCC and AAFC) has been established to coordinate risk management and risk communication activities. As the lead in managing the potential human health risks related to health products and food that could contain cervid materials, Health Canada's HPFB has considered the initial findings of this research within the context of known and accepted science and evidence related to the transmissibility of CWD to cervids, other animals, transgenic mice, and its potential to be transmissible to humans, to provide an updated advisory opinion of the potential risk to human health. This opinion is provided to the working group to inform the assessment of current CWD control policies in Canada as well as the advice related to the potential risks posed by CWD through the consumption of cervid food products.

Health Canada's Current Position on TSEs in Health Products and Food:

HPFB has previously addressed concerns regarding human exposure to BSE, and remains alert to the possibility that other animal TSEs such as scrapie and CWD may also pose risks to human health. HPFB maintains a precautionary stance in relation to human exposure to TSEs through health products and food.

In 2003, HPFB adopted the position that no material derived from an animal known to be infected with any TSE (including CWD) should be used or consumed by humans or animals. This position was, and continues to be, consistent with the position of the WHO.

HPFB requires pre-market review and approval of all human therapeutics, biologics and genetic therapies, veterinary drugs and natural health products intended for sale in Canada. This includes a requirement for license holders of these products to maintain documentation and provide information for any materials of animal origin that may be used within their products, including therapeutic substances, reagents and excipients. This documentation can include letters of attestation, Certificates of Suitability or Veterinary Certificates. While there are no specific federal regulations related to the use(s) of cervids in foods, current federal animal disease control policies support the diversion of known CWD-infected farmed animals away from the food and feed supply. Outreach, communications, and monitoring programs related to wild cervids, as well as disease surveillance for farmed cervids, fall within the jurisdiction of the Provincial and/or Territorial governments.

Hazard Characterization

In 2003, Health Canada's TSE secretariat assessed the potential for CWD to pose a hazard to human health. Given the lack of scientific evidence of the potential for CWD to become a human pathogen, it was stated that the most prudent course of action was to consider that CWD could have the potential to infect humans, and thus take a precautionary approach to its management.

Following nearly two decades of ongoing human prion disease surveillance and retrospective review by PHAC and the Centers for Disease Control and Prevention (CDC), there have been no identified cases of human prion disease or any other outcome attributed to CWD in Canada, the USA, or elsewhere.

In 2017, PHAC published a systematic literature review of the evidence for the transmissibility of CWD to humans, which included evidence of successful transmission of CWD intracranially and orally to squirrel monkeys. From this review, it was concluded that CWD transmission to humans has not been recorded. In five epidemiological studies no association between CWD exposure and human prion disease was identified. Some cases of CJD had a history of exposure to cervids and venison in CWD affected regions, but no definitive link to CWD could be found. The assessment of the evidence captured in this systematic review does not support the hypothesis that CWD is readily transmitted to humans; however, the positive evidence of interspecies transmission from *in vivo* and *in vitro* experiments indicates that the species barrier is not absolute. The initial findings from the APRI/ALMA-funded macaque experiment are consistent with this conclusion.

Potential Sources of Exposure to Cervids and Cervid-derived Materials:

Canadians may be exposed to cervids, and materials derived from cervids through a variety of sources, and routes of exposure, including in their diet and through the use of natural health products that contain antler velvet. There is also the potential for Canadians to be exposed to cervids through farming (including veterinary services), slaughter, velvet harvest, as well as through field dressing of hunted animals, preparing trophies and/or the use of cervid-derived materials (e.g., urine) as hunting lures. While monitoring and control programs are in place to reduce the likelihood that animals known to be infected with CWD reach the marketplace, the possibility cannot be excluded that some of these sources of exposure may be derived from animals with CWD.

Cervid meat (venison) is available in many of the same cuts and processed meat products as for other meat products. While consumption survey estimates for the general Canadian population (2004 Canadian Community Health Survey, Cycle 2.2) indicate that overall venison consumption is quite low, there are known subpopulations, including rural and Indigenous populations that have higher dietary exposures to this food. In addition, populations that rely on cervids as an important source of protein are more likely to hunt and/or consume wild cervids.

There are no human biologics or genetic therapies licensed in Canada that contain ingredients of cervid origin, and it is considered unlikely that cervid materials or ingredients would be used in the manufacture

of these human therapeutic products, including medical devices. There are approximately 200 licenced natural health products (NHPs) that contain ingredients of cervid origin such as antler velvet.

Impact of New Findings on Human Health Risk Assessment:

There have been no known cases of human prion disease or any other outcome attributable to CWD identified to date. National surveillance of all forms of CJD by PHAC has yielded no direct evidence that CWD has infected humans in Canada. However, in the absence of definitive information related to the transmissibility of CWD to humans, and in light of the evidence that BSE can be transmitted to humans, HPFB has maintained a precautionary position with respect to CWD that is in agreement with the WHO's 2012 recommendation that "No tissue that is likely to contain the BSE agent, nor part or product of any animal which has shown signs of a TSE should enter the (human or animal) food chain.".

The initial findings from the experimental non-human primate transmission study do not change HPFB's position with respect to food and health products, and a continued precautionary approach to the management of the potential risks of exposure through food and health products is warranted.

HPFB continues to recommend avoiding consumption of foods from known infected or any diseased animals, and taking precautions when handling cervid carcasses. In addition, in areas where CWD is known to occur in wild cervids, continued consistent Federal and P/T communications, warning and precautions should be provided to groups who may be expected to have higher exposures to cervids through hunting and diet (e.g., rural and Indigenous populations).

While current animal disease control policies support the diversion of known CWD-infected animals away from the food and feed supply, research and development of sensitive detection methods and antemortem sampling techniques remain crucial for ensuring accurate diagnoses. Continued research into TSEs and continued epidemiologic surveillance for human prion diseases are required.

HPFB will continue to review and monitor scientific literature related to CWD, as well as these initial findings and other emerging research related to the potential transmissibility of CWD to humans. The Branch will continue to update its position on animal TSEs as new scientific evidence indicates the need for further protection of public health.

Reviewed by:
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