INTERNATIONAL WORKSHOP ON EMERGING ASPECTS OF PRION DISEASES: SCIENCE, IMPLICATIONS, AND APPROACHES TO RISK MANAGEMENT

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Executive Summary

This international workshop was intended to elicit commentary on continuing and emerging issues in prion diseases. Participants were from industry, government and academia, and were familiar with one or more of the diseases considered: bovine spongiform encephalopathy, chronic wasting disease, scrapie and Creutzfeldt-Jakob disease.

Bovine Spongiform Encephalopathy (BSE)

Some countries, including Canada, have had incidences of classical BSE in cattle born after the introduction of the most stringent feed bans, leading to discussion about the absolute effectiveness of the bans. Need for vigilance and promotion on issues such as good husbandry, good management practices and biosecurity were emphasized. Countries should rethink their feed ban policies in light of the recent history of BSE and the variance in feed bans.

More information about the pathogenesis of atypical BSE and potential to transfer to other species is needed. There was concern that the OIE downplays atypical BSE and does not consider it in its risk assessments or in country classifications. Countries with negligible risk status are not inclined to implement rigorous surveillance and BSE control measures. The OIE position on atypical BSE risk might need to be challenged.

Surveillance remains an important part of BSE control, but surveillance systems should be re-examined to achieve optimal risk-benefit. The OIE standards are based on 20-year-old science. Vaccines for BSE control are unlikely to emerge due to technical challenges and lack of industry and regulator interest because of a poor cost-benefit ratio.

Live testing for cattle is not seen as a useful food safety approach by industry and regulators. Improving reliability of current sensitive tests in complex matrices such as meat and bone meal was seen as desirable. Some saw a reliable sensitive test as desirable for end-product testing for food and feed.

Other areas seen as requiring study: implications of atypical BSE and of BSE cases born after rigorous initiation of feed bans; the basis of prion strains; and, prion decontamination.

Chronic Wasting Disease (CWD)

Chronic wasting disease is a highly-contagious form of prion disease that has been found in 23 American states, two Canadian provinces, South Korea and Norway. There is some possibility that CWD might occur in farmed animals through contaminated feed. Birds could also be contributors to the spread of CWD. The possibility that CWD might also be occurring spontaneously cannot be eliminated.

Aboriginal people, hunters and those in the cervid industry would be most impacted by continued geographical spread and increasing prevalence. A possible spread of the disease to caribou was of particular concern because ranges of white-tailed deer and caribou are starting to overlap. There does not seem to be any barrier to transmission between cervid species. The finding of CWD in a reindeer in Norway in March 2016 heightens this concern.

There is no epidemiological evidence for CWD being zoonotic. Experimental interspecies transmission has been found via intracranial injection of infected material, a route not considered realistic in a field sense. Issues around the occurrence of different prion strains, the wide distribution of infectivity in cervid tissues, and some mixed results with infection of non-human primates leave unanswered questions. The European Food Safety Authority placed CWD in a category where zoonotic potential was considered possible, but there was no evidence for a causal link between CWD and human disease.

Developing effective management strategies with good control rather than eradication was seen as an achievable aim. The farming of cervids in Canada is highly regulated by the Canadian Food Inspection Agency. Cervid farms are also subject to provincial rules, and the management of wild cervids is a provincial responsibility. Surveillance will remain important, but there is a need for more emphasis on control. The Canadian National CWD Control Strategy needs to be reviewed. It is desirable to combine forces across Canadian and American jurisdictions to find effective and common means of control.

An effective control strategy would need to include a comprehensive communication and public education strategy. Some participants saw vaccines as being of more importance and usefulness to cervid farmers than for use in the wild. Targeted herd reduction around CWD hotspots could be implemented, but they would require significant public education and acceptance. Should a resistant allele be identified, it could lead to a possible selective breeding program of benefit to industry. Some saw a reliable pre-mortem test for CWD as being of substantial benefit for industry and possibly for surveillance in the wild. There was concern that the market might be too small to attract sufficient investment to achieve development of such a test.

Scrapie

Scrapie occurs in both classical (long-known) and atypical (relatively recently described) forms. A number of strains of scrapie prions have been identified. Classical scrapie has been controlled in some countries by aggressive depopulation and through selective breeding for a resistant allele in the prion protein gene. Resistance alleles have not been identified for atypical scrapie. The prevalence of atypical scrapie has not changed much in most countries over the past few years.

Control measures to reduce the possibility of transmission of scrapie through control of contents of feed and human food are more stringent in Europe than in North America. The sheep industry generally feels that measures such as removal of SRM in small ruminants are not necessary given the long-known occurrence of scrapie without any known transmission to other species. But some recent experiments with strains of classical scrapie in transgenic mice have suggested that they there might not be an impermeable species barrier to transmission. Atypical scrapie has not been analyzed for interspecies transmission. Current active and passive surveillance processes likely do not provide ideal information that lead to a full measure of protection from interspecies transmission. This is particularly true for atypical scrapie.

There was concern that policy and regulations have not kept up with recent research. Additional research is needed with respect to the species barriers for scrapie and the nature of the pathogenesis of the diseases, especially atypical scrapie.

Human Prion Diseases

In the UK there has not been a person who developed variant Creutzfeldt-Jakob disease (vCJD) born after the SRM removal regulation was instigated in 1989. Experience in other countries has varied a little due to different times of implementation of precautionary measures, among other factors. There is strong evidence that BSE is a zoonotic disease and is the cause for vCJD.

The occurrence of vCJD in the UK and Europe led to an erosion of public confidence in government and regulatory agencies due to the failure to properly communicate human risk. This experience points to the continuing need for good data to inform risk assessment and for better risk communication.

The zoonotic potential of other prion diseases remains unresolved. Recently, after the finding that scrapie could infect humanized transgenic mice under some circumstances, the European Food Safety Agency issued a statement based on considerations of an expert group that there was no absolute barrier to zoonotic transmission of scrapie, but given that scrapie displayed three of the nine Bradford Hill Criteria of Causation, there is only a possible link between scrapie and human disease (see Scrapie, above). Other animal prion diseases such as CWD fall into this category. Tracking of sCJD in Australia, Iceland and Cyprus did not find a link between sCJD and scrapie. Surveillance, monitoring for evolution of the animal disease and research to better understand pathogenesis need to continue.

The experience of BSE suggests that protective measures should be imposed based on the best-available science and modified in the light of new science. It is recognized that there are scientific and political considerations in all regulations and advice to the public. Risk and benefit, and the communication about them, can only be done well in the presence of good scientific data to assist with the risk assessment.

More unified approaches by scientists and all levels of government are needed to deal with possible zoonotic diseases such as CWD. Current policies, regulations, control measures and communication about CWD are disjointed over many agencies and jurisdictions. Effort to bring the jurisdictions together is urgently needed to share scientific data to inform decision making and to develop common plans and communications for dealing with the disease, including a preparedness plan for use in the event that CWD turns out to be zoonotic.

Lessons and Priorities for Moving Forward

Participants provided views of specific targets for research and regulatory activities. These are provided in more detail in the sections at the end of the workshop report.

Introduction and Purpose

The Workshop on Emerging Aspects of Prion Diseases brought together international experts to discuss emerging prion science, implications for regulatory agencies and industry, and approaches to risk management associated with three animal prion diseases: bovine spongiform encephalopathy (BSE), chronic wasting disease (CWD) and scrapie. The risks that animal prion diseases present to human health were also a focus of the workshop. This report presents a summary of the presentations and discussions, along with suggestions for future research priorities. Note: Comments and suggestions are not meant to imply consensus.

The workshop was jointly hosted by the Alberta Livestock and Meat Agency (ALMA), the Alberta Prion Research Institute (APRI), and the Canadian Food Inspection Agency (CFIA).

- The **Alberta Prion Research Institute**, a part of **Alberta Innovates Bio Solutions**, is funded by the Government of Alberta to support top researchers working on solutions to the serious scientific and socioeconomic challenges associated with prion diseases in animal and prion and prion-like diseases in humans. prioninstitute.ca
- The **Canadian Food Inspection Agency** is dedicated to safeguarding food, animals and plants to enhance and protect the well-being of Canada's people, environment and economy. Mitigating risks to food safety is the CFIA's highest priority. The CFIA, in collaboration with industry, consumers, and federal, provincial and municipal organizations, works to protect Canadians from preventable health risks related to food and zoonotic diseases. inspection.gc.ca
- The **Alberta Livestock and Meat Agency** is a provincial government agency committed to growing competiveness, profitability and sustainability in Alberta's agricultural industry. Through collaboration with industry and government partners, ALMA supports projects that encourage knowledge transfer, innovation and adoption of best practices. alma.alberta.ca

Comments from Workshop Co-Hosts

Kevin Keough, Executive Director, APRI, welcomed participants to the workshop. He noted that the discussion portions of the workshop would be conducted under a modified Chatham House Rule[1], which does not attribute remarks to speakers, thereby encouraging open discussion and information sharing. According to the rule, participants are free to use the information received, but they may not attribute comments to individuals unless given permission to do so. In that light, Kevin noted that he looks forward to interesting and spirited discussions about this very important part of science and its implications for industry and policy makers.

Bruce Archibald, President, CFIA, noted that the CFIA relies on high-quality, timely and relevant science as the basis for program design and regulatory decision-making. Through the Agency's modernization efforts, there is increased focus on disease prevention and implementation of proactive measures. Collaboration is key to addressing shared priorities, including working with provincial/territorial partners and industry and research partners such as ALMA and APRI.

[1] See more at: https://www.chathamhouse.org

Canada is the only country that has had all the known animal prion diseases (classical and atypical BSE, classical and atypical scrapie, transmissible mink encephalopathy and CWD). Enormous investments have been made and continue to be made around the world to control these diseases and to better understand and explain them. However, despite having learnt a great deal, prion diseases remain an enigma to a large degree with many challenges remaining and some surprises emerging.

In the case of scrapie, for example, we have known about it since the 1700s during which time there has been a long-held belief that it does not transmit to humans. However, this might be challenged by a recent report of its successful experimental transmission to a closely-related primate species, a cynomolgus macaque, following a 10-year incubation period. It remains to be determined to what extent this finding is informative of the zoonotic potential of scrapie under natural field conditions. This study highlights one of the greatest challenges in dealing with prion diseases, which is their prolonged incubation period. As a result, long-term studies continue to be needed to assess their zoonotic potential, together with long term commitments and investments to maintain and refine our measures to protect both human and animal health. This is particularly relevant for BSE at this time, where past successes could be undermined over time if control measures are rolled back too far in response to various pressures.

Although BSE has been successfully brought under control in the cattle population globally, primarily as a result of breaking the transmission cycle through a feed ban, many questions remain. For example, what are the implications of atypical strains? How many are there? Do they represent a sporadic form of BSE? Are they transmissible to cattle and/or other species? Do they pose a public health threat?

While it is clear that environmental contamination plays a significant role in the transmission of CWD and scrapie, it's much less clear what role, if any, it plays in the transmission of BSE. Traditionally, it has not been considered to be a risk pathway as cattle are not known to shed prions in their bodily excretions, unlike sheep affected with scrapie or cervids affected with CWD. Whether some disposal practices associated with cattle mortalities on farm are likely to lead to sufficient pasture contamination that could pose a threat to cattle or other species is unknown.

In addition to the uncertainties, challenges and knowledge gaps highlighted so far, there are many more including the need for a better understanding of the dissemination, persistence and degradation of prions in the environment, the role of plant uptake of prions in disease transmission along with ways to detect prions in soil, plants and water.

From a regulatory perspective, a live animal test on easily-accessible tissues would be an invaluable disease control and surveillance tool, especially early in the disease process before animals begin to shed prions. In addition, a feed test that could reliably discriminate between ruminant and non-ruminant species with a sufficient level of specificity would enhance compliance oversight and facilitate future modifications to a feed ban.

Because it is carried and shed by wild cervids, CWD spreads easily. A vaccine would provide a significant tool to combat CWD. Advances in genetic testing and breeding for resistance would benefit all species at risk of prion diseases.

This workshop provides the opportunity to share information and best practices and to learn from one another. Better understanding of ongoing and emerging issues related to animal prion diseases will help

decision makers in industry, academia, and government set direction for the future, including funding for research and prevention.

David Chalack, Board Chair, ALMA, noted that the livestock and meat industry is Alberta's most important renewable sector. Public health, the economy and trade are all at risk from the impacts of prion diseases. ALMA, whose stakeholders include producer groups, researchers, and agri-food businesses, invests in programs to enhance productivity and sustainability, increase market access and consumer awareness, and stimulate new product development. ALMA's largest activity is research. A key outcome of the workshop would be the identification of new research opportunities. ALMA takes a One Health approach – covering the entire spectrum of the intersection of animal health, human health and the environment.

Prior to the start of the workshop, Bob Church, Professor Emeritus, University of Calgary, reminded the group of some of the history of prion disease in North America and some of his early discussions about the spread of the disease into Canada. He pointed out that the large cervid population within the Suffield Station in southern Alberta, which he estimates might contain as many as 10,000 elk, could be a significant reservoir for chronic wasting disease. Dr. Church pointed out the ongoing challenges to animal and human health that are presented by emerging infectious agents and their intermediate hosts, citing the examples of Lyme disease and Zika and other emerging viruses. He was of the view that high vigilance and appropriate investment in dealing with such diseases should be essential components of moving forward on human and animal health strategies.

Bovine Spongiform Encephalopathy

Presentation: Towards BSE Control and Eradication: How Far Have We Gotten?

Dr. Torsten Seuberlich, University of Berne, Switzerland

Switzerland has had 466 cases of BSE since 1990, with the largest number occurring in 1995. There were no cases between 2007 and 2010. However, there were cases in 2011 and 2012.

Disease control measures in Switzerland since 1990 include those related to animal health (ban on meat and bone meal (MBM) in feeds) and measures related to human health (removal of specified risk material (SRM) from the food supply). Appropriate surveillance programs are required to determine if those animal health and human health measures are effective. For example, the effect of feed bans on BSE incidence requires tracking based on the year of the animal's birth rather than the year of BSE detection. Following the MBM in ruminant feed ban in 1990, there was a drop in BSE cases in Switzerland. However, it was clear that additional measures were required, which led to the removal of SRM from livestock feed in 1996 and MBM from livestock feed in 2000. Voluntary testing by the meat industry provides larger samples (30K with active surveillance versus 150K through voluntary testing) and helps maintain consumer confidence.

Classical BSE cases have recently (2015-2016) been detected in animals born many years after the reinforced feed ban (BARB): Canada and the UK (animals born in 2009), Ireland (animal born in 2010), and France (animal born in 2011). It is difficult to explain where/how these animals were infected, as these countries all have efficient feed bans in place. These cases have an impact on trade: one case can change the export status of a country.

For atypical BSE (H- and L-types), there have been fewer than 100 cases worldwide, mostly detected in cattle older than eight years and in countries with low BSE risk and no history of classical BSE cases. Transmission studies have indicated that L-type BSE has zoonotic potential.

Various hypotheses exist about the origin of BSE, which makes disease control and risk assessment challenging. Theories on the origin include:

- Atypical BSE was recycled in the cattle population.
- Sporadic C-type BSE was recycled in the cattle population.
- Scrapie prions crossed the species barrier to cattle.
- Prions of other species crossed the species barrier to cattle.

Other gaps and challenges in knowledge about BSE include:

- Significance of atypical and C-type BARB cases.
- Molecular basis of prion strains.
- Limitation of diagnostics (all are post-mortem).
- Treatment/immunoprophylaxis.
- Prion decontamination.
- Maintenance of effective disease surveillance.

The BSE cases in Switzerland in 2011 and 2012 were unusual. Extensive study of the animals indicated that transmission did not induce a spongiform encephalopathy or prion disease. The PrP aggregates that were found in brain and muscle samples suggested a seeded PrP aggregation. Whether PrP aggregates relate to the pathogenesis of neuronal or muscular disease remains to be determined.

Bovine Spongiform Encephalopathy Discussion

There remains uncertainty regarding BSE, and a lot more work is needed on the origin and evolution of prions and prion diseases. Better surveillance is needed to ensure decisions are based on the true risk to animal health and human health.

BSE classification (C-, H- and L-types) is done only on the basis of an immunological and histological profile. Prion strain or phenotype definition is much broader. If additional cases are detected, the isolates would have to be examined further to determine if they are truly C-type.

Residual feed or feed contamination is usually considered the cause of BSE in animals born after the feed ban. The risk is greater for countries that do not have a well-implemented or monitored feed ban. Modelling shows that these types of cases could still occur through to 2019 in the UK.

Good management practices, biosecurity protocols and risk management remain important BSE control measures, including removal of SRM. Environmental contamination has been assumed to not be an issue with BSE. However, farm practices (clean-up of old feed, land fill, etc.) could be considered as potential infection pathways. For example, in the EU, on-farm mortalities have to be disposed of off-farm, whereas in North America on-farm mortalities may be disposed of on-farm. On-farm investigations in the UK include tracking feed supplies, cleaning history of silos, and other factors to try to determine the source of the occurrence. There does not seem to be an age barrier for an animal to acquire the disease.

Canada's[2] original 1997 ruminant feed ban prohibits the feeding of ruminant animals (cattle, sheep, goats, deer, elk and other species) with most proteins derived from mammals. Exceptions to this ban apply to proteins derived from swine and equines as well as such animal derived products as milk,

[2] Canada's comprehensive feed ban consists of a combination of two measures:

> 1. Prohibition to feed most mammalian-derived proteins collectively referred to as prohibited material, to ruminant animals (cattle, sheep, goats, deer, elk and other species), proteins derived from pure swine or equine materials, blood, milk and milk products of any species as well as gelatin and tallow containing no more than 0.15% insoluble impurities are exempt; and
>
> 2. Total ban of Specified Risk Material from the entire terrestrial and aquatic animal feed chains as well as fertilizer.

gelatin, animal fat and blood products from all species. Also excluded are proteins derived from non-mammalian species such as fish and poultry. Nevertheless, proteins prohibited from feeding to ruminants can, be used to feed non-ruminant livestock such as poultry and swine or used in pet food. In 2007, the enhanced feed ban regulations retained the 1997 provisions including the exemptions but prohibited bovine specified risk material (SRM) as defined from all animal feed, pet food and fertilizer and added a permit system to control the collection, transport, treatment and disposal of bovine SRM.

Current understanding about atypical BSE strains raises questions about their potential risk to human health. There is some concern that the OIE has made a clear statement on atypical BSE and its relevance to animal and human and does not considered it in any risk assessment or in their country classification decision. More strategic conversations with OIE might be needed to draw attention to atypical BSE risks. Countries that have never had BSE, and therefore have a negligible risk status, don't normally implement BSE control measures to protect the human food supply (e.g. removal of brain and spine from the food supply). The OIE position regarding the status of countries with atypical BSE might need to be challenged to ensure public health is protected.

While control of animal diseases is often through the use of vaccines, BSE research does not seem to be heading this way. There are issues related to the economic viability of a BSE-specific vaccine: it is a rare disease; it doesn't circulate in the blood at high rates; and it is unlikely there could be 100 per cent protection. It is also unlikely that a vaccine would work against atypical types, especially if they prove to be spontaneous.

Uptake of a BSE vaccine (which protects animal health) is expected to be low, given that there has been only a low uptake of the E.coli vaccine (which protects human health). However, the effectiveness of the E.coli vaccine has been inconsistent, which might be a contributing factor to its poor uptake. A BSE vaccine providing a low level of protection would not likely be used in the field and it would not lessen the need for the other disease prevention measures. If a vaccine were provided at no cost, perhaps there would be greater uptake.

Some of the available tests for detecting BSE (e.g. PMCA), work well in extracted tissues but when other samples are involved, such as meat and bone meal and soil, sensitivity and specificity are greatly diminished. For the targeted surveillance in North America, there are sufficient, validated and approved tools available. Additional/new tools could include:

- Live animal tests (desired in particular by the cervid industry, but might not be relevant for regulatory or research purposes).
- Tests with increased sensitivity and specificity.
- Rigorous validation regimes for tests.
- End product (food and feed) testing – need a reliable, relatively inexpensive way to detect threats to human and animal health.

OIE considers the number of samples tested, but there isn't clarity on the significance of these numbers. OIE standards are based on 20-year-old science. Countries and regulators need to look at the science in terms of risk: what would the risk-benefit analysis be today? Variations in how animals are raised, climate, age, etc., might limit the effectiveness of a standard based solely on the number of samples tested in one country versus another.

In addition, the OIE disease-based system discourages low-risk status countries from undertaking proper surveillance (i.e. if you start looking you might find something and then your status will change with ensuing trade impacts). Perhaps a fundamental rethink on BSE standards is needed.

In Switzerland, surveillance has been effective, especially during times of high awareness of the disease. Disease awareness is now very low (even when BSE cases are reported in the media, reaction is low). One of the strategies being considered is to extend the surveillance from BSE to also include other diseases.

Chronic Wasting Disease

Presentation: Chronic Wasting Disease Overview

Dr. Glenn Telling, Colorado State University

Prions diseases include those affecting animals (Bovine Spongiform Encephalopathy, Chronic Wasting Disease, Scrapie and Transmissible Mink Encephalopathy) and Creutzfeldt-Jakob Disease (CJD) which affects humans. In addition, Alzheimer's and Parkinson's diseases have similarities to prion diseases. It is not clear how prions replicate. From a molecular perspective, there is a unique hypothesis in which the prion protein converts into a different protein conformation, which can induce a change that produces more abnormal PrP. This becomes an exponential process, similar to viral replication.

Prion diseases of animals can be naturally occurring (scrapie, CWD) or feed borne (BSE). They have long incubation periods, but once symptoms appear they progress rapidly. The central involvement of a prion protein (PrP) is key. While scrapie has been around for several hundred years, CWD was first identified as a prion disease in the early 1980s.

Chronic wasting disease is a highly contagious prion disorder of captive and wild cervids. Species affected by CWD include black-tailed deer, white-tailed deer, mule deer, Rocky Mountain elk, and, more recently, moose. The disease is expanding in its geographic range. First discovered in the so-called endemic region of Northeastern Colorado to Southeastern Wyoming, by 2002 it was found in free-ranging populations of white-tailed deer east of the Mississippi. CWD cases have been seen in wild and/or farm-raised cervids in 23 states and two Canadian provinces (Saskatchewan and Alberta). There have also been outbreaks in South Korea and most recently a case in Norway. The prevalence of the disease is likely vastly under-estimated.

Management of CWD is challenging. Most US states and Canadian provinces have introduced surveillance programs, ranging from targeted surveillance to mandatory testing of suspect animals.

The highly contagious nature of the disease also creates research challenges, as it is difficult to maintain control groups. Transgenic mice, non-human primates, cell-culture models and other laboratory tests are useful research tools. Diagnosis can only be made post-mortem.

The origins of CWD are unclear. Although sheep had previously been housed on the land where CWD was first encountered, a definitive connection to scrapie has not been made. It could be possible that a sporadic disease was the origin.

Incubation tends to be up to about two years. Clinical symptoms appear in animals three to seven years of age. The natural route of transmission is not precisely known, but ingestion of contaminated

materials could be the source of CWD in the wild. CWD prions are present in saliva, blood, urine, feces and antler velvet. CWD prions also bind to soil particles and remain infectious.

Risk of transmission to livestock is unclear. The risk to human health is also unclear. But because BSE proved to be zoonotic, the risk of CWD transmission to human health is of significant concern. The unprecedented contagious spread of CWD, the discovery of two distinct CWD strains, and the presence of CWD prions in muscle, fat and other animal derivatives destined for human consumption or exposure suggest a high risk and the need for public health concern.

Key research concerns and challenges include:

- The expansion of the geographic range of CWD seems irrevocable.
- Persistence in the environment is a major complicating issue.
- New strains can emerge in ways that are not fully understood. Infection of additional species such as caribou would have serious impacts.
- Better experimental models are needed to study peripheral pathogeneses to help determine why CWD is so highly contagious.
- Deer, elk and moose species produce prions with different biological characteristics.

Chronic Wasting Disease Discussion

CWD is a highly-contagious disease that is spreading in an unprecedented way. There is no evidence of atypical CWD; no discernible difference has been found by Western blotting profile of any material from either deer, elk or moose. Atypical CWD is possible, but unlikely considering the timelines to date. But the potential for sporadic CWD should not be ruled out. The strain profile is radically different between elk and mule deer in transmission experiments. CWD strains tend to be co-propagated in the brains of mule deer, whereas elk can propagate either type-1 or type-2. CWD's zoonotic potential remains unclear.

It is clear, however, that CWD will have major ecological and environmental effects. There is a very narrow window of time to do something meaningful: Canada is currently in that period.

In Alberta, wild cervids have been tested since 1998, with the first detection of CWD in 2005. There are enough cases now to demonstrate changing occurrence patterns. It is spreading along watersheds, which are primary deer habitats. This appears to be a real spread, not an outcome of improved diagnostics or increased surveillance. The pattern of disease in Alberta wildlife appears to be driven by mule deer.

The threat to caribou is looming. White-tailed deer are moving north due to industrial development and climate change; they could provide a transmission point to caribou. Interestingly, the spread pattern of CWD is discontinuous (i.e. there are areas of no infection that break the swath of geographical infection). The disease spread from an endemic region to other non-connected states and provinces likely occurred as the result of unregulated transport of infected cervids out of the endemic region. Risk mapping can provide predictions of where spread will occur.

In April 2016, the Norwegian Veterinarian Institute confirmed CWD in one free-ranging reindeer. This will have Europe looking to North America for control strategies. The possible connection to scrapie as the source was raised as there is scrapie in Norway; some researchers believe cervids might be susceptible to some scrapie strains. There is also some emerging evidence, as shown in a recent study

from the University of Saskatchewan, that birds can spread CWD. Birds such as crows that scavenge on carcasses of cervids that died from CWD might act as mechanical vectors by shedding CWD prions in their faeces after flying substantial distances.

Surveillance, containment, and rigorous epidemiology can be effective management and control measures for CWD, but controlling the disease in the wild is challenging given the unusual biological characteristics of the infectious agent. Vaccines and selected breeding might be effective, but both are long-term strategies. A risk assessment has led to a ban on imports of deer urine (used by hunters as a lure) into the EU; however, the practice continues in North America.

Realistic goals are important: it is unlikely that CWD will be eliminated from wildlife. But it should be possible to limit the rate of increase in infected areas and limit the rate of spread into new areas. Although the transmission method is still unclear (source of CWD, how one animal infects another, role of environmental CWD, whether transmission varies by species, etc.), there is fairly good understanding of the demographics of CWD in the wild. The ideas and strategies that emerged from the 2011 CWD management meeting should be reviewed, as many have not been implemented. The Canadian National CWD Control Strategy is excellent at a strategic/policy level, but it is lacking in terms of operationalization/ implementation.

Limiting the spread of CWD in wild populations requires working with the primary tool available: hunter harvest. If the harvest targets the sector of the cervid population known to most likely be infected, then perhaps the rate of infection/spread can be limited by their removal. However, harvesting specific animals or culling herds in CWD positive areas can be difficult to implement due to public perceptions and backlash.

In addition, targeted harvesting raises questions about potential health risks given the pressures on hunters to consume the meat. Most states and provinces require holders of a recreational hunting licence to consume the meat of any big game animal taken (i.e. the meat cannot be wasted). To change this well-entrenched ethos would require well-based scientific evidence of zoonosis. There are also cultural rituals related to hunting and the consumption and usage of certain parts of the animal.

Alberta has a surveillance program that tracks hunter-submitted samples in addition to targeted samples and road kill. Since 2006, zones identified as CWD endemic are classified as mandatory sample submission zones. With an annual harvest of 45K+ animals, the mandatory areas limit the number of testing samples to a more manageable level. When a positive result is obtained, the hunter is contacted. Information is provided according to World Health Organization guidelines: ‘CWD does not affect humans; however, if an animal is known to be positive, it is recommended that its meat not enter the food chain.’ The hunter is left to make his own personal decision. In most cases, the meat is consumed. If the hunter does choose to dispose of the meat, no penalty (e.g. wastage charge) is applied.

Whether CWD prions can cause human prion disease is unclear. In an APRI-funded transmission study on non-human primates, the incubation period is now at six years. Two animals that were exposed to deer and elk CWD-infected skeletal muscle have displayed some signs of neurological disease. This supports taking a precautionary approach to the consumption of deer and elk meat from endemic areas.

As noted, public attitudes play a role in whether control measures such as no longer maintaining high populations of bucks for trophy hunting or banning the use of urine as hunting lure, banning baiting, or are accepted. Until there are changes in public perception, these types of control measures will be difficult to implement. Changing attitudes would require demonstration of the impact of CWD on

wildlife (for example that it only takes a 20 per cent incidence rate to have significant impact). Public education should lead to public support, which will lead to government funding/action. All stakeholders need to be involved to develop a reasonable approach, to avoid public fear and lack of understanding of the issues. Important populations of cervids live on private land; property owners also need to be engaged.

The farming of cervids is a highly regulated industry. When a positive case is detected on-farm, the animal is kept out of the food chain, and the rest of the herd is destroyed and tested. Zoning is an unwanted additional requirement from a producer perspective.

On-farm outbreaks might result from direct or indirect contact with infected wild cervids (CWD infectivity has been found in soil, dust, and run-off). Feed is also being considered as a source of CWD in farmed cervids. Further study of how on-farm cervids are infected is needed, with the collaboration of industry, regulators and researchers.

CWD contamination appears to be able to remain in the environment for five, 10 or more years without significant loss of infectivity. Some types of soil and some types of soil minerals might be more conducive to prion binding. Different environments might lead to/effect different strains, and soil types might also figure into the longevity of prion presence in an area. Knowing which soil types are more conducive is important in identifying areas for containment/clean-up. There is also evidence of the take-up of CWD prions by plants (wheat in Alberta). An Alberta study showed that while prions were evident in roots, they were not detected in stems or leaves. A study done in the US detected the evidence of the uptake of prions into plant tissues. In addition, there are many species that interact with a deer carcass in the wild, which increases the risk of other species being infected or carrying CWD prions elsewhere.

Prion research is extremely slow and the disease is complex; it is important to manage expectations and realize that there likely won't be a one-size or single solution. Because transgenic mice experiments are expensive and time consuming, other means for discerning strains have been considered. For example, the use of cell culture, which enables identification of different strains through propagation under different conditions, and the generation of antibodies against the CWD prion protein to create different responses leading to "fingerprints" for identifying, characterizing and differentiating prion strains can be used.

What is most important is that the research community works together. Researchers need to be able to share research and specimens across borders, which requires support from the CFIA and US counterparts. Collectively, there is enough data from the wildlife management side to identify best practices and successful strategies. Perhaps it is time to shift the focus from tracking the disease to developing management tools that can be applied in the field to control the disease at a level that minimizes impact to the environment and the economy.

Some participants saw the need for a vaccine, which could be effective for farmed cervids but mightnot be for wildlife. Other participants noted that experience with the rabies vaccine provides an example of successful containment of a wildlife virus. Rabies in the wild has not been eradicated but it has been controlled. In this context, a CWD vaccine could be a valuable tool for both farmed and wild cervids.

Some participants saw the need for a live test. It was stated by some participants that development of a live test should be a national priority. It was also noted that live tests are problematic in terms of confidence in negative results; laboratory testing can only report as "detected" or "undetected." Implementation of live testing would be expensive and time consuming; an industry partner would be

needed. Some felt that development of a live test would not offer a return on investment, as the size of the market likely doesn't support it. Others considered it a viable approach because of the many tissues, saliva, etc., in which the prions appear.

Just as there is a need for collaboration on research, cross jurisdictional (federal-provincial) collaboration on policy development is important. However, federal-provincial responsibility and relationships for CWD are complicated:

- The CFIA has authority to deal with CWD as it is a reportable disease, but game farms also fall under the jurisdiction of provincial agricultural and/or environment ministries;
- Environment Canada has limited legislative authority over big game (e.g. for species at risk); it does have a role in managing migratory birds;
- If CWD crosses to an endangered species (e.g. certain caribou populations), Environment Canada could become involved; and
- If CWD was recognized as a persistent organic pollutant[3], Environment Canada could possibly exercise some authority.

Similarly, increased dialogue among provinces and states would be helpful. For example, the Western States Association of Fish and Wildlife used to have a CWD information sharing meeting with various jurisdictions about every two years. Participants suggested that this meeting be reinstated and expanded. The Canadian Wildlife Directors Committee has a sub-group dealing with CWD; this could be a way to maintain a high profile for the disease.

Scrapie

Presentation: Scrapie – it is not so easy to get rid of old friends

Dr. Olivier Andreoletti, Ecole Nationale Vétérinaire de Toulouse

First identified more than 300 years ago, scrapie is possibly the archetypical prion disease and offers many lessons and insights. But there is still much unknown about it.

There are two main types of scrapie. Classical scrapie is considered a rare disease (nine positive results out of 10,000 tested animals), but there is wide variability of presence among countries and flocks. Atypical scrape was first identified in Norway in 1998 and has since been detected in numerous countries, including New Zealand and Australia. In Europe, prevalence is six positives in 10,000 tested animals; this level of prevalence tends to be the same in all areas.

There are multiple strains of classical scrapie. Transmissible scrapie prions are present in many tissues and body fluids, including milk, blood, urine and skeletal muscle, and they have long persistence in the environment (pastures, barns, etc.). ARR allele carriers display a very high level of resistance to classical scrapie infection.

Atypical scrapie can affect all genotypes, including ARR. Research has demonstrated that infectivity is present in peripheral tissues. However, the OIE does not consider atypical scrapie to be a TSE that is transmissible in natural situations.

[3] **Persistent organic pollutants** (**POP**s) are organic compounds that are resistant to environmental degradation through chemical, biological, and photolytic processes: https://en.wikipedia.org/wiki/Persistent_organic_pollutant

Similar to strategies for controlling BSE, an integrated approach to prevent circulation and exposure to scrapie agents includes feed bans, removal of specified risk materials (SRM) from the food chain, and epidemiological surveillance. Nonetheless, infected animals do enter the food chain: an estimated 30K in the EU in 2011. Despite SRM measures, a significant amount of the infectivity contained in the tissues of apparently healthy but scrapie infected sheep were slaughtered and entered into the food chain.

Breeders and the sheep industry feel that because scrapie has been known for so long it is unlikely to be dangerous to other animals or to human health, and that expensive measures such as removal of SRM and active surveillance programs are not really necessary.

However, the species barrier for scrapie has been shown to be permeable. Experiments with humanized transgenic mice indicate that there is potential for transmission to humans, possibly leading to a sporadic prion disease (sCJD). In addition, there is indication that classical scrapie could propagate without an apparent transmission barrier in bovine expressing hosts, while atypical scrapie appears to have a substantial but porous transmission barrier. The human species barrier is also permeable to atypical scrapie. Food chain protection measures should remain in place.

In bovine PrP transgenic mice, no species barrier appears to limit the propagation of certain scrapie strains. Moreover the incubation period with these strains appears to be shorter than for BSE. These data suggest a real potential for the propagation of these agent in cattle. Genetic selection for controlling or eradicating scrapie has been implemented in the EU for the past decade. Resistance has been demonstrated in sheep with ARR allele carriers and in goats with an equivalent allele (K222); however, transmission of classical scrapie is still possible. There is no efficient genetic protection against atypical scrapie. Genetic selection in conjunction with properly applied control measures (feed bans, SRM removal, surveillance) can decrease the prevalence of classical scrapie. A frequency of 60-80% of ARR carriers in flocks appears to control spread. But achieving that level takes decades and sustained investment of both effort (including focus of policy makers) and funding.

Other control strategies include hunt and destroy and active surveillance and testing. With hunt and destroy, flocks that test positive are culled to eradicate the disease. However, this approach does not consider potential subsequent environmental transmission. Active surveillance and testing does not consider the typically long incubation period of TSEs; a negative test result in a young animal can be a positive result years later. Eradicating small ruminant TSEs in the field on a testing basis in not practical – for every 1 detected, 10 to 20 cases are undetected and enter the food chain.

There are still many uncertainties about scrapie, including its ability for transmission across species barriers. Feed bans and removal of SRM from the food chain need to continue.

Scrapie Discussion

Portugal has the highest incidence of atypical scrapie. The prevalence of atypical scrapie has not really diminished (between 2007 and 2011), but it did not statistically increase, except the UK is experiencing an unexplained increase. The detection of atypical scrapie with the current rapid testing process is more difficult than for classical scrapie. Therefore, there might be a greater incidence of atypical scrapie in flocks than reported. It is important that vigilance is maintained.

Scrapie is most often transmitted from mother to lamb around birth (the placenta and birthing fluids, colostrum and milk) rather than contaminated feed. Scrapie can also be found in sheep milk. Some studies have shown that infection might occur from repeated small doses over time. Scrapie research

also suggests that the scrapie prion agent is prone to adaptation; this means there is higher risk for lateral transmission. A key difference between surveillance and testing for BSE and scrapie is that BSE looks to identify individual cases, whereas for scrapie it is incidence within the flock.

In Canada there are no specific regulatory requirements to exclude those tissues from the human food or animal feed chains likely to harbour scrapie infectivity (SRM[4]) from small ruminants. However, considering that there is a specific regulatory prohibition on animal feeds containing proteins derived from the carcass of any ruminant, other than cattle, that died or have been condemned before they would otherwise have been slaughtered for human consumption, small ruminants as well as cervids would not be rendered for the production of meat and bone meal destined for incorporation in animal feed. For infected flocks, animals over 12 months of age cannot be sent to slaughter (food chain). All goats and genetically susceptible sheep over 12 months must be destroyed and disposed of by on farm burial, incineration or through designated rendering plants that process cattle SRM. Sheep and goats that are under 12 months can be sent for slaughter at an abattoir.

Breeding for resistance has been shown to reduce susceptibility. However, the introduction of resistant alleles is not possible in all sheep and goat breeds. To date there have been no negative outcomes (e.g. dropping of desired traits) resulting from breeding for scrapie resistance. It is important to introduce resistance slowly to maintain genetic diversity and to avoid creating "bottlenecks" that can reduce genetic viability. In Ontario and Quebec (where most of the scrapie in Canada occurs), producers are introducing resistant alleles. In some other parts of Canada, however, producers are more reluctant unless the breeding program is fully funded by the government.

It is difficult to compare the effectiveness of breeding for resistance to scrapie in sheep (farmed animals) versus CWD resistance in wild cervids. There might be a resistance allele in cervids, but the number of species further complicates its potential. Because prion disease does not prevent reproduction, there is no evolutionary pressure on the gene that controls neurodegenerative disease. Progress on resistance for scrapie has been made only recently through animal husbandry practices, even though scrapie has existed for hundreds of years. Resistance could be in the form of lengthened incubation period or susceptibility. Breeding for resistance could help reduce susceptibility of farmed cervids.

Existing knowledge about scrapie needs to be better incorporated into policy and regulatory decision-making. For example, the OIE does not consider atypical scrapie to be a TSE. Participants suggested that this position should be challenged by OIE members in light of current knowledge.

In terms of research areas for scrapie, participants suggested that a team of experts could be convened to consider the risk and potential of scrapie to cross the human species barrier. It could be useful to review the history of BSE research and how/when the link to CJD was confirmed. This will help determine whether the precautionary approach is demanded.

Participants suggested that basic research is still needed to better understand the transmission process and barriers to transmission, including the factors of the infectious agents that enable or prevent transmission across the species barrier, replication (how, where, cellular factors), and human health

[4] SRM for sheep and goats in the EU are defined as the spleen and the ileum from animals of all ages and for animals over 12 months of age, the skull including the brains and eyes, tonsils, spinal cord (point 1 of Annex V of EC Regulation 999/2001).

considerations. Research to develop new models and new tests is also needed. Above all, a sense of importance about investing in this research needs to be created.

Human Prion Diseases

Presentation: Animal Prion Diseases and Risk to Human Health

Dr. Robert Will, University of Edinburgh, UK

Variant CJD (vCJD) is the form of Creutzfeldt-Jakob disease that is closely linked to BSE exposure. As the incidence of BSE in the UK declined from 1988 to 2014 due to the ban on meat and bone meal in feed, so too did incidence of vCJD after 2000.

The UK population was exposed to CJD through the food chain. Yet there have only been 174 cases of vCJD to date. While there are a number of hypotheses as to why the infection rate was so low given the wide exposure, such as genetic factors, no clear explanation emerged for why some individuals get this disease while others do not. Some models suggest that there must be a threshold level of exposure to BSE in the human food chain. The reason might be because it is actually difficult to infect humans.

A public inquiry in the 1990s concluded that although the UK government introduced measures to guard against the risk of BSE for both cattle and humans, the possibility of risk to humans was not properly communicated to the public or to those whose job it was to implement and enforce the precautionary measures. The government did not lie to the public about BSE. The government was preoccupied with preventing an alarmist over-reaction to BSE because it believed that the risk was remote. When it finally did announce that BSE had probably been transmitted to humans, the public felt that they had been betrayed.

In the UK, the major measure to protect human health (SRM removal from food chain) was introduced in 1989. There has not been a case of vCJD in anyone born after that date in the UK. In continental Europe where precautionary measures were not introduced until a few years later, there have been for cases in people born after 1989.

The EU also conducted inquiries into the BSE crisis, leading to significant legislation for protection against possible BSE risk. However, misplaced confidence that there was no BSE in cattle in some countries and limited surveillance led to the erosion of public confidence in government risk communications after abattoir testing and more active surveillance led to the detection of BSE in a number of EU countries in 2000.

The reason for continuing uncertainty in the UK for public health is partly because the pathogenesis of vCJD is different from other forms of CJD in that there is significant infectivity in peripheral tissues, including the appendix. Projected results from examination of more than 32K appendix samples placed the rate of infection at one in 2,000 in the general population. This raised further concerns about the potential for secondary transmission, for example through blood transfusion.

A subsequent study looked at whether there is a link between blood donors with vCJD and recipients being infected. To date, four individuals have been infected after receiving a blood transfusion from someone who later developed vCJD. This is of high concern, given the potential rate of infected individuals (one in 2,000). But the prevalence rate projected in the appendix study does not match the actual number of transfusion-transmitted cases. A further appendix study is underway. There is still

concern in the UK that there could be additional outbreaks of vCJD in people of different genetic makeup.

Sporadic CJD (sCJD) is caused by a spontaneous conversion of normal PrP into the disease-associated form. This might also explain why there are hereditary cases as gene mutations could lead to instability of prion protein. A consistent finding of studies is that the age-specific incidence of sCJD declines in the elderly, which is different from Alzheimer's where the older the individual, the more frequent the disease. The reason for these results could be poor ascertainment in the elderly.

Data on the geographic distribution of sCJD appears to show that it is a random disease. However, when past residence is viewed over 20 plus years, there appears to be proximity linkages among some people with sCJD. This raises the notion that perhaps sCJD might not be spontaneous.

The apparent increase in mortality rates for definite and suspected sCJD cases in the UK might be attributed to improved diagnostics and awareness. Population demographics might also contribute to the increase, as the number of individuals over the age of 60 has increased. However, the increase in sCJD has also been seen in other countries.

Hereditary forms of the disease are associated with mutations of the prion protein gene. The general view is that the mutation causes the disease; but some researchers believe the mutation is associated with an increased susceptibility to external infection.

The connection to BSE raises questions about the zoonotic potential of ovine scrapie. One research study showed that the serial transmission of different scrapie isolates in transgenic mice led to the propagation of prions that are phenotypically identical to those causing sCJD. These results demonstrate that scrapie prions have a zoonotic potential and raise new questions about the possible link between animal and human prions. However, the infection of the test animals was through intracerebral inoculation of high doses, whereas human exposure is oral. Another study showed the transmission of scrapie prions to a non-human primate after an extended silent incubation period.

In light of those studies, the EU asked the European Food Safety Authority (EFSA) to report on whether there is evidence that scrapie and atypical scrapie were pathogenic to humans. The conclusions, published in 2015, were:

- There is no evidence of an absolute species barrier. There are many factors that influence the ability of any TSE agent to infect a host, regardless of whether the infection occurs across a species barrier;
- The host factor that has been shown to play a very key role in the overall susceptibility to TSE is the amino acid sequence of the host PRNP gene, and its associated species specific polymorphisms;
- For disease to develop there must be exposure to a sufficient dose of the agent, the agent must be taken up from the gastrointestinal tract, enter the nervous system and be successfully transported to the neuronal cell bodies in the central nervous system. The infecting agent must then be able to "convert" the cellular PrP^{C} to PrP^{Sc} at a rate which enables accumulation of sufficient PRP^{Sc} to cause disease within the life-span of the host;
- It is impossible to define an experimental model that encompasses this potential variability and to directly measure zoonotic potential. These experiments are important, but they are unable to answer the question if these diseases are zoonotic; and
- The level of exposure to TSE agents influences the likelihood of successful infection. The level of exposure of consumers to TSE agents through oral exposure is largely determined by the prevalence

of animal TSE and by the amount of infectivity in animal tissues entering the food chain. The latter is reduced by current SRM measures.

The Bradford Hill Criteria of Causation[5] are minimal conditions necessary to provide adequate evidence of a causal relationship between an incidence and a possible consequence (e.g. smoking and cancer). With BSE and CJD, these criteria are fulfilled. Other prion diseases (small ruminant BSE, atypical BSE (L and H types), CWD, and classical and atypical scrapie) met three (plausibility, analogy and experiment) of the nine criteria. As a result, the EFSA report further concluded that there is a possibility that these other prion diseases are zoonotic, but there is no evidence of a causal link between classical or atypical scrapie and human TSE. The possibility of scrapie-related public health risks from consumption of ovine products cannot be assessed. No consistent risk factors have been identified for sCJD.

Continued surveillance of animal and human TSE is recommended to monitor the evolution of the diseases, allow their epidemiological comparisons and investigate their associations in the future.

Human Prion Diseases Discussion

During the UK outbreak, the average age of death of a patient with vCJD was 29. In France, which had the second largest number of cases, patients were about five years older. This might be explained by the pattern of dietary exposure to the BSE agent over time. It is also likely that most of the cases in the EU were related to UK exports and not to indigenous BSE in those countries.

Disease investigators were able to obtain a lot of background information about each patient (e.g. medical history, including surgery and dental procedures, diet, occupation, habits, etc.). There did not appear to be any obvious risk factor, such as location commonality (e.g. proximity to an abattoir), occupational similarity or other linkages among cases. The only similarity among patients was young age and dietary exposure to the agents. A case control study indicated that the risk of developing vCJD was significantly associated with consumption of various foods, particularly those containing mechanically recovered meat (MRM). Another study, which looked at dietary surveys from the 1980s, showed a clear regional difference in exposure to foods containing MRM, which was consistent with regional differences in vCJD incidence. In addition to exposure through agents in the food chain, there is likely an age-related susceptibility factor. By exclusion of other causes, the only reasonable hypothesis is that vCJD is food borne.

The issue of withdrawing control measures is not only a scientific one, but it is also a political and economic issue. In 1999, the over 30-month (OTM) rule (cattle could not be sold for food if over 30 months of age) was introduced in the UK. In 2005, cattle OTM could be sold if they tested negative for BSE. The age level for testing was subsequently raised to 72 months in 2011. Removing the OTM and testing measures was based on a cost analysis: how many lives were being saved at what cost? However, SRM rules and their associated costs remain in place. Because of the cost to industry, there is some desire to end the practice. However, as there is still uncertainty the prudent course is to continue to minimize human exposure to potentially infective agents through the SRM rule. Maintaining and/or expanding feed bans has to be clearly linked to reducing real risks or there will be low compliance and difficulties with implementation.

[5] http://www.drabruzzi.com/hills_criteria_of_causation.htm

Tracing all animal tissues for how they are used/consumed/disposed of is important. Some believe that this was never properly done for cattle in the UK. All farmed cervids slaughtered for human consumption are tested for CWD for surveillance purposes, not for food safety.

Perhaps all prion diseases have zoonotic potential, though some might have stronger potential than others. More than experimental evidence is required to determine zoonosis: there must also be epidemiology and observed cases of an atypical prion disease in humans along with additional evidence from transmission studies showing that the agent has different characteristics from sCJD. A major advance would be a blood test that could detect preclinical cases of vCJD, and thereby enable removal of blood from the transfusion system if positive. Although each is a prion disease, BSE, CWD and scrapie are different from one another. Tracking of sCJD cases in Australia, Iceland and Cyprus did not find a link to scrapie.

When the BSE crisis occurred in the UK, risk of transmission to humans was thought to be unlikely and therefore no contingency plan was put in place. A preparedness plan for CWD would be useful to protect public health. If CWD is shown to be transmissible to humans in the near future, addressing public concerns will be easier if a plan is in place.

The science indicates that transmission (or not) of a zoonotic disease depends on the dose, the level of exposure and the effectiveness of any measures that are taken to mitigate exposure. The science is then balanced against industry and economic positions. It would be reasonable to take action to reduce human exposure to CWD in ways that are not too expensive and acceptable to all stakeholders. In addition, feed that includes meat and bone meal of cervids should be part of the feed ban.

The consumption and use of wild cervids is broad. The largest exposure risk is for hunters: 30-40K deer are harvested annually in each CWD positive province. Even when animals are known to be positive, people choose to eat the meat. First Nations people are heavily reliant on cervids for food and other uses (e.g. brain is used in the hide tanning process). Legally, people cannot be prohibited from eating or handling CWD infected animals. A legal means to stop consumption of infected animals is needed. It is difficult to separate CWD in wild cervids versus farmed cervids: unless there is a vaccine or other means to prevent disease transmission (biosecurity), there will continue to be cross-over.

With BSE, the disease agents are more in the brain and spinal cord, rather than the muscle. If this is also true for CWD, this could inform the information/advice regarding consumption. CWD has been shown to be present in the lymph nodes as well, and one of the most common ways of eating deer is in sausage form, which includes offal. Consumption advice depends on the distribution of infection in the animal with the intent of reducing exposure to highly infected tissue. Surveillance measures should include monitoring of hunters versus the general population of areas where there is high incidence of CWD to see if there are more cases of sCJD.

Prior to 1996, there was no evidence that animal TSEs were zoonotic. But then it became clear that vCJD was actually BSE in humans: therefore, it was a zoonosis; therefore, caution about human exposure should be exercised for other animal TSEs. The precautionary approach needs to be considered. If there is a link made to another animal TSE we have to be held accountable. What was known? What was done to mitigate risk?

Governments need to take a more direct approach and responsibility for clarification, updating, and consistency of advice. The messages currently on government websites are contradictory. On the one

hand, they state that there is no direct link. On the other, the World Health Organization recommends not consuming any part of an animal infected with a prion disease.

The Canadian government (Health Canada and the CFIA) should establish a national policies for CWD and scrapie that relate to potential threats to the human food supply, similar to regulations that exist for BSE. It will be important to determine what priorities to be addressed, areas requiring policy and regulatory changes (for example, based on existing science should SRM rules be changed?) and who needs to be informed.

Funds and efforts can be directed towards those areas and specific actions can be put in place to reduce risk. Researchers, clinicians, politicians, farmers need to work together to issue a joint statement that identifies acceptable level of risk and ways to reduce exposure. The full spectrum of stakeholders needs to be engaged, including governments, academia, industry, producer groups, hunters and consumer groups.

It will be important to acknowledge that it might be theoretical risk, but exposure can be reduced by not consuming specific animal parts (recommend SRM removal from food chain). The European Food Safety Authority (EFSA) reports could be used to support risk claim. The detection of CWD in Norway will push the need for a report/ communication piece.

Research Priorities

A reasoned, strategic, long-term plan for investment in prion research is needed – one that is implemented before the first case of human CWD, scrapie or atypical BSE occurs. It is important to invest in research capacity (people and facilities). Co-funding strategies are needed to pool resources across sectors (CWD and scrapie) and jurisdictions (states, provinces and federal governments).

An overall research strategy that defines specific outcomes would help guide and focus limited research funds by targeting areas with high potential for progress. This has been effective in Canada's beef industry, which takes a national approach to research priorities and funding.

It is also important to review what has already been done to reduce duplication, and apply new technologies as appropriate. A repository of data, research, results, etc. would be useful. Collaboration and sharing of lessons learned with colleagues are crucial.

Participants emphasized the need for research investments to:

- Define the molecular characteristics of the infectious agent;
- Identify strains;
- Define the mechanism and factors of replication;
- Define the parameters controlling interspecies transmission or lack thereof;
- Develop improved or new diagnostic tools, especially for use in the field;
- Investigate prion uptake in plants, especially food plants;
- Develop vaccines; and
- Better understand decontamination and prion destruction (for example, is there potential for alternate uses of SRM?).

CWD Research

Participants emphasized that it is important that steps to control CWD are taken now based on existing knowledge while science continues to make progress. Because it affects wildlife, CWD requires different approaches than for BSE and scrapie. Knowledge of the different species of wild cervids, their habits (movement, behaviour, knowledge of where different species intersect, etc.) and habitats are important in the management of CWD. Public education will be needed to increase awareness and reduce barriers to control measures and surveillance, for example restricted access to privately owned land.

Suggestions for CWD-focused research included:

- Research is needed to better understand the efficiency and effectiveness of current CWD control measures so as to manage the disease in wild cervids to protect the environment, ecosystems and human health. Such research must take a long-term view (5- to 10-year projects). Funding is a key challenge, as ministries of environment tend to have the lowest budgets.
- Ongoing surveillance is needed along with long-term field trials to test the results of modeling that has shown the potential to change prevalence with increased gradation, different hunting strategies, or different population densities. This will help demonstrate to the public, to landowners and to hunters the effectiveness of various control measures. Long-term funding from provinces, states and federal governments is needed to support such trials.
- There is a need to investigate CWD infection of moose. They are moving to new areas, they overlap with deer, and their feeding habitats are changing.
- Research is needed on CWD and caribou and reindeer. Canada needs to show leadership in this area, particularly in light of the detection of CWD in reindeer in Norway and the First Nations reliance on caribou.
- The effect of human intervention should be explored (for example, the effect of raising deer for antler production).

Key Messages

- The need to renew policy and regulations as science changes – both domestically and in terms of international organizations such as OIE.
- A large animal study on L-type BSE is needed to determine its potential for inter-species transmission. Such a study is challenging because it would be very expensive; would need to be funded by both private and public sectors.
- The history and knowledge of scrapie tells us that it is not a major zoonotic disease. Atypical scrapie needs more investigation to determine its zoonotic potential.
- Effective surveillance on both animal and human sides is crucial.
- Human health is the main driver, but there are other considerations (wildlife, ecosystems, environment and economy).
- For CWD, a live diagnostic test would be helpful to both cervid farmers and wildlife specialists.
- CWD's potential as a zoonotic disease remains unknown. We need to apply what is known now to do a risk assessment and to take actions for intervention and control. It might be prudent to develop a contingency plan now in case CWD does prove to be zoonotic.

Finally, participants suggested that a committee could be formed to review the outcomes of this workshop and develop strategic research priorities.

Closing Remarks

Susan Novak, Alberta Livestock and Meat Agency, thanked participants for their frank and open discussions. She noted that ALMA and APRI frequently work together on research projects. ALMA's mandate is not prion research per se but rather the industry itself – market access, productivity, and sustainability. We consider issues in terms of, what would happen if we didn't fund? We fund prion research to be proactive and to inform policy. It is important nationally and for Canada to remain credible internationally. A key message arising from the workshop is the need to convene a national level conversation to determine our priorities as a country. We need to answer questions about funding, coordination and collaboration, including with the US and internationally, how we can best enable future research, and how we can best communicate what is already known.

Ian Alexander, Canadian Food Inspection Agency, expressed appreciation that participants took the time away from their own work to share their knowledge with colleagues. As a science-based regulator, it is important to CFIA that we have these conversations with acknowledged experts in the fields so that we better understand the challenges and what the science is telling us about new directions for policy, regulations and risk. The Agency recently signed a memorandum of collaboration with EFSA, which is now even more important in light of the detection of CWD in reindeer in Norway. A number of themes emerged over the course of the workshop, including:

- Surveillance – the importance and value of surveillance, on both the animal and human sides, the need for the right type of surveillance and clear understanding of what we are tracking and why.
- Risk assessment – what is the science telling us? There are opportunities for joint risk assessment work that need to be further explored.
- Research – from basic research to create deeper understanding of prion diseases, to diagnostics and alternative control measures such as vaccines, to epidemiological work.
- Collaboration – across borders and disciplines to leverage what is happening both in Canada and in other countries.
- Communication – need to be transparent, need to determine who will communicate, what will be communicated and when.

Kevin Keough, Alberta Prion Research Institute, also expressed his appreciation to participants. He noted that APRI supports research and intervention trials that are aligned with the organization's mandate and that have an Alberta-based partner. Researchers from other provinces and international partners also have opportunity to work with APRI through a cost-sharing program in which APRI provides 75 per cent of the funding and the partner provides the remaining 25 per cent. Alberta is the major funder of prion research in Canada, but to make a difference on a national basis there needs to be other players, including regulatory policy makers from Health Canada, Environment Canada and CFIA.

Appendix A: List of Participants

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Coulthart	Michael	Public Health Agency of Canada
Czub	Stefanie	Canadian Food Inspection Agency
Delver	Larry	VM Agriculture Consulting Ltd.
Djillali	Bachir	Canadian Food Inspection Agency
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Hauer	Gerald	Government of Alberta
Hills	Bob	Health Canada
Hope	James	Animal and Plant Health Agency
Keough	Kevin	Alberta Prion Research Institute
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Laycraft	Dennis	Canadian Cattlemen's Association
Lovett	Donn	Social Media ROI
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Merrill	Evelyn	University of Alberta
Mitchell	Gordon	Canadian Food Inspection Agency
Moore	Robyn	Alberta Lamb Producers
Mohri	Shirou	Tohoku University
Murray	Noel	Canadian Food Inspection Agency
Napper	Scott	University of Saskatchewan
Novak	Susan	Alberta Livestock and Meat Agency
O'Hara	Diana	Alberta Elk Commission
Ortegon	Hernan	Government of Alberta
Parker	Kathy	Alberta Sheep Breeders' Association
Pybus	Margo	Government of Alberta
Schatzl	Hermann	University of Calgary
Schmid	Karen	Alberta Beef Producers

Seuberlich	Torsten	University of Berne
Seutter	Connie	Alberta Elk Commission
Sim	Valerie	University of Alberta
Telling	Glenn	Colorado State University
Walton	Bryan	Alberta Cattle Feeders Association
Will	Bob	National CJD Surveillance Unit