SLU

Welcome to a conference on

Prion diseases in animal and man

18 November, 2019, 09.00 -17.00

Location: Park Inn by Radisson
Storgatan 30, Uppsala, Sweden

Organizers:
Department of Anatomy, Physiology and Biochemistry and
Department of Wildlife, Fish, and Environmental Studies
with help from Swedish Centre for animal welfare
and sponsored by SLU Future Animals, Nature and Health

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Abstract and program

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Department of Anatomy, Physiology and Biochemistry and Department of Wildlife, Fish, and Environmental Studies, Swedish University of Agricultural Sciences. SLU Future Animals, Nature and Health grant the meeting/conference. The meeting/conference is arranged with help from Swedish Centre for Animal Welfare (SCAW), Swedish University of Agricultural Sciences, SLU, Uppsala Sweden.

Program

Time	Subject	Speaker
09.00-09.50	**Fika and registration**	Park Inn
09.50-09.55	Information by Park Inn	Park Inn
0.9.55-10.00	Welcome and introduction	Margareta Stéen, Swedish University of Agricultural Sciences (SLU)
10.00-10.30	Polymorphism in PrP and its relevance for moose and public health/Polymorfism hos PrP och dess relevans för älgen och folkhälsan	Sofia Mikko, SLU
10.30-11.00	The chemistry of amyloids and prions/Amyloiders och prioners kemi	Per Hammarström; University of Linköping (LiU)
11.00-11.30	A reductionistic approach to investigation of mammalian prion diseases/En reduktionistisk strategi för studier av däggdjurs prionsjukdomar	Sofie Nyström, LiU

11.30-12.00	Experimental models of prion diseases/Experimentella modeller av prionsjukdomar	Walker Jackson, LiU
12.00-12.30	Detection of aggregated prion proteins through rolling circle amplification of proximity ligation immuno markers/Detektion av aggregerade prionproteiner med PLARCA.	Erik Pelve, SLU
12.30-13.30	**Lunch**	
13.30-14.00	Chronic wasting disease (CWD) strain emergence and *PRNP* poly-morphism in North America/CWD olika stammar och PRNP polymorfism i Nordamerika	Sabine Gilch, University of Calgary, Canada
14.30-15.00	Chronic Wasting Disease (CWD) in Norwegian cervids/Skrantesjuke (avmagringssjuka) hos norska hjortdjur	Jørn Våge, Norwegian Veterinary Institute (NVI)
15.00-15.30	**Fika and mingel**	
15.30-16.00	The prion strains affecting the Norwegian CWD cases are different from those reported in the North American CWD cases/ Prionstammar hos norska CWDfall avviker från de rapporterade i Norge.	Sylvie Benestad, NVI
16.00-16.30	Chronic Wasting Disease (CWD) in Sweden/Avmagringssjukan i Sverige	Maria Nöremark, Statens veterinärmedicinska anstalt (SVA)
16.30-17.00	Early warning systems for diseases with environmental persistence /Varningssystem för sjukdomar med miljöbeständighet - behov av övervakning och analys	Frauke Ecke, Dept. of Wildlife, Fish, and Environmental Studies, SLU
17.00-17.05	Thanks and Goodby	Margareta Stéen, SLU

INTRODUCTION

MARGARETA STÉEN

Margareta Stéen, Scientist (Assoc. prof in Wild Animal Health) and supervisor at the Dept. of Anatomy, Physiology and Biochemistry, and Vice Director at the Swedish Centre for Animal Welfare (SCAW), Swedish University of Agricultural Sciences (SLU), Uppsala Sweden.

Presentation: *I am engaged in wildlife research as well as in animal welfare. My interest and research in wildlife medicine is connected with environment and society, with basic and advanced questions in single wildlife and semi-domesticated species, as well as holistic on a global arena.*

Chronic Wasting Disease (CWD) has been detected in Scandinavian deer, in wild reindeer and moose in Norway, a moose in Finland and at three moose in Sweden. CWD is a transmissible brain disease (TSE) as well as Scrapie in sheep, BSE in cows and Creutzfeldt-Jacobs disease in humans. The prion protein (PrP) is a body protein in mammals that in altered form gives rise to disease in humans and animals. For Sweden and the Nordic countries, knowledge about prions is limited and limited research has been done in this area in our part of the world. With the findings of CWD in Scandinavia, EU has decided on a monitoring of deer. Monitoring is important for detecting cases of the disease and information is important for epidemiological analyzes. But ONLY monitoring is not sufficient for understanding the prevalence, spread and source of prion diseases, major research efforts are needed. One of the moose diagnosed with CWD in Sweden had a GPS (global positioning system) collar and analysis of movement of this and other diseased animals can give important insights on potential contamination and risk areas.

ABSTRACTS

SOFIA MIKKO

Polymorphism in PrP and its relevance for moose and public health/ Polymorfism hos PrP och dess relevans för älgen och folkhälsan

Mikko S[1], Arifin M[1,2], Linné T[1], Ågren E O[3], Laikre L[4], Ryman N[4], Thulin C-G[1], Stéen M[1]. [1]Dept. of Anatomy, Physiology and Biochemistry, Swedish University of Agricultural Sciences, Uppsala, Sweden, [2]Gilch Lab, Dept. of Ecosystem and Public Health, University of Calgary, Canada, [3]Dept. of Pathology and Wildlife Diseases, National Veterinary Institute, Uppsala, Sweden, [4]Dept. of Zoology, Stockholm University, Stockholm, Sweden.

Sofia Mikko, Researcher, teacher, Dept. of Animal Breeding and Genetics and Dir. of Undergraduate Studies at the Dept. of Anatomy, Physiology and Biochemistry, Swedish University for Agricultural Sciences (SLU), Uppsala, Sweden.

***Presentation**: I have a strong interest in understanding the biology behind different traits and diseases in animals. I search for more knowledge about biologic functions to investigate the genome, and by functional genomics, to understand the underlying biology.*

A present missense mutation in the *PRNP* gene of Scandinavian moose leads to a change of lysin (K) to glutamine (Q) in amino acid position 109, which may affect the proteolytic processing of PrP. Amino acid variations at this critical position in PrP could potentially influence pathology, disease susceptibility, incubation time, and disease transmission between species, if the mutated PrP is transformed into prions. We have investigated allele- and genotype frequencies of this potential harmful mutation in past and present Swedish moose populations. We have also investigated the protein cleavage pattern to elucidate potential associations between the polymorphism and moose health. In moose affected by Moose Wasting Syndrome (MWS, Älvsborgssjukan), Cu and Zn levels are known to be severely altered, and research has shown that major cleavage sites of PrP^C may vary in response to Cu2+ and Zn2+. Therefore, we further studied the association between proteolytic pattern, metal ion level, genotype and MWS. Our working hypothesis is that small changes in a PK-sensitive prion protein could be associated with health condition in wild and domestic ungulates. Moreover, mutations that introduce small changes in prion protein sequence, and are spread in a population, could over time increase the risk of induction of a prion strain. The clinical picture and transmissibility may then vary, depending on the type of previous PrP mutation. This could possibility be of concern, especially considering the unknown background of the recent outbreak of Chronic Wasting Disease (CWD) in reindeer, moose, and red deer in Norway. Recently, CWD cases have also been reported in moose in Sweden and Finland.

PER HAMMARSTRÖM

The chemistry of amyloids and prions/Amyloiders och prioners kemi.

Per Hammarström, Professor, IFM-Chemistry, Linköping University, Linköping, Sweden.

Presentation: *I have worked for over 20 years in the field of protein folding, molecular chaperone function, protein misfolding and amyloid formation. I received my PhD at LiU 2000, Post doc at Scripps Research 2000-2002, and became Professor of Protein Chemistry at LiU 2008. I have been awarded the Göran Gustafsson Prize 2014, the Tage Erlander Award 2011 and The Svedberg Prize 2009.*

Proteins are generated as the active molecules of the cell, being transcribed and translated from genes of our genome. To function properly, a protein must adopt a specific folded three-dimensional structure, also known as the native conformation. Folding occurs spontaneously under permissive conditions as shown by Anfinsen in the 1960:ies. The sequence of DNA determines the sequence of amino acids in a protein which in turn determines the fold - like a self-folding origami. Occasionally normal proteins misfold and thereby aggregate and accumulate in living tissue. Protein misfolding and aggregation is associated with a large group of diseases, e.g. Alzheimer's disease, Creutzfeldt Jakob disease, and systemic amyloidosis. Here misfolded proteins form amyloid fibrils which are highly symmetric fiber structures that spawn by recruiting protein molecules for growth and self-propagation. This mechanism appears very similar for all known amyloid and prion diseases. Basic research in this field has been instrumental for the understanding that protein aggregation cause disease but not how nor how to target this process. The issue is a molecular problem. Misfolding cause conformational polymorphism, i.e. a multiple of conformations, and appear to counter the Anfinsen postulate of one-sequence one-fold. This polymorphism is apparent in common diseases like Alzheimer's disease but has been mostly understood in the field of prions describing so called prion strains. Here identical proteins with different structures determines disease phenotype. By using protein chemistry and chemical biology approaches we try to understand the molecular mechanisms behind amyloid fibril polymorphism and its importance for amyloid and prion diseases. More about our research: https://liu.se/en/research/hammarstrom-lab

SOFIE NYSTRÖM

A reductionistic approach to investigation of mammalian prion disease/En reduktionistisk strategi för studier av däggdjurs prionsjukdomar.

Sofie Nyström, Assoc. prof., protein chemist, IFM-Chemistry, Linköping University; Linköping, Sweden.

Presentation: *I work with proteins that misfold into amyloid and cause disease, eg Aβ causing Alzheimer´s disease, SAA causing systemic amyloidosis and PrP causing prion disease. In particular, the connection between amyloid structure and disease progression has been in focus during the last decade.*

Chronic wasting disease (CWD) is one of many prion protein (PrP) associated diseases found in mammals. Other prion disease, often referred to as TSEs (Transmissible spongiform encephalopathy) are BSE in cattle, Scrapie and Nor98 in sheep and goats and Creutzfeldt Jakob's disease in humans. Prion disease propagate in the host mechanism by a domino effect, starting with one misfolded prion particle that recruits the PrP expressed by the host cell. The culprit prion particle can arise within the host or be acquired from the outside via different routes of transmission. The former leading to a sporadic prion disease and the latter giving rise to an infectious prion disease. PrP is present in all mammals and is most abundantly present on the surface of neurons. The amino acid sequence/primary sequence of PrP differs between different species. There are also several known intra species differences in the amino acid sequence that modulate disease susceptibility and progression. Some are protective and some dominantly give rise to disease. For most infectious disease, there is a species barrier that prevents or delays disease transmission between different species. The same is true for prion infection. However, the species barrier for prion disease is not absolute, as became evident in the BSE/vCJD outbreak in 1980-1990:ies. Over 50 different species are known to be affected by prion disease. Most of these have been infected by BSE. The possibility to express mammalian proteins in bacterial cells and purify them in test tubes (recombinant expression) has revolutionized the understanding of proteins, their natural function and their roles in disease processes. In our lab we have worked with recombinantly expressed prion proteins during the past 15 years. We study the impact of naturally occurring and synthetic point mutations of the human PrP sequence. Several other mammalian sequences have also caught our attention. During latter years, we have increased our interest in PrPs from cervids. Using our cost- and time efficient seeding assay (similar to RT-QuIC) we have analyzed several brain homogenates from the Norwegian cases of CWD to see if there is potential in these samples to convert native PrPs. We observe a striking specificity and PrP sequence dependence when seeding cervid and human PrP sequences with homogenates from CWD positive and negative moose and reindeer. The implications of these results will be speculated on.

WALKER JACKSON

Experimental models of prion diseases/Experimentella modeller av prionsjukdomar

Walker Jackson, Senior Lecturer, Dept. of Clin. and Exp. Med. (IKE), Div. of Neurobiology (NEUROB), Linköping University; Linköping, Sweden.

Presentation: *I study how specific brain regions are targeted in various neurodegenerative diseases and how gene regulation in specific cell types is affected by neurodegenerative disease and sleep loss, using genetically encoded tools and next generation sequencing techniques. Manipulation of gene sequence and activity with CRISPR/Cas based methods is also a strength of the lab.*

Chronic wasting disease (CWD) is unique among prion diseases in that it affects animals living in the wild. This poses challenges for basic research when the living conditions between diseased and non-diseased animals needs to be as similar as possible. Although consistent living conditions are readily achieved by maintaining animals indoors, this is difficult to apply to large animals such as deer or moose, especially when many replicates and many parallel experiments are desired. However, this is not an issue for experimental rodents. Moreover, some rodents are easy to genetically modify, enabling studies not feasible in large animals. This lecture will present some important findings about prion diseases through studies with rodent models and highlight how applying these methods to Scandinavian CWD studies will provide an invaluable system to characterize and monitor these emerging diseases.

ERIK PELVE

Detection of aggregated prion proteins through rolling circle amplification of proximity ligation immune-markers/Detektion av aggregerade prionproteiner med PLARCA

Erik Pelve, PhD, lecturer, assistant director of department studies, Dept. of Anatomy, Physiology and Biochemistry (AFB), Swedish University for Agricultural Sciences (SLU), Uppsala, Sweden.

Presentation: *I have a background in microbial cell biology and ecology, and did my postdoc at MIT in USA and is now working on the gut microbiome.*

Proximity Ligation Assay - Rolling Circle Amplification (PLARCA) is a sensitive method to detect aggregated prion proteins (PrP). The method utilizes detection by ligation and rolling circle amplification of two nucleotide ligands attached to antibodies specific for PrP. In this way, only antibodies bound to PrP in close proximity to each other will give a signal, while antibodies bound to single PrP will not give signal. This increased sensitivity give PLARCA the potential to detect aggregated PrP in low concentrations. We have utilized this technique to detect aggregated PrP in brain tissue from sheep diagnosed with scrapie. We have also detected aggregated PrP in moose and deer diagnosed with Chronic Wasting Disease (CWD). By applying this method to preserved samples from moose sampled in the 1980:ies diagnosed with Moose Wasting Syndrome (MWS, Älvsborgssjukan), we can see a signal that suggest the presence of aggregated PrP.

SABINE GILCH

CWD strain emergence and Prnp polymorphism in North America/ CWD olika stammar och PRNP polymorfism i Nordamerika

S Gilch, M Arifin, S C Chang, S Hannaoui, Calgary Prion Research Unit, Dept. of Comparative Biology and Experimental Medicine, Faculty of Veterinary Medicine, University of Calgary; Calgary, Canada.

Sabine Gilch, Calgary Prion Research Unit, Dept. of Comp. Biology and Exp. Med., Faculty of Veterinary Medicine, University of Calgary; Calgary, Canada, Email: sgilch@ucalgary.ca

Presentation: *I am working with colleagues to understand Chronic Wasting Disease (CWD), a highly infectious and fatal neurological disease that is spreading across North America and threatening elk, moose, mule and white-tailed deer. Caribou are also susceptible to CWD, and new strains of the disease may threaten more wild mammals.*

Chronic wasting disease (CWD) is a prion disease of wild and farmed cervids, including deer, elk, reindeer and moose in North America, South Korea and Scandinavia. Prion diseases are transmissible and strictly fatal neurodegenerative disorders that can occur in humans and animals. Prions consist of a distorted form, called PrP^{Sc}, of a host-encoded protein, designated PrP^{C}. PrP^{Sc} is prone to build up clumps or protein aggregates in the brain, which eventually results in the death of neurons. CWD-infected animals accumulate prions not only in the brain, but also in muscle tissue, antler velvet, tissues of the immune system, and release prions into the environment through feces, urine and saliva. This contributes to transmission between animals, the geographic expansion and the annually increasing case numbers of CWD. Natural transmission of CWD to non-cervid species or humans has not been reported to date. However, the discovery of increasing numbers of CWD strains, conformational variants of prions that can have a different host range raises concerns that strains may exist which are able to cross the barrier to humans or wild or domesticated non-cervid animals. Understanding factors that can trigger the emergence of CWD prion strains and characterize their profiles is important for assessment of transmission risks and development of management strategies.

JØRN VÅGE

Chronic Wasting Disease (CWD) in Norwegian cervids/Skrantesjuke (avmagringssjuka) hos norska hjortdjur.

J. Våge, S. L. Benestad, P. Hopp, K. Madslien, C.G. Das Neves, T. Vikøren and H. Viljugrein, Veterinary Institute, Oslo, Norway.

J. Våge, Veterinarian (DVM), PhD (molecular genetics), Researcher, Veterinary Institute (NVI), Oslo, Norway.

Presentation: *I work with wildlife health and I am the institutes coordinator and project leader for Chronic Wasting Disease (CWD). The role as CWD-coordinator is substantial in liaison activity towards governmental bodies responsible for regulation, animal disease and wild species management. Apart from CWD research, I work with wildlife health issues in general and tasks of contingency work of wildlife diseases.*

In 2016, Chronic Wasting Disease (CWD) was detected in Norway. This was the first European occurrence of CWD and the first natural occurrence in reindeer (*Rangifer tarandus*). Historically, CWD has been a health challenge for deer in North America. The disease was described clinically in Colorado in the late 1960s and recognized as a transmissible spongiform encephalopathy (TSE) in 1980. Today, CWD is a well-known prion disease in deer, in line with similar disease in sheep (scrapie), cattle (BSE) and human (Creutzfeldt-Jakob Disease, CJD). CWD is a 100% fatal neurodegenerative disorder without known possibility of treatment or prevention. North American incidence has increased significantly over the past 15-20 years. In Norway CWD was detected in wild reindeer, living isolated under alpine conditions (Nordfjella). In order to limit the possibility of spread, the entire sub-population (2424 animals) was removed and tested for the presence of infection. Post detection, the national monitoring program for CWD was expanded from 2016 and now tests about 30,000 deer (moose, reindeer, red deer and roe deer) annually. By October 2019 the total number of animals tested, passed 90 000. Of 42863 reindeer (10 695 wild reindeer and 32 161 domestic reindeer), 19 wild reindeer have tested positive. 21 035 moose have been tested with 5 positive. Only one of 18 816 red deer has been found positive for abnormally folded prion protein (Prp^{SC}).

SYLVIE BENESTAD

The prion strains affecting the Norwegian CWD cases are different from those reported in the North American CWD cases/Prionstammar hos norska CWD-fall avviker från de rapporterade i Nordamerika

Benestad SL[(1)], Tran L[(1)], Vuong T[(1)], Madslien K[(1)], Pirisinu L[(2)], Vaccari G[(2)], Bian J[(3)], Moreno JA[(3)], Kim S[(3)], Telling GC[(3)], R Moda F[(4)], Bistaffa E[(4)], Diack A[(5)], Andréoletti O[(6)], Nonno R[(2)], Vikøren T[(1)], Våge J[(1),] (1) Norwegian Veterinary Institute, Oslo, Norway, (2) Istituto Superiore di Sanità, Department of Veterinary Public Health, Nutrition and Food Safety, Rome, Italy, (3) Colorado State University, Prion Research Center, Fort Collins, CO USA, (4) Istituto Neurologico Carlo Besta, Milan, Italy, (5) The Roslin Institute, University of Edinburgh, UK, (6) INRA/ EVT Toulouse, France

Sylvie Benestad, PhD (Neurophysiology), Senior researcher, Professor competency, Veterinary Institute (NVI), Oslo, Norway.

***Presentation**: I work almost exclusively with TSE diagnostic and research and is the head of the National Reference Laboratory for TSE in animals. I am working with aim to characterize the CWD strains detected in Norway and compare them with CWD detected in North America. I am together with others working on the establishment of ultra-sensitive methods to detect small amounts of prions in different tissues and excreta, the detection of prions in living animals, as well as genetics of the Norwegian cervid populations. I obtained my PhD in Neurophysiology in 1994 as a collaboration between the University of Marseille-Aix (France) and the University of Oslo (Norway). I have been working at the Norwegian Veterinary Institute since end of 1997.*

Chronic wasting disease (CWD) has been detected in North America (Colorado) for the first time in 1967 and is now diagnosed in captive and free-ranging cervids [mule deer (*Odocoileus hemionus*), white-tailed deer (*Odocoileus virginianus*), elk/wapiti (*Cervus canadensis*) and moose (*Alces alces*)] in 26 American states and 3 Canadian provinces. CWD is still spreading despite considerable efforts to restrain the disease. CWD has also been diagnosed in red deer (*Cervus elaphus*) and sika deer (*Cervus nippon*) in South Korea as the result of importing CWD infected elk from North America. CWD is considered as the most contagious of the prion diseases, transmitted by direct contact from deer to deer, or in some extend from mother to offspring, or indirectly through contact with environment contaminated by feces, saliva, urine or carcass from infected animals. In April 2016 CWD was diagnosed for the first time in Europe, in a wild reindeer (*Rangifer tarandus*), in the Nordfjella area in Southern Norway (Benestad et al. 2016). CWD in the Norwegian reindeer showed characteristic indistinguishable from those of the CWD cases identified in North America. Preliminary bioassay results show that both the CWD type of the moose that displayed clear differences in the host (Pirisinu et al. 2018), and the CWD prion type in reindeer, even if displaying similarities with the North American CWD, are different from what has been reported in North America. Finland and Sweden have diagnosed CWD in respectively one and three old moose, and the preliminary analyses revealed similarities with the CWD type of the Norwegian moose. Further research is ongoing to characterize the disease, especially the red deer, which shows some peculiar characteristics also distinct from reindeer and moose type. This suggests that multiple strains affect European cervids and that they are different from the ones described in North America.

MARIA NÖREMARK

Chronic Wasting Disease (CWD) in Sweden/Avmagringssjukan i Sverige

Maria Nöremark, PhD (Veterinary Epidemiology), Dept. of disease control and epidemiology, National Veterinary Institute (SVA), Uppsala, Sweden.

***Presentation**: I work with surveillance of prion-diseases, and have done that since 1999, starting with BSE (Mad Cow Disease, Galna kosjukan), and I am involved in European Research projects to understand the epidemiology of atypical scrapie.*

In March 2019 the first Swedish case of Chronic Wasting Disease (CWD) was detected in a free ranging moose (*Alces alces*) in Norrbotten county. In May, a second case was detected, and in September a third case. All the cases were in female moose and all were detected in the same county. The two first cases were both 16-year-old animals euthanized after being observed emaciated with behavioural changes, while the third case was in a 10 -year-old moose shot during ordinary hunting. The Swedish cases shows similar features with cases of atypical CWD (Nor16CWD) previously described in Norwegian moose, such as being confirmed in older moose with brain and brainstem positive, but so far with no detectable prions in lymph-node. Further analysis of the cases is ongoing, e.g. at the National Veterinary Institute of Norway, which is OIE reference laboratory for CWD, and the European Union reference laboratory for TSE in Italy. The detection of a three case of CWD in Swedish moose in a limited geographical area can easily give the impression that a contagious variant of the disease present in the region, but there may be other explanations. It is hypothesised that the CWD cases in older moose may not be contagious, but rather a spontaneous variant of CWD occurring in old animals (Prisinu et al*). Spontaneous prion diseases occur in other species (e.g. atypical BSE and atypical scrapie), predominantly in older animals, and detected prevalence vary between the species. Increased sampling in areas where cases in old moose have been detected will contribute with epidemiological data indicating if these cases in old moose are contagious or not. In the area where the three cases were found, it has been decided to sample all adult moose shot during the hunting season, and a sample of reindeer during the slaughter season. The region has a hunting management which leads to a high proportion of old female moose in the local population. As age seem to be an important relevant factor, jaws are collected from the sampled animals to enable determination of age. Surveillance in the rest of the country is just as important and ongoing. The surveillance had a late start and too few animals have been sampled to draw any conclusion. A map displaying surveillance and cases is available at: https://www.sva.se/en/animal-health/wildlife/map-of-chronic-wasting-disease-cwd. *Prisinu et al 2018, Novel Type of Chronic Wasting Disease Detected in Moose (Alces alces), Norway, Emerg Infect Dis. 2018 Dec;24(12):2210-2218.

FRAUKE ECKE

Early warning systems for diseases with environmental persistence/Varningssystem för sjukdomar med miljöbeständighet - behov av övervakning och analys

Frauke Ecke, Associate Professor, Dept. of Wildlife, Fish, and Environmental Studies, Swedish University for Agricultural Sciences (SLU), Umeå, Sweden.

Presentation: *My background is in landscape ecology of rodents and my research interest is in disease ecology. In my work, I integrate environmental and population monitoring with targeted field studies and experiments towards increased understanding of pathogen transmission and disease outbreaks.*

Many wildlife-borne diseases are horizontally transmitted among animal hosts via close non-sexual contact such as grooming, biting, scratching or aerosols. To prevent or mitigate such contact, we need good knowledge on behaviour, including movement, of potential host species. Information on where, when and why susceptible animals aggregate increases our understanding on transmission ecology. In addition, many pathogens causing wildlife-borne diseases show environmental persistence, i.e. the pathogen can survive – for varying and in many cases unknown periods – outside animal reservoirs. Chronic wasting disease (CWD) is an example of a disease with both horizontal transmission mode and environmental persistence. Early warning systems are important to mitigate the magnitude of outbreaks of infectious diseases. Traditionally, early warnings of outbreaks of CWD and other wildlife-borne diseases rely on disease alerts, i.e. early reports of animal and/or human disease. However, such warnings require readiness with short notice in case of an outbreak. Here, I present a framework for surveillance and early warning of CWD in Sweden. The framework builds on comprehensive and existing Swedish environmental monitoring programs and suggests amongst others testing the use of animal sentinels for outbreaks of CWD. Such an approach would also further our understanding of the ecology of CWD.