SURVEILLANCE OF INFECTIOUS DISEASES IN ANIMALS AND HUMANS IN SWEDEN 2019

Chapter excerpt -
Leptospirosis

SVA NATIONAL VETERINARY INSTITUTE
Jordbruksverket Swedish Board of Agriculture
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Editor: Karl Ståhl
Department of Disease Control and Epidemiology, National Veterinary Institute (SVA), SE-751 89 Uppsala, Sweden.

Authors: Charlotte Axén, Mia Brytting, Ioana Bujila, Erika Chenais, Rikard Dryselius, Helena Eriksson, Pernille Etterlin, Eva Forsgren, Malin Grant, Gittan Gröndahl, Gunilla Hallgren, Anette Hansen, Gete Hestvik, Marika Hjertqvist, Mia Holmberg, Cecilia Hultén, Helena Höök, Cecilia Jernberg, Jerker Jonsson, Ulrika König, Elina Lahti, Emelie Larsdotter, Mats Lindblad, Anna Lundén, Emma Löf, Hans-Olof Nilsson, Oskar Nilsson, Maria Nöremark, Anna Ohlson, Ylva Persson, Karin Persson-Waller, Thomas Rosendal, Karl Ståhl, Robert Söderlund, Kaisa Sörén, Magnus Thelander, Karin Troell, Anders Wallensten, Per Wallgren, Stefan Widgren, Ulrika Windahl, Beth Young, Nabil Yousef, Siamak Zohari, Erik Ågren, Estelle Ågren, Elina Åsbjer

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Reporting guidelines: Reporting guidelines were introduced in 2018 for those those chapters related to purely animal pathogens. The guidelines build on experiences from several EU projects, and have been validated by a team of international experts in animal health surveillance. The aim is to develop these guidelines further in collaboration within the global surveillance community and they have therefore been made available in the form of a wiki on the collaborative platform GitHub (https://github.com/SVA-SE/AHSURED/wiki). Feel free to contribute!

Layout: The production of this report continues to be accomplished using a primarily open-source toolset. The method allows the source text, produced by authors, to be edited independently of the template for the layout which can be modified and reused for future reports. Specifically, the chapter texts, tables and captions are authored in Microsoft Word and then converted using pandoc and R to the LaTeX typesetting language. Most figures and maps are produced using the R software for statistical computing. Development for 2019 has further improved the importing of content from Word to LaTeX. The method can now import text, tables and figure captions from Word, as well as the newly designed 'IN FOCUS' sections of some chapters. The tool is available as an R-package at GitHub (https://github.com/SVA-SE/mill/). This year the report was also built with a continuous integration pipeline on Microsoft's Azure DevOps platform, allowing every committed change to the content to be built and tested automatically. The report generation R-package and process was designed by Thomas Rosendal and Stefan Widgren. In 2019, figures and the final typsetting were done by Wiktor Gustafsson and Thomas Rosendal with contributions from the report authors.

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SVA NATIONAL VETERINARY INSTITUTE

visiting address. Ulls väg 2B **address.** 751 89 Uppsala
telephone. +46 18-67 40 00 **fax.** +46 18-30 91 62
e-mail. sva@sva.se **web.** www.sva.se

Leptospirosis

BACKGROUND

Several species of the spirochetal bacterium *Leptospira* can cause leptospirosis. All mammals, including humans, are susceptible to one or several *Leptospira* serovars. Leptospirosis occurs worldwide but the dominant serovars vary by region. Cattle and pigs are considered to be reservoirs for *L.* Hardjo and *L.* Pomona, respectively. Serovars known to infect and cause clinical disease in dogs include *L.* Icterohaemorrhagiae, *L.* Canicola, *L.* Grippotyphosa, *L.* Pomona, *L.* Sejroe and *L.* Australis. These are all serovars also known to infect and cause disease in humans.

Serovars that can cause disease in horses include *L.* Icterohaemorrhagiae, *L.* Grippotyphosa, *L.* Pomona and *L.* Bratislava.

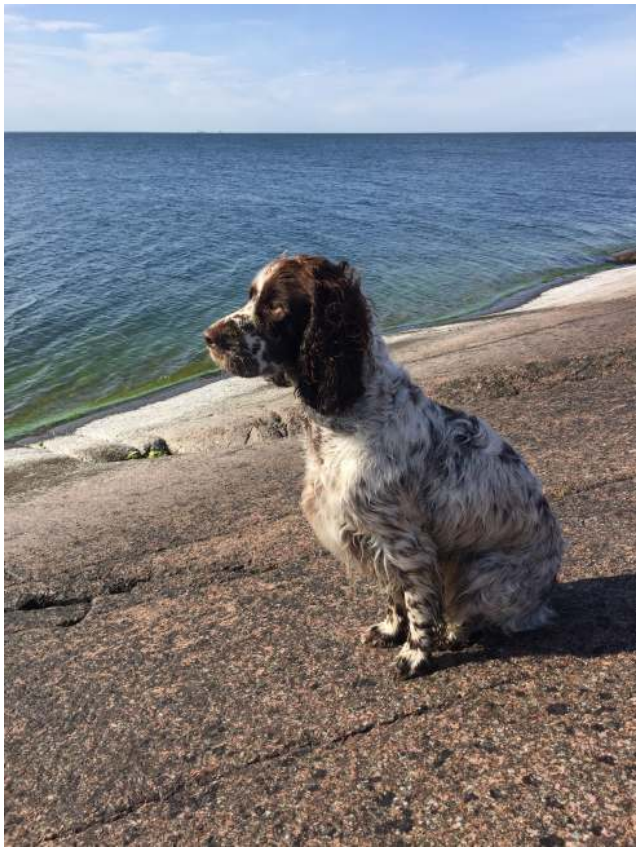
Seropositivity to *Leptospira* spp other than *L.* Pomona are occasionally confirmed in Swedish pigs, mostly to an indigenous serovar of *L.* Sejroe, *L.* Bratislava and *L.* Icterohaemorrhagiae.

An even lower prevalence to the indigenous strain of *L.* Sejroe in cattle has been recorded.

Between 1994 and 2006 sampling and testing for antibodies to *L.* Hardjo and *L.* Pomona in cattle and pigs respectively, was performed each year and after 2006 every third year. The commercial cattle and pig populations in Sweden are considered free from *L.* Hardjo and *L.* Pomona based on only negative results from this surveillance system.

Surveillance in other animal species including dogs and horses is passive only.

Leptospira may be transmitted directly between animals or environmentally (i.e. indirectly). The bacteria do not multiply outside the host but may survive for long periods in the environment.



Several *Leptospira* serovars known to be pathogenic for humans as well as other animal species have been shown to be present in both healthy and severely ill Swedish dogs. Seropositivity is however currently underreported and prevalence of clinical disease and death in Swedish dogs due to leptospiral infection is currently not readily available. Photo: Mia Holmberg.

DISEASE

Animals

L. Hardjo is one of several pathogenic serovars and is associated with disease in cattle, sheep, goats and horses. In cattle, infections may be acute or chronic; asymptomatic, mild or severe. Acute disease is more often seen in calves. Disease in adults may go unnoticed, because the early clinical signs of fever and depression are often transient and mild. Infected herds may have problems with abortions, decreased fertility and decreased milk yield as well as increased mortality in calves.

The clinical signs in sheep and goats are similar to those in cattle. Both sheep and cattle can act as asymptomatic reservoir hosts.

Leptospira infections in pigs may also be asymptomatic or may give rise to reproductive failure. In piglets, fever, gastrointestinal disorders and jaundice may be present.

The clinical presentations in dogs infected with *Leptospira* range from subclinical to severe clinical illness and death; liver and/or kidney affection as well as varying degrees of vasculitis is typical. A peracute pulmonary form with high mortality rate is not uncommon.

In horses, most infections are subclinical and when clinical signs are present, they resemble those seen in dogs. Late abortions and recurrent uveitis have also been described.

Humans

Leptospirosis in humans ranges from asymptomatic or mild influenza-like illness to a severe infection with renal and hepatic failure, pulmonary distress and death.

LEGISLATION

Animals

Since 2004, leptospirosis is a notifiable disease on laboratory confirmation in Sweden (SJVFS 2013:23), in all animal species concerned. Single serologically positive samples are reported. Reporting is not serovar specific *i.e.* to which serovar or serovars antibodies are detected is not reported.

Based on the legislation on testing of animals (SFS 2006:806), the Swedish Board of Agriculture can decide to initiate an epidemiological investigation in case of clinical disease consistent with leptospirosis in animals.

Humans

Leptospirosis in humans is notifiable according to the Communicable Disease Act (SFS 2004:168 with the amendments of SFS 2013:634).

SURVEILLANCE

Animals

Active surveillance in cattle and pigs is at present performed every third year. The aim is to demonstrate freedom from *L.* Hardjo in cattle and *L.* Pomona in pigs. Animals sampled for export and in breeding centres adds to the active surveillance.

All serological analyses included in the active surveillance are performed at the National Veterinary Institute. The diagnostic test used for *L.* Hardjo is an indirect ELISA (PrioCHECK® *L.* Hardjo, Antibody detection ELISA, Lelystad, Holland) for both serum and bulk milk samples. Positive serum samples are further tested with MAT (Microscopic agglutination test) with results reported as positive at 1:100 or above. For positive or doubtful ELISA results on bulk milk samples, an investigation is carried out in the herd and additional individual samples are taken. Antibodies against *L.* Pomona are analysed using the microscopic agglutination test (MAT) with results reported as positive at 1:100 or above.

The surveillance in cattle is based on serum and bulk milk samples selected by systematic random sampling from the surveillance programme for bovine viral diarrhoea virus (BVDV) and evenly distributed throughout the sampling period. See chapter on BVDV for details on sampling and population. The surveillance was designed using a between-herd design prevalence of 0.2%, a within-herd design prevalence of 40% (based on anticipated prevalence in naïve herds) and a risk of introduction of 1 in 50 years. In domestic pigs, the active surveillance is based on samples collected for the abattoir sampling part of the surveillance carried out by Farm & Animal Health for porcine reproductive and respiratory syndrome (PRRS). See chapter on PRRS for details on sampling and population. The surveillance was designed using a between-herd design prevalence of 0.5%, a within-herd design prevalence of 40% and a risk of introduction of 1 in 25 years.

The number of samples and herds needed is calculated yearly taking the outcome of the surveillance in previous years into account. For 2019, the calculated number of samples required for the active surveillance of *L.* Hardjo in cattle was 450 bulk milk samples and 1100 serum samples and for *L.* Pomona in pigs 405 serum samples.

Passive surveillance in animals including dogs and horses consists of mandatory reporting of positive results from onsite tests detecting antibodies used at veterinary clinics, PCR-positive samples, and seropositivity confirmed at laboratories, including titers as low as 1:100 regardless of serovar. Furthermore, all positive results are reported regardless of whether clinical suspicion of disease is present or if previous vaccination might be the cause of the detected antibodies. Serum samples submitted to the National Veterinary Institute for MAT-testing are currently tested for L. Icterohaemorrhagiae, L. Canicola, L. Grippotyphosa, L. Bratislava, L. Saxkoebing, L. Sejroe, L. Automnalis and sometimes L. Australis.

Humans

Notification of human cases is mandatory and surveillance is based on identification of the disease by a treating physician or by laboratory diagnosis. Both are obligated to report identified cases to the regional and national level to enable further analyses and adequate intervention measures.

RESULTS

Animals

During 2019, 1089 serum samples and 471 bulk milk samples were analysed in cattle and 390 serum samples in pigs. All cattle samples were negative for *L.* Hardjo antibodies and all pig samples were negative for antibodies to *L.* Pomona. With these results it is concluded that the active surveillance in cattle and pigs in 2019 fulfilled the purpose to demonstrate freedom from disease at the specified level.

In dogs, thirty leptospira-positive laboratory analyses were reported of which twenty (60%) from the National Veterinary Institute. The National Veterinary Institute reported thirteen seropositive and seven PCR positive analyses. Methods used in the remaining 26% of reported results, including whether a validated test-method was used or not, is unknown. The reasons for samples being submitted to the National Veterinary institute include clinical suspicion of acute disease as well as sampling of clinically healthy dogs and horses due to export requirements or suspected leptospirosis in other animals in the household.

Furthermore, a serologically positive sample was reported from one cat and one pig, respectively. The pig was sampled as part of an investigation of reproductive failure and had a positive serological reaction to *L.* Icterohaemorrhagiae. After further investigation in the herd including paired serological samples with no increase in titers to *L.* Icterohaemorrhagiae it could be concluded that the reproductive failure was not caused by infection with *Leptospira.*

One seropositive horse was reported during 2019, which equals the average yearly number of reported cases since 2014: one horse yearly.

Humans

In 2019, seven cases of leptospirosis were reported. The median age was 34 (range 23–49 years) and five of the cases were male. Two of the cases were reported to have acquired their infections in Sweden. Five cases were noted as infected abroad, three in Asia one in Central America and one in Africa. One of the cases of domestic leptospirosis was identified during the summer 2019. The case had been bitten by a rat two weeks before symptom onset and suffered from kidney failure and jaundice and was admitted to hospital. Serum samples were analysed with one week between sampling dates. The first sample was positive in PCR but negative in ELISA. The second sample was positive in ELISA

but negative in PCR illustrating the development of the disease. The case was diagnosed with Weil's disease, the severe form of leptospirosis, and was treated with relevant antibiotics and was fully recovered. The incident is regarded as a very rare event in Sweden.

DISCUSSION

Leptospirosis occurs worldwide, but the predominant serovars vary by geographic region. The disease is an important zoonosis as well as being associated with reproductive losses in livestock causing significant economic costs worldwide.

The commercial cattle and pig populations in Sweden are considered free from *L.* Hardjo and *L.* Pomona based on only negative results from the surveillance system since 1994. Seropositvity to *Leptospira* spp other than *L.* Pomona are occasionally confirmed in Swedish pigs, mostly to an indigenous serovar of *L.* Sejroe, *L.* Bratislava and *L.* Icterohaemorrhagiae. An even lower prevalence to the indigenous strain of *L.* Sejroe in cattle has been recorded. Since 2006, the surveillance programme in cattle and pigs is no longer performed on a yearly basis as the probability of introduction is very low and the serological screening of *Leptospira* is considered of less importance compared to screening programmes of other contagious animal diseases.

Several *Leptospira* serovars have been shown to be present in Swedish dogs by detection of seropositivity to *L.* Icterohaemorrhagiae, *L.* Canicola, *L.* Grippotyphosa, *L.* Bratislava, *L.* Saxkoebing, *L.* Sejroe *and L.* Automnalis. Serovars including e.g. *L.* Bratislava and *L.* Grippotyphosa) have also been detected in wild rats caught in Swedish cities in research studies, a further indication of presence of leptospiral serovars in Sweden.

Currently, all positive MAT results in dogs are reported without knowledge of vaccination status, travel history and whether clinical disease is suspected or not. Furthermore, in clinical cases paired samples (sometimes three samples) are needed for diagnosis as the immune response providing specific antibodies to the causing serovar often is delayed. A negative result is common during the acute phase of illness, as is cross reactions leaving the causative serovar unidentified.

As all laboratory diagnostics must be paid for by the dog owner there is a lack of such paired samples. In addition, not all dogs survive the infection and autopsies are rare due to the cost to the owner as well as the emotional aspect. Furthermore, the number of samples sent to laboratories abroad, and to what extent possible positive results are being reported or not by the referring veterinarians, is currently unknown. In 2018 and 2019, the number of samples sent to SVA for PCR analyses instead of MAT analyses increased. In 2019 only a quarter of all samples sent to SVA for Leptospira-analyses were for serologic examination. This is reflected in a lowered number of reported positive serological results. PCR is expected to be negative in the majority of cases, including dogs with severe clinical illness.

Furthermore, an onsite ELISA test not distinguishing between different serovars is now available and in use in several small-animal hospitals and clinics. The number of reported seropositive results from use of such tests during 2019 is one, or at the most six dogs (only one report specifies onsite test as the method used). The number of positive onsite test results retrospectively mentioned during phone calls to the National Veterinary Institute from clinically active small-animal veterinarians far exceeds that number, indicating that underreporting is common. Reliable data on how common underreporting is however lacking.

In short, seropositivity to leptospiral serovars in Swedish dogs is currently underreported and data on seropositivity can neither be compared to or between previous years. Furthermore, prevalence of clinical disease in Swedish dogs due to leptospiral infection is currently not reflected in the surveillance data and not readily available.

A limited collaborative study (Swedish university of Agricultural Sciences and National Veterinary institute) seroprevalence study is ongoing with so far 300 canine serum samples collected during autumn 2019. Further studies are however warranted, as the number of suspected or confirmed clinical cases is rising, indicating an increase in exposure- but confirmatory data is lacking. There is currently no available system to aid in reporting and evaluating suspicion of Leptospiral infection as the true cause of disease in clinical cases. Information on presence or absence of clinical disease or results from any confirmatory laboratory investigations carried out is currently not included in the data reported.

The reporting procedures and challenges in horses are largely the same as in dogs.

Few cases of human infections are reported each year and the majority are travel-associated. The primary diagnostics of human cases is mainly based on serology. However, with increasing awareness of molecular based techniques for diagnosis could probably lead to an increase in incidence.

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