

Tularaemia and Australian wildlife

Fact sheet

Introductory statement

Tularaemia, first identified in the United States in 1911, is disease resulting from infection with the bacterium *Francisella tularensis*. *F. tularensis* is commonly found in a range of wildlife species across the northern hemisphere but, until recently, was believed to be absent from Australia. Overseas, it has been responsible for periodic epidemics and mass mortalities particularly of lagomorphs, beavers and muskrats but usually cycles at a low level in the local rodent and lagomorph populations. *F. tularensis* has the potential to be transmitted to humans via contact with infected wildlife, via ticks, biting insects and mosquitoes. The situation in Australia is evolving. In September 2016, *F. tularensis* was detected for the first time in Australian animals, in common ringtail possums (*Pseudocheirus peregrinus*), that had died in two separate events in NSW in 2002 and 2003 (Eden et al. 2017). Two cases of tularaemia in humans in Tasmania in 2011 appeared to be associated with exposure to common ringtail possums.

Aetiology

F. tularensis is an aerobic, Gram negative, pleomorphic, bacterial rod measuring 0.2 x 0.2-0.7 µm in size. It is an obligate intracellular parasite divided into several subspecies, with varying degrees of virulence. There are several other related species in the genus.

F. tularensis tularensis (Type A), and *F. tularensis holarctica* (Type B) are the most common cause of disease in humans and other mammals. *F. t. tularensis* causes life threatening illness in humans; *F. t. holarctica* results in less severe disease. *F. t. mediasiatica* has similar virulence to *F. t. holarctica* and *F. t. novicida* is the least virulent subspecies, having been isolated only rarely in North America.

Natural hosts

F. tularensis has an extremely broad host range, having been reported from 190 species of mammals, 23 species of birds, three species of amphibians and 88 species of invertebrates. Despite this tularaemia is primarily a disease of lagomorphs and rodents (Mörner and Addison 2001).

World distribution

F. tularensis tularensis is only found in North America; *F. tularensis holarctica* is found throughout the northern hemisphere; *F. tularensis mediasiatica* has only been found in central Asia; *F. tularensis novicida* has been isolated only rarely in North America.

Occurrences in Australia

Although recent studies indicate the presence of tularaemia in Australian wildlife, the situation remains unclear.

A different species of *Francisella*, *F. hispanensis*, has been isolated from a man in the NT in 2003 (this organism was previously classified as a *novicida*-like subspecies of *F. tularensis* (Whipp et al. 2003; Sjödin et al. 2012). A strain of *Francisella*, resembling *F. hispanensis* was recently implicated in disease in a woman in WA (Aravena-Román et al. 2015).

In February and September 2011, a diagnosis of *F. t. holarctica* biovar *japonica* was made based on PCR, supported by typical clinical presentation, in two women who were scratched and bitten by common ringtail possums between Queenstown and Zeehan in Tasmania (Veitch and Cooley 2011; Jackson et al. 2012). Testing of a small number of possums from western Tasmania and other areas did not reveal evidence of tularaemia.

In September 2016, tularaemia was detected for the first time in Australian animals, following next generation molecular analysis of archived samples, collected from two separate clusters of common ringtail possum deaths that had occurred in NSW in 2002 and 2003. Findings of *F. tularensis holarctica* were confirmed by PCR and were found to be genomically very similar to that found in the 2011 Tasmanian human cases (Eden et al. 2017).

Epidemiology

F. tularensis is highly infectious and spread by blood feeding arthropods including ticks, biting insects and mosquitoes, contact with blood or tissues of infected animals, inhalation of aerosols or particles, or ingestion of contaminated water or meat (Mörner and Addison 2001). Tularaemia is not transmissible from person to person and the organism can survive in water and mud for several months (Tärnvik and Berglund 2003). In the northern hemisphere, tularaemia in wildlife may present as an acute mass mortality event, particularly in rabbits and hares.

Although it has been confirmed that the organism is present in Australia, there is limited information on the presence, prevalence or epidemiology of tularaemia in the Australian context. Further work is indicated.

Follow-up surveys of possums from those areas of Tasmania where the two women who were scratched and bitten by possums (above) failed to identify any evidence of tularaemia infection or exposure.

Clinical signs

Clinical signs are vague and variable, including sudden death, depression, pyrexia, local inflammation or ulceration at the portal of entry and enlargement of lymph nodes draining the affected area. The course of the disease is two to ten days in sensitive species ((Mörner and Addison 2001). Mass mortalities may be seen.

Diagnosis

Tularaemia can be diagnosed at necropsy by making impression smears of liver, spleen, bone marrow, kidney or lung. These will reveal large numbers of very small Gram negative organisms. Identity can be confirmed using immunofluorescence, immunohistochemistry or PCR. The organism can be cultured from heart blood, liver, spleen or bone marrow but is slow growing and grows poorly on most ordinary bacterial culture media.

Serological tests such as tube agglutination, ELISA and Western blot can also be used to detect antibodies in species that live long enough (see WHO guidelines 2007 and the link to the APHIS update on tularaemia and *F. tularensis* microagglutination assay being used for surveillance

https://www.aphis.usda.gov/wildlife_damage/nwdp/pdf/Tularemia%20update%20Vol1%20Iss1.pdf).

The inability to culture an organism on specialized media in the Tasmanian cases probably was caused by prolonged ciprofloxacin treatment before the specific culture attempt. This case met the definition for probable tularemia according to the 2007 WHO guidelines; however, the combination of clinical, serologic, and molecular evidence strongly supported the diagnosis of infection with *F. tularensis holarctica*. This conclusion is consistent with recent reports of tularemia in which case definitions included a compatible clinical syndrome and positive *F. tularensis* real-time PCR or DNA sequencing (Jackson et al. 2012).

For more details on sample collection and submission see the WHA “National guidelines for sample submission tularaemia – exclusion testing”

www.wildlifehealthaustralia.com.au/Portals/0/Documents/ProgramProjects/National_Guidelines_Sample%20Submission_Tularaemia_Dx_Testing_v1.0_June17.pdf

Pathology

Acutely affected mammals are usually found dead, in good body condition, with pale foci of necrosis in the liver, bone marrow and spleen, which is generally enlarged. The lungs are usually congested and there may be a fibrinous pneumonia and pleuritis. Foci of caseous necrosis are often present in lymph nodes particularly in the abdominal cavity. Multifocal necrosis is usually absent in affected birds, with splenic enlargement the only obvious lesion.

In chronic cases, granulomas can be found in the lymph nodes, liver, spleen, lungs and kidneys.

Microscopically acute cases have multifocal areas of coagulation necrosis in the spleen, liver, lymph nodes, bone marrow and lungs without the presence of neutrophils or macrophages. Lesions in chronic cases are granulomatous with areas of central necrosis surrounded by macrophages, epithelioid cells and giant cells (Mörner and Addison 2001; Mörner 2007).

Differential diagnoses

Differential diagnoses include any diseases that cause necrotizing, suppurative or granulomatous lymphadenitis, multifocal hepatitis and splenitis, such as plague, pseudotuberculosis, mycobacterial infections, salmonellosis, Tyzzer’s disease, and herpesvirus infections.

Laboratory diagnostic specimens

Care should be taken when handling animals or carcasses with suspected tularaemia, as the organism can cause serious disease in humans. Good hygiene and infection control measures are required (see NSW DPI bulletin www.dpi.nsw.gov.au/data/assets/pdf_file/0011/679619/CVO_Bulletin_Tularaemia_veterinarians.pdf). A

necropsy should be performed and a complete set of tissues collected fresh and in formalin. Impression smears of affected organs can also be submitted. If there are any concerns about the ability to manage the carcass safely, the whole carcass should be sent, (chilled) to the state or territory diagnostic laboratory for testing. Contact the laboratory to provide advanced notice of the submission.

Laboratory procedures

Because *F. tularensis* is highly contagious and zoonotic, necropsies of suspect cases and culture attempts should only be carried out in laboratories with physical containment level 3 facilities. *F. tularensis tularensis*, *holarctica* and *mediasiatica* are fastidious and require media containing cystine or cysteine for growth while *F. tularensis novicida* is non-fastidious. Cultures should be incubated at 37 °C for 72 to 96 hours. For contaminated tissues, adding an antibiotic to the culture agar will improve recovery of the organism. Freezing of tissues as soon as possible after death will also improve culture recovery rates. Positive colonies appear non-haemolytic, and greenish-grey. *F. tularensis tularensis*, *mediasiatica* and *novicida* ferment glycerol while *F. tularensis holarctica* does not (Quan 1993; Whipp et al. 2003; Petersen et al. 2004; Aravena-Román et al. 2015).¹

Treatment

Streptomycin is reported to be the drug of choice. Aminoglycosides, tetracyclines and quinolones are effective alternatives. Betalactams, macrolides, lincosamides and trimoxazole are not recommended. The human infection from the Northern Territory resolved after a combined treatment with flucloxacillin and doxycycline (Mörner and Addison 2001; Tärnvik and Berglund 2003; Whipp et al. 2003). One of the Tasmanian human cases responded promptly to a 14 day course of intravenous gentamicin (Jackson et al. 2012).

Prevention and control

Generally, tularemia outbreaks cannot be controlled in the source population. However, steps have been taken overseas to ameliorate the effect of the disease on people and livestock. These include control of reservoir hosts through poisoning and hunting and attempting to reduce vector numbers. People at risk should take hygiene and infection control precautions, such as wearing rubber gloves when handling potentially infected animals, thoroughly cooking meat, disinfecting water by boiling or chlorination and using insect repellents to decrease the probability of bites from potentially infected arthropods (Mörner and Addison 2001).

Surveillance and management

Wildlife disease surveillance in Australia is coordinated by the Wildlife Health Australia. The National Wildlife Health Information System (eWHIS) captures information from a variety of sources including Australian government agencies, zoo and wildlife parks, wildlife carers, universities and members of the public. Coordinators in each of Australia's States and Territories report monthly on significant wildlife cases identified in their jurisdictions. NOTE: access to information contained within the National Wildlife Health Information System dataset is by application. Please contact admin@wildlifehealthaustralia.com.au.

A survey was conducted in November 2011, collecting samples within a five km radius of where the two human cases had been bitten by common ringtail possums in Tasmania. Over 40 samples, including carcasses,

¹ In the USA, tularemia is considered a biodefense threat and therefore work with the agent is highly regulated.

faeces and nesting material were examined. There was no evidence of exposure or infection with *F. tularensis* (www.dhhs.tas.gov.au/peh/current_public_health_issues/tularaemia).

It has been suggested that to find 2% prevalence, with 95% confidence (assuming perfect test sensitivity and specificity), 300 wild common ringtail possums would need to be randomly sampled. The forests of western Tasmania are wild and isolated and there are considerable challenges associated with sampling in these areas. Significant resources would be required. Passive surveillance is on-going in Tasmania and includes general practitioners, hospitals, veterinarians and wildlife carers.

Research

Although it has been confirmed that the organism is present in Australian wildlife, further work is needed to better understand the distribution, prevalence and epidemiology of tularaemia in the Australian context. In other countries, tularemia has emerged several times in non-endemic areas after the importation/translocation of infected wildlife or changes in ecologic and climate conditions, or in settings of post-war social disruption.

Human health implications

Care should be taken when handling animals or carcasses with suspected tularaemia, as the organism can cause serious disease in humans. Clinical signs are determined by the route of infection. After an arthropod bite or other cutaneous exposure, an ulcer develops at the site of infection along with abscessation of draining lymph nodes. Consumption of contaminated water or meat leads to pharyngitis, tonsillitis and swelling of lymph nodes in the neck. Inhalation of the organism results in an influenza-like illness with fever and pneumonia. *F. t. tularensis* is more virulent than the other strains causing pneumonia, septicaemia and death in 5 to 10% of untreated cases. The infective dose is extremely low, 10 bacteria when injected subcutaneously and 25 when given as an aerosol. Tularaemia is not transmissible from person to person (Tärnvik and Berglund 2003). In general, infection with *F. t. holarctica* causes less severe disease than *F. t. tularensis*.

The two women from Tasmania were bitten and scratched by common ringtail possums prior to developing ulcers at the site of the injury and a prominent lymphadenitis. One of the women had swollen epitrochlear lymph nodes, fever, rigor, myalgia and night sweats. Axillary lymphadenopathy was palpable on day 14, and by day 17 the epitrochlear nodes had formed a spontaneously discharging sinus (Jackson et al. 2012).

Conclusions

The Australian status with respect to tularaemia is evolving. *F. t. holarctica* has been confirmed in archived samples from common ringtail possums in NSW, and in two human cases in Tasmania. Tularaemia should be considered in any acute mortality events in wildlife, in particular in possums, rabbits, hares and rodents. Wildlife carers and those working closely with Australian wildlife should be aware of tularaemia and take appropriate hygiene and infectious control precautions. If bites or scratches occur, people are advised to seek medical advice from their local public health department.

References and other information

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See also:

WHA National guidelines for sample submission tularaemia – exclusion testing

www.wildlifehealthaustralia.com.au/Portals/0/Documents/ProgramProjects/National_Guidelines_Sample%20Submission_Tularaemia_Dx_Testing_v1.0_June17.pdf

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www.promedmail.org/direct.php?id=20111122.3425

CDC www.cdc.gov/tularemia/

CFSPH Fact sheet: www.cfsph.iastate.edu/Factsheets/pdfs/tularemia.pdf and PowerPoint presentation:

www.cfsph.iastate.edu/DiseaseInfo/ppt/Tularemia.ppt

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To provide feedback on this fact sheet

We are interested in hearing from anyone with information on this condition in Australia, including laboratory reports, historical datasets or survey results that could be added to the National Wildlife Health Information System. If you can help, please contact us at admin@wildlifehealthaustralia.com.au.

Wildlife Health Australia would be very grateful for any feedback on this fact sheet. Please provide detailed comments or suggestions to admin@wildlifehealthaustralia.com.au. We would also like to hear from you if you have a particular area of expertise and would like to produce a fact sheet (or sheets) for the network (or update current sheets). A small amount of funding is available to facilitate this.

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