

Leptospirosis: key things to know about this quintessential zoonotic pathogen



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Leptospirosis is a human and veterinary illness caused by spirochete bacteria in the genus *Leptospira*. In symptomatic infection the clinical presentation ranges from non-specific febrile illness to fulminant organ system failure with a high case fatality rate. Leptospire are excreted in the urine of infected mammals with rodents being the main source for human exposures. Leptospire can survive for months in urine-contaminated water and moist soil and humans can acquire infection via direct exposure to urine from infected animals or indirectly through contact with urine-contaminated water and wet soil. While leptospirosis occurs worldwide, it is more common in tropical and sub-tropical climates where it is estimated to cause more than a million illnesses and result in almost 60 000 deaths annually. Flood-related leptospirosis outbreaks have been documented in many settings, including Australia, and are expected to increase with climate change. The largest outbreak of human leptospirosis in Australia occurred in 2018 when 84 cases were identified among workers on a berry farm in New South Wales. In 2019 unprecedented clusters of fatal canine leptospirosis occurred in urban areas of Sydney and Melbourne. It is not yet known whether the recent leptospirosis outbreaks among dogs and humans are an aberration or herald a growing threat to public and veterinary health in Australia. A One Health approach is critical to understanding the emergence of leptospirosis in an era of climate change, population growth, changes to agricultural practices, increased travel and urbanisation, both in Australia and abroad.

Leptospirosis, a disease that affects humans and animals, is caused by spirochete bacteria in the genus *Leptospira*¹. There are 10 pathogenic species, and more than 250 pathogenic serovars².

*Leptospire*s are excreted in the urine of infected animals, principally rodents, but also dogs, pigs, horses and bats³. Many species of wildlife can become infected, including Australia's iconic kangaroos and Tasmanian devils, and in developing countries in Africa and the Pacific Islands, subsistence livestock are also an important source of exposure. The bacteria can survive for weeks to months in urine-contaminated water and moist soil. Pathogenic leptospire can penetrate mucous membranes, the conjunctiva, or enter through the skin if there are cuts or abrasions¹. Humans acquire infection either directly via exposure to urine from infected animals, indirectly through contact with urine-contaminated water and wet soil, or by ingestion of contaminated food or water¹. Human-to-human transmission is very rare but has been documented through sexual contact and breastfeeding².

Limited data from prospective surveillance studies suggest that many human leptospirosis infections are asymptomatic or mild, but the clinical course is highly variable^{1,3}. Symptomatic infection in humans typically appears 5–14 days after exposure, with a range of 2–30 days. The clinical presentation ranges from non-specific febrile illness to fulminant, life-threatening organ system failure³.

High-risk activities include both recreational and occupational exposure to surface water and mud that may be contaminated with animal urine⁴. Direct contact with infected animals through farming and slaughtering is also a risk. While leptospirosis occurs worldwide, it is more common in tropical or sub-tropical climates.

Here are some key things to know about the increasing risk to human and veterinary public health posed by this pervasive, but often under-appreciated, pathogen.

(1) Leptospirosis is a leading cause of zoonotic morbidity and mortality worldwide

According to the US Centers for Disease Control and Prevention leptospirosis is considered to be the most widespread zoonotic disease in the world². This assertion is supported by modelled estimates from 2015, which found that worldwide there are more than a million symptomatic leptospirosis infections each year

resulting in almost 60 000 deaths⁵. These figures make leptospirosis a leading zoonotic cause of human morbidity and mortality with the number of deaths attributable to leptospirosis approaching or exceeding those caused by viral haemorrhagic fever and canine rabies⁶. Given that these estimates were largely derived from hospital-based surveillance studies using passive case ascertainment, they likely underestimate the true global burden of leptospirosis.

(2) The case-fatality rate for severe human leptospirosis illness is high

Most ill persons will experience fever, chills, muscle aches, headaches. Other symptoms may include photophobia, conjunctivitis, anorexia, vomiting, diarrhea, abdominal pain, jaundice, cough, lethargy, arthralgia, calf tenderness, and less commonly, a rash^{2,3}. Approximately 10 percent of people with leptospirosis progress to severe disease involving one or more of the following: kidney or liver failure, coagulopathy, pulmonary haemorrhage, myocarditis, arrhythmia, shock, optic neuritis, transverse myelitis, meningitis, and encephalitis. Since a broad array of organ systems can be affected, the signs and symptoms are diverse and protean. As a result, leptospiral infections are often incorrectly attributed to other causes of acute febrile illness, such as malaria, dengue, or enteric fever⁵. There is now growing recognition that leptospirosis is an important cause of an acute febrile illness in tropical environments, and may be responsible for more than 60% of acute undifferentiated, non-malarial febrile illnesses⁵.

Unfortunately, in the case of leptospirosis, misdiagnosis can lead to sub-optimal or delayed clinical management and this contributes to poor outcomes. Early initiation of appropriate antibiotics is associated with a significantly shortened duration of illness and, combined with rigorous ICU-level supportive care (e.g. dialysis, ventilation), can improve the prognosis⁷. Still, the case fatality rate for patients with severe clinical illness is very high, ranging from 5 to 15%, a figure comparable to that of meningococcal meningitis.

(3) Challenges in diagnosing leptospirosis directly contribute to its status as a neglected disease

In addition to the difficulty of making a clinical diagnosis, challenges in obtaining laboratory confirmation for leptospirosis contribute to it being under-appreciated as an important human pathogen. Historically, case confirmation has relied on demonstrating antibody seroconversion between acute and convalescent-phase samples using the microscopic agglutination test (MAT)⁸. Because the MAT is time-consuming and difficult to perform, various screening tests for detecting IgM antibodies have been developed, but poor sensitivity early in the course of illness means they have limited

utility for diagnosing leptospirosis at the time when important therapeutic decisions need to be made⁸.

More recently, PCR tests designed to detect the presence of *Leptospira* DNA in blood (and other tissues) shortly after illness onset have been used in both clinical and research settings for humans and other mammals^{9–13}. After a 20-year hiatus, leptospirosis was reinstated as a nationally notifiable disease in the United States in 2014 and criteria for a confirmed case includes ‘detection of pathogenic *Leptospira* DNA by PCR from a clinical specimen’¹⁴. In contrast, human leptospirosis illness has been notifiable in Australia for decades, however, the case definition has not been updated since 2004 and completely omits mention of diagnostic PCR testing¹⁵. Given its utility for diagnosing leptospirosis in the early phases of illness, the case definition used for national surveillance in Australia should be revised¹².

(4) Although it is typically thought of as a ‘tropical disease’, leptospirosis can cause outbreaks in unexpected places

A nearly ubiquitous pathogen, leptospirosis can emerge in some surprising places. The largest outbreak ever reported in the US occurred in 1998 when 110 individuals, most of them athletes competing in a triathlon, were infected in Springfield, Illinois^{16,17}. Another atypical cluster occurred among inner-city residents of Baltimore, Maryland who were exposed through percutaneous injuries subsequently contaminated by rat urine in alleys¹⁸.

(5) Leptospirosis has caused recent outbreaks among humans and their pets in Australia

Over the 29-year period for which the data are publically available, there have been an average of 149 human leptospirosis illnesses diagnosed and reported in Australia each year (range: 72–319; Figure 1). While the majority (57%) of cases during this period were reported from Queensland, every jurisdiction has had cases¹⁹.

Some of the leptospirosis infections reported in Australia would certainly have been acquired while travelling abroad in high-incidence countries. For persons living in developed countries, activities involving water exposure and eco-tourism are well documented risk factors for acquiring leptospirosis overseas. This underscores the need for clinicians to obtain travel histories on patients presenting with febrile illness and to include leptospirosis in the differential diagnosis for those at risk.

Leptospirosis can also be locally acquired in Australia resulting in sporadic cases and outbreaks²⁰. In 2018, the largest outbreak of human leptospirosis in Australia occurred in New South Wales when 84 cases were identified over a 5-month period among

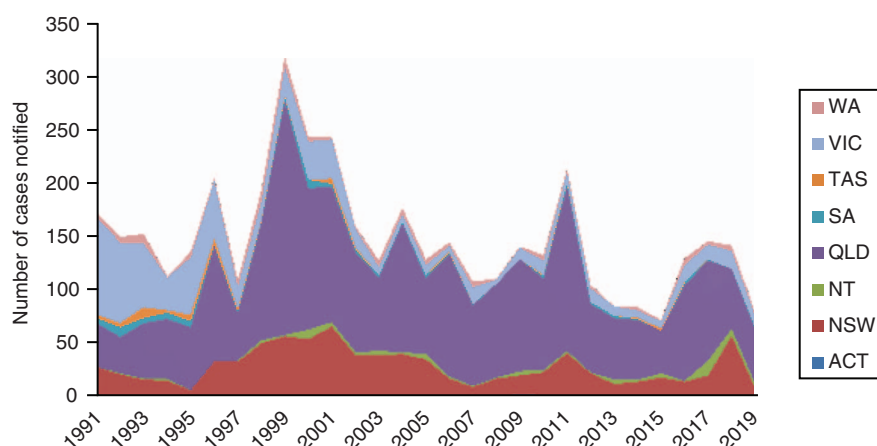


Figure 1. Number of notifications of Leptospirosis, Australia, by jurisdiction and year, 1991–2019.

raspberry workers from a berry farm¹². The farm workers were exposed through scratches obtained while picking raspberries that then became contaminated with leptospires excreted into the environment by infected mice. Three of 13 mice that were trapped as part of the investigation tested positive for *Leptospira borgpetersenii* serovar Arborea.

In 2019 the first ever outbreak of canine leptospirosis was identified in Sydney, NSW when seven fatal leptospirosis infections occurred among pets in inner city suburbs²¹. Dr Jacqueline Norris, Professor of Veterinary Microbiology and Infectious Diseases at the University of Sydney was quoted as saying, ‘We haven’t seen leptospirosis in Sydney dogs ... so something has changed’. Displacement of rat populations and pooling water caused by light rail construction works were hypothesised to be potential contributing factors.

Later in 2019, an unprecedented spate of canine deaths was reported from Melbourne, Victoria. According to statements attributed to Victoria’s Chief Veterinary Officer, three fatal canine leptospirosis infections were reported from eastern Melbourne, a phenomena that veterinarians who treated the dogs said they had never seen before²². However, serological evidence of canine leptospirosis in Australia suggests that the disease is more widespread than previously appreciated. A serosurvey of almost 1000 dogs sampled at shelters in Queensland, New South Wales, Victoria, Western Australia and the Northern Territory found that 1–2.5% were seropositive, with *Leptospira interrogans* serovar Copenhageni being most prevalent of the 11 different serovars detected²³. Whether the recent outbreaks of leptospirosis among dogs in major Australian cities are simply a ‘one-off’ event or signal a growing urban hazard remains to be seen.

(6) Climate change will likely increase the risk of future leptospirosis outbreaks

Extreme weather events resulting in flood-related disasters are predicted to increase with climate change^{24,25}. Flood-related

leptospirosis outbreaks have already been documented in many parts of the world, in both developing and developed countries, including Australia, and may be becoming more common^{26,27}. Pacific Island countries already have the highest leptospirosis disease burden in the world and experience frequent outbreaks. Improved surveillance for leptospirosis in human and veterinary medicine will be important for assessing and responding to the impact of climate change on this prevalent, but still emerging, zoonosis.

(7) Australia is well positioned to help address emergence of leptospirosis locally and internationally

Australia has one of the best leptospirosis laboratories in the world. The Leptospirosis Reference Laboratory in Queensland is accredited by the World Health Organization and the Office International des Epizooties (OIE)²⁸. This laboratory provides expert advice and diagnostic support to public health authorities at local, national and international levels, and collaborates extensively with universities and government departments to support research and surveillance in the human and veterinary fields. Australia is also fortunate to have experienced clinicians and researchers whose expertise in leptospirosis is respected globally; the work of some of these individuals is cited in this article.

In addition, Australia has been a leader in advocating for a One Health approach to address zoonotic infectious diseases²⁹. One Health recognises that developing effective strategies to mitigate the threat to human and animal health posed by zoonotic pathogens will require the engagement of professionals with a diverse set of skills and from a range of disciplines. This approach will be critical to fully understanding the emergence of leptospirosis in an era of climate change, population growth, changes to agricultural practices, increased travel and urbanisation³⁰. Fortunately, given its expertise and laboratory capacity, Australia is well positioned to

make significant contributions, both at home and abroad, for responding to the threat posed by this quintessential – but often neglected – zoonotic pathogen.

Conflicts of interest

The author declares no conflicts of interest.

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Biography

Paul Effler received a Doctorate in Medicine from the University of California and a Master of Public Health from the University of Hawaii. On completing a residency in Public Health Medicine, Dr Effler served as an Officer in the Epidemic Intelligence Service at the US Centers for Disease Control. In 1994 he became the State Epidemiologist for Hawaii, where he directed the public health response to leptospirosis and other communicable diseases. In 2008 Dr Effler moved to Perth where he works in communicable disease control. He is a Clinical Professor at the University of Western Australia School of Medicine, an Associate Editor for *Emerging Infectious Diseases*, and serves on the Steering Committee for the Global Outbreak and Response Network and the Technical Advisory Group for the Asia Pacific Strategy for Emerging Diseases and Public Health Emergencies with WPRO/WHO.