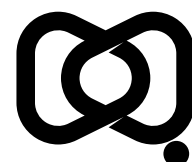




# Ratting out leptospirosis: investigation of a revealing urban case associated with socioeconomic disadvantage in Sydney, Australia

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## Abstract

Classically reported in Australia in association with travel or occupational exposures, leptospirosis in the urban setting is a disease of lower socioeconomic status with the risk of rat exposure inversely proportional to conditions of living. Whilst this has been widely reported elsewhere in the world, urban-acquired cases of leptospirosis are rare in Australia. Here we report on the fifth locally acquired case in Sydney, Australia, during the period 2003–2024. This case coincided with a severe rat infestation in the case's social housing block. A collaborative environmental health investigation followed, involving members of the Public Health Unit and Department of Primary Industries and Regional Development. Twelve rats captured within a 1.5 km radius of the case's residence underwent polymerase chain reaction testing for leptospirosis and were all negative. This prompted consideration of other potential reservoirs, including native species. This case demonstrates persisting social inequities in metropolitan Sydney, and the consequences for health.

Keywords: leptospirosis; rats; Sydney; socioeconomic status; environmental health; public health; investigation

## Introduction

Leptospirosis is a zoonosis of global concern widely reported in association with certain occupations and adventure travellers, owing to exposure to animal and freshwater reservoirs of the *Leptospira* spirochaete.<sup>1,2</sup> However, as will be seen in this case, it is also a disease of low socioeconomic status, found in urban areas with poor living conditions and sanitation.<sup>3</sup>

Leptospirosis may be asymptomatic, or may present with fevers, myalgia, nausea and vomiting, jaundice, renal impairment, conjunctival suffusion, and even pulmonary haemorrhage in severe cases.<sup>1</sup> Icteric leptospirosis, formerly referred to as Weil's Disease, is associated with multiorgan failure and a mortality rate of 5–15%.<sup>2,4</sup>

A highly motile aerobic spirochete, the genus *Leptospira* has 18 different species and over 200 serovars.<sup>5</sup> These can be divided by phylogenetic analysis and corresponding virulence into saprophytic, intermediate (moderately pathogenic but with unclear role in human and animal disease) and pathogenic species.<sup>6</sup> All species have been found to persist in environmental reservoirs in water and soil for several weeks.<sup>6</sup>

The spirochetes of pathogenic species can also reside in the proximal renal tubules of wild and domestic mammalian hosts, from which they may be shed asymptotically and continuously for prolonged periods of time.<sup>7,8</sup> Percutaneous or mucosal contact with the infected urine of these animals, or with urine-contaminated water or soil, can lead to human transmission and disease after an incubation period of 1–30 days.<sup>2,6</sup>

Rats are the main reservoir of leptospirosis in urban environments.<sup>1,9</sup> Pathogenic *Leptospira* spp. have been identified in rats worldwide, with a demonstrated prevalence in Australia ranging from 8% in Sydney (based on sampling of rat kidney tissue) to 70–80% among rats in Queensland.<sup>5,9–11</sup> Locally acquired human cases reported in the cities of Tokyo, Baltimore, New York and Marseille all had a history of exposure to rats.<sup>12–15</sup> Rare urban cases in Sydney have also been linked to rats and water suspected to be contaminated with rat urine.<sup>16</sup> There was some geographical overlap found between *Leptospira* polymerase chain reaction (PCR) positive Sydney rats and a cluster of canine cases in 2019, suggesting a possible role for rats in transmission to dogs as well as humans, or common exposure to environmental reservoirs.<sup>5</sup>

Many studies, mostly from South America, have reported poor living conditions as a risk factor for leptospirosis in people.<sup>17</sup> This is particularly true for urban cases, which are more likely to be related to domestic rat exposures than rural cases, which are predominantly occupation-related.<sup>18,19</sup> Significant associations have been demonstrated with income, education, housing type, household crowding, proximity to sewerage or garbage, and sanitation.<sup>3,14,17,20</sup> Homelessness and incarceration are also predisposing risks.<sup>15,21</sup> Even dogs were found to be more at risk if the house they lived in had incomplete plumbing facilities and/or a greater degree of poverty.<sup>17</sup>

Here we report on the investigation of a case of locally acquired leptospirosis in inner-city Sydney, Australia, in association with rat-infested social housing. Written informed consent was provided by the case for publication of a clinical case report.

## Case

At the beginning of May 2024, an Aboriginal man in his fifties presented to Emergency with five days of fevers, malaise, myalgias, headache, mildly productive cough, abdominal pain, nausea and vomiting. His background was notable for Vohwinkel syndrome—an inherited condition causing hyperkeratosis and hearing loss—as well as recent intravenous drug use and pack-a-day cigarette smoking. He was unemployed and living in a ground floor unit of an inner-city social housing block with his dog. There was no history of recent travel or other reported animal exposures.

On review, he was febrile to 38.2 °C, hypotensive with blood pressure of 85/55 mm Hg despite aggressive fluid resuscitation. He became increasingly hypoxic, requiring 4L/min of nasal prong oxygen, necessitating transfer to the intensive care unit for vasopressor support and intubation. Examination was remarkable for jaundice and scleral icterus, crepitations at the left lung base, and generalised abdominal tenderness without guarding or rigidity. He had marked palmoplantar keratosis (in keeping with known Vohwinkel syndrome) with associated deep skin breaks and cracks. Flucloxacillin, gentamicin and hydrocortisone were commenced for sepsis of unknown origin.

Investigations revealed mixed hyperbilirubinaemia, progressing to a peak just above 400 µmol/L (normal range < 20 µmol/L), and acute anuric kidney injury from a normal baseline (serum creatinine 274 µmol/L; estimated glomerular filtration rate [eGFR] 22 mL/min). There was a leukocytosis of  $15.2 \times 10^9/L$  (reference range  $4.0\text{--}11.0 \times 10^9/L$ ) with predominant neutrophilia of  $14.6 \times 10^9/L$  (reference range  $2.0\text{--}7.5 \times 10^9/L$ ) and raised C reactive protein (306 mg/L, normal < 5 mg/L). Liver enzymes were moderately deranged with a gamma-glutamyl transferase (GGT) test result ten times upper limit of normal and alkaline phosphatase (ALP) almost three times upper limit of normal, without a commensurate derangement in transaminases and normal synthetic hepatic function. Computed tomography of the chest demonstrated widespread bilateral peribronchovascular tree-in-bud and ground glass changes, worse on the left. No biliary tract obstruction or other structural abnormalities were seen on abdominal imaging. Transthoracic echocardiography revealed no evidence of endocarditis. Microbiological investigations included blood, urine and bronchoscopy cultures, respiratory virus PCR testing, human immunodeficiency virus (HIV) and hepatitis serologies. These were all negative.

The patient was commenced on continuous renal replacement therapy and had antibiotics ceased at seven days after completing a course of flucloxacillin and ceftriaxone covering presumptively for community acquired pneumonia or possible skin source of sepsis. His hepatic impairment spontaneously improved over three weeks, and his renal function recovered after four weeks on dialysis. He was discharged home on day 35 with ongoing outpatient follow-up.

Serology for leptospirosis done on day five of illness was positive for immunoglobulin M (IgM) but negative on microagglutination testing. Convalescent serology four weeks later remained IgM positive and now had a strongly positive microagglutination test for the *Leptospira* Copenhageni serovar (titre of 3200, where a titre of > 200 is considered diagnostically significant). This prompted a notification to the Public Health Unit at the end of June 2024 and initiation of follow-up.

## Public health response

Due to hearing impairment, a case interview was conducted with the patient's mother. She confirmed a lack of any recent travel history or occupational exposure. The case's dog was well and had been previously vaccinated against leptospirosis, although it had missed a couple of recent annual boosters. Note was made of significant rat exposures and concerns over the standard of living in the social housing block. She reported other residents routinely piling garbage in the corridor outside the patient's unit, attracting large numbers of rats. The case would often hose down the corridor whilst barefoot to clean up the garbage and rat faeces.

Given this history, an investigation was initiated by Environmental Health Officers (EHOs) from the local Public Health Unit. This revealed a history of severe rat infestation that had come to the attention of the local council in August 2023 and required a formal clean up order. The council's initial inspection found dead rats, rat burrows and rat droppings throughout the premises. The order cited 'poor waste management practices, lack of adequate cleaning and maintenance'.<sup>22</sup>

When the EHOs attended for inspection in June 2024, one week after the case's confirmatory convalescent serology results were notified, significant work had already been undertaken with regular rodent baiting, improved garbage storage and clean up, and planned landscaping to remove established rat burrows. Evidence of persisting rat holes was seen (Figure 1), but no live vermin. Garbage disposal areas appeared clean and tidy. However, reports from housing residents suggested this was not always the case. A repeat inspection in August 2024 still found evidence of rat faeces, particularly near the case's unit. The landscaping works were completed at the end of October 2024.

Veterinary colleagues from the New South Wales Department of Primary Industries and Regional Development (DPIRD) were engaged to discuss testing local rats and the case's dog for asymptomatic carriage of leptospirosis. The ability of dogs to act as maintenance hosts with prolonged asymptomatic urinary shedding of *Leptospira* is well established.<sup>23</sup> Investigation of the case's dog would have entailed a urinary PCR test and serology, but unfortunately the case declined to pursue this.

Twelve Brown rats (*Rattus norvegicus*; speciation made based on phenotypic traits noted by the DPIRD veterinarian involved), captured within a 1.5 km radius of the case's unit, underwent PCR testing to investigate possible active infection or shedding of pathogenic *Leptospira*. The 1.5 km radius was chosen on the basis of available funding for testing and numbers of rats found. Rat carcasses were collected from traps between the end of August and mid-October 2024, 1–3 days from time of death. The kidneys were dissected and stored at -80 °C until DNA extraction. Real-time PCR testing was performed on kidney tissue using the assay developed by Smythe et al.,<sup>24</sup> with no positive detections. This assay targets the *rrs* (16S) gene and detects DNA from both pathogenic and intermediate *Leptospira* organisms.<sup>24</sup> It has been used to detect *Leptospira* DNA in rats, flying foxes, and environmental samples.<sup>25,26</sup> If positive, further PCR testing, including a serogroup-based assay, would have been performed. Serological testing was not done as the rats were collected 1–3 days post-mortem, and it would only have been informative regarding prior exposure rather than active infection and environmental shedding.

**Figure 1: Photograph of a rat hole (indicated by blue arrow) in the garden beds of the social housing block, Sydney, Australia, 2024**



## Discussion

This is only the fifth human leptospirosis case to be acquired locally in suburban Sydney, out of 71 notified cases in New South Wales during the period 1 January 2003 – 18 December 2024.<sup>27</sup> The other 66 cases have regional, rural or overseas acquisition. It is also the only New South Wales metropolitan case associated with poor living conditions and rat infestation.<sup>16</sup> Suspected rat or urine-contaminated water exposure has been common across all five notified suburban Sydney cases, based on Public Health interviews investigating possible sources. In this instance, the social housing rat infestation and issues with garbage storage around the case's unit increased his risk of exposure. In addition, Vohwinkel syndrome is known to predispose to skin and soft tissue infections due to disrupted skin integrity, presumably also increasing risk for percutaneous transmission of leptospirosis.<sup>28</sup>

Most studies linking urban leptospirosis to lower socioeconomic status and poor conditions of living are from lower income nations, particularly in South America.<sup>18,19,29–31</sup> In more affluent countries, leptospirosis may not always be considered as a potential diagnosis in cases lacking classic occupational or water activity histories,<sup>1</sup> raising the possibility of other missed local cases. Confounding social determinants of health like unemployment, food insecurity, substance use, limited social support and low levels of educational attainment may exacerbate vulnerability to infection with leptospirosis, severity of presentation, and clarity of diagnosis.<sup>18,29,31</sup> People identifying as Aboriginal or Torres Strait Islander, such as this case, are over-represented in social housing, comprising around 17% of residents, while making up just under 4% of the total Australian population.<sup>32–34</sup> Not only is there disparity in risk of exposure through poor living conditions, but a lack of access to culturally safe healthcare may hamper appropriate and timely medical management.

*Rattus norvegicus* is ubiquitous in urban environments worldwide and has been identified as one of two species of rat with the highest prevalence of *Leptospira* spp.<sup>9</sup> Carriage of serovar Copenhageni is documented globally, and the Icterohaemorrhagiae serogroup it sits within is reported most frequently in rat studies.<sup>9</sup> Chronic asymptomatic carriage and urinary shedding of *Leptospira* spp. by *Rattus norvegicus* can persist for upwards of 200 days.<sup>8</sup> Despite this, none of the rats tested as part of the Public Health investigation into this case had a positive PCR

for leptospirosis on kidney tissue, including a rat retrieved from the dog park immediately adjacent to the social housing block. Previous papers have found that live-trapped rats were more likely to test positive on PCR, suggesting that degradation of DNA in rat carcasses could have contributed to false negative PCR results.<sup>5</sup> The small sample size of 12 may also have been too small to detect the previously documented prevalence rate of 8% in Sydney rats.<sup>5</sup>

If the negative results do truly reflect a lack of leptospirosis carriage in the local rat population, then alternate reservoirs need to be considered. Native common brushtail possums, flying-foxes and bandicoots have all been suggested as potential reservoir species, with evidence of chronic *Leptospira* carriage and shedding,<sup>11,26,35,36</sup> while feral and domestic cats are also known carriers.<sup>37,38</sup> A recent study suggested that pathogenic *Leptospira* may even be ubiquitous in recreational parks in Sydney.<sup>25</sup>

Interestingly, cases of canine leptospirosis have recently been reported in the local area. Figure 2 shows a sign present at the time of inspection in the dog park adjacent to the case's residence.

**Figure 2: Photograph of a sign in the dog park adjacent to the social housing block regarding canine leptospirosis cases in the area, Sydney, Australia, 2024**



An outbreak of leptospirosis in Sydney dogs started in 2017 and continues, with 34 total cases as of December 2023.<sup>25</sup> Thirteen of 17 cases up to 2020 fell within the City of Sydney Council area, in which our case resides, and all but two tested positive for serovar Copenhageni, the same serovar seen in this human case.<sup>39</sup> It was postulated that the dogs had contracted leptospirosis through contact with rat urine or eating rats, so owners within a 3 km radius of affected suburbs were advised to get their dogs vaccinated against serovar Copenhageni.<sup>5</sup>

It is possible that our case's dog had contracted leptospirosis, become a chronic asymptomatic carrier, and was the actual source of transmission. However, a systematic review of risk factors for human leptospirosis found that the odds ratio for dog ownership was close to one, implying a limited role as a source.<sup>20</sup> This is possibly because dogs shed much lower concentrations of infectious leptospires in their urine than rats or humans.<sup>40</sup> Although unconfirmed, it was also reported that the case's dog had previously been vaccinated against *Leptospira* spp. The only canine vaccine available in Sydney at the time was Protech<sup>®</sup> C2i, an inactivated vaccine targeting *Leptospira interrogans* serovar Copenhageni.<sup>41</sup> Regardless, it is unfortunate that the possibility of canine transmission was not able to be ruled out with diagnostic testing of the dog.

On balance, transmission from rats is assumed to be the most plausible route of acquisition for this case. There is extensive literature supporting rats as the primary urban reservoir for leptospirosis, with risk of disease correlating with increased rat exposure.<sup>1,9</sup> Eight percent of Sydney rats have been found to carry *Leptospira*,<sup>5</sup> and the case's social housing complex was known to have a severe concurrent rat infestation. Further surveillance and testing of other potential local animal reservoirs, including domestic and feral animals, and native wildlife, may provide better clarity.

## Conclusion

This case, representing the fifth case of locally acquired leptospirosis in metropolitan Sydney over the last two decades, highlights the potential increased risk of rat exposure from socioeconomic disadvantage and poor living conditions. These are well-recognised risks for leptospirosis in other countries but have not previously been linked with the rare urban cases in Sydney. There is a chance that other urban cases associated with these factors may have been missed, and increased clinician awareness and suspicion is required. Urban-acquired leptospirosis is an example of persisting social inequity, even in affluent cities like Sydney. Addressing broader issues of housing standards and security, and other social determinants of health, should be a priority in conjunction with heightened diagnostic awareness. Not enough is known about other potential reservoir species in the city, and this should also be further investigated.

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## Ethics approval

With respect to human ethics considerations, the information collected for this study was for the purpose of a public health investigation, for which human ethics approval was not required. Consent was sought from, and provided by, the case for publication of this case study.

The rats examined were not euthanised for the purposes of this investigation. The City of Sydney Council independently organised a licenced contractor to carry out widespread rat management across the council area. Rat euthanasia was carried out in accordance with the relevant sections of the *Australian Code for the Care and Use of Animals for Scientific Purposes* (Clauses 3.3.33–3.3.44), in particular humane killing. Rat carcasses were opportunistically collected by the New South Wales Department of Primary Industries and Regional Development (DPIRD) and stored at -80 °C by the investigator MW in case they were ever useful for disease testing in the future. As the rats analysed in this study were not collected for the purposes of this case report and were tested retrospectively, after this case emerged, animal ethics approval was not required.

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