Musara and Kapungu
Tropical Diseases, Travel Medicine and Vaccines (2025) 11:16
https://doi.org/10.1186/s40794-025-00250-7

Tropical Diseases,
Travel Medicine and Vaccines

REVIEW

Open Access

Addressing the burden of leptospirosis in Africa

Colin Musara[1*] and Frank Kapungu[2]

Abstract

Leptospirosis is a zoonosis of global distribution. The U.S. Centers for Disease Control and Prevention has designated leptospirosis a nationally notifiable disease. There is need to raise awareness of the burden of leptospirosis among health care givers and policy makers in Africa. The aim of this review was to highlight the current situation of leptospirosis in Africa and suggest a One Health approach of addressing its status as a leading zoonosis. In tropical regions, the nonspecific symptoms of fever, myalgia and arthralgia result in misdiagnosis of leptospirosis with malaria, yellow fever, typhoid fever, dengue fever, brucellosis, rickettsiosis, and babesiosis. Urinalysis presents an inexpensive diagnostic aid for leptospirosis. Humans with leptospirosis exhibit proteinuria, glucosuria, pyuria, haematuria and granular casts resulting from acute kidney injury. Therapeutic guidelines for empirical treatment of febrile patients should be considered. Febrile patients who test negative for malaria and yellow fever can benefit from doxycycline, which also treats brucellosis, rickettsiosis and typhoid fever. Control of leptospirosis should also address *Leptospira* infection in domestic animal reservoirs through vaccination of cattle, sheep, goats, pigs and dogs in endemic areas. Treatment of sick animals with streptomycin eliminates the carrier status, curbing leptospiruria and spread of infection. Rodents are important in transmission of *Leptospira* to humans in urban slums and rural settings therefore rodent control strategies help in reducing transmission of leptospirosis. Indirect transmission of *Leptospira* occurs through contact with water, vegetation, or soil contaminated with infected urine. Drinking water should be drawn from protected sources or chlorinated before household use.

Keywords Leptospirosis, Zoonosis, Urinalysis, Doxycycline, Streptomycin, Vaccination, Rodent control, Chlorination, Africa

Introduction

Leptospirosis is a zoonosis of global distribution. The syndrome of icteric leptospirosis with renal failure was first reported in humans by Adolf Weil in 1896 and subsequently named Weil's disease [1]. The aetiology of leptospirosis was first demonstrated by Stimson in 1907, who named the causative organism *Spirochaeta interrogans* [2], now known as *Leptospira interrogans*. The role of the rat as a source of human infection was first established in 1917 by Ido and co-workers [3]. In humans, severe leptospirosis is often, but not always, caused by serovars of the Icterohaemorrhagiae serogroup [4]. According to the World Health Organization (WHO) estimates, the global endemic human leptospirosis rate is 5 cases per 100,000 people per year, whilst the epidemic human leptospirosis rate stands at 14 cases per 100,000 people per year [5]. The incidence rate in tropical areas is higher, at 10–100 cases per 100,000 people per year [6]. About 30% of acute leptospirosis cases become chronic, resulting in long-term health issues [7]. Human leptospirosis is largely an occupational and environmental hazard. Vulnerable populations include communities living in habitations

*Correspondence:
Colin Musara
cmusara@unam.na
[1] University of Namibia, Private Bag 13301, Pioneers Park, Windhoek, Namibia
[2] University of Zimbabwe, P.O. Box MP167, Mount Pleasant, Harare, Zimbabwe

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

exposed to rodents, people working or living in close contact with infected farm animals, and communities with poor sanitation or lack of safe drinking water [7–12]. The U.S. Centers for Disease Control and Prevention (CDC) has designated leptospirosis a nationally notifiable condition [13] and the World Health Organization as a major direct zoonosis with epidemic potential [14, 15]. In spite of its significance, leptospirosis remains underreported in Africa largely because of the high technological requirements for its definitive diagnosis. At 3.4 cases per 100 000 people per year, southern Africa has the lowest documented incidence of leptospirosis worldwide [16]. There is need to raise awareness of the human health burden of leptospirosis in Africa among health care givers and policy makers. The contribution of domestic animals to transmission of leptospirosis to humans in Africa is now well- established [17] and ought to be taken into consideration in addressing the human burden. In addition, the high temperatures and high rainfall associated with the summer season in tropical regions of Africa favour survival and transmission of *Leptospira* pathogens [18], presenting an environmental component to the scourge of leptospirosis. In this review, we give a synopsis of leptospirosis in Africa and suggest a One Health approach of bringing the disease under control. This concept encompasses interventions at human, animal and environmental levels. Additional information for safety of travellers coming to Africa from non-endemic temperate climates is presented at the end.

Epidemiology

The epidemiology of leptospirosis in Africa is best contextualized into national, regional and continental levels.

National level

At the national level, Crump investigated the epidemiology of leptospirosis in 7804 patients presenting with fever in Malawi, Mozambique, Zimbabwe and Laos [19]. A total of 149 (2.2%) cases of confirmed leptospirosis were diagnosed by PCR, of which 1.2% were from Malawi, 0.4% from Mozambique, 1.6% from Zimbabwe and 6.2% from Laos. The results denote crude prevalence rates encompassing multiple variables including age, sex, exposure to animals, working in rice fields and swimming or bathing in river water. The higher prevalence in Laos was associated with rice field workers. Three species of *Leptospira* were detected in southern Africa namely *L. interrogans*, *L kirschneri* and *L. borgpetersenii*, in descending order of prevalence. Icterohaemorrhagiae and Ballum were the predominant serogroups in the southern Africa countries, as opposed to Australis in Laos. The two serogroups detected in Malawi, Mozambique and Zimbabwe suggest that rats and mice, respectively, are significant reservoirs for human leptospirosis in these countries. In a serological survey of bovine leptospirosis in Malawi, 275 serum samples from cattle were tested for *Leptospira* antibody titres [20]. Fifty-nine (21.4%) of the animals were positive for leptospirosis, titres to serovars hardjo and pomona being the most prevalent. Cattle thus also contribute to the pool of reservoirs for human leptospirosis in Malawi. In Namibia, where a seroprevalence of 2.8% has been reported in humans in one survey, antibodies to *Leptospira* organisms have been detected in wildlife species including impala and rhinoceros [21]. In Kenya, a country with a diversity of wildlife hosts similar to Namibia but having much higher annual rainfall, seropositivity in community populations was between 2.5% and 25.7% [22]. Statistical tests showed a shared spectrum of *Leptospira* serogroups among humans, domestic animals and wildlife. The exact contribution of wildlife to transmission of leptospirosis to humans is yet to be established, but direct contact between wild mammals and humans is minimal.

Regional level

At regional level, Comia et al. [23] conducted a meta-analysis of the epidemiology of human leptospirosis in Southern African Development Community (SADC) countries. This region is composed of 16 countries, namely Angola, Botswana, Democratic Republic of Congo, Comoros, Eswatini, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Tanzania, Zambia and Zimbabwe. The pooled prevalence of leptospirosis in the SADC region, based on the meta-analysis, was 19%. The three species of *Leptospira* detected by Crump in Malawi, Mozambique and Zimbabwe [19] were also the predominant species reported for the SADC region as a whole. A total of 23 serogroups were identified in SADC countries, of which the most prevalent were Icterohaemorrhagiae, Grippotyphosa, Australis, Sejroe, Ballum and Hebdomadis. The Icterohaemorrhagiae serogroup was isolated from rodents as well as cattle and pigs. This signifies the role of livestock as reservoirs of this serogroup, previously believed to be solely rodent-maintained. A relationship was found between *Leptospira* genotypes circulating in livestock and humans, particularly among farm workers.

Continental level

At continental level, the prevalence of acute human leptospirosis ranged from 2.3% to 19.8% in hospital patients with febrile illness [24]. It was noted that acute *Leptospira* infection was geographically widespread across the African continent and should be considered as an important differential diagnosis in acute undifferentiated febrile illness (AUFI). Data from across Africa indicated that

human disease incidence ranged from 25 to 120 cases per 100,000 people per year. Most naturally-occurring leptospiral infections in animal reservoirs were reported in South Africa, Zimbabwe and Tanzania. Leptospiral infection was documented in a broad range of animal hosts including livestock (cattle, pigs, goats), pets (dogs, cats), rodents (rats, mice) and feral animals (bats, shrew tenrecs, streaked tenrecs, gerbils, mongooses). Rodents were the most important reservoirs of human infection, followed by cattle and pigs. The prevalence rate in rodents was up to 65.8%, compared to 18.2% for cattle. Cattle were identified as reservoirs for the largest range of *Leptospira* serogroups including Icterohaemorrhagiae, Grippotyphosa, Pomona, Sejroe, Australis, Hebdomadis, Pyrogenes, Tarrasovi and Bataviae. African grass rats and black rats were also important reservoir hosts for multiple serogroups. Less frequently isolated serogroups included Canicola, Automnalis, Djasiman, Wolfi and Mini.

Control

Leptospira pathogens are maintained by chronic infection of the renal tubules of carrier animals, resulting in intermittent leptospiuria [25–27]. The source of infection for humans is direct contact with the urine of an infected animal, or indirect contact with soil or water contaminated with infected urine. The portals of entry are through the skin, conjunctiva and respiratory passages. Control of leptospirosis requires the adoption of the One Health model, which considers the connection between *Leptospira* infection in humans and animal reservoirs together with the role of the environment in the epidemiology of leptospirosis [24, 28].

Leptospirosis in humans

In tropical regions the non-specific clinical symptoms of fever, myalgia and arthralgia often results in misdiagnosis of leptospirosis with other endemic febrile diseases like malaria, yellow fever, typhoid fever, dengue fever, brucellosis, rickettsiosis and babesiosis. Concurrence of fever with icterus is presumptive of yellow fever, malaria or icteric leptospirosis. Leptospirosis accounts for up to 40% of AUFI [29]. The standard method for definitive diagnosis of leptospirosis is through detection of antibodies against the infecting serovar in plasma using the Microscopic Agglutination Test (MAT) [30, 31]. More recently, molecular methods like Polymerase Chain Reaction (PCR) on urine or blood samples have become increasingly pertinent in diagnosis of leptospirosis [32, 33]. Both MAT and PCR are expensive assays that require sophisticated technology in terms of laboratory personnel, equipment and facilities. Acute leptospirosis is therefore easily misdiagnosed at primary healthcare centres in Africa due to limited availability of both tests [34]. Urinalysis presents a useful and inexpensive diagnostic aid for leptospirosis in Africa. In humans with leptospirosis, urine analysis demonstrates abnormal results caused by acute kidney injury, including proteinuria, glucosuria, pyuria, haematuria, low urine specific gravity and granular casts [35–37]. In icteric leptospirosis, bilirubinuria will also be present. Haemoglobinuria may be observed secondary to haemolysis caused by haemolysins produced by certain serovars. Abnormal urinalysis findings are not currently part of the diagnostic criteria for leptospirosis although they are a common feature in many investigations in both humans and animals. Urinalysis can only be used as an ancillary diagnostic test owing to its low specificity and sensitivity. Of the dipstick parameters mentioned above, only the leukocyte esterase test for pyuria shows sufficient sensitivity for bacteriuria when compared with a quantitative urine culture [38]. When it is used alone, the leukocyte esterase test has a sensitivity of 48–86% and specificity of 17–93% in detecting urinary tract infection [39]. Combining the results of leucocyte esterase test with other dipstick parameters will improve both sensitivity and specificity.

Commercial rapid diagnostic tests (RDTs) for leptospirosis based on the detection of IgG or IgM antibodies to *Leptospira* pathogens in blood or plasma are available at point of care. In one RDT, Leptocheck-WB®, the sensitivity was found to be 47,7%, and specificity of 80.65% [40]. In the same study another RDT, ImmuneMed Leptospira IgM Duo®, had a sensitivity of 21.05% and specificity of 90.32%. These results compare well with urinalysis. Rapid diagnostic tests are user-friendly as well as affordable and therefore offer a valuable avenue for diagnosis of leptospirosis in low-resource settings. The main limitation of rapid diagnostic tests is that they can easily miss the acute septicaemic phase of leptospirosis in the first week of the disease. During this phase antibody levels are still low, but the pathogen is multiplying in blood and disseminating to various organs and tissues resulting in severe clinical symptoms [41, 42]. Anti-leptospira IgM antibodies are only detectable 4–5 days after onset of symptoms whist IgG and agglutinating antibodies appear even later [43]. It should also be noted that IgM antibodies can persist in the blood for years following recovery from infection, a situation which may yield false-positive results in spot tests [36].

The development of therapeutic guidelines for the empirical treatment of febrile patients should be a priority in resource-limited primary health care centres. Leptospira is susceptible to several classes of antimicrobial agents including tetracyclines, penicillins, third generation cephalosporins, macrolides, fluoroquinolones and aminoglycosides [44–47]. Febrile patients who test

negative for malaria and yellow fever can immediately be placed on a course of broad-spectrum antimicrobial agents like doxycycline. Besides treating leptospirosis, doxycycline is also effective against other febrile illnesses including brucellosis [37], rickettsiosis [48] and typhoid fever [49]. When used in combination with a fast acting schizontocidal agent like quinine, doxycycline is also highly effective for treatment of malaria [50]. Ceftriaxone is recommended for treatment of leptospirosis in cases that are refractory to doxycycline [51].

Although vaccines against *Leptospira* spp. are available, human immunization is not widely practised in many countries including developing nations in Africa. Contemporary anti-leptospirosis vaccines are bacterins composed of whole inactivated *Leptospira* [52–54]. Typically, they induce only a short-term serovar-specific immunity, therefore necessitating annual immunization [55]. The use of specific vaccines against targeted serovars would undoubtably reduce the incidence of infection in endemic regions. However, given the prevailing broad range of pathogenic serovars in Africa, it is unlikely that any single vaccine will be able to fully protect against human leptospirosis on the continent. In addition, the requirement for annual revaccination makes vaccination programs less appealing and more expensive compared to treatment. Other reasons for vaccine apathy include low effectiveness and adverse side effects [56]. These drawbacks have resulted in the current scenario where no single anti-leptospirosis vaccine is licenced for use in the whole of Africa. Nonetheless, outbreak response immunization with polyvalent vaccines should be considered a viable control strategy in the face of epidemics.

Leptospirosis in animals

With respect to infection in animals, knowledge of reservoir animal hosts is essential for understanding the epidemiology, transmission and control of leptospirosis. The most significant maintenance hosts for human leptospirosis are rodents, dogs and farm animals. Rats and mice are maintenance hosts for serovars of the serogroups Icterohaemorrhagiae and Ballum respectively [6]. Dogs harbour serovar canicola; cattle harbour harjo, pomona, and grippotyphosa; pigs harbour pomona, tarassovi and bratislava; and sheep harbour harjo and pomona [57]. Emerging evidence indicates that control measures to prevent human leptospirosis should focus not only on the traditional rodent reservoirs, but also on domestic animals. Farm animals are important reservoirs of *Leptospira* infection in Africa and play a bigger role in transmission of the disease to humans than was previously recognised. Control of *Leptospira* infection in livestock species would therefore considerably reduce animal-to- human transmission of leptospirosis by reducing the prevalence of leptospiruria [58, 59]. This requires regular surveillance and monitoring of *Leptospira* infections in livestock and at slaughterhouses. Vaccination of animal hosts is recommended in endemic areas. Commercial vaccines against leptospirosis are available for cattle, sheep and goats (hardjo, pomona), pigs (tarassovi, pomona) and dogs (icterohaemorrhagiae, canicola). Treatment of sick animals with streptomycin eliminates the carrier status in animals thus curbing leptospiruria and the risk of animal-to-human infection [60]. Although rodents have been implicated as important in transmission of *Leptospira* pathogens to humans mainly in high density urban slums, they are domiciliated species in rural settings of Africa as well, particularly in granaries and traditional thatched houses. Implementation of rodent control strategies therefore helps to reduce transmission of leptospirosis in both rural and urban areas. Recent reports on isolation of *Leptospira* pathogens from a variety of both small and large mammals in wildlife may pose yet another challenge to control of leptospirosis on the African continent. However, direct and indirect contact between these feral reservoirs and humans is minimal.

Leptospira spp. in the environment

The environment plays an important role in the transmission cycle of *Leptospira* pathogens in both humans and animals. Indirect transmission of *Leptospira* occurs through contact with water, vegetation, or soil contaminated with infected urine. The transmission of pathogenic *Leptospira* is thus exacerbated by high rainfall as well as contact with soil during farming activities [61].) In a case study on pathogenic *Leptospira* spp. in open water sources conducted in Cotonou, Benin, contamination was reported in 5.5% of samples collected from temporary water bodies, permanent ponds and underground water during the wet season [62]. Waterborne leptospirosis thus poses a potential public health hazard during the rainy season due to overflow of contaminated surface water. High sanitary standards should be observed, especially when it comes to drinking water. Where the necessary infrastructure is present, drinking water should only be drawn from protected wells or boreholes. Water drawn from open sources, for example dams and rivers, needs to be chlorinated before household use. Water purification tablets containing chlorine are widely available and affordable in most parts of Africa. In areas where chlorination is not possible for economic or other reasons, water should be boiled to make it potable. The public should be educated on the risk of living close to stagnant pools of water which, besides presenting breeding grounds for mosquitoes, are prone to contamination with urine

from livestock, dogs and feral reservoirs. Accordingly, adequate drainage should be maintained during the rainy season.

Soil is an important natural habitat for *Leptospira* spp. The pathogens can survive for more than a year and then multiply and disseminate following waterlogging [63]. This gives rise to the concept of soilborne leptospirosis. Whilst it is not possible to avoid hand contact with soil during agricultural activities, protective footwear reduces transmission of *Leptospira* organisms from contaminated soil via the feet. *Leptospira* pathogens are highly susceptible to desiccation [64]. In this respect, low precipitation during the dry season in southern Africa provides a natural respite to transmission of leptospirosis.

Leptospirosis and travellers

Tourists travelling to tropical African countries during the rainy season should be aware of the potential risk of exposure to leptospirosis, particularly if they will be engaging in activities like water sports and ecotourism [65]. There is currently no drug that is effective for prophylaxis of leptospirosis. Travellers from countries like Japan, China, France and Cuba where anti-leptospirosis vaccines are licenced [55] may consider vaccination as a prophylactic measure prior to travel. Knowledge of the clinical symptoms of leptospirosis among travellers is also invaluable for early recognition of the disease and prompt treatment. Two clinical forms of *Leptospira* infections are recognised in humans; icteric and non-icteric [66–68]. Icteric leptospirosis is characterised by haemolysis, haemoglobinuria, jaundice or icterus, bilirubinuria, and a fever of up to 39˚C. The main serovars associated with haemolysis and jaundice are icterohaemorrhagiae, ballum, pomona, hardjo, tarassovi and canicola [66]. Anicteric leptospirosis, on the other hand, is typified by myalgia, abdominal pain and vomiting, conjunctivitis with or without conjunctival suffusion, renal dysfunction (oliguria), leptospirosis pulmonary haemorrhagic syndrome (dyspnoea, coughing and haemoptysis), aseptic meningitis (convulsions, neurological impairment) and a low-grade biphasic fever in the absence of icterus. A presumptive diagnosis of leptospirosis should still be considered even in the absence of icterus as both icteric and non-icteric forms warrant prompt treatment to prevent deterioration [6]. Since the incubation period of pathogenic *Leptospira* spp. is between 2 and 20 days [41], it is still possible for travellers to develop clinical symptoms for up to three weeks after visiting an endemic area. On a conciliatory note, direct transmission of leptospirosis between humans is rare [69] therefore public amenities are safe to use.

Conclusion

At continental level, the prevalence of acute human leptospirosis ranged from 2.3% to 19.8% in hospital patients with febrile illness. In tropical Africa, there are many serovars infecting humans and animals due to a large number of reservoir species which include domestic animals and small mammals such as rats, mice, mongooses, tenrecs, gerbils and bats. *Leptospira* serogroups that have been isolated from cases of acute human leptospirosis and animal reservoirs include Australis, Automnalis, Ballum, Canicola, Djasiman, Grippotyphosa, Hebdomadis, Icterohaemorrhagiae, Mini, Pomona, Pyrogenes, Sejroe, Tarassovi and Wolfii. The standard MAT method for diagnosis of leptospirosis is only available in reference laboratories therefore leptospirosis is easily misdiagnosed at primary healthcare centres. In addition, the nonspecific symptoms of leptospirosis overlap with other endemic febrile diseases like malaria, yellow fever, typhoid fever, dengue fever, brucellosis, rickettsiosis, and babesiosis, confounding definitive diagnosis of leptospirosis. Urinalysis and RDTs present affordable differential diagnostic tools for leptospirosis at primary healthcare level. Doxycycline reduces the duration and severity of illness in human leptospirosis, and is also effective against brucellosis, typhoid fever and rickettsiosis. For treatment of animal leptospirosis, streptomycin or dihydrostreptomycin are recommended because they eliminate the carrier status. Vaccination, however, is the most effective means for control of leptospirosis in domestic animals. Adequate rodent control strategies should be implemented in both urban slums and rural areas to interrupt transmission from rats and mice. The environment plays an important role in the transmission cycle of *Leptospira* pathogens in both humans and animals exposed to water, vegetation, or soil contaminated with infected urine. Transmission of pathogenic *Leptospira* is thus enhanced by high rainfall, flooding and contact with soil during farming activities. High sanitary standards should be observed when it comes to potable water, and appropriate personal protective equipment worn during agricultural activities.

Abbreviations

CDC	The United States Centres for Disease Control and Prevention
WHO	World Health Organization
SADC	Southern African Development Community
AUFI	Acute Undifferentiated Febrile Illness
MAT	Microscopic Agglutination Test
PCR	Polymerase Chain Reaction
RDT	Rapid Diagnostic Test

Acknowledgements

Not applicable.

Authors' contributions
C.M. conceived the review and compiled the original draft of the manuscript. F.K. revised the first draft and added more scientific content. Both authors edited the final draft before submission for consideration for publication.

Funding
Not applicable.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 30 January 2025 Accepted: 12 March 2025
Published online: 07 June 2025

References

1. Weil A. Ueber eine eigentu¨mliche, mit Milztumor, Icterus und Nephritis einhergehende akute Infektionskrankheit. Dtsche Arch Klin Med. 1886;39:209–32.
2. Stimson AM. Note on an organism found in yellow-fever tissue. Public Health Rep. 1907;22:541.
3. Ido Y, Hoki R, Ito H, Wani H. The rat as a carrier of *Spirochaeta icterohaemorrhagiae*, the causative agent of Weil's disease (spirochaetosis icterohaemorrhagica). J Exp Med. 1917;26:341–53. https://doi.org/10.1084/jem.26.3.341.
4. Levett PN. Leptospirosis. Clin Microbiol Rev. 2001;14(2):296–326. https://doi.org/10.1128/CMR.14.2.296-326.2001.
5. World Health Organization. Leptospirosis fact sheet. WHO Regional Office for South East Asia; 2011. p. 1–12. Available from: http://apps.who.int/rest/bitstream/retrieve . Accessed 23 Mar 2023.
6. Sellors P, Watson RF, Bate R, Bentham GL, Haigh K. Clinical features and severity of Leptospirosis cases reported in the Hawke's Bay Region of New Zealand. J Trop Med. 2021;2021: 5567081. https://doi.org/10.1155/2021/5567081.
7. Haake DA, Levett PN. Leptospirosis in humans. Curr Top Microbiol Immunol. 2015;387:65–97. https://doi.org/10.1007/978-3-662-45059-8_5.
8. Campagnolo ER, Warwick MC, Marx HL, Cowart RP, Donnell HD, Bajani MD, et al. Analysis of the 1998 outbreak of leptospirosis in Missouri in humans exposed to infected swine. J Am Vet Med Assoc. 2000;216:676–82. https://doi.org/10.2460/javma.2000.216.676.
9. Chan OY, Paul DR, Sng EH. Leptospirosis among abattoir workers—a serological study. Singapore Med J. 1987;28:293–6.
10. Demers RY, Frank R, Demers P, Clay M. Leptospiral exposure in Detroit rodent control workers. Am J Public Health. 1985;75:1090–1. https://doi.org/10.2105/ajph.75.9.1090.
11. Anderson DC, Geistfeld JG, Maetz HM, Patton CM, Kaufmann AF. Leptospirosis in zoo workers associated with bears. Am J Trop Med Hyg. 1978;27:210–1. https://doi.org/10.4269/ajtmh.1978.27.210.
12. Thornley CN, Baker MG, Weinstein P, Maas EW. Changing epidemiology of human leptospirosis in New Zealand. Epidemiol Infect. 2002;128(1):29–36. https://doi.org/10.1017/s0950268801006392.
13. Centres for Disease Control and Prevention. Leptospirosis case definition and reporting. Available at: https://www.cdc.gov/leptospirosis/php/surveillance/index.html. Accessed 2 Mar 2025.
14. World Health Organisation. Leptospirosis fact sheet. Available from: https://iris.who.int/bitstream/handle/10665/205437/B4221.pdf. Accessed 25 Feb 2025.
15. World Health Organisation. Human Leptospirosis: guidance for diagnosis, surveillance and control. Available from: https://www.who.int/publications/i/item/human-leptospirosis-guidance-for-diagnosis-surveillance-and-control. Accessed 25 Feb 2025.
16. Muñoz-Zanzi C, Dreyfus A, Limothai U, Foley W, Srisawat N, Picardeau M, Haake DA. Leptospirosis—improving healthcare outcomes for a neglected tropical disease. OFID. 2025;12(2):1–9. https://doi.org/10.1093/ofid/ofaf035.
17. Onafruo D, Dreyfus A, Erume J, Kankya C, Jubara A, Kokas I, Odoch T, Munyeme M, Alinaitwe L, Kitale E, Marin P, Sabbath E, Klein J. Leptospira seroprevalence and associated risk factors among slaughterhouse workers in Western Bahr El Ghazal State, South Sudan. PLoS Negl Trop Dis. 2024;18(12): e0012700. https://doi.org/10.1371/journal.pntd.0012700.
18. Mukadi Kakoni P, Munyeku Bazitama Y, Nepomuceno JR, Pukuta-Simbu E, Kawhata Mawika F, Kashitu Mujinga G, Palla L, Ahuka-Mundeke S, Muyembe Tamfum JJ, Koizumi N, Kubo Y, Ariyoshi K, Smith C. Leptospirosis as a cause of fever associated with jaundice in the Democratic Republic of the Congo. PLoS Negl Trop Dis. 2021;15(8): e0009670. https://doi.org/10.1371/journal.pntd.0009670.
19. Crump JA. Leptospirosis among patients presenting with fever in a multicenter Febrile Illness Evaluation in a Broad range Endemicities (FIEBRE) study. FIEBRE-ASTMH-leptospirosis-2022;1–13. Available from: https://www.lshtm.ac.uk. Accessed 24 Sep 2024.
20. Myburgh JG, Staley GP, van der Merwe SM. Serological evidence of bovine leptospirosis in Malawi. Onderstepoort J Vet Res. 1989;56(4):285–6.
21. de Vries SG, Visser BJ, Nagel IM, Goris MG, Hartskeerl RA, Grobusch MP. Leptospirosis in sub-Saharan Africa: a systematic review. Int J Infect Dis. 2014;28:47–64. https://doi.org/10.1016/j.ijid.2014.06.013.
22. Wainaina M, Wasonga J, Cook EAJ. Epidemiology of human and animal leptospirosis in Kenya: a systematic review and meta-analysis of disease occurrence, serogroup diversity and risk factors. PLoS Negl Trop Dis. 2024;18(9): e0012527. https://doi.org/10.1371/journal.pntd.0012527.
23. Comia IR, Miambo RD, Noormahomed EV, Mahoche M, Pondja A, Schooley RT, et al. A systematic review and meta-analysis of the epidemiology of Leptospirosis in HIV uninfected and in people living with HIV from the Southern African development community. PLoS Negl Trop Dis. 2022;16(12): e0010823. https://doi.org/10.1371/journal.pntd.0010823.
24. Allan KJ, Biggs HM, Halliday JEB, Kazwala RR, Maro VP, Cleaveland S, et al. Epidemiology of Leptospirosis in Africa: a systematic review of a neglected zoonosis and a paradigm for 'one health' in Africa. PLoS Negl Trop Dis. 2015;9(9): e0003899. https://doi.org/10.1371/journal.pntd.0003899.
25. Awad-Masalmeh A, Willinger H. Evaluation of 2-mercaptoethanol treatment in serodiagnosis of swine leptoispirosis. Microbiologica. 1983;6:133–43.
26. Baelen E, Roustan J. Leptospirosis associated with acute acalculous cholecystitis. J Clin Gastroenterol. 1997;25:704–6. https://doi.org/10.1097/00004836-199712000-00038.
27. Rathinam SR, Rathnam S, Selvaraj S, Dean D, Nozik RA, Namperumalsamy P. Uveitis associated with an epidemic outbreak of leptospirosis. Am J Ophthalmol. 1997;124:71–9. https://doi.org/10.1016/s0002-9394(14)71646-0.
28. Gizamba JM, Mugisha L. Leptospirosis in humans and selected animals in sub-Saharan Africa, 2014–2022: a systematic review and meta-analysis. BMC Infect Dis. 2023;23(1):649. https://doi.org/10.1186/s12879-023-08574-5.
29. Abela-Ridder B, Sikkema R, Hartskeerl RA. Estimating the burden of human leptospirosis. Int J Antimicrob Agents. 2010;36(1):S5–7. https://doi.org/10.1016/j.ijantimicag.2010.06.012.
30. Limmathurotsakul D, Turner EL, Wuthiekanun V, Thaipadungpanit J, Suputtamongkol Y, Chierakul W, et al. Fool's gold: why imperfect reference tests are undermining the evaluation of novel diagnostics: a reevaluation of 5 diagnostic tests for leptospirosis. Clin Infect Dis. 2012;55:322–31. https://doi.org/10.1093/cid/cis403.
31. Grooms DL, Bolin CA. Diagnosis of fetal loss caused by bovine viral diarrhea virus and Leptospira spp. Vet Clin North Am: Food Anim Pract. 2005;21:463–72. https://doi.org/10.1016/j.cvfa.2005.02.010.

32. Pinna AE, Martins G, Hamond C, Lilenbaum W, Medeiros MA. Molecular diagnostics of leptospirosis in horses is becoming increasingly important. Vet Microbiol. 2011;153(3–4):413. https://doi.org/10.1016/j.vetmic.2011.06.015.
33. Otaka DY, Martins G, Hamond C, Penna B, Medeiros MA, Lilenbaum W. Serology and PCR for bovine leptospirosis: herd and individual approaches. Vet Rec. 2012;170(13):338. https://doi.org/10.1136/vr.100490.
34. Musso D, La Scola B. Laboratory diagnosis of leptospirosis: a challenge. J Microbiol Immunol Infect. 2013;46(4):245–52. https://doi.org/10.1016/j.jmii.2013.03.001.
35. de Brito T, Freymu¨ller E, Penna DO, Santos HS, Soares de Almeida S, Galva˜o PAA, et al. Electron microscopy of the biopsied kidney in human leptospirosis. Am J Trop Med Hyg. 1965;14:397–403.https://doi.org/10.4269/ajtmh.1965.14.397.
36. Budihal SV, Perwez K. Leptospirosis diagnosis: competancy of various laboratory tests. J Clin Diagn Res. 2014;8(1):199–202. https://doi.org/10.7860/JCDR/2014/6593.3950.
37. Solera J, Espinosa A, Martínez-Alfaro E, Sánchez L, Geijo P, Navarro E, et al. Treatment of human brucellosis with doxycycline and gentamicin. Antimicrob Agents Chemother. 1997;41:80–4. https://doi.org/10.1128/aac.41.1.80.
38. Lohr JA. Use of routine urinalysis in making a presumptive diagnosis of urinary tract infection in children. Pediatr Infect Dis J. 1991;10(9):646–50. https://doi.org/10.1097/00006454-199109000-00004.
39. Devillé WL, Yzermans JC, van Duijn NP, Bezemer PD, van der Windt DA, Bouter LM. The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy. BMC Urol. 2004;4: 4. https://doi.org/10.1186/1471-2490-4-4.
40. Alia SN, Joseph N, Philip N, Azhari NN, Garba B, Masri SN, Sekawi Z, Neela VK. Diagnostic accuracy of rapid diagnostic tests for the early detection of leptospirosis. J Infect Public Health. 2019;12(2):263–9. https://doi.org/10.1016/j.jiph.2018.10.137.
41. Turner LH. Leptospirosis I. Trans R Soc Trop Med Hyg. 1967;61:842–55. https://doi.org/10.1016/0035-9203(67)90045-4.
42. Langston CE, Heuter KJ. Leptospirosis: a re-emerging zoonotic disease. Vet Clin N Am: Small Anim Pract. 2003;33(4):791–807. https://doi.org/10.1016/s0195-5616(03)00026-3.
43. Silva MV, Camargo ED, Batista L, Vaz AJ, Brandão AP, Nakamura PM, Negrão JM. Behaviour of specific IgM, IgG and IgA class antibodies in human leptospirosis during the acute phase of the disease and during convalescence. J Trop Med Hyg. 1995;98(4):268–72.
44. Alexander AD, Rule PL. Penicillins, cephalosporins, and tetracyclines in treatment of hamsters with fatal leptospirosis. Antimicrob Agents Chemother. 1986;30:835–9. https://doi.org/10.1128/AAC.30.6.835.
45. McClain JBL, Ballou WR, Harrison SM, Steinweg DL. Doxycycline therapy for leptospirosis. Ann Intern Med. 1984;100:696–8. https://doi.org/10.7326/0003-4819-100-5-696.
46. Watt G, Padre LP, Tuazon ML, Calubaquib C, Santiago E, Ranoa CP, et al. Placebo-controlled trial of intravenous penicillin for severe and late leptospirosis. Lancet. 1988;1(8583):433–5. https://doi.org/10.1016/s0140-6736(88)91230-5.
47. Edwards CN, Nicholson GD, Hassell TA, Everard COR, Callender J. Penicillin therapy in icteric leptospirosis. Am J Trop Med Hyg. 1988;39:388–90. https://doi.org/10.4269/ajtmh.1988.39.388.
48. Binder AM, Armstrong PA. Patient characteristics, treatment patterns, and outcomes of Rickettsial diseases among a commercially insured population in the United States, 2005–2017. Sci Rep. 2021;11(1):18382. https://doi.org/10.1038/s41598-021-96463-9.
49. Basnyat B. The treatment of enteric fever. J R Soc Med. 2007;100(4):161–2. https://doi.org/10.1258/jrsm.100.4.161.
50. Tan KR, Magill AJ, Parise ME, Arguin PM. Doxycycline for malaria chemoprophylaxis and treatment: report from the CDC expert meeting on malaria chemoprophylaxis. Am J Trop Med Hyg. 2011;84(4):517–31. https://doi.org/10.4269/ajtmh.2011.10-0285.
51. Kritikos K, Mililis P, Mpahara A, Kouvariotis G, Kritikos N, Chaliotis G. Increasing awareness of physicians against severe leptospirosis: a treatable but potentially fatal zoonotic infection. J Family Med Prim Care. 2017;6(1):148–50. https://doi.org/10.4103/2249-4863.214955.
52. Chen T. Development and present status of leptospiral vaccine and technology of vaccine production in China. Jpn J Bacteriol. 1985;40:755–62. https://doi.org/10.3412/jsb.40.755.
53. Laurichesse H, Gourdon F, Smits HL, Abdoe TH, Estavoyer JM, Rebuke H, et al. Safety and immunogenicity of subcutaneous or intramuscular administration of a monovalent inactivated vaccine against Leptospira interrogans serogroup Icterohaemorrhagiae in healthy volunteers. Clin Microbiol Infect. 2007;13(4):395–403. https://doi.org/10.1111/j.1469-0691.2007.01662.x.
54. Martinez Sanchez R, Obregon Fuentes AM, Perez Sierra A, Baly Gil A, Diaz Gonzalez M, Baro Suarez M, et al. The reactogenicity and immunogenicity of the first Cuban vaccine against human leptospirosis. Rev Cuba Med Trop. 1998;50:159–66.
55. Azevedo IR, Amamura TA, Isaac L. Human leptospirosis: in search for a better vaccine. Scand J Immunol. 2023;98(5): e13316. https://doi.org/10.1111/sji.13316.
56. Adler B. Vaccines against leptospirosis. In: Adler B, editor. Leptospira and leptospirosis. Current topics in microbiology and immunology, vol 387. Berlin, Heidelberg: Springer; 2015.
57. Bolin C. Leptospirosis. In: Brown C, Bolin C, editors. Emerging diseases of animals. Washington DC: ASM Press; 2000. p. 185–200.
58. Mughini-Gras L, Bonfanti L, Natale A, Comin A, Ferronato A, La Greca E, Patregnani T, Lucchese L, Marangon S. Application of an integrated outbreak management plan for the control of leptospirosis in dairy cattle herds. Epidemiol Infect. 2014;142(6):1172–81. https://doi.org/10.1017/S0950268813001817.
59. Vallée E, Ridler AL, Heuer C, Collins-Emerson JM, Benschop J, Wilson PR. Effectiveness of a commercial leptospiral vaccine on urinary shedding in naturally exposed sheep in New Zealand. Vaccine. 2017;35(9):1362–8. https://doi.org/10.1016/j.vaccine.2016.04.037.
60. Guadelupe B, Balaro MFA, Brandão FZ, Martins GMS, Lilenbaum W. Streptomycin treatment of genital carriers of Leptospira in experimentally infected sheep on different estrous phases. Res Vet Sci. 2022;152:579–81. https://doi.org/10.1016/j.rvsc.2022.09.027.
61. Faine S. *Leptospira* and leptospirosis. Boca Raton: CRC Press; 1994.
62. Houéménou H, Gauthier P, Houéménou G, Mama D, Alassane A, Socohou A, Dossou HJ, Badou S, Picardeau M, Tweed S, Leblanc M, Dobigny G. Pathogenic Leptospira and water quality in African cities: a case study of Cotonou, Benin. Sci Total Environ. 2021;20(774):145541. https://doi.org/10.1016/j.scitotenv.2021.145541.
63. Yanagihara Y, Villanueva SYAM, Nomura N, Ohno M, Sekiya T, Handabile C, Shingai M, Higashi H, Yoshida S, Masuzawa T, Gloriani NG, Saito M, Kida H. Leptospira is an environmental bacterium that grows in waterlogged soil. Microbiol Spectr. 2022;10:e02157–221. https://doi.org/10.1128/spectrum.02157-21.
64. Philip N, Garba B, Neela VK. Long-term preservation of *Leptospira* spp.: challenges and prospects. Appl Microbiol Biotechnol. 2018;102:5427–35. https://doi.org/10.1007/s00253-018-9047-9.
65. Lau CL, Townell N, Stephenson E, van den Berg D, Craig SB. Leptospirosis: an important zoonosis acquired through work, play and travel. Aust J Gen Pract. 2018;47(3):105–10. https://doi.org/10.31128/AFP-07-17-4286.
66. del Real G, Segers RP, van der Zeijst BA, Gaastra W. Cloning of a hemolysin gene from *Leptospira interrogans* serovar *hardjo*. Infect Immun. 1989;57:2588–90. https://doi.org/10.1128/iai.57.8.2588-2590.1989.
67. El-Tras WF, Bruce M, Holt HR, Eltholth MM, Merien F. Update on the status of leptospirosis in New Zealand. Acta Trop. 2018;188:161–7. https://doi.org/10.1016/j.actatropica.2018.08.021.
68. Bharti AR, Nally JE, Ricaldi JN, Matthias MA, Diaz MM, Lovett MA, et al. Leptospirosis: a zoonotic disease of global importance. The Lancet Infect Dis. 2003;3(12):757–71. https://doi.org/10.1016/s1473-3099(03)00830-2.
69. Bal AE, Gravekamp C, Hartskeerl RA, de Meza-Brewster J, Korver H, Terpstra WJ. Detection of leptospires in urine by PCR for early diagnosis of leptospirosis. J Clin Microbiol. 1994;32:1894–8. https://doi.org/10.1128/jcm.32.8.1894-1898.1994.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.