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Daschner C., Schübler A.-S., Jung M., Ayasse N., Yücel G., Husain-Syed F., Leipe J., Krämer B.K., Yazdani B.

Severe leptospirosis with acute kidney injury: a case description and literature review

(2024) *Nephron*, 148 (11-12), pp. 832 - 839

DOI: 10.1159/000540300

ABSTRACT: Introduction: Leptospirosis is a globally transmitted zoonotic disease caused by *Leptospira* spp., a highly mobile, obligate aerobic, spiral-shaped bacteria. Described first by Adolf Weil in 1886, leptospirosis in Germany is rare, leading to a delayed diagnosis due to diverse symptoms. Most cases are mild, but severe forms, like Weil's disease, cause life-threatening complications such as fever, jaundice, haemoptysis, and acute kidney injury (AKI). The aim of this work was to provide a literature review of leptospirosis with renal manifestation based on a case report. Case Presentation: We report the case of an 81-year-old male patient with initially unclear oliguric AKI, bilateral pulmonary infiltrates, and jaundice. After excluding common AKI causes, the expanded patient history suggested possible rat contact in his chicken coop. Finally, we serologically identified an infection with *Leptospira* spp. by positive IgM, proving that the illness was compatible with classical Weil's disease. The patient underwent temporary haemodialysis and antibiotic treatment with intravenous penicillin G for 2 weeks. Under therapy, the AKI, hyperbilirubinemia, and clinical condition of the patient improved. The patient was discharged after 2 weeks. In the following controls, slightly impaired kidney function was observed, indicating a progress of his chronic kidney disease (CKD). Conclusion: Although leptospirosis is rare, there are some cases with a fulminant course. Impairment of renal function often correlates with severity of the disease requiring antibiotic treatment. In some cases, AKI progresses to CKD demonstrating the need to raise awareness for leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Foltran B.B., Gaspar J.P., Silva I.R.M., Pires H.M., Andrade F.B., Costa G.M., Paixao J.E.L., Fernandes L.G.V., Teixeira A.F., Nascimento A.L.T.O.

New insights into the putative role of leucine-rich repeat proteins of *Leptospira interrogans* and their participation in host cell invasion: an in silico analysis

(2024) *Frontiers in Cellular and Infection Microbiology*, 14, art. no. 1492352

DOI: 10.3389/fcimb.2024.1492352

ABSTRACT: Pathogenic *Leptospira* are spirochetes that cause leptospirosis, a worldwide zoonotic disease. Leptospirosis affects humans and animals, with approximately 1 million human infections and 60,000 deaths per year. The diversity of leptospiral strains and serovars allied to the fact that pathogenesis is not yet fully understood, make the development of an effective vaccine against leptospirosis a challenge. Outer membrane and secreted proteins are considered potential antigens since they play a vital role in mediating interactions with host molecules. Several domains or motifs have been reported to participate in the leptospiral infection process. Among them, leucine-rich repeat (LRR) proteins have been highlighted as attractive multipurpose proteins, exhibiting a broad spectrum of ligands and having a putative role in bacterial pathogenesis. Indeed, genome annotation of leptospiral species pointed out that LRR proteins are predominant in pathogenic strains, a feature that corroborates this hypothesis. A few LRR proteins of *L. santarosai*, *L. borgpetersenii* and *L. interrogans* have been studied and their possible role in virulence was proposed. Yet, a mechanistic and broad investigation of LRR proteins was not fully performed. In this review, a comprehensive in silico analysis of 21 LRR proteins of *L. interrogans* was performed in relation to structure, function, dynamics and virulent potential

that will contribute to understanding the key role of these domains in the underlying mechanisms of leptospiral infection.

LANGUAGE OF ORIGINAL DOCUMENT: English

Vidal Del Río M.M., Jiménez Villa M.A.

Risk of human and animal leptospirosis in Ecuador: a multisectoral approach [Riesgo de leptospirosis humana y animal en Ecuador. Enfoque multisectorial]

(2024) Revista Cubana de Investigaciones Biomedicas, 43, art. no. e3633

ABSTRACT: Leptospirosis is a global zoonotic disease caused by a spirochete-shaped bacterium called *Leptospira*, which is often neglected in Latin American countries. In Ecuador, it is endemic in both rural and urban areas, with outbreaks reported in humans and animals in tropical regions with high morbidity and mortality rates. The objective of this study was to analyze the current situation of animal leptospirosis in Ecuador, its main risk factors, and preventive measures for disease control through a literature review. A systematic descriptive literature review was conducted to present information on the epidemiological status of the disease in Ecuador. It was found that human and animal leptospirosis in Ecuador is a major concern for public health and animal health authorities, as there is an annual increase in reported cases, with the highest incidence in coastal regions where heavy rainfall occurs due to climate change. The study concludes that disease control should be prioritized using a multisectoral approach, particularly in areas where people are exposed to animals, especially rodents, which are considered the main carriers of the disease.

LANGUAGE OF ORIGINAL DOCUMENT: Spanish

Abdul Razak A.A., Shatar L., Ramli A., Kassim S., Mohd Ghazali M.S., Chee H.Y., Zakaria R., Mahdi M.A., Suhailin F.H.

Surface-enhanced raman spectroscopy (SERS) substrates based on photonic crystal embedded bi-metallic nanoparticles for leptospiral DNA detection

(2024) Applied Spectroscopy

DOI: 10.1177/00037028241303780

ABSTRACT: Leptospirosis is an acute bacterial febrile disease affecting humans and animals in many tropical and subtropical countries. This work presents an optimization of surface-enhanced Raman spectroscopy (SERS) substrates to probe vibrational spectroscopic detail from *Leptospira* deoxyribonucleic acid (DNA). The pathogenic gene of LipL32 was used as a biomarker. The SERS substrates were based on a photonic crystal (PC) structure embedded with bi-metallic gold and silver nanoparticles (PC@AuAg NPs). The localized plasmonic resonance of AuAg NPs was coupled to the Raman modes of the target through SERS interaction. Prior to detection, the AuAg NPs were functionalized with chemical linkers to facilitate specific conjugation between metallic surfaces and DNA biomolecules. The immobilization and hybridization of probe DNA to their complementary target DNA (cDNA) created duplex formation for detection. The configuration was also tested with non-complementary DNA to verify detection specificity. Prominent SERS peaks were recorded, and the characteristic intensity decreased after cDNA hybridization due to less base interaction after complementary pairing. Distinct SERS behavior from the negative control test was also observed in non-complementary interaction. The configuration is highly attractive and can be potentially extended for sensitive and label-free detection of leptospiral DNA, paving the way for alternative diagnosis of leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Nakornpakdee Y., Techawiwattanaboon T., Prasai S., Komanee P., Sangkanjanavanich N., Boonkea S., Patarakul K.

In silico prediction and experimental evaluation of LIP3228 of pathogenic *Leptospira* as a potential subunit vaccine target against leptospirosis

(2025) Biochemical and Biophysical Research Communications, 745, art. no. 151229

DOI: 10.1016/j.bbrc.2024.151229

ABSTRACT: A protein subunit vaccine comprising conserved surface-exposed outer membrane proteins (SE-OMPs) is considered a promising platform for leptospirosis vaccine. The search for novel vaccine candidates that confer high protective efficacy against leptospirosis is ongoing. The LIP3228 protein was previously identified as a conserved and abundant SE-OMP with the potential to serve as an effective vaccine candidate. However, it is crucial to explore the immunological properties of this vaccine antigen before proceeding with animal experiments. This study aimed to assess the immunological characteristics of LIP3228 through in silico prediction and to validate its immunogenicity and protective efficacy in a hamster model of acute leptospirosis. The LIP3228 vaccine candidate was predicted in silico to be immunogenic, with strong binding B-cell and T-cell epitopes. In the immune simulator, it demonstrated stable interactions with Toll-like receptors 2 (TLR2) and 4 (TLR4) and induced immune responses, potentially stimulating host immune responses in vivo. The animal experiment showed that immunization with recombinant LIP3228 protein, formulated with AddaVax adjuvant, induced high and specific IgG responses in hamsters, with IgG2 being the predominant subclass. Although no significant improvement in survival was observed compared to the negative control after a homologous challenge with virulent leptospires, the vaccinated hamsters showed a reduction in histopathological changes and severity of lesions in target organs compared to unvaccinated hamsters. These results suggest that the immunoinformatic prediction is effective in predicting immunogenicity but not protective efficacy. Therefore, LIP3228 could be considered a potential vaccine candidate for mitigating severe tissue damage. These findings may have significant implications for the development of subunit vaccines in the future.

LANGUAGE OF ORIGINAL DOCUMENT: English

Jiang W., Zhang S., Ma L., Zhang M., Xie X., Lv T., Ding Y., Zhang W., Chang Y.-F., Cao Y.

Leptospirosis in China: current status, insights, and future prospects

(2024) Zoonoses (Ireland), 4 (1), art. no. 36

DOI: 10.15212/ZOONOSES-2024-0040

ABSTRACT: Leptospirosis is a re-emerging zoonotic disease that significantly impacts animals and human health worldwide. China has diverse climate types, providing a suitable environment for transmitting and surviving pathogenic *Leptospira* and its host animals. Despite the substantial reduction in the prevalence of leptospirosis, it continues to be a significant zoonotic disease of public health concern in China. This literature review aimed to provide a concise overview of the current status of leptospirosis in China, the findings from epidemiologic studies on leptospirosis, and the impact of animal and environmental factors on leptospirosis. Leptospirosis is commonly observed in subtropical and tropical cities in China, especially cities with ample water resources in the southern Yangtze River basin. Epidemiologic studies have identified *Leptospira interrogans* and *L. borgpetersenii* as the predominant pathogenic species responsible for leptospirosis in China. *Leptospira* serotypes prevalent in one part of China are related to the serotypes prevalent in the

dominant local rodent species and these animals may threaten public health safety as carriers. Given the potential increase in the risk of leptospirosis due to extreme climate change, it is crucial to raise awareness among stakeholders and promote the adoption of a comprehensive approach to prevent and control the continuous transmission and sudden outbreaks of leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Saranya E., Ramya M.

Epitope analysis of hypothetical proteins in *Leptospira interrogans* serovar Lai reveals potential diagnostic markers

(2024) Journal of Pure and Applied Microbiology, 18 (4), pp. 2482 - 2495

DOI: 10.22207/JPAM.18.4.20

ABSTRACT: Leptospirosis is a neglected zoonosis caused by a pathogenic spirochete, *Leptospira interrogans*. The mode of infection in humans is through an abrasion in human skin or the conjunctiva and mucous membrane. Infected patients usually show different symptoms resembling bacterial or viral infections such as the flu. Hence, diagnosing leptospirosis in the early stage is complex, and can be easily confused with other infections. A strategical pathway was developed to analyze the hypothetical proteins in *L. interrogans* and unveil their potential as diagnostic markers. Subcellular localization tools such as PSORTb, CELLO, SOSUI-GramN, and ProtCompB were used to segregate the outer membrane and surface proteins from the overall pool of hypothetical proteins. The shortlisted proteins were checked for their virulency, and antigenicity through tools such as VirulentPred, and VaxiJen, respectively. Proteins with the highest scores were fed into ElliPro which predicted both linear and discontinuous epitopes in each protein. Proteins with many epitopes were further analyzed with BepiPred 3.0, which provided the epitope probability for each protein's amino acid. Epitope probability of the potential proteins was compared with the standard diagnostic marker, LipL32. The comparison revealed that a protein (UniProt ID D4YW28) has better immunogenic potential than the gold standard marker, LipL32. In conclusion, this protein can be used as a diagnostic marker for the detection of leptospirosis and it will also serve as a better vaccine candidate.

LANGUAGE OF ORIGINAL DOCUMENT: English

Guida Acevedo G.N., Franco Delgado R.M., Aguilar Berrezueta R.J., Castillo Aveiga K.J.

Evaluation of knowledge level about leptospirosis in rural area “San Gabriel del Baba”, Ecuador [Evaluación del nivel de conocimiento sobre leptospirosis en zona rural “San Gabriel del Baba”, Ecuador]

(2024) Revista Cubana de Investigaciones Biomedicas, 43, art. no. e3601

ABSTRACT: Leptospirosis is an emerging zoonotic disease with a worldwide distribution, particularly prevalent in tropical and subtropical regions. In Ecuador, the incidence of this disease is high due to environmental and socioeconomic conditions favorable to its transmission. The objective of this study was to evaluate the level of knowledge about leptospirosis in the rural area of “San Gabriel del Baba,” in Santo Domingo de los Tsáchilas, Ecuador. A qualitative investigation with an action-research design was conducted, utilizing a structured survey of 27 questions administered to 110 residents of the rural area. The results revealed that, although 79 % of the respondents had heard of leptospirosis and 91 % understood its association with floods, there are significant gaps in knowledge about the vectors and symptoms of the disease. Only 77.9 % correctly identified rats as carriers, and a significant percentage did not recognize severe symptoms such as kidney damage.

Additionally, 19.8 % of the respondents work in high-risk conditions, and 30.2 % do not use adequate personal protection. While the majority of the population has access to basic services, 16.3 % still lack these, increasing their risk of infection. Conclusions: Although there is a basic knowledge of leptospirosis in "San Gabriel del Baba," significant gaps remain that need to be addressed. Continuous education and improvements in access to basic services and personal protective equipment are required to mitigate the risks associated with this disease in the studied community.

LANGUAGE OF ORIGINAL DOCUMENT: Spanish

Zhang X.-C., Lei X.-Q., Sun Y., Shan N.-B.

Leptospirosis manifested with severe pulmonary hemorrhagic syndrome successfully treated with veno-venous extracorporeal membrane oxygenation. A case report and literature review

(2024) Medicine (United States), 103 (51), pp. e40942

DOI: 10.1097/MD.00000000000040942

ABSTRACT: Rationale: The mortality rate associated with pulmonary hemorrhage induced by leptospirosis is notably high. Available treatment modalities are limited, and their efficacy has not been fully demonstrated. Here, we present the case report of a patient with leptospirosis-induced pulmonary hemorrhagic syndrome. A 49-year-old male patient was admitted to the Surgical Ward of the Department of Intensive Care Medicine of Fuyang Infectious Disease Clinical College of Anhui Medical University. The patient had initially sought medical attention at a local hospital due to symptoms of fever persisting for 4 days and chest tightness accompanied by hemoptysis for 1 day. Patient concerns: We present the case report of a patient with leptospirosis-induced pulmonary hemorrhagic syndrome. Hemoptysis persisted in our patient during VV-ECMO, although we adjusted the heparin regimen to maintain an activated partial thromboplastin time target value of 50 to 55 seconds. Diagnoses: Leptospirosis-induced pulmonary hemorrhagic syndrome. Interventions: He was immediately intubated and mechanically ventilated and then transferred to our hospital for further medical intervention. Upon arrival at our hospital, he was treated with veno-venous extracorporeal membrane oxygenation (VV-ECMO). Consequently, he was administered penicillin and omacycline for anti-infective therapy. Anti-inflammatory agents, high-dose vasoactive drugs to enhance blood pressure, continuous renal replacement therapy, tracheal sputum aspiration, and ventilator-assisted ventilation were also administered as part of the treatment protocol. Outcomes: After treatment, his inflammation index was significantly decreased, the amount of pulmonary bleeding was reduced, his oxygenation ratio was improved, and the pulmonary lesions were absorbed. Consequently, he was discharged on the 34th day of hospitalization. Lessons: We successfully treated a case of leptospirosis pulmonary hemorrhagic syndrome using VV-ECMO combined with prudent anticoagulant therapy.

LANGUAGE OF ORIGINAL DOCUMENT: English

Stepanov A., Holub M., Zlamal M., Beran O., Bartovska Z., Ptacek M.

Infectious diseases: leptospirosis

(2024) Ocular Manifestations of Systemic Diseases, pp. 507 - 509

DOI: 10.1007/978-3-031-58592-0_12

ABSTRACT: This chapter offers an extensive examination of infectious diseases and their ocular manifestations. Covering a wide array of pathogens, from Lyme Disease to Brucellosis, the authors explore systemic symptoms alongside ocular complications. They delve into Bartonellosis, Leptospirosis, and Herpetic

Infections, providing valuable insights into their ocular implications. The discussion extends to various other infectious diseases, including Cytomegalovirus, Measles, Histoplasmosis, Candidiasis, Cryptococcosis, Toxoplasmosis, Pneumocystosis, Larval Toxocariasis, Onchocerciasis, Schistosomiasis, and Ocular Myiasis. Through thorough examination of pathophysiology, clinical features, diagnosis, and management, this chapter serves as an invaluable resource for clinicians seeking to understand and address ocular manifestations in infectious diseases.

LANGUAGE OF ORIGINAL DOCUMENT: English

Suárez-Galaz A., Reyes-Novelo E., Cruz-Romero A., Ramos-Vázquez R., Panti-May J.A., Ruiz-Piña H., Sánchez-Montes S., Torres-Castro M.

The relationship between the spatial occurrence of *Leptospira* exposed animals and the characteristics of the peridomiciles they inhabit in a locality of Southeastern Mexico

(2024) Pathogens, 13 (12), art. no. 1037

DOI: 10.3390/pathogens13121037

ABSTRACT: The occurrence of *Leptospira* in mammals is an indicator for assessing potential health risks, particularly in tropical regions. Understanding their hosts' habitat characteristics and spatial occurrence is essential to surveil them. This study aimed to determine the characteristics of the peridomiciles associated with the spatial occurrence of *Leptospira* hosts. We inventoried the characteristics of the peridomiciles. Blood serum was gathered from dogs, opossums, and rodents for a microagglutination essay to detect exposure to several serogroups of *Leptospira*. A generalized linear model with binomial distribution helped estimate risk ratios and 95% confidence intervals between a seropositive animal's occurrence and the peridomiciles' characteristics. For estimates with the occurrence of one or more seropositive animals, a multinomial model was fitted. The seroprevalence in rodents was 81.8%; in opossums 31.2%; and 56.5% for dogs. The most frequent serogroup in dogs and rodents was Canicola. In opossums, the seroreaction was against Tarassovi, Ballum, Sejroe, and Cynopteri. The results showed that the peridomicile area (m²), the geographic polygon, and the accumulation of plastic containers (PET) were characteristics related to the occurrence of seropositive animals. The results revealed that the peridomicile's characteristics and spatial distribution in the locality help explain the occurrence of *Leptospira* hosts.

LANGUAGE OF ORIGINAL DOCUMENT: English

Jyothi J., Sree M.B.

Leptospirosis

(2024) The handbook of zoonotic diseases of goats, pp. 232 - 235

DOI: 10.1079/9781800622852.0019

ABSTRACT: Leptospirosis is a typical zoonotic illness affecting both humans and agricultural animals. Even though sheep and goats with leptospiral infection do not show any symptoms, they are especially important in the spread of *Leptospira* bacteria through urine. Young animals are frequently affected by severe disease, which is linked to accidental serovars. The main signs of subclinical infection include reproductive issues such as infertility, abortion, stillbirths and weak lambs or goat kids. For a precise infection diagnosis, laboratory testing is necessary. The most typical indirect diagnostic for leptospirosis is the microscopic agglutination test. Leptospirosis in small ruminants should be diagnosed using the PCR technique. Leptospirosis control

measures include locating and treating carriers and other infection sources, keeping acquired animals in isolation and routine inoculation with commercial vaccines.

LANGUAGE OF ORIGINAL DOCUMENT: English

Antima, Banerjee S.

Understanding the dynamics and drivers of leptospirosis in tropical and subtropical regions: a mathematical and epidemiological approach

(2025) Nonlinear Dynamics

DOI: 10.1007/s11071-024-10767-9

ABSTRACT: Leptospirosis, a neglected tropical zoonotic disease of emerging concern, poses a significant public health threat, particularly in regions vulnerable to heavy rainfall and flooding. This study investigates the dynamics of leptospirosis by employing a comprehensive mathematical model incorporating the temperature-dependent square root growth rate of *Leptospira*, the causative bacteria. Delving into intricate transmission dynamics, we conduct a stability analysis, identify transcritical bifurcation, and estimate parameters, including the sensitivity index of the reproduction number. Numerical results demonstrate the theoretical results, underscoring the substantial influence of rainfall, climate, and agriculture on leptospirosis prevalence in tropical India, with specific predictions for cases in Kerala and Ratnagiri. In conclusion, our study urges urgent preventive measures, including enhanced surveillance, impactful awareness campaigns, targeted interventions, and improved hygiene practices, which are necessary to curb leptospirosis and improve public health in India.

LANGUAGE OF ORIGINAL DOCUMENT: English

Senthilkumar K., Nirmala K., Tirumurugan K.G., Ravikumar G., Aravindbabu R.P., Senthilkumar T.M.A.

Development and evaluation of recombinase polymerase amplification assay for diagnosis of canine leptospirosis

(2024) Indian Journal of Animal Research, 58 (12), pp. 2209 - 2213

DOI: 10.18805/IJAR.B-5060

ABSTRACT: Background: Canine Leptospirosis is a life-threatening disease and zoonosis. Usually, PCR assay is carried out for early diagnosis but requires a thermal cycler and post-PCR procedures. This limits its use in resource-limited areas. Hence, the isothermal amplification of nucleic acid by recombinase polymerase amplification assay was developed as a versatile alternative for the diagnosis of canine leptospirosis in this study. Methods: The RPA assay to detect *Leptospira* DNA was optimized with *Leptospira* reference strains and its performance characteristics such as analytical, diagnostics and reproducibility were assessed. Result: The limit of detection of RPA assay was estimated as 102 copies of genomic DNA and specific to amplify the pathogenic *Leptospira*. Out of 150 dog samples screened, *Leptospira* DNA was detected in 64 (42.6%) by RPA assay and 67 (44.6%) by PCR. The diagnostic sensitivity and specificity of the RPA assay were 92.5% and 97.59% respectively. The RPA assay has a good diagnostic agreement with a kappa value of 0.905. The reproducibility assessment with the third-party testing laboratory revealed a better agreement with a kappa value of 0.81. The simplicity, rapid and less expensive enable this assay to perform at resource-limited laboratories or point-of-care testing.

LANGUAGE OF ORIGINAL DOCUMENT: English

Wang G., Aguero-Rosenfeld M.E.

Lyme disease, relapsing fever, and leptospirosis

(2024) Manual of molecular and clinical laboratory immunology, 9th Edition: Volume 1-2, 1, pp. 412 - 461

DOI: 10.1128/9781683674023.ch40

ABSTRACT: Lyme disease, or Lyme borreliosis, relapsing fever, and leptospirosis are infections caused by spirochetes, a phylogenetically ancient and distinct group of microorganisms. Three genera of spirochetes, *Borrelia*, *Leptospira*, and *Treponema*, are pathogenic to humans and are associated with Lyme borreliosis and relapsing fever, leptospirosis, and syphilis, respectively. This chapter focuses on the immunological laboratory methods used in the diagnosis of Lyme borreliosis, relapsing fever, and leptospirosis. Leptospire are maintained in nature by chronic renal infection of carrier animals. The most important reservoirs are rodents and other small mammals. Infected animals may excrete leptospire in their urine intermittently or continuously throughout life. The microscopic agglutination test can be used for confirmation and presumptive diagnosis of human leptospirosis cases, especially for febrile patients with nonspecific symptoms in areas of endemicity. The IgM enzyme-linked immunosorbent assays (ELISA) is a useful screening tool for testing few or large numbers of specimens.

LANGUAGE OF ORIGINAL DOCUMENT: English

Jayaramu V., Zulkafli Z., Rahmat F.

Spatio-temporal prediction of leptospirosis in kuantan using hydrometeorological variables and random forest machine learning

(2024) International Exchange and Innovation Conference on Engineering and Sciences, 10, pp. 916 - 922

DOI: 10.5109/7323369

ABSTRACT: Leptospirosis, a zoonotic disease prevalent in tropical regions with consistent rainfall, has been extensively studied using hydrometeorological data. This study focuses on developing a spatio-temporal model to predict leptospirosis in the Kuantan district, Pahang, known for its heavy rainfall and high disease incidence. Utilizing the random forest machine learning algorithm, we integrated hydrometeorological variables such as rainfall, streamflow, water level, relative humidity, and temperature across four model scenarios, lagging them from zero to 12 weeks at four-weeks intervals. Our models achieved an average testing accuracy of 73.4%, with sensitivity and specificity of 83.8% and 62.9%, respectively. Notably, we observed a minimal variation among the model scenarios, contrasting with previous studies where lag time improved the results. These findings underscore the potential of our models as a predictive tool for leptospirosis, enhancing spatial and temporal understanding in the Kuantan district. This improved insight can inform targeted disease prevention strategies, ultimately aiding in better management of leptospirosis outbreaks.

LANGUAGE OF ORIGINAL DOCUMENT: English

Linhares G.P., Zequiao T., Buso G.M., Cruz J.A.W., Tuon F.F.

Burden of leptospirosis in Brazil in the last decade

(2024) Revista de saude publica, 58, pp. 53

DOI: 10.11606/s1518-8787.2024058005859

ABSTRACT: To correlate the incidence of leptospirosis with sociodemographic data in the Brazilian Unified Health System from 2011 to 2022. This ecological study used national health and economic secondary data sources. Secondary analyses summarized the scenario of disease-related hospitalizations among federative units. In total, two analyses were conducted: variable description for relationship analysis and a secondary analysis with population health and sanitation indicators and economic indicators from the Instituto Brasileiro

de Geografia e Estatística (IBGE - Brazilian Institute of Geography and Statistics). The statistical analysis following this framework summarized raw data by year-month-federative unit. A time series regression was conducted, comparing the time variable with other national-level variables. Then, several simple linear regressions were performed. Linear regressions show the relationship between the reduction in cases and improved access to treated water and sewage collection, whereas an increase in per capita income seems to be inversely related to leptospirosis incidence. Geospatial distribution shows higher incidence in the Brazilian South and Southeast. Disease lethality varied over time but without significant change during the period. The average treatment cost remained constant over the years, despite its complexity. Leptospirosis incidence in Brazil from 2011 to 2021 decreased and was associated with improvements in socioeconomic conditions despite no changes in lethality.

LANGUAGE OF ORIGINAL DOCUMENT: English

Paz L.N., de Moraes L., Santos L.A., Hamond C., Pinna M.H.

AUTHOR FULL NAMES: Paz, Lucas Nogueira (57192557684); de Moraes, Laise (57193995017); Santos,

Insights into host-pathogen interaction based on the comparison of genomes of *Leptospira interrogans* isolated from dogs, humans, and a rodent in the same epidemiological context: a one health approach

(2025) Heliyon, 11 (1), art. no. e41531

DOI: 10.1016/j.heliyon.2024.e41531

ABSTRACT: Leptospirosis is a zoonotic infectious disease that significantly impacts animal and public health. Comparative genomics can aid in understanding poorly understood aspects of leptospirosis pathogenesis, including infection mechanisms, antimicrobial resistance, and host interactions across different epidemiological scenarios. This study aimed to compare the genomes of *Leptospira interrogans* serogroup Icterohaemorrhagiae strains isolated from three host species in a single epidemiological scenario. Four strains of *L. interrogans* serogroup Icterohaemorrhagiae from naturally infected and clinically symptomatic dogs (C20, C29, C51, and C82) were processed for whole genome sequencing (WGS). These results were compared against WGS data from two other rodent and human strains. Phylogenetic and genomic similarity analyses demonstrated high identity and synteny between the strains isolated from humans, canines, and rodents. Small regions of divergence were observed, especially in the genome obtained from a rodent sample. The presence of 23 genes potentially associated with biofilm formation was notable, with the identification of missense mutations in eight genes. Considering the need to better understand the molecular basis involved in biofilm formation, it is of fundamental importance to elucidate the effect of mutations on the expression of the phenotype (biofilm) among different strains. The present findings highlight the necessity of One Health-based collaborative interventions to address the complex dynamics of leptospirosis transmission, involving both common hosts such as rodents and dogs, as well as less-recognized hosts.

LANGUAGE OF ORIGINAL DOCUMENT: English

Furlanello T., Mazzotta E., Bertasio C., D'Incau M., Bellinati L., Lucchese L., Natale A.

The challenge of bacterial strain identification: *Leptospira interrogans* serovars Australis in a dog and long-term clinical follow-up

(2024) Tropical Medicine and Infectious Disease, 9 (12), art. no. 285

DOI: 10.3390/tropicalmed9120285

ABSTRACT: Leptospirosis is a widespread disease throughout the world, presenting in severe clinical forms in dogs. The pathogenicity of the different serovars in field infections is not fully documented, and clinical diagnosis is often limited to a combination of serological tests and molecular analyses. The latter, although a fundamental tool, cannot identify the infecting strain without further analysis. This study reports the use of various indirect (microscopic agglutination test, MAT) and direct (microbiological culture, real-time PCR) laboratory techniques, followed by typing protocols (Multi-locus Sequence Typing (MLST), Multiple Loci Variable number tandem repeat Analysis (MLVA), serotyping) that allowed for the identification of the *Leptospira* serovar Australis in a symptomatic and previously vaccinated dog (vaccine containing heterologous strains). This study reports long-term clinical follow-up (0–640 days) and describes the possible role of the infection in the development of chronic renal failure. This study aims to highlight how a combination of different techniques can be useful to better characterise the environmental circulation of zoonotic agents. Therefore, the identification and isolation of circulating *L.* strains would facilitate the updating of epidemiological data, enhance the knowledge of pathogenicity and long-term clinical effects, and provide a valuable resource for improving the efficacy of a specific serovar vaccination.

LANGUAGE OF ORIGINAL DOCUMENT: English

Gomes L.R., Correia L.I.V., Reis T.F.M.D., Peres P.A.B.M., Sommerfeld S., Silva R.R., Fonseca B.B., Silva A.C.A., Lima A.M.C.

In vitro evaluation of the antimicrobial effect of ZnO:9Ag nanoparticle and antibiotics on standard strains of *Leptospira* spp.

(2025) Microbial Pathogenesis, 199, art. no. 107259

DOI: 10.1016/j.micpath.2024.107259

ABSTRACT: Silver nanoparticles are recognized for potent antimicrobial properties against pathogenic bacteria, crucial in addressing the severity of leptospirosis, where an ideal treatment is lacking. This study focuses on assessing the antimicrobial efficacy of silver-doped zinc oxide nanoparticles (ZnO:9Ag) on standard *Leptospira* spp. strains (six species and ten serovars). Comparisons with conventional antibiotics were made. In vitro characterizations, including minimum inhibitory concentration (MIC), cell viability, membrane permeability, intracellular content release, and broth microdilution checkerboard assay, evaluated streptomycin, penicillin G, doxycycline, tetracycline, and ZnO:9Ag effects on *Leptospira*. The safety and toxicological effects of ZnO:9Ag were explored using the chicken embryo in vivo model. All treatments displayed notable anti-*Leptospira* effects. Penicillin G had a lower MIC (<0.048), contrasting ZnO:9Ag's higher MIC (6.25–50 µg/mL). Despite this, ZnO:9Ag exhibited pronounced inhibitory effects, making it a viable therapeutic option. At 100 µg/mL, ZnO:9Ag reduced cell viability in 50 % of strains, notably in *L. interrogans*, *L. kirschneri*, and *L. noguchii* species. ZnO:9Ag induced a significant permeability change ($p < 0.05$) and substantial intracellular content extravasation across all species. The checkerboard method revealed a significant synergistic antibacterial effect of the ZnO:9Ag combination with doxycycline, penicillin G, streptomycin, and tetracycline against the *L. interrogans* species. In vivo, ZnO:9Ag differed significantly ($p < 0.05$) from the negative control in the GGT enzyme parameter. In conclusion, ZnO:9Ag shows promising potential as an alternative antibacterial agent against *Leptospira* spp., inhibiting growth with a relatively safe and low toxicity level.

LANGUAGE OF ORIGINAL DOCUMENT: English

Selemani M., Makundi R.H., Massawe A.W., Katakweba A.S.

Serological survey of leptospira spp. in livestock and rodents from different settlements in the Kilombero Wetland, Tanzania

(2024) Pathogens, 13 (12), art. no. 1059

DOI: 10.3390/pathogens13121059

ABSTRACT: Background: The circulation of *Leptospira* has been linked to various occupational activities globally. This study investigated the seroprevalence of *Leptospira* spp. in rodents and livestock (cattle and goats) in three settlements/villages involved in agriculture, livestock keeping, and mixed agriculture and livestock in the Kilombero district, Tanzania. Methods: Data were collected during the wet and dry seasons. A total of 179 rodents were live-captured from selected habitats. Livestock samples were collected from 80 cattle in a livestock settlement and 120 goats from both livestock and mixed agricultural–livestock settlements. The microscopic agglutination test was utilized to identify *Leptospira* serovars. Results: The seroprevalence of *Leptospira* spp. was 17.3% in rodents (21.7% in *Mastomys natalensis* and 3.9% in *Rattus rattus*) and 8.3% in livestock (13.5% in cattle and 12.6% in goats). The prevalence among rodents and livestock differed between settlements ($p = 0.01$). A higher prevalence was observed among rodents in the agricultural settlement relative to the other settlements. A higher prevalence of antibodies in livestock was observed in the livestock settlement compared with the mixed agricultural–livestock settlement. The *Leptospira* serovars Sokoine (serogroup Icterohaemorrhagiae) and Hebdomadis (serogroup Hebdomadis) were detected in both rodents and livestock. The serovars Hardjo (serogroup Sejroe) and Gripothyphosa (serogroup Gripothyphosa) were found exclusively in cattle, whereas the serovars Pomona (serogroup Pomona) and Lora (serogroup Australis) were identified in rodents. *Leptospira* antibodies were found to be elevated during the rainy season compared with the dry season ($p = 0.05$) in all settlements, with the exception of rodents in the mixed agricultural–livestock settlement. Conclusions: This study demonstrates the presence of anti-*Leptospira* antibodies in rodents and livestock related to occupational activities in human settlements. It further demonstrates that wild animals (rodents) and livestock are reservoirs of *Leptospira* and are important in the epidemiology of leptospirosis. Management and control strategies should target both rodents and livestock.

LANGUAGE OF ORIGINAL DOCUMENT: English

Biswas S., Ganesh B.

Leptospirosis

(2024) Neglected Zoonoses and Antimicrobial Resistance: Impact on One Health and Sustainable Development Goals, pp. 183 - 206

DOI: 10.1016/B978-0-443-16062-2.00010-1

ABSTRACT: Leptospirosis has become a deadly infectious disease on a global scale in the last several decades. Nonetheless, the pathophysiology of leptospirosis is still unclear from the perspective of scientific research. Most of the time in animals and human being, this infection has no symptoms at all. To date, with the development of different standard diagnostic procedure, the infected animals can be detected. Standard treatment protocols can be followed to both human and animals with promising results. Human leptospirosis vaccines are only available commercially in a few countries; however, there are worldwide vaccines for dogs, pigs, and cattle. Some new advanced vaccines are in experimental process to ensure more safety with strong immunity. In this chapter, we aim to elaborately discuss the distribution/epidemiology, etiology, hosts, mode of transmission, disease process, changeover of the traditional clinical symptoms into the current one, economic

importance, modern diagnostic techniques, treatment protocol, antibacterial resistance, prevention and control strategy, vaccines used recently or under development.

LANGUAGE OF ORIGINAL DOCUMENT: English

Kappagoda C., Senavirathna I., Agampodi T., Agampodi S.B.

Role of tToll-like receptor 2 during infection of *Leptospira* spp: a systematic review

(2024) PLoS ONE, 19 (12), art. no. e0312466

DOI: 10.1371/journal.pone.0312466

ABSTRACT: The involvement of Toll-like receptor 2 (TLR2) in leptospirosis is poorly understood. Our systematic review examined its role across in-vitro, in-vivo, ex-vivo, and human studies. Original articles published in English up to January 2024, exploring the role of TLR2 during leptospirosis, were selected from databases including PubMed, Web of Science, Scopus, Trip, and Google Scholar. Cochrane guidelines and Preferred Reporting Items for Systematic Reviews and Meta-Analyses were followed by this systematic review. The National Institute of Health Quality Assessment tool, Systematic Review Centre for Laboratory Animal Experimentation risk of bias tool, and Office of Health Assessment and Translation extended tool were used to assess the risk of bias of the studies. Out of 2458 studies retrieved, 35 were selected for the systematic review. These comprised 3 human, 17 in-vitro, 5 in-vivo, 3 ex-vivo, and 7 studies with combined experimental models. We assessed the direct TLR2 expression and indirect TLR2 involvement via the secretion/mRNA expression of immune effectors during leptospirosis. Notably, we observed the secretion/mRNA expression of several cytokines (IL6, IL8, IL-1 β , TNF α , IFN γ , IL10, CCL2/MCP-1, CCL10, COX2, CXCL1/KC, CXCL2/MIP2) and immune effectors (hBD2, iNOS, Fibronectin, Oxygen, and Nitrogen reactive species) as key aspects of host TLR2 responses during leptospirosis. Even though increased TLR2 expression in in-vivo and in-vitro studies was evident, human studies reported mixed results showing that the postulated effect of TLR2 response based on other studies may not be valid for human leptospirosis. Besides the role of TLR2 in response to leptospirosis, the involvement of TLR4 and TLR5 was identified in in-vitro and in-vivo studies. TLR2 expression is inconclusive during human leptospirosis and further studies are needed to examine the immune effector regulation, through TLR2 for mitigating the harmful effects and promoting effective immune responses.

LANGUAGE OF ORIGINAL DOCUMENT: English

Kumar B., Sinha R.K., Kumar A.

Dynamical behavior of leptospirosis: a comparative analysis of delayed and non-delayed eco-epidemic models

(2025) Modeling Earth Systems and Environment, 11 (1), art. no. 49

DOI: 10.1007/s40808-024-02226-6

ABSTRACT: Understanding the parameters affecting disease transmission dynamics in leptospirosis is crucial for developing effective disease control and prevention strategies. The parameters influencing disease transmission dynamics, such as incubation period delay, handling time, and disease transmission rate, can significantly impact the spread of the disease. This study's findings have important implications for public health policy and practice, highlighting the need for targeted interventions to reduce the transmission rate of infected animals and prevent disease outbreaks. This study investigates the dynamical behavior of leptospirosis, a zoonotic disease, by incorporating two discrete delays, including the incubation period delay. The impact of

incubation delay on disease transmission is examined, along with the effects of handling time on the model's dynamics. The positivity of solutions, equilibrium analysis, and stability are thoroughly examined. Bifurcation analysis is conducted for different cases of time delay parameters, revealing oscillatory behaviour when the time delay parameter is introduced, and chaotic behaviour with respect to handling time in the disease transmission function for infected animals. Hopf bifurcations are obtained for parameters τ_1 and h . Both analytical and numerical approaches are employed, with numerical simulations performed using MATLAB and Maple.

LANGUAGE OF ORIGINAL DOCUMENT: English

Engida H.A., Fisseha D.

Malaria and leptospirosis co-infection: a mathematical model analysis with optimal control and cost-effectiveness analysis

(2025) Scientific African, 27, art. no. e02517

DOI: 10.1016/j.sciaf.2024.e02517

ABSTRACT: Malaria and leptospirosis are emerging vector-borne diseases that pose significant global health problems in tropical and subtropical regions. This study aimed to develop and analyze a mathematical model for the transmission dynamics of malaria-leptospirosis co-infection with optimal control measures. The model's dynamics are examined through its two sub-models: one for malaria alone and the other for leptospirosis alone. We apply a next-generation matrix approach to derive the basic reproduction numbers for the sub-models. By using the reproduction number, we demonstrate the local and global asymptotic stability of both disease-free and endemic equilibria in these sub-models. We perform numerical experiments to validate the theoretical outcomes of the full co-infection model. The graphical results show that malaria-leptospirosis co-infection will be eradicated from the population through time if $R_{0ml} < 1$. Conversely, if $R_{0ml} > 1$, the co-infection will persist in the population. Furthermore, we investigate an optimal control model to demonstrate the impact of various time-dependent controls in reducing the spread of both diseases and their co-infection. We use the forward-backward sweep iterative method to perform numerical simulations of the optimal control problem. Our findings of the optimal control problem imply that strategy D, which incorporates all optimal controls, namely malaria prevention $\omega_1(t)$, leptospirosis prevention $\omega_2(t)$, insecticide control measure for malaria $\omega_3(t)$, control sanitation rate of the environment $\omega_4(t)$ is the most effective in minimizing our objective function. We also conduct a cost-effectiveness analysis to identify the predominant strategy in terms of cost among the optimal strategies.

LANGUAGE OF ORIGINAL DOCUMENT: English

Zhou Y., Wang X., Li H., Wu Z., Pan N., Ning H., Liu S., Ye X., Qiu C.-C., Wu K., Shi J.

Epidemiological trends and clinical characteristics of human leptospirosis in Wenzhou, Zhejiang Province, China, 2020–2022

(2024) Journal of Infection in Developing Countries, 18 (11), pp. 1709 - 1714

DOI: 10.3855/jidc.18434

ABSTRACT: Objective: To observe the clinical characteristics and epidemic trends of human leptospirosis in Wenzhou, Zhejiang Province, China, from 2020 to 2022 and to provide a scientific basis for prevention and control in this area. Methods: Descriptive epidemiological methods were used in Wenzhou, China, from 2020 to 2022. Leptospira antibodies were detected by a microscopic agglutination test (MAT), and laboratory tests

were conducted to analyse the prevalence of *Leptospira* in the population. Results: From 2020 to 2022, a total of 41 cases of human leptospirosis were reported in Wenzhou, China, with no deaths and an average annual incidence of 0.1428/100,000. The highest incidence was in 2021 (30 cases, incidence rate: 0.31/100,000), and the lowest incidence was in 2022 (three cases, incidence rate: 0.04/100,000). The high-incidence season was from August to October, in which a total of 36 cases were reported, accounting for 87.80% of total cases, most of which were males. The main occupation was farming, which accounted for 70.7% of the total number of cases. 90.2% of cases had fever symptoms, and the body temperature was between 36.5 °C and 40.1 °C. A total of 32 positive samples were detected by MAT in six main groups, mainly the Autumnalis serogroup. Conclusions: The incidence of leptospirosis in Wenzhou, China, was at a moderate level from 2020 to 2022. Localities should actively strengthen the monitoring of leptospirosis host animals and populations, understand the infection rate and floral changes and prevent leptospirosis outbreaks.

LANGUAGE OF ORIGINAL DOCUMENT: English

de Araújo Portela R., Limeira C.H., Bezerra J.A.B., Martins C.M., da Costa D.F., Santos C.D.S.A.B., Alves C.J., Azevedo S.S.D.

Insights on the pooled prevalence and global distribution of leptospirosis in goats: systematic review and meta-analysis

(2024) *Microorganisms*, 12 (12), art. no. 2391

DOI: 10.3390/microorganisms12122391

ABSTRACT: *Leptospira* spp. infection in small ruminants is usually asymptomatic or presents nonspecific clinical signs and has an economic impact on goat farming and public health. The aim of this study was to carry out a systematic review with meta-analysis on the global seroprevalence and distribution of leptospirosis in goats. The methodology was based on the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), and the review project was registered in the International Prospective Register of Systematic Reviews (PROSPERO—ID: CRD42023405693). Overall, 79 articles were included in the study. The global prevalence of leptospirosis in goats was 18.6% (CI 95% = 15.08–22.71%), with no publication bias and high heterogeneity. The records originated from South America (n = 32), Asia (n = 26), Europe (n = 8), North America (n = 7), and Africa (n = 6), and seropositivities were 17%, 19%, 12%, 34%, and 22%, respectively. It is concluded that *Leptospira* spp. infection is widespread in goat herds, including regions with semi-arid and arid climates, and it is suggested that the prospects for controlling the disease should focus on avoiding environmental contamination and improving management measures and sanitary practices. This important information provides guidance for actions to protect against human contamination and to control animal leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Plá N., Videla Y.P., Burucúa M.M., Cheuquepán Valenzuela F.A., Marin M.S., Quintana S.

***Leptospira* spp. is recognized by TLR2 and induces IFN- β and IFN- λ expression in smegma from naturally infected bulls**

(2025) *Comparative Immunology, Microbiology and Infectious Diseases*, 117, art. no. 102291

DOI: 10.1016/j.cimid.2024.102291

ABSTRACT: Leptospirosis, a zoonosis with a wide worldwide distribution, causes significant reproductive losses in cattle. The genital presentation of the disease has been reported, and its understanding is crucial for

the implementation of adequate sanitary measures. Although *Leptospira* spp. modulate innate immunity, the response in the genital mucosa of bulls is unknown. The objective of this work was to evaluate the expression of innate immune receptors and cytokines in smegma from bulls with genital infection by *Leptospira* spp. To do so, routine preputial scraping samples were selected from breeding bulls from four establishments in the Azul District, Buenos Aires, Argentina with no reproductive problems, which were previously evaluated for the presence of *Leptospira* spp. DNA by qPCR detection of the *secY* gene. The relative gene expression of TLR2, TLR4, IFN- β and IFN- λ in the smegma samples of animals infected with *Leptospira* spp. was determined by RT-qPCR, with subsequent analysis of the results using REST software. The expression of TLR2 was significantly increased in animals infected with *Leptospira* spp. compared to uninfected control animals (4-fold), while TLR4 did not show differences. Likewise, both IFN- β and IFN- λ were significantly increased in smegma of infected animals (3.5 and 3.1-fold, respectively). Therefore, this work shows that genital infection of *Leptospira* spp. in bulls generates and modulates a local innate immune response, with an association between the presence of *Leptospira* spp. DNA and the expression levels of TLR2, IFN- β and IFN- λ .

LANGUAGE OF ORIGINAL DOCUMENT: English

Amamura T.A., Courrol D.D.S., Barbosa A.S., Silva-Junior I.A., da Silva T.F., Midon L.M., Cruz M.C., Heinemann M.B., Chura-Chambi R.M., Morganti L., Isaac L.

Proteolytic activity of secreted proteases from pathogenic leptospires and effects on phagocytosis by murine macrophages

(2025) *Microbes and Infection*, art. no. 105469

DOI: 10.1016/j.micinf.2025.105469

ABSTRACT: Leptospirosis is a zoonosis caused by spirochete *Leptospira*. Pathogenic leptospires evade the Complement System, enabling their survival upon contact with normal human serum in vitro. In a previous study, we demonstrated that proteases secreted by pathogenic leptospires cleave several Complement proteins, including C3 and the opsonins C3b and iC3b. We hypothesize that these *Leptospira* proteases, such as thermolysin and leptolysin, may decrease the phagocytic activity of murine peritoneal macrophages. We observed decreased amounts of CR3 and CR4 using flow cytometry when these cells were treated with supernatant from the culture of pathogenic leptospires (SPL) for 24 h. Through confocal microscopy, we observed a reduction in TLR2, CD11b, and CD206 (mannose receptor) levels when these cells were treated with SPL or recombinant thermolysin for 24 h. Furthermore, opsonins such as C3b/iC3b deposited on the surface of pathogenic leptospires were clearly degraded in the presence of recombinant thermolysin or recombinant leptolysin. Consequently, when opsonized bacteria and macrophages were previously incubated with these proteases, phagocytic activity was diminished. These observations lead us to suggest that proteases secreted by pathogenic leptospires could degrade opsonins present in normal serum or deposited on the bacterial membrane, as well as cleave or inhibit macrophage surface molecules. Therefore, these proteases could interfere with the recognition and internalization by murine macrophages, favoring the spread of leptospires in the host.

LANGUAGE OF ORIGINAL DOCUMENT: English

Lee N., Smith C., Bailey R., Ariyoshi K., Smith S., Black N., Edwards T.

Core Outcome Set development for LEptospirosis trials (COS-LEP): a study protocol to develop a core outcome set for the evaluation of clinical therapeutic interventions for human leptospirosis

(2025) *Trials*, 26 (1), art. no. 6

DOI: 10.1186/s13063-024-08713-6

ABSTRACT: Background: Leptospirosis is a zoonotic bacterial infection occurring worldwide. It is of particular public health concern due to its global distribution, epidemic potential and high mortality without appropriate treatment. The method for the management of leptospirosis, particularly in severe disease, is clouded by methodological inconsistency and a lack of standardized outcome measures. The study this protocol details aims to develop a core outcome set (COS) for leptospirosis research. A COS is a set of outcomes with international consensus as a minimum for reporting in future studies focusing on leptospirosis. Establishing a COS will contribute to harmonizing Leptospirosis treatment research and will be instrumental in constructing a high-quality evidence base to feed into a planned future rigorous international clinical trial on leptospirosis. Methods: The COS-LEP study will employ a COS development methodology standardized by the COMET initiative framework. This includes (1) a systematic review of available quantitative and qualitative literature reporting therapeutic response and safety outcomes and measures; (2) focused interviews with healthcare professional and people treated for leptospirosis exploring outcomes of interests using qualitative methodology; (3) narrowing the choice of outcomes by international consensus using a Delphi survey process; and (4) undertaking a hybrid consensus meeting with key stakeholders to build the final COS. Discussion: This protocol describes the method to develop the first core outcome set for use in human leptospirosis studies. This will not only be a key feature in the design of a future definitive randomized controlled trial, but also provide a structure for clinicians and researchers collecting treatment cohort data in the various settings where leptospirosis is a public health issue.

LANGUAGE OF ORIGINAL DOCUMENT: English

Kamarulbahri T.M.S.T., Yahaya R.

Diagnostic conundrum: A rare case of psychosis in leptospirosis among siblings with folie à trois

(2024) *Klinik Psikiyatri Dergisi*, 27 (4), pp. 331 - 334

DOI: 10.5505/kpd.2024.87528

ABSTRACT: Folie à Trois is a rare presentation of psychosis. It has been described in several case reports, but there is a lack of studies to understand the mechanism and management of this disease. We presented a case of three siblings who share the same delusional idea initially induced by one of the sisters who had neuropsychiatric manifestations of leptospirosis. The siblings exhibited a shared pattern of aggressive behaviors, auditory hallucinations, and persecutory delusions toward each other. Intriguingly, two of the sisters displayed improvement even without pharmacological intervention. The case highlights the complexity of differentiating shared psychotic disorder from organic etiologies, emphasizing the importance of multidisciplinary assessments in unraveling intricate clinical presentations. The distinctive temporal resolution of psychiatric symptoms among the siblings underscores the need for nuanced diagnostic considerations in shared psychotic disorders. This case report contributes to the understanding of the interplay between infectious diseases and psychiatric manifestations, urging clinicians to exercise meticulous scrutiny in cases of shared psychotic disorders masquerading as organic illnesses.

LANGUAGE OF ORIGINAL DOCUMENT: English

Ayral F., Botman J., Le Guyader M., Ramery E., Gourlay P.

Chronic carriage of *Leptospira interrogans* genotype associated with the Australis serogroup by naturally-infected hedgehogs (*Erinaceus europaeus*) at a wildlife health centre in Northwestern France

(2025) Zoonoses and Public Health

ABSTRACT: Background: Leptospirosis is a widespread zoonosis caused by bacteria in the genus *Leptospira*. Basic epidemiological information is crucial to mitigating disease risk but is lacking for leptospirosis; notably, the hosts responsible for maintaining *Leptospira* remain largely unknown. Frequently observed near human habitations, hedgehogs (*Erinaceus europaeus*) are taken to wildlife rescue centres when found sick or injured. Thus, they may pose a risk to human and animal health if they carry pathogenic *Leptospira*. Aims: This study aimed to describe *Leptospira* carriage in a hedgehog population and the potential clinical impacts of the infection. Material and Method: We investigated *Leptospira* carriage frequency and diversity in urine samples from 69 hedgehogs at a wildlife rescue centre, between April and June 2022. We used quantitative PCR, typing of the 16S rRNA and *lfb1* genes, variable number tandem repeat and multispacer sequence typing to characterise *Leptospira* DNA. An analysis of urinary biochemical parameters was conducted to assess renal function. Results: We detected *Leptospira* DNA in 25 (35%) of the urine samples, of which 21 were successfully typed. The latter analysis revealed a limited degree of genetic diversity. *L. interrogans* (n = 19) predominated, and the only genotype detected was related to the Australis serogroup (n = 17). We also noted the presence of *L. borgpetersenii* (n = 1) and *L. kirschneri* (n = 1). There was no relationship between infection status and urinalysis parameters. Conclusion: These results suggest hedgehogs may act as long-term shedders of *Leptospira* in natural ecosystems.

LANGUAGE OF ORIGINAL DOCUMENT: English

Şahin A.M., Çetin S., Şenel İ., Erdem-Çakır T., Aydın E., Yetkin M.A.

The role of clinical and laboratory finding in the differential diagnosis of hantavirus and leptospirosis infections

(2024) Journal of Vector Borne Diseases, 61 (4), pp. 601 - 606

DOI: 10.4103/JVBD.jvbd_54_24

ABSTRACT: Background & objectives: Hantavirus and leptospirosis infections are zoonotic diseases with similar clinical and laboratory findings. The aim of this study is to identify the distinguishing features of these two diseases, for which a definitive diagnosis can take a long time. Methods: Between September 2021 and June 2023, a total of 45 patients who were admitted to our hospital and were diagnosed with hemorrhagic fever with renal syndrome (HFRS) or leptospirosis were retrospectively evaluated. Patients were compared in terms of demographic data, clinical, and laboratory parameters. The role of these variables in predicting HFRS or leptospirosis was investigated. The two diseases were compared with regard to outcomes. Receiver operating characteristics were employed for the calculation of cut-off values, sensitivity, specificity, and positive and negative predictive values for parameters showing significant differences. A statistical significance level of $p < 0.05$ was considered. Results: Fifteen patients diagnosed with HFRS and thirty patients diagnosed with leptospirosis were included in the study. In both groups, hospital admissions were observed with non-specific and similar symptoms. There was no statistically significant difference observed between the two groups in terms of length of hospital stay, blood product transfusion, requirement for hemodialysis, intensive care unit admission, the rate of return to normal renal function and mortality. Elevated ferritin levels were statistically

significant in favor of HFRS, while lymphopenia, elevated bilirubin, CRP, and ESR were statistically significant in favor of leptospirosis. Interpretation & conclusion: The use of laboratory findings and clinical symptoms can aid in the challenging task of accurately diagnosing and using appropriate treatment for these two diseases.

LANGUAGE OF ORIGINAL DOCUMENT: English

Viskontene A.L., Radyuk E.V., Shapkin O.A., Khizhkin E.A., Bulanenko V.P., Voytsekhovskaya Y.A., Medvedev S.G., Karan L.S.

In search of pathogenic *Leptospira* species in *Myotis* and other vesper bats, Russia

(2025) Acta Tropica, 262, art. no. 107506

DOI: 10.1016/j.actatropica.2024.107506

ABSTRACT: Various bat species worldwide have been identified as *Leptospira* carriers, especially in tropical regions. In this study, we investigated the infection of Vespertilionidae bats by pathogenic *Leptospira* in north-west Russia. Out of 264 bats from 13 species, the urine of 24 specimens tested positive according to a polymerase chain reaction test. The infected species were exclusively *Myotis* bats: *M. brandtii* (1/56; 1.8 %); *M. dasynceme* (9/40; 22.5 %); and *M. daubentonii* (14/47; 29.8 %). The detected *Leptospira* strains were similar to *L. kirschneri* and *L. borgpetersenii*.

LANGUAGE OF ORIGINAL DOCUMENT: English

Tran P.N.T., Limothai U., Dinhuzen J., Tachaboon S., Sukmark T., Dokpong C., Roytrakul S., Haake D.A., Srisawat N.

MicroRNA biomarkers and host response pathways in severe pulmonary hemorrhagic syndrome due to leptospirosis: A multi-omics study

(2025) Journal of Infection, 90 (2), art. no. 106400

DOI: 10.1016/j.jinf.2024.106400

ABSTRACT: Background: Severe pulmonary hemorrhagic syndrome (SPHS) remains a fatal complication of leptospirosis with poorly understood mechanisms and an urgent need for effective biomarkers. Methods: A nested case-control analysis was conducted using blood specimens from two previous Thai leptospirosis cohorts. Candidate microRNAs were initially discovered through a global profiling of 798 serum microRNAs in five SPHS and seven non-SPHS patients, and then validated using real-time polymerase chain reactions in 168 patients. Pathways enriched from microRNA targets were compared to those from an integrated transcriptomic-proteomic analysis. Proteins pertaining to the key resulting pathway were measured to validate significance and reveal correlation with microRNA biomarkers. Results: Serum microRNA profiling revealed a total of 81 significantly expressed microRNAs, of which seven were selected for further validation in the whole cohort of 168 leptospirosis patients, including 28 in SPHS and 140 nonSPHS groups. Among the selected microRNAs, miR-5010-3p and miR-147b-3p had significantly higher expression in SPHS group compared to nonSPHS group, with consistently higher expression after adjusting for age, sex, days of illness, comorbidity, smoking status or recruitment site. The two had area under the curve (AUC) values of 0.76 (95% CI: 0.67–0.85) and 0.70 (95% CI: 0.56–0.81) for discriminating SPHS, respectively. These microRNAs also exhibited consistent AUC values in patients tested before chest radiograph shadows manifested. Combination of miR-5010-3p with miR-548ai and miR-224-5p, as selected by Bayesian Model Averaging algorithm, substantially boosts the AUC value to 0.86 (95% CI: 0.77–0.94). The miRNA biomarkers also enhanced the predictive values of a previously validated clinical model, increasing AUC value from 0.87 to 0.92 with a significant

reclassification net index. Multi-omics pathway analysis incorporating microRNA targets and transcriptomic-proteomic data suggested TNF signaling as among the key pathways. In validation, seven out of ten pathway proteins were significantly different between groups, with principal components correlated with severity and miR-5010-3p. Conclusions: MiR-5010-3p and miR-147b-3p are novel biomarkers with good predictability and potential relevance with TNF signaling pathway, an important host response mechanism in leptospirosis SPHS.

LANGUAGE OF ORIGINAL DOCUMENT: English

Nieves D.J.

Leptospirosis

(2025) Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 9th Edition: 2-Volume Set, 1-2, pp. 1320 - 1331.e6

DOI: 10.1016/B978-0-323-82763-8.00143-6

LANGUAGE OF ORIGINAL DOCUMENT: English

Tufa T.B., Postigo-Hidalgo I., Fuchs A., Orth H.M., Häussinger D., Luedde T., Kaiser M., Patel P., Landt O., Drexler J.F., Feldt T.

Detection of bacterial infections and malaria among blood culture-negative samples of hospitalized febrile patients from a tertiary hospital in Ethiopia

(2025) The American journal of tropical medicine and hygiene, 112 (1), pp. 79 - 84

DOI: 10.4269/ajtmh.23-0663

ABSTRACT: Febrile illnesses contribute significantly to morbidity and mortality in sub-Saharan Africa, but the lack of diagnostic facilities and the broad spectrum of pathogens can lead to inadequate clinical management. The timely and reliable identification of the causative pathogens in febrile patients is the basis for the administration of optimal treatment. We aimed to evaluate the performance of a multiplex polymerase chain reaction (PCR) among blood culture-negative patients presenting with febrile diseases in Central Ethiopia. From April 2016 to June 2018, we collected blood samples from adults and children ≥ 1 year of age admitted with febrile diseases to the Asella Referral and Teaching Hospital, which is located at an altitude of 2,400 m. Total nucleic acids were extracted from frozen plasma samples using a MagNA Pure 96 instrument (Roche, Mannheim, Germany). The multiplex PCR assays were used in combination with LightCycler multiplex DNA master mix (Roche) on a LightCycler 480 instrument (Roche). We used the pathogen-specific assays targeted to *Plasmodium* spp., *Borrelia* spp., *Rickettsia* spp., *Leptospira* spp., *Salmonella* spp., and arboviruses. We tested plasma samples of 511 patients and found positive results for *Plasmodium* spp. (13, 2.5%), *Borrelia* spp. (12, 2.3%), and *Rickettsia* species (7, 1.3%); in total, pathogens were detected in 32 of the samples (6.3%). No pathogen was detected by multiplex PCR in 94% of blood culture-negative samples. Even if the pathogens identified by PCR were not necessarily causes of fever, molecular testing using a multiplex PCR can contribute to pathogen diagnosis in a proportion of febrile patients in the highland part of Ethiopia and help to improve the clinical management.

LANGUAGE OF ORIGINAL DOCUMENT: English

Hamond C., Tibbs-Cortes B., Fernandes L.G.V., LeCount K., Putz E.J., Anderson T., Camp P., Stuber T., Hicks J., van der Linden H., Dos Santos Ribeiro P., Bayles D.O., Schlater L.K., Nally J.E.

Leptospira gorisiae sp. nov, L. cinconiae sp. nov, L. mgodei sp. nov, L. milleri sp. nov and L. iowaensis sp. nov: five new species isolated from water sources in the Midwestern United States

(2025) International journal of systematic and evolutionary microbiology, 75 (1)

DOI: 10.1099/ijsem.0.006595

ABSTRACT: Isolates of *Leptospira* spp. were cultured from water sources at five different sites in central Iowa in the Midwestern United States and characterized by whole-genome sequencing. Isolates were helix-shaped and motile. Genome sequence analyses determined that the isolates could be clearly distinguished from other species described in the genus *Leptospira* and included one species that belonged to the pathogen subclade P1, one species that belonged to the pathogen subclade P2 and three species that belonged to the saprophyte subclade S1. The names *Leptospira gorisiae* sp. nov. (type strain WS92.C1T=NVSL-WS92.C1T=KIT0303T), *Leptospira cinconiae* sp. nov. (type strain WS58.C1T=NVSL-WS58.C1T=KIT0304T), *Leptospira mgodei* sp. nov. (type strain WS4.C2T=NVSL-WS4.C2T=KIT0305T), *Leptospira iowaensis* sp. nov. (type strain WS39.C2T=NVSL-WS39.C2T=KIT0306T) and *Leptospira milleri* sp. nov. (type strain WS60.C2T=NVSL-WS60.C2T=KIT0307T) are proposed.

LANGUAGE OF ORIGINAL DOCUMENT: English

Griebsch C., Kirkwood N., Norris J.M., Ward M.P.

A comparison of risk factors for canine leptospirosis and seropositivity in New South Wales, Australia

(2025) Australian Veterinary Journal

DOI: 10.1111/avj.13411

ABSTRACT: This study aimed to identify and compare risk factors associated with canine leptospirosis and *Leptospira* seropositivity in New South Wales, Australia. Seventy-nine canine cases of confirmed leptospirosis (clinical cases) and 16 healthy dogs seropositive to *Leptospira* (seropositive cases) were included in the study; these were separately compared to 394 healthy dogs seronegative to *Leptospira* (controls) in at-risk areas. A questionnaire investigated rat contact, stagnant water, dog park access and household number of dogs and cats. Associations between these factors, signalment and risk of leptospirosis or *Leptospira* seropositivity were screened using Pearson Chi-Square test and logistic regression was used to estimate odds ratios of association. Significantly associated with both leptospirosis risk and seropositivity risk was rat contact ($P < 0.01$) which increased the risk 4.3- and 4.5-fold, respectively. Other factors significantly associated with leptospirosis risk were breed ($P < 0.01$) and age ($P < 0.01$). Being a herding dog or Terrier increased leptospirosis risk 27.2-fold and 8-fold, respectively and being a young adult dog increased leptospirosis risk 3.9-fold. Frequenting dog parks decreased leptospirosis risk (OR 0.12). In contrast, no other significant risk factors were identified for seropositivity risk. Exposure to *Leptospira* through contact with reservoir hosts resulted in seropositivity as well as clinical leptospirosis. However, host factors like breed and age seem to be important factors in determining if exposure results in clinical disease. Increased urbanisation and landscape fragmentation could result in increased exposure to reservoir hosts. Environmental sampling is needed to identify sources of infection. Risk mitigation includes reducing contact with reservoir hosts and contaminated environments and increased pest control.

LANGUAGE OF ORIGINAL DOCUMENT: English

Rai T.K., Chakravarty J., Kashyap S., Chatterjee S., Tiwari V.D., Rai U.G., Gangwar M., Sundar S., Nath G.

Etiology of acute encephalitis syndrome in adults in a tertiary care center in Eastern Uttar Pradesh

(2025) The American journal of tropical medicine and hygiene, 112 (1), pp. 194 - 199

DOI: 10.4269/ajtmh.24-0118

ABSTRACT: Seasonal outbreaks of acute encephalitis syndrome (AES) with high case fatality rates have been commonly reported among adults in India. With an increase in Japanese encephalitis virus (JEV) vaccination, the etiology of AES is also changing. However, most studies on AES in India have focused only on children and on JEV. This study was conducted in the Department of Medicine, Institute of Medical Sciences, Banaras Hindu University between 2020 and 2022 to determine the etiology of AES in adults. Blood and cerebrospinal fluid (CSF) were collected from patients 18 years or older with fever and altered sensorium for ≤ 15 days. We did IgM ELISA for dengue, chikungunya, West Nile virus, scrub typhus, leptospirosis from serum, CSF-IgM for JEV, and CSF-polymerase chain reaction for herpes simplex virus 1 and 2, varicella-zoster virus, enterovirus, and cartridge-based nucleic acid amplification test (CBNAAT) for tuberculous meningitis (TBM). The most common cause of AES identified in our study was TBM (16.7%), followed by leptospirosis (15.1%) and scrub typhus (11.9%). The high occurrence of TBM in our study highlights the importance of CSF-CBNAAT for all AES patients. As leptospirosis and scrub typhus are easily treatable, early detection and treatment of these infections should be recommended.

LANGUAGE OF ORIGINAL DOCUMENT: English

Ismail Z.B., Widemann L., Daradkeh Y., Al-Omari O., Fahmawi A., Lakaideh M., Sha'fout B., Mellhem H., Al-Bayari L., Al-Omari S., Talafha H., Hijazeen Z., Al-Omari B., DeMarco J., Karesh W.B., Abu-Basha E.A.

Seroprevalence of *Leptospira* spp. antibodies in humans and livestock at various human-animal interfaces in Jordan

(2025) Veterinary World, 18 (1), pp. 1 - 7

DOI: 10.14202/vetworld.2025.1-7

ABSTRACT: Background and Aim: Leptospirosis, caused by *Leptospira* spp., affects humans and animals, posing significant health and economic burdens. This multidisciplinary One Health study aimed to estimate the prevalence of *Leptospira* spp.-specific antibodies in humans and livestock at the human-animal interfaces in Jordan. Materials and Methods: Study sites were selected across Jordan based on previous research showing a high likelihood of zoonotic pathogen circulation. The study population comprised 500 individuals and 400 livestock (sheep, goats, cattle, and camels). Blood samples were collected from both humans and livestock at baseline and at follow-up after 1.5 years. Humans were followed longitudinally, whereas livestock were sampled opportunistically. The samples were tested for *Leptospira* spp.-specific Immunoglobulin G antibodies using a commercially available enzyme-linked immunosorbent assay kit. For humans, seroprevalence was calculated from baseline data, and incidence was calculated using follow-up data. In livestock, seroprevalence was calculated at baseline and follow-up. Results: At baseline, the seroprevalence of leptospirosis in humans was 4.0% (95% confidence interval [CI]: 2.5–6.1), with exposure detected across all five sites. The incidence rate of human leptospirosis was 1145 cases/100,000 person-years (95% CI: 455–2,321). In livestock, the baseline seroprevalence was 1.7% (95% CI: 0.79–3.7), which increased to 4.3% (95% CI: 2.6–6.9) at follow-up. *Leptospira* spp. antibodies were detected only in sheep and goats at both sampling times, with no cases found in camels or cattle. Conclusion: This study highlights the presence and dynamics of leptospirosis at the human-animal interface in Jordan, revealing a baseline human seroprevalence of 4.0% and an incidence rate

of 1145 cases per 100,000 person-years. Among livestock, seroprevalence increased from 1.7% to 4.3% over the study period, with exposure limited to sheep and goats. These findings underscore the importance of targeted public health and veterinary interventions to address zoonotic leptospirosis in endemic areas.

LANGUAGE OF ORIGINAL DOCUMENT: English

Kalasi K.K., Fitzpatrick D., Stone D., Guttin T., Alhassan A.

Grenadian cats as potential reservoir for *Leptospira*

(2024) PLoS Neglected Tropical Diseases, 18 (12), art. no. e0012784

DOI: 10.1371/journal.pntd.0012784

ABSTRACT: Leptospirosis is a spirochetal disease caused by *Leptospira* spp. bacteria with global distribution affecting multiple mammalian species, including humans. The disease is endemic in many geographic areas and is of particular concern in tropical regions with abundant rainfall, such as the Caribbean. Currently, there are no published reports on *Leptospira* exposure or infection in Grenadian cat populations, and the role of cats in the epidemiology of the disease is unknown. Our hypothesis is that Grenadian cat population may be a reservoir host for zoonotic *Leptospira* on the island. During 2019–2021, 160 feral cats were captured from three parishes in Grenada, and their urine and blood were tested for *Leptospira*. Urine from 4 of 148 (2.7%) cat samples tested PCR-positive for *Leptospira*. Serum from 6 of 136 (4.4%) cat samples tested PCR-positive for *Leptospira*. Sequence analysis of the *Leptospira* *rpoB* gene showed 86–100% similarity to known or presumed pathogenic *Leptospira* species. The findings of this study suggest that Grenadian cat populations are infected with and are shedding *Leptospira* genotypes that are phylogenetically related to known pathogenic *Leptospira*, including known zoonotic strains. These observations support the hypothesis that Grenadian cat populations may be a reservoir host for zoonotic *Leptospira* on the Island.

LANGUAGE OF ORIGINAL DOCUMENT: English

Gerras J., Young K., Roberts D., Waldman G., Salmon J.H., Gilger B.C.

Uveitis and blindness in a closed herd of Equidae following leptospiral infection

(2024) Frontiers in Veterinary Science, 11, art. no. 1504990

DOI: 10.3389/fvets.2024.1504990

ABSTRACT: Objective: To describe the ocular findings, chronology of disease, and serum leptospiral titers in a group of horses, mules, and donkeys following an outbreak of leptospirosis. Methods: Fifty Equidae in central North Carolina had ophthalmic examinations and serum leptospiral microscopic agglutination test (MAT) titers performed every 3–6 months for 24 months followed by a final examination at 34 months. Results: Throughout the nearly three-year study period, 17 horses (34%; 17/49 horses) developed signs of uveitis; 20 eyes (20/34; 58.8%) of these 17 horses were visual at the initial examination, but only four eyes (11.8%) remained visual at the final examination. Serum titers (serogroups Pomona and Bratislava) in horses with uveitis were significantly elevated compared to Equidae without uveitis ($p < 0.02$). In the 32 horses, donkeys, and mules that did not develop uveitis, a subgroup of 11 horses and one donkey had negative or low serum leptospiral titers (titers $\leq 1:800$) while a second subgroup of 16 horses, three mules, and one donkey had high leptospiral titers ($> 1:800$) but never developed uveitis. Water sources in the pasture were found to have high levels of leptospira. Conclusion: Approximately 1/3 of horses on a farm exposed to *Leptospira* developed uveitis and blindness. Serum titers to *L. Pomona* and *L. Bratislava* were significantly elevated in horses with uveitis. However, despite exposure, some horses, even with very high serum titers, never developed ocular disease.

These data indicates that further research is warranted to investigate the genetic and immunological aspects of the pathogenesis and susceptibility of leptospiral-associated uveitis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Nilles E.J., Paulino C.T., Galloway R., de St. Aubin M., Mayfield H.J., Cadavid Restrepo A., Dumas D., Garnier S., Caroline Etienne M., Duke W., Peña F., Iihoshi N., Abdalla G., Lopez B., Cruz L.L., Henríquez B., Durski K., Baldwin M., Loevinsohn G., Rees E.M., Martin B., Sartorius B., Skewes-Ramm R., Gutiérrez E.Z., Kucharski A., Lau C.L.

Seroepidemiology of human leptospirosis in the Dominican Republic: a multistage cluster survey, 2021

(2024) PLoS Neglected Tropical Diseases, 18 (12), art. no. e0012463

DOI: 10.1371/journal.pntd.0012463

ABSTRACT: Little is known about the epidemiology of leptospirosis in the Dominican Republic, the second most populous country in the Caribbean. We report on findings from a multi-stage household survey across two regions in the country that reveals a previously under-estimated burden of human *Leptospira* infection. Our findings, based on the reference-standard microscopic agglutination test, indicate a complex picture of serogroup diversity, spatial heterogeneity in infection and risk, and a marked discrepancy between reported cases and serologically estimated infections. Given an overall seroprevalence of 11.3% (95% CI: 10.8–13.0%) and a lower estimated force of infection (0.30% per year [0.27%–0.35%]) the number of infections may exceed national reported case data by 145-fold or more. *Icterohaemorrhagiae*, associated with severe Weil's disease, was the most commonly identified serogroup with a serogroup-specific prevalence of 4.4%. Consistent with other settings, risk factors including age, male sex, and rat exposure were associated with higher seroprevalence. Our study highlights the need for targeted public health interventions informed by serogroup-specific dynamics, detailed spatial analyses, knowledge of local animal reservoirs, and strengthened laboratory surveillance to effectively control this pathogen.

LANGUAGE OF ORIGINAL DOCUMENT: English

Wang W., Gao Y., Ji J., Huang Z., Xiong B., Xiang S.

Trends and advances in *Leptospira*, a bibliometric analysis

(2024) Frontiers in Microbiology, 15, art. no. 1514738

DOI: 10.3389/fmicb.2024.1514738

ABSTRACT: Background: Leptospirosis is an acute zoonotic disease caused by pathogenic *Leptospira*, primarily transmitted to humans through contact with water or soil contaminated by the bacteria. It is globally distributed, with heightened prevalence in tropical regions. While prior studies have examined the pathophysiology, epidemiology, and risk factors of leptospirosis, few have explored trends and emerging topics in the field. This study applies bibliometric analysis to generate a visual knowledge map, identifying research hotspots and forecasting future trends in leptospirosis investigations. Methods: Data were extracted from the Web of Science Core Collection (WOSCC), encompassing all publications up to May 1, 2024. CiteSpace and VOSViewer software were used to analyze annual publication trends, as well as contributions from countries, institutions, journals, authors, references, and keywords, thereby pinpointing current research priorities and potential future directions. Results: A total of 5,244 articles were included, sourced from 4,716 institutions, 955 journals, and 156 countries or regions. The United States led with 1,315 publications and had the most significant influence in the field. "PLOS Neglected Tropical Diseases" published the highest number of articles

(166), while “Infection and Immunity” garnered the most citations (6,591). Prominent research areas included restriction endonucleases, monoclonal antibodies, outer membrane proteins, water environments, detection methods, and antimicrobial agents. Research focus has shifted from early genomic and antigenic studies to investigations into outer membrane protein functions and environmental persistence, culminating in recent advances in molecular mechanisms and diagnostic technology development. Conclusion: This bibliometric analysis provides a comprehensive snapshot of leptospirosis research, emphasizing collaborations and impact among authors, countries, institutions, and journals. It offers valuable insights into ongoing trends and serves as a reference for future collaboration and research opportunities in the field.

LANGUAGE OF ORIGINAL DOCUMENT: English

Chandit C., Hengphasatporn K., Donsuy P., Shigeta Y., Wangkanont K.

Structure and catalytic activity of a dihydrofolate reductase-like enzyme from *Leptospira interrogans*

(2025) International Journal of Biological Macromolecules, 298, art. no. 139931

DOI: 10.1016/j.ijbiomac.2025.139931

ABSTRACT: A dihydrofolate reductase (DHFR)-like enzyme from *Leptospira interrogans* (LiDHFR) was cloned and the recombinant protein was characterized. Sequence alignment suggested that the enzyme lacked the conserved catalytic residues found in DHFR. Indeed, LiDHFR did not catalyze the reduction of dihydrofolate by either NADH or NADPH. X-ray crystallography revealed that LiDHFR bound NADP(H) tightly, but its active site architecture was vastly different from that of *Escherichia coli* DHFR (EcDHFR) and other DHFRs. Interestingly, vanillin could serve as a substrate for LiDHFR, demonstrating that LiDHFR is a functional enzyme. A putative vanillin binding mode was proposed.

LANGUAGE OF ORIGINAL DOCUMENT: English

Kin M.S., Sanchez M.C., Esteban M., Martinez M.L., Brihuega B.F., Hamer M., Saraullo V., Cayron E.D., Cayron G.P., Giménez H., Cayron C.R., Fort M.

First record of the presence of antibodies against *Leptospira* in *Lagostomus maximus*, and *Leptospira weilii* serogroup Celledoni in *Chaetophractus villosus*, Argentina

(2025) Comparative Immunology, Microbiology and Infectious Diseases, 117, art. no. 102302

DOI: 10.1016/j.cimid.2025.102302

ABSTRACT: Leptospirosis is a zoonosis with a worldwide distribution, which is transmitted through direct contact with infected animals or by contact with contaminated water or soil. Objectives was to examine the presence of antibodies against 23 serogroups of *Leptospira* in *Lagostomus maximus* and *Chaetophractus villosus* in La Pampa province, Argentina. Ninety-four serum samples from *L. maximus* (80) and *C. villosus* (14) were taken. The samples were analysed by microscopic agglutination test (MAT). Only 5/94 (5.3 %) serum samples presented antibodies against *Leptospira* sp. Three (21.4 %) serum samples from *C. villosus*, were reactive to the serogroups, Ballum, Grippotyphosa, Canicola and Celledoni, and two samples (2.5 %) of *L. maximus* to Pomona, Canicola and Ballum. This constitutes the first record of the presence of antibodies serogroup Celledoni in *C. villosus* and serogroups Pomona, Canicola and Ballum in *L. maximus* in Argentina.

LANGUAGE OF ORIGINAL DOCUMENT: English

Jain D., Gupta R., Mehta R., Prabhakaran P.N., Kumari D., Bhui K., Murali D.

Revisiting the synergistic in vitro antimicrobial and antibiofilm potential of chlorhexidine gluconate and cetrime in combination as an antiseptic and disinfectant agent

(2025) Microbiology Research, 16 (1), art. no. 16

DOI: 10.3390/microbiolres16010016

ABSTRACT: Chlorhexidine and cetrime are often used as antiseptics and disinfectants. While their individual activities are well-documented, their synergism has rarely been evaluated. Here, we attempted to evaluate the antimicrobial and antibiofilm effects of the combination of these two antimicrobial agents against two environment isolates, viz., *P. aeruginosa* and *S. aureus*. The synergism was assayed by determining the fractional inhibitory concentrations, while the antibiofilm effects were determined using crystal violet staining and the resazurin assay. Further, the effects on the biofilms were visualized using brightfield and confocal laser scanning microscopy. Our results show that the combination of these antimicrobials resulted in synergistic inhibition of *P. aeruginosa* growth. When tested at concentrations below the individual MICs (one-quarter of the MICs), the combination was able to significantly reduce the adherence of *S. aureus* biofilms to a polystyrene surface, while no effect was observed for *P. aeruginosa*. The combination was also able to significantly reduce the viability of pre-formed biofilms of both bacteria, thereby showing its antibiofilm potential. Next, we evaluated the performance of this combination against a wide array of micro-organisms. This fixed-dose combination formulation exhibited a significant reduction in the viability of an array of clinically relevant micro-organisms, including ESKAPE pathogens, *Mycobacterium* sp., MRSA, *Leptospira*, *Candida* sp., norovirus and adenovirus. Overall, it can be inferred that the combination of chlorhexidine and cetrime is a potential biocide that continues to be relevant for use in antisepsis and disinfection against infection-causing pathogens.

LANGUAGE OF ORIGINAL DOCUMENT: English

Halmenschlager V., de Almeida A.N., Ribeiro F.G., da Trindade C.S.

The effects of hydrological disasters on the population's health in the Northeast Region of Brazil

(2025) Health Economics (United Kingdom)

DOI: 10.1002/hec.4939

ABSTRACT: The Northeast region of Brazil is characterized by long periods of drought. However, the region is also frequently affected by floods. The socioeconomic characteristics of the locality make the population more vulnerable to the impacts of these disasters. Therefore, the aim of this article is to investigate the short to long-term impacts of hydrological disasters in northeastern Brazil on morbidity and mortality rates, by age groups. For this purpose, the difference-in-differences method proposed by Callaway and Sant'Anna was applied to a monthly panel data spanning the period from 2000 to 2012. The results indicate that in the short term there is an increase in the mortality rate associated with drowning. In the medium term, there are effects particularly on morbidity rates, with emphasis on leptospirosis and acute respiratory diseases. For the long-term diseases analyzed, no effects of hydrological disasters were observed.

LANGUAGE OF ORIGINAL DOCUMENT: English

Visnardi A.B., Ribeiro R.A., de Souza A.S., Churasacari Vences T.G., Llontop E.E., de Almeida Ferrari A.S., França Henrique P.A., Valdivieso D., Sánchez-Limache D.E., Silva G.R., Soares E.P., Santos T.W.C., Farah C.S., Sassonia R.C., Salinas R.K., Guzzo C.R., de Souza R.F.

Insertion of a Divergent GAF-like Domain Defines a Novel Family of YcgR Homologues That Bind c-di-GMP in Leptospirales

(2025) ACS Omega

DOI: 10.1021/acsomega.4c09917

ABSTRACT: The Leptospiraceae family, which includes the genera *Leptospira*, *Leptonema*, and *Turneriella*, is an ecologically diverse group that includes saprophytic strains from soil and water as well as important pathogenic strains. Adaptation to these multiple environments relies strongly on signal transduction to adjust their morphology, motility, and metabolism to the changing environmental conditions. Members of the genus *Leptospira* distinguish themselves among spirochetes for having an elevated number of signal transduction genes. In this study, we describe a novel signal transduction protein that has gained multiple paralogues in the Leptospiraceae. These proteins are members of the YcgR/DgrA/MotI family, whose orthologs in several bacterial lineages have been shown to regulate the flagellar motor upon binding to c-di-GMP through their N-terminal PilZ domain. Unlike previously described versions of YcgR, the spirochetal proteins are characterized by the insertion of a divergent GAF domain within their N-terminal PilZ domain. We show that one member of this protein family from *Leptospira interrogans* is still a monomeric c-di-GMP binding protein and that these novel YcgR-like proteins have mostly replaced other members of the YcgR family in Leptospiraceae. Marked divergence among the paralogs suggests this family's expansion was accompanied by neofunctionalization, with the likely emergence of novel interactions in the signal transduction network controlling the flagellum rotor and other processes affected by changes in levels of c-di-GMP.

LANGUAGE OF ORIGINAL DOCUMENT: English

Di Azevedo M.I.N., Kremer F., Ezepha C., Greco J.P.G., da Silva I.C.V., Bourhy P., Lilenbaum W.

Comparative genomics of *Leptospira santarosai* reveals genomic adaptations in bovine genital strains

(2024) Frontiers in Microbiology, 15, art. no. 1517151

DOI: 10.3389/fmicb.2024.1517151

ABSTRACT: Bovine genital leptospirosis (BGL) is a silent and chronic reproductive syndrome associated with reproductive failures that result in animal suffering and substantial financial losses for farmers. Important aspects of the interactions between the host and the pathogen during chronic leptospirosis have been well described in the kidney, but little is known about the genital infection mechanisms. The present study sheds light on the pathophysiology of BGL based on comparative genomic analysis of renal versus genital isolates of *Leptospira santarosai* genomes, an endemic species on Latin America. A significant number of genes were exclusive of the genital strains, with emphasis on genes associated with cell wall/membrane/envelope biogenesis, mobilome: prophages and transposons, and signal transduction mechanisms. Overall, these gene clusters play crucial roles in bacterial colonization and evasion of the immune response, which can reflect leptospiral tissue tropism to the genital niche. We provide new insights into the pathophysiology of an important and neglected syndrome in bovine, helping to elucidate the evolution of adaptation of leptospires in the genital tract of cows. Copyright

LANGUAGE OF ORIGINAL DOCUMENT: English