UNIVERSITI PUTRA MALAYSIA

SEROLOGICAL AND MOLECULAR DETECTION, ISOLATION AND CHARACTERIZATION OF LEPTOSPIRA INTERROGANS FROM CATS IN PENINSULAR MALAYSIA

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SEROLOGICAL AND MOLECULAR DETECTION, ISOLATION AND CHARACTERIZATION OF LEPTOSPIRA INTERROGANS FROM CATS IN PENINSULAR MALAYSIA

By

ABDULRAHMAN ALASHRAF

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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DEDICATION

We were strong, times were rough
But the family was tough, stood side by side all along

Growing up with them was easy, the time had flew on by
The years began to fly, They aged and so did I

Then one day Papa said, "Son, I'm proud of how you've grown"
He said, "Go out and make it on your own. Don't worry. We are OK alone"

He said, "There are things that you must do, there's places you must see"
And his eyes were sad as he said goodbye to me

The leaves were brown, and the sky was grey
I've been for a long walk, on such a winter's day

Stopped into a prayer room, I passed along the way
I got down on my knees, And I started to pray

The preacher likes the cold, and that I'm going to stay
If I did leave, I would not be here today

Every time, Papa words ring true:
"Whatever your dream is, as you really work for, there is no way it won't get true"

- I dedicate this project to **Allah Almighty** my creator, my strong pillar, my source of inspiration, strength, wisdom, knowledge and understanding, on His wings only I have soared.
- To my father & teacher, **Dr. Talal Alashraf** and my mother & soul, **Nashwa Kalo**, who have encouraged me all the way and whose support have made sure that I give it all it takes.
- To my siblings, my backbone, **Anas**, **Nour** and **Hiba** who have influenced me in every possible way by this quest.
- To the kind love of my siblings-in-law, **Khaled Al-Najjar** & **Zouhur Azrak**.

My love for you all can never be quantified,
Much love and God bless.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

SEROLOGICAL AND MOLECULAR DETECTION, ISOLATION AND CHARACTERIZATION OF LEPTOSPIRA INTERROGANS FROM CATS IN PENINSULAR MALAYSIA

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ABDULRAHMAN ALASHRAF

August 2020

Chairman : Associate Professor Lau Seng Fong, PhD
Faculty : Veterinary Medicine

Leptospirosis is one of the most common zoonotic diseases worldwide and it has been frequently reported in tropical regions, the annual cases of leptospirosis have exceeded more than one million worldwide with high mortality rates in humans. There is a paucity of data regarding the leptospiral infection in cats. Investigation on leptospiral infection in cats is necessary for further understanding the susceptibility of cats towards *Leptospira* spp. and to increase the public health awareness. In this study, a total of 192 blood samples were collected from cats from four shelters in Peninsular Malaysia. The sero-detection against *Leptospira* spp. was as high as 21.3% (n= 41/192). Bataviae was the predominant serogroup found in cats, the antibodies titres ranged from 1:100 to 1:1600. Additionally, the blood, urine and kidneys from 82 cats were tested using PCR and bacterial culture. The results showed that 4.8% cats (n= 4/82) had pathogenic leptospiral DNA in urine and 4.8% cats (n= 4/82) showed positive cultures from urine and/or kidney. The leptospires isolates were identified using serological and molecular methods as pathogenic *L. interrogans* serogroup Bataviae. Furthermore, 21 cats that were diagnosed positive for *Leptospira* spp. were proceeded for renal examination. The kidney showed histopathological changes from mild to severe and interstitial nephritis was the most observed lesion, whilst 95.2% cats (n=20/21) were positively stained for lipL32 in the lumen of kidney tubules. The isolated leptospiral strain from this study (Alashraf U53-UPM; MK391605) was proceeded for further genomic analysis. The genome analysis revealed genes involved in pathogeneses, environmental tolerance (pH and temperature resistance) and tissue invasion. Moreover, 99% Average Nucleotide Identity (ANI) similarity was revealed with previously isolated Bataviae strains in rats and humans in Malaysia and Thailand respectively. The current study shows that leptospiral infection is common in cats in Malaysia. Locally and globally, the results provide evidence to improve existing knowledge of leptospiral infection in cats.

This study presents the first report of the ability of cats to act as a reservoir harbour the pathogenic *Leptospira* spp. in kidney and shed the pathogens in urine to environment. The infected cats with leptospires had histopathological changes in kidney with expression of lipL32. The isolated leptospires were pathogenic and closely related to a highly pathogenic Copenhageni strain Fiocruz L1-130. The genome characteristics of the isolates contribute to further comparative analysis of pathogenic leptospiral evolution.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

JANGKITAN LEPTOSPIRA: PENGESANAN SECARA SEROLOGI, MOLEKULAR, ISOLASI DAN PENCIRIAN LEPTOSPIRA INTERROGANS DARIPADA KUCING DI SEMENANJUNG MALAYSIA

Oleh

ABDULRAHMAN ALASHRAF

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Leptospirosis adalah salah satu penyakit zoonotik yang paling dikenali di seluruh dunia dan sering dilaporkan di kawasan tropika. Laporan tahunan kes leptospirosis telah melebihi lebih dari satu juta di seluruh dunia dengan kadar kematian yang tinggi dikalangan manusia. Secara umum, terdapat kekurangan data berkenaan jangkitan leptospira pada kucing. Kajian mengenai jangkitan leptospira pada kucing adalah penting untuk memahami kerentanan kucing terhadap Leptospira spp. dan untuk meningkatkan kesedaran kesihatan awam. Dalam kajian ini, 192 sampel darah dikumpulkan dari kucing dari empat tempat perlindungan di Semenanjung Malaysia. Pengesanan sero terhadap Leptospira spp. setinggi 21.3% (n = 41/192). Bataviae adalah serogroup dominan yang terdapat pada kucing, titer antibodi berkisar antara 1: 100 hingga 1: 1600. Selain itu, sampel darah, air kencing dan ginjal dari 82 kucing turut diuji menggunakan PCR dan kultur bakteria. Hasil kajian menunjukkan bahawa 4.8% kucing (n = 4/82) mempunyai DNA leptospira patogen dalam air kencing dan 4.8% kucing (n = 4/82) menunjukkan kultur positif dari air kencing dan / atau buah pinggang. Asingan leptospires dikenal pasti menggunakan kaedah serologi dan molekul sebagai patogenik L. interrogans serogroup Bataviae. Selanjutnya, 21 kucing yang didiagnosis positif Leptospira spp. dilanjutkan untuk pemeriksaan ginjal. Ginjal menunjukkan perubahan histopatologi dari nefritis ringan hingga teruk dan interstisial adalah lesi yang paling banyak diperhatikan, sementara 95.2% kucing (n = 20/21) bernoda positif untuk lipL32 di lumen tubulus ginjal. Strain leptospira terpencil dari kajian ini (Alashraf U53-UPM; MK391605) dilanjutkan untuk analisis genomik selanjutnya. Analisis genom menunjukkan gen yang terlibat dalam patogen, toleransi persekitaran (ketahanan pH dan suhu) dan pencerobohan tisu. Lebih-lebih lagi, persamaan 99% Purata Identiti Nukleotida (ANI) dinyatakan dengan strain Bataviae yang sebelumnya diasingkan pada tikus dan manusia di Malaysia dan Thailand. Kajian semasa menunjukkan bahawa jangkitan leptospira sering terjadi pada kucing di Malaysia.

Kajian ini membentangkan laporan pertama mengenai kemampuan kucing bertindak sebagai takungan yang menyimpan patogen Leptospira spp. di buah pinggang dan memindahkan patogen dalam air kencing ke persekitaran. Kucing yang dijangkiti dengan leptospire mengalami perubahan histopatologi pada buah pinggang dengan ekspresi lipL32. Leptospire terpencil patogen dan relevan dengan strain Copenhageni Fiocruz L1-130 yang sangat patogen. Ciri-ciri genom isolate menyumbang kepada analisis perbandingan lebih lanjut mengenai evolusi leptospira patogen.

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This thesis was submitted to the Senate of the Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

%	Percentage
5-AS	5-amino-salicylic acid
5-FU	5-fluorouracil
°C	The Degree Celsius
µM	Micromolar
µl	Microliter
N	Negative
n	Number
P	Positive
ANI	Average nucleotide identity
AKI	Acute kidney injury
ARDS	Acute respiratory distress syndrome
BLAST	Basic local alignement search tool
BSA	Bovine serum albumin
CI	Confidence Interval
DNA	Deoxyribonucleic acid
dNTP	Deoxynucleotide triphosphate
ECM	Extracellular Matrix
EDTA	Ethylene-diamine-tetraacetic-acid
ELISA	Enzyme-linked immunosorbent assay
EMJH	Ellinghausen and McCullough modified by Johnson and Harris
H&E	Haematoxylin and Eosin
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IHC	Immunohistochemistry
IN	Interstitial nephritis
LPS	Lipopolysaccharide
LPHS	Lethal pulmonary haemorrhages syndrome
MAT	Microscopic agglutination test
mg	Milligram
ml	Millilitre
mM	Millimolar

NaCl	Sodium chloride
NCBI	National centre for biotechnology information
ND	Not determined
OMP	Outer membrane proteins
PBS	Phosphate buffered saline
PCR	Polymerase chain reaction
PD	Polydipsia
PU	Polyuria
PGs	Prostaglandins
pH	Potential hydrogen
PRR	Pattern recognition receptor
RNA	Ribonucleic acid
rpm	Rounds per minute
Str	Strain
TLR	Tol-like receptor
VF	Virulence factor
VHF	Viral haemorrhagic fever
WGS	Whole genome sequence
WHO	World health organization
WSS	Warthin starry silver

CHAPTER 1

INTRODUCTION

Leptospirosis is one of the most common zoonotic diseases in the world and it has been frequently reported in tropical regions (Benacer et al., 2016). High mortality rates in humans correlated with leptospirosis have surpassed serious diseases such as viral hemorrhagic fevers (VHFs), the annual cases of leptospirosis have exceeded more than one million worldwide (Lozano et al., 2012; Costa et al., 2015). The causative agent of the disease is *Leptospira* spp., a bacterium belongs to the spirochetes phylum (Levett, 2001). Leptospirosis can be transmitted in two modes, either through direct contact with infected urine and indirectly by the access to contaminated environment (Musso & La Scola, 2013). More than 250 virulent serovars have been reported to date, causing the infection to more than 150 mammals (Adler & Moctezuma, 2010; Ko et al., 2012). The prevalent serovars differed due to geographical variability, serovars endemicity and the infected hosts (Hartmann et al., 2013), such as serovar Icterohaemorrhagiae in Europe (Levett, 2001). Rodents are the primary reservoir host of *Leptospira* spp. that can harbour and excrete the bacteria asymptotically through lifetime (Levett, 2001), other domestic animals may act as hosts for designated serovars such as Hardjo in cattle (Adler & Moctezuma, 2010).

In most cases, leptospirosis is an asymptomatic disease in both animals and humans (Bharti et al., 2003b). Clinical symptoms are usually non-specific and vary widely, the common clinical signs in human include jaundice, fever and nausea (Levett, 2001; Bharti et al., 2003). As for animals, the clinical signs differ among species of animals, for example, symptoms in cattle manifest the reproductive system and mainly due to serovar Hardjo (Miyama et al., 2018), and the ocular system in horses that are infected with serovar Bratislava are found to be impaired (Rohrbach et al., 2005). In Malaysia, leptospirosis is endemic with human cases recorded increasing from 263 in 2004 to 7,806 in 2014 (Benacer et al., 2016; Garba et al., 2017). The high humidity and temperatures in Malaysia provide an ideal environment for the survival of the *Leptospira* species.

Cats showed susceptibility towards leptospiral infection with percentage ranged in-between 4.8-48% (Agunloye & Nash, 1996; Luciani, 2004; Markovich et al., 2012; Rodriguez et al., 2014). A wide range of serovars have been reported in cats that belong to two species, namely, *L. interrogans* and *L. kirschneri* (Hartmann et al., 2013). Clinical signs of leptospirosis in cats are yet to be investigated, despite in previous studies, cats with polyuria and polydipsia (PU/PD) had been reported more likely to have anti-*Leptospira* antibodies (Luciani, 2004; Fessler & Morter, 1964). Recently, both stray and household cats were reported to have DNA from pathogenic *Leptospira* species in urine (Chan et al., 2014; Fenimore et al., 2012; Weis et al., 2017). Therefore, cats might be reservoir host or incidental host of *Leptospira* spp., while the role of cats as potential source of the infection is always a subject of discussion (Hartmann et al., 2013). In Malaysia, cats are the most common companion animals and live in vicinity to human,

but there is a paucity of published data regarding leptospirosis in cats (Benacer et al., 2017).

This preliminary study investigated feline leptospiral infection among the sheltered cat in Peninsular Malaysia; determined the susceptibility of cats, the predominant serogroups, the carrier and shedding status; and the renal involvement in naturally infected cats with *Leptospira* spp.

1.1 Problem Statement

The problem statements can be capitulated as follows:

1. Leptospirosis is one of the common zoonotic diseases in Malaysia, with high occurrence in humans in recent years.
2. Cats are the most common companion animal in Malaysia, however, their exposure to *Leptospira* spp. is uncertain.
3. Cats are speculated to be either a reservoir host or an incidental host of *Leptospira* spp., the role of cats as a source is unknown.
4. The renal pathological changes in naturally and sub-clinically infected with *Leptospira* spp. cats are under-reported.

1.2 Objectives

The objectives of this study are:

1. To sero-detect anti-*Leptospira* spp. antibodies among shelter cat population in Malaysia and to determine the most common infective leptospiral serogroups.
2. To determine the exposure, shedding and carriage status of leptospires in shelter cats in Malaysia using serological, molecular and bacteriological methods.
3. To describe the renal changes in naturally infected cats with *Leptospira* spp. and to demonstrate leptospires in the renal cats' tissue using special stain Warthin-Starry Stain Impregnation (WSS) stain and Immunohistochemistry (IHC) using rabbit antiserum against the leptospiral major outer membrane protein (lipL32).
4. To study leptospiral isolates obtained from cat urine and to analyse the genome in terms of its evolution and the virulence factors using Whole Genome Sequence (WGS).

1.3 Hypotheses

The hypotheses of this study are:

1. In Malaysia, the sero-detection of leptospiral infection in cats will be as high as other domestic animals such as dogs and cattle.
2. Infected cats with *Leptospira* spp. in Malaysia are carriers and are able to transmit leptospires to the environment.
3. The histological examination of the renal sections from naturally infected cats with *Leptospira* spp. will show changes in the kidney.
4. Leptospiral isolates obtained from cats urine and kidney will be highly virulent.

REFERENCES

Abgueguen, P., Delbos, V., Blanvillain, J., Chennebault, J. M., Cottin, J., Fanello, S., & Pichard, E. (2008). Clinical aspects and prognostic factors of leptospirosis in adults. Retrospective study in France. *Journal of Infection*, *57*(3), 171–178. https://doi.org/https://doi.org/10.1016/j.jinf.2008.06.010.

Abiayi, E. A., Inabo, H. I., Jatau, E. D., Makinde, A. A., Sar, T. T., & Dangeri, M. A. (2015). Occurrence of leptospirae antibodies in abattoir workers in parts of north central Nigeria. *Research Journal of Immunology*, *8*(1), 27–34. https://doi.org/10.3923/rji.2015.27.34.

Adler, B. (1967). *Leptospira and Leptospirosis*. *Archives of Neurology* (Vol. 17). https://doi.org/10.1001/archneur.1967.00470290112018.

Adler, B. (2014). Pathogenesis of leptospirosis: Cellular and molecular aspects. *Veterinary Microbiology*, *172*(3–4), 353–358. https://doi.org/10.1016/j.vetmic.2014.06.015.

Adler, B., & Moctezuma, A. (2009). Leptospira and leptospirosis. *Journal of Veterinary Microbiology Journal*, *140*, 287–296. https://doi.org/10.1080/00219266.1991.9655201.

Adler, B., & Moctezuma, A. (2010). *Leptospira* and leptospirosis. *Veterinary Microbiology*, *140*(3–4), 287–296. https://doi.org/10.1016/j.vetmic.2009.03.012.

Adler, B., Lo, M., Seemann, T., & Murray, G. L. (2011). Pathogenesis of leptospirosis : The influence of genomics. *Veterinary Microbiology*, *153*(1–2), 73–81. https://doi.org/10.1016/j.vetmic.2011.02.055.

Agudelo-Florez, P., Murillo, V. E., Londono, A. F., & Rodas, J. D. (2013). Histopathological kidney alterations in rats naturally infected with Leptospira. *Biomedica : Revista Del Instituto Nacional de Salud*, *33 Suppl 1*, 82–88.

Agunloye, C. a, & Nash, S. (1996). Investigation of possible leptospiral infection in cats in Scotland. *The Journal of Small Animal Practice*, *37*(3), 126–129. https://doi.org/10.1111/j.1748-5827.1996.tb02360.x.

Ahmad, S. N., Shah, S., & Ahmad, F. M. (2005). Laboratory diagnosis of leptospirosis. *Journal of Postgraduate Medicine*, *51*(3), 195–200.

Ahmed, N., Devi, S. M., Valverde, Á., Vijayachari, P., Machang, R. S., Ellis, W. A., & Hartskeerl, R. A. (2006). Multilocus sequence typing method for identification and genotypic classification of pathogenic Leptospira species, *10*, 1–10. https://doi.org/10.1186/1476-0711-5.

Ajayi, O. L., Antia, R. E., Ojo, O. E., Awoyomi, O. J., Oyinlola, L. A., & Ojebiyi, O. G. (2017). Prevalence and renal pathology of pathogenic *Leptospira* spp. in wildlife in Abeokuta, Ogun State, Nigeria. *Onderstepoort J Vet Res*, *84*(1), 1–9. https://doi.org/10.4102/ojvr.v84i1.1210.

Akira, S., Uematsu, S., & Takeuchi, O. (2006). Pathogen Recognition and Innate Immunity. *Cell*, *124*(4), 783–801. https://doi.org/10.1016/j.cell.2006.02.015.

Al Kattan, G., Bahaman, A. R., Bejo, S. K., Zakaria, Z., & Garba, B. (2017). Serological and molecular prevalence of Leptospira infection in Rat populations in Kuala Lumpur. *Australian Journal of Basic and Applied Sciences Aust. J. Basic & Appl. Sci*, *11*(111), 62–72.

Alashraf, A. R., Lau, S. F., Khor, K. H., Khairani-Bejo, S., Bahaman, A. R., Roslan, M. A., … Radzi, R. (2019). Serological Detection of Anti-Leptospira Antibodies in Shelter Cats in Malaysia. *Topics in Companion Animal Medicine*, *34*, 10–13. https://doi.org/10.1053/j.tcam.2018.12.002,

Albert I. Ko & Goarant. C. (2012). Leptospira: The Dawn of the Molecular Genetics Era. *Natural Review Microbiology*, *7*(10), 736–747. https://doi.org/10.1038/nrmicro2208.

Alt, D. P., Welder, J. H., Bayles, D. O., Cameron, C., Adler, B., Bulach, D. M., … Zuerner, L. (2015). Complete Genome Sequence of Leptospira interrogans Serovar. *Genome Announcments*, *3*(3), 1–2. https://doi.org/10.3390/pathogens3020280.2.

Alves, F., Vianna, M. R., Yasuda, P. H., & De Brito, T. (1987). Detection of leptospiral antigen in the human liver and kidney using an immunoperoxidase staining procedure. *The Journal of Pathology*, *151*(2), 125–131. https://doi.org/10.1002/path.1711510205.

Amran, F., Mohd, M. K. N., Mohamad, S., Mat Ripen, A., Ahmad, N., Goris, M. G. A., … Noor Halim, N. A. (2016). Draft Genome Sequence of Leptospira interrogans Serovar Bataviae Strain LepIMR 22 Isolated from a Rodent in Johor, Malaysia. *Genome Announcements*, *4*(5), e00956-16. https://doi.org/10.1128/genomeA.00956-16.

Andrade, L., de Francesco Daher, E., & Seguro, A. C. (2008). Leptospiral nephropathy. *Seminars in Nephrology*, *28*(4), 383–394. https://doi.org/10.1016/j.semnephrol.2008.04.008.

André-Fontaine, G. (2006). Canine leptospirosis-Do we have a problem? *Veterinary Microbiology*, *117*(1), 19–24. https://doi.org/10.1016/j.vetmic.2006.04.005.

Arbour, J., Blais, M.-C., Carioto, L., & Sylvestre, D. (2012). Clinical Leptospirosis in Three Cats (2001-2009). *Journal of the American Animal Hospital Association*, *48*(4), 256–260. https://doi.org/10.5326/JAAHA-MS-5748.

Athanazio, D. A., Silva, E. F., Santos, C. S., Rocha, G. M., Vannier-santos, M. A., Mcbride, A. J. A., … Reis, M. G. (2008). Rattus norvegicus as a model for persistent renal colonization by pathogenic Leptospira interrogans. *Acta Tropica*, *105*, 176–180. https://doi.org/10.1016/j.actatropica.2007.10.012.

Atzingen, M. V., Barbosa, A. S., De Brito, T., Vasconcellos, S. A., De Morais, Z. M., Lima, D. M. C., … Nascimento, A. L. T. O. (2008). Lsa21, a novel leptospiral protein binding adhesive matrix molecules and present during human infection. *BMC Microbiology*, *8*, 1–16. https://doi.org/10.1186/1471-2180-8-70.

Azócar-Aedo, L., Smits, H. L., & Monti, G. (2014). Leptospirosis in dogs and cats: Epidemiology, clinical disease, zoonotic implications and prevention. *Archivos de Medicina Veterinaria*, *46*(3), 337–348. https://doi.org/10.4067/S0301-732X2014000300002.

Azócar-Aedo, G., & Jara, R. (2014). Leptospira spp. in domestic cats from different environments: Prevalence of antibodies and risk factors associated with the seropositivity. *Animals*, *4*(4), 612–626. https://doi.org/10.3390/ani4040612.

Bahaman, A. R., & Ibrahim, A. L. (1988). A review of leptospirosis in Malaysia. *Veterinary Research Communications*, *12*(2–3), 179–189. https://doi.org/10.1007/BF00362799.

Bal, A. E., Gravekamp, C., Hartskeerl, R. A., De Meza-Brewster, J., Korver, H., & Terpstra, W. J. (1994). Detection of leptospires in urine by PCR for early diagnosis of leptospirosis. *Journal of Clinical Microbiology*, *32*(8), 1894–1898.

Barbosa, A. S., Abreu, P. A. E., Neves, F. O., Atzingen, M. V, Watanabe, M., Vieira, L., … Sa, U. (2006). A Newly Identified Leptospiral Adhesin Mediates Attachment to Laminin. *Infection and Immunity*, *74*(11), 6356–6364. https://doi.org/10.1128/IAI.00460-06.

Beaudu-Lange, C., & Lange, E. (2014). Unusual clinical presentation of leptospirosis in a cat. *Revue Veterinaire Clinique*, *49*(3), 115–122. https://doi.org/10.1016/j.anicom.2014.05.001.

Becker, D. J., & Lowe, J. B. (1999). Leukocyte adhesion deficiency type II. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, *1455*(2–3), 193–204.

Benacer, D., Thong, K. L., Ooi, P. T., Souris, M., Lewis, J. W., Ahmed, A. A., & Mohd Zain, S. N. (2017). Serological and molecular identification of Leptospira spp. In swine and stray dogs from Malaysia. *Tropical Biomedicine*, *34*(1), 89–97.

Benacer, D., Mohd Zain, S. N., Ahmed, A. A., Mohd Khalid, M. K. N., Hartskeerl, R. A., & Thong, K. L. (2016). Predominance of the ST143 and ST50 Leptospira clones in the urban rat populations of Peninsular Malaysia. *Journal of Medical Microbiology*, *65*(6), 574–577. https://doi.org/10.1099/jmm.0.000262.

Benacer, D., Mohd Zain, S. N., Sim, S. Z., Mohd Khalid, M. K. N., Galloway, R. L., Souris, M., & Thong, K. L. (2016). Determination of Leptospira borgpetersenii serovar Javanica and Leptospira interrogans serovar Bataviae as the persistent Leptospira serovars circulating in the urban rat populations in Peninsular Malaysia. *Parasites and Vectors*, *9*(1), 1–11. https://doi.org/10.1186/s13071-016-1400-1.

Benacer, D., Thong, K. L., Min, N. C., Verasahib, K. Bin, Galloway, R. L., Hartskeerl, R. A., … Zain, S. N. M. (2016). Epidemiology of human leptospirosis in Malaysia, 2004-2012. *Acta Tropica*, *157*, 162–168. https://doi.org/10.1016/j.actatropica.2016.01.031.

Benacer, D., Thong, K. L., Verasahib, K. Bin, Galloway, R. L., Hartskeerl, R. A., Lewis, J. W., & Mohd Zain, S. N. (2016). *Human Leptospirosis in Malaysia: Reviewing the Challenges after 8 Decades (1925-2012). Asia-Pacific Journal of Public Health* (Vol. 28, pp. 290–302). https://doi.org/10.1177/1010539516640350.

Benacer, D., Zain, S. N. M., Amran, F., Galloway, R. L., & Thong, K. L. (2013). Isolation and molecular characterization of Leptospira interrogans and Leptospira borgpetersenii Isolates from the urban rat populations of Kuala Lumpur, Malaysia. *American Journal of Tropical Medicine and Hygiene*, *88*(4), 704–709. https://doi.org/10.4269/ajtmh.12-0662.

Bernheimer, A. W., & Bey, R. F. (1986). Copurification of Leptospira interrogans serovar pomona hemolysin and sphingomyelinase C. *Infection and Immunity*, *54*(1), 262–264.

Betance, L., Peda, A., Conan, A., & Ribeiro, J. (2017). Seroprevalence of Leptospirosis in the Feral Cat Population of. *Journal of Animal Research and Technology*, 38–42. https://doi.org/10.5147/jart.2017.0161.

Bharti, A. R., Nally, J. E., Ricaldi, J. N., Matthias, M. A., Diaz, M. M., Lovett, M. A., … Vinetz, J. M. (2003). Leptospirosis: a zoonotic disease of global importance. *The Lancet Infectious Diseases*, *3*(12), 757–771. https://doi.org/10.1016/S1473-3099(03)00830-2.

Birnbaum, N., Barr, S. C., Center, S. A., Schermerhorn, T., Randolph, J. F., & Simpson, K. W. (1998). Naturally acquired leptospirosis in 36 dogs: serological and clinicopathological features. *The Journal of Small Animal Practice*, *39*, 231–236. https://doi.org/10.1111/j.1748-5827.1998.tb03640.x.

Blanco, R. M., Dos Santos, L. F., Galloway, R. L., & Romero, E. C. (2016). Is the microagglutination test (MAT) good for predicting the infecting serogroup for leptospirosis in Brazil? *Comparative Immunology, Microbiology and Infectious Diseases*, *44*, 34–36. https://doi.org/10.1016/j.cimid.2015.12.003.

Bolin, C. A., & Koellner, P. (1988). Human-to-human transmission of Leptospira interrogans by milk. *The Journal of Infectious Diseases*. *1*, 246-247 United States. https://doi.org/10.1093/infdis/158.1.246.

Börkü, M. K., Kurtdede, A., Aydın, Y., Durgut, R., Pekkaya, S., & Özkanlar, Y. (2000). Clinical, laboratory and pathological findings in cats and dogs exhibiting chronic renal failure signs. *Ankara Universitesi Veteriner Fakultesi Dergisi*, *47* (3), 281–289.

Bourhy, P., Collet, L., Lernout, T., Zinini, F., Hartskeerl, R. A., van Der Linden, H., … Giry, C. (2012). Human Leptospira isolates circulating in Mayotte (Indian Ocean) have unique serological and molecular features. *Journal of Clinical Microbiology*, *50*(2), 307–311.

Bryson, D. G., & Ellis, W. A. (1976). Leptospirosis in a British domestic cat. *Journal of Small Animal Practice*, *17*(7), 459–465. https://doi.org/10.1111/j.1748-5827.1976.tb06986.x.

Budihal, S. V., & Perwez, K. (2014). Leptospirosis diagnosis: Competancy of various laboratory tests. *Journal of Clinical and Diagnostic Research*, *8*(1), 199–202. https://doi.org/10.7860/JCDR/2014/6593.3950.

Burth, P., Younes-Ibrahim, M., Santos, M. C. B., Castro-Faria, N., & de Castro Faria, M. V. (2005). Role of nonesterified unsaturated fatty acids in the pathophysiological processes of leptospiral infection. *The Journal of Infectious Diseases*, *191*(1), 51–57. https://doi.org/10.1086/426455.

Thompson, J., & B. W. Manktelow. (1986). Pathogenesis and red blood in haemoglobinaemic cell destruction leptospirosis. Journal of Comparative Pathology, *96(5)*, 529-540.

Cachay, E. R., Vinetz, J. M., & E.R., C. (2005). A global research agenda for leptospirosis. *Journal of Postgraduate Medicine*, *51*(3), 174–178.

Campagnolo, E. R., Warwick, M. C., Marx, H. L. J., Cowart, R. P., Donnell, H. D. J., Bajani, M. D., … Ashford, D. A. (2000). Analysis of the 1998 outbreak of leptospirosis in Missouri in humans exposed to infected swine. *Journal of the American Veterinary Medical Association*, *216*(5), 676–682.

Carlos, E. R., Kundin, W. D., Watten, R. H., Tsai, C. C., Irving, G. S., Carlos, E. T., & Directo, A. C. (1971). Leptospirosis in the Philippines: feline studies. *American Journal of Veterinary Research*, *32*(9), 1455–1456.

Catley, J. M. (2009). *The prevalence of leptospira serovars causing infections in dogs in South Africa*. *Masters thesis, university of Pretoria, South Africa*.

Cerqueira, G. M., & Picardeau, M. (2009). A century of Leptospira strain typing. *Infection, Genetics and Evolution*, *9*(5), 760–768. https://doi.org/10.1016/j.meegid.2009.06.009.

Chan, K.-W., Hsu, Y.-H., Hu, W.-L., Pan, M.-J., Lai, J.-M., Huang, K.-C., & Chou, S.-J. (2014). Serological and PCR detection of feline leptospira in southern Taiwan. *Vector Borne and Zoonotic Diseases*, *14*(1), 118–123. https://doi.org/10.1089/vbz.2013.1324.

Chitale, S., Ehrt, S., Kawamura, I., Fujimura, T., Shimono, N., Anand, N., … Riley, L. W. (2001). Recombinant Mycobacterium tuberculosis protein associated with mammalian cell entry. *Cellular Microbiology*, *3*(4), 247–254.

Choy, H. A., Kelley, M. M., Chen, T. L., Møller, A. K., Matsunaga, J., & Haake, D. A. (2007). Physiological Osmotic Induction of Leptospira interrogans Adhesion : LigA and LigB Bind Extracellular Matrix Proteins and Fibrinogen. *Infection and Immunity*, *75*(5), 2441–2450. https://doi.org/10.1128/IAI.01635-06.

Cinco, M., Banfi, E., & Soranzo, M. R. (1981). Studies on the Interaction between Macrophages and Leptospires. *Journal of General Microbiology*, 409–413.

Cosson, J. F., Picardeau, M., Mielcarek, M., Tatard, C., Chaval, Y., Suputtamongkol, Y., … Morand, S. (2014). Epidemiology of Leptospira Transmitted by Rodents in Southeast Asia. *PLoS Neglected Tropical Diseases*, *8*(6).

Costa, F., Hagan, J. E., Calcagno, J., Kane, M., Torgerson, P., Martinez-Silveira, M. S., … Ko, A. I. (2015). Global Morbidity and Mortality of Leptospirosis: A Systematic Review. *PLoS Neglected Tropical Diseases*, *9*(9). https://doi.org/10.1371/journal.pntd.0003898.

De Brito, T., Menezes, L. F., Lima, D. M. C., Lourenco, S., Silva, A. M. G., & Alves, V. A. F. (2006). Immunohistochemical and in situ hybridization studies of the liver and kidney in human leptospirosis. *Virchows Archiv : An International Journal of Pathology*, *448*(5), 576–583. https://doi.org/10.1007/s00428-006-0163-z.

de Souza, L., & Koury, M. C. (1992). Isolation and biological activities of endotoxin from Leptospira interrogans. *Canadian Journal of Microbiology*, *38*(4), 284–289.

de Vries, S. G., Visser, B. J., Nagel, I. M., Goris, M. G. A., Hartskeerl, R. A., & Grobusch, M. P. (2014). Leptospirosis in Sub-Saharan Africa: A systematic review. *International Journal of Infectious Diseases*, *28*, e47–e64. https://doi.org/10.1016/j.ijid.2014.06.013.

Del Real, G., Segers, R. P. A. M., Van Der Zeijst, B. A. M., & Gaastra, W. (1989). Cloning of a hemolysin gene from Leptospira interrogans serovar hardjo. *Infection and Immunity*, *57*(8), 2588–2590.

Dellagostin, O. A., Grassmann, A. A., Rizzi, C., Schuch, R. A., Jorge, S., Oliveira, T. L., … Hartwig, D. D. (2017). Reverse Vaccinology: An Approach for Identifying Leptospiral Vaccine Candidates. *International Journal of Molecular Sciences*, *18*(1), 158. https://doi.org/10.3390/ijms18010158.

Demers, R. Y., Frank, R., Demers, P., & Clay, M. (1985). Leptospiral exposure in Detroit rodent control workers. *American Journal of Public Health*, *75*(9), 1090–1091. https://doi.org/10.2105/ajph.75.9.1090.

Desvars, A., Naze, F., Benneveau, A., Cardinale, E., & Michault, A. (2013). Endemicity of leptospirosis in domestic and wild animal species from Reunion Island (Indian Ocean). *Epidemiology and Infection*, *141*(6), 1154–1165. https://doi.org/10.1017/S0950268812002075.

Dhaliwal, G. S., Murray, R. D., Dobson, H., Montgomery, J., & Ellis, W. A. (1996). Reduced conception rates in dairy cattle associated with serological evidence of Leptospira interrogans serovar hardjo infection. *The Veterinary Record*, *139*(5), 110—114. https://doi.org/10.1136/vr.139.5.110.

Diament, D., Brunialti, M. K. C., Romero, E. C., Kallas, E. G., & Salomao, R. (2002). Peripheral blood mononuclear cell activation induced by Leptospira interrogans glycolipoprotein. *Infection and Immunity*, *70*(4), 1677–1683. https://doi.org/10.1128/iai.70.4.1677-1683.2002

Dickeson, D., & Love, D. N. (1993). A serological survey of dogs, cats and horses in south-eastern Australia for leptospiral antibodies. *Australian Veterinary Journal*, *70*(10), 389–390.

Dolhnikoff, M., Mauad, T., Bethlem, E. P., & Carvalho, C. R. R. (2007). Leptospiral pneumonias. *Current Opinion in Pulmonary Medicine*, *13*(3), 230–235. https://doi.org/10.1097/MCP.0b013e3280f9df74

Doukkali, C. (2011). Leptospira : Morphology , Classification and Pathogenesis Bacteriology & Parasitology Leptospira : Morphology , Classification and Pathogenesis. *Journal of Bacteriology & Parasitology*. *2*(6), 2-6 https://doi.org/10.4172/2155-9597.1000120

Dybing, N. A., Jacobson, C., Irwin, P., Algar, D., & Adams, P. J. (2017). Leptospira Species in Feral Cats and Black Rats from Western Australia and Christmas Island. *Vector-Borne and Zoonotic Diseases*, *17*(5), 319–324.

https://doi.org/10.1089/vbz.2016.1992

Eichorst, S. A., Breznak, J. A., & Schmidt, T. M. (2007). Isolation and characterization of soil bacteria that define Terriglobus gen. nov., in the phylum Acidobacteria. *Applied and Environmental Microbiology*, *73*(8), 2708–2717. https://doi.org/10.1128/AEM.02140-06

Ellis, W. A. (1994). Leptospirosis as a cause of reproductive failure. *The Veterinary Clinics of North America. Food Animal Practice*, *10*(3), 463–478. https://doi.org/10.1016/S0749-0720(15)30532-6

Eshghi, A., Becam, J., Lambert, A., Sismeiro, O., Dillies, M.-A., Jagla, B., … Picardeau, M. (2014). A Putative Regulatory Genetic Locus Modulates Virulence in the Pathogen <span class="named-content genus-species & Leptospira interrogans; *Infection and Immunity*, *82*(6), 2542 LP – 2552. https://doi.org/10.1128/IAI.01803-14

Eshghi, A., Henderson, J., & Trent, M. S. (2015). Leptospira interrogans lpxD Homologue Is Required for Thermal Acclimatization and Virulence. *Infection and Immunity, 83*(11), 4314–4321. https://doi.org/10.1128/IAI.00897-15.Editor

Eshghi, A., Pappalardo, E., Hester, S., Thomas, B., & Pretre, G. (2015). Pathogenic Leptospira interrogans Exoproteins Are Primarily Involved in Heterotrophic Processes. *Infection and Immunity, 83*(8), 3061–3073. https://doi.org/10.1128/IAI.00427-15

Esseveld, H., & Collier, W. A. (1938). Leptospirosis in Cats in Java. *Zeitschrift fur Immunitatsforschung und Experimentelle Therapie*, *93*, 512–528.

Ettinger, S J; Feldman, Edward C.; Côte, E. (2016). *Textbook of Veterinary Internal Medicine*. *Textbook of Veterinary Internal Medicine: Diseases of The Dog and The Cat*.

Evangelista, K. V., Hahn, B., Wunder, E. A., Ko, A. I., Haake, D. A., & Coburn, J. (2014). Identification of Cell-Binding Adhesins of Leptospira interrogans. *PLoS Neglected Tropical Diseases*, *8*(10). https://doi.org/10.1371/journal.pntd.0003215

Evangelista, K. V, & Coburn, J. (2010). Leptospira as an emerging pathogen: a review of its biology, pathogenesis and host immune responses Karen. *Future Microbiology*, *5*(9), 1413–1425. https://doi.org/10.2217/fmb.10.102.Leptospira

Everard, C. O., Cazabon, E. P., Dreesen, D. W., & Sulzer, C. R. (1979). Leptospirosis in dogs and cats on the Island of Trinidad: West Indies. *International Journal of Zoonoses*, *6*(1), 33–40.

Faine, S. (1982). Guidelines for the control of leptospirosis. *WHO Offset Publication*.

Fanton d'Andon, M., Quellard, N., Fernandez, B., Ratet, G., Lacroix-Lamand??, S., Vandewalle, A., … Werts, C. (2014). Leptospira Interrogans Induces Fibrosis in the Mouse Kidney through Inos-Dependent, TLR- and NLR-Independent Signaling Pathways. *PLoS Neglected Tropical Diseases*, *8*(1), 11. https://doi.org/10.1371/journal.pntd.0002664

Farr, R. W. (1995). Leptospirosis. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America*, *21*(1), 1–8.

Felt, S. A., Wasfy, M. O., El-Tras, W. F., Samir, A., Rahaman, B. A., Boshra, M., … Pimentel, G. (2011). Cross-species surveillance of Leptospira in domestic and peri-domestic animals in Mahalla City, Gharbeya Governorate, Egypt. *American Journal of Tropical Medicine and Hygiene*, *84*(3), 420–425. https://doi.org/10.4269/ajtmh.2011.10-0393

Fenimore, A., Carter, K., & Lunn, K. F. (2012). Detection Of Leptospiruria In Shelter Cats In Colorado. *Journal of Veterinary Internal Medicine*, *26*(3), 783.

Fernandes, L. G., Morais, Z. M. De, Vasconcellos, S. A., & Nascimento, A. L. T. O. (2015). Leptospira interrogans reduces fibrin clot formation by modulating human thrombin activity via exosite. *Pathogens and Disease*, 1–13. https://doi.org/10.1093/femspd/ftv001

Fernandes, L. G., Siqueira, G. H., Teixeira, A. R. F., Silva, L. P., Figueredo, J. M., Cosate, M. R., … Nascimento, A. L. T. O. (2016). Leptospira spp .: Novel insights into host – pathogen interactions. *Veterinary Immunology and Immunopathology*. https://doi.org/10.1016/j.vetimm.2015.12.004

Fessler, J. F., & Morter, R. L. (1964). Experimental feline leptospirosis. *Cornell Veterinarian thesis*, *54*, 176–190.

Fonseca, C. de A., Teixeira, M. M. G., Romero, E. C., Tengan, F. M., Silva, M. V. da, & Shikanai-Yasuda, M. A. (2006). Leptospira DNA detection for the diagnosis of human leptospirosis. *Journal of Infection*, *52*(1), 15–22. https://doi.org/10.1016/j.jinf.2005.02.022

Fouts, D. E., Matthias, M. A., Adhikarla, H., Adler, B., Amorim-Santos, L., Berg, D. E., … Vinetz, J. M. (2016). What Makes a Bacterial Species Pathogenic?:Comparative Genomic Analysis of the Genus Leptospira. *PLoS Neglected Tropical Diseases*, *10*(2), 1–57. https://doi.org/10.1371/journal.pntd.0004403

Fraga, T. R., Barbosa, A. S., & Isaac, L. (2011). Leptospirosis : Aspects of Innate Immunity , Immunopathogenesis and Immune Evasion From the Complement System. *Scandinavian Journal of Immunology*, 408–419. https://doi.org/10.1111/j.1365-3083.2010.02505.x

Gao, X., Mu, Z., Yu, X., Qin, B., Wojdyla, J., Wang, M., & Cui, S. (2018). Structural insight into conformational changes induced by ATP binding in a type III secretion-associated ATPase from Shigella flexneri. *Frontiers in Microbiology*, *9*(JUL), 1–15. https://doi.org/10.3389/fmicb.2018.01468

Garba, B., Bahaman, A. R., Khairani-Bejo, S., Zakaria, Z., & Mutalib, A. R. (2017). Retrospective Study of Leptospirosis in Malaysia. *EcoHealth*, *14*(2), 389–398. https://doi.org/10.1007/s10393-017-1234-0

Gasque, P. P., Christine, M., & Bandjee, J. (2015). Running title : Immunobiology of skin melanocytes. *Journal of Infection*. https://doi.org/10.1016/j.jinf.2015.06.006

Gaywee, J., Xu, W., Radulovic, S., Bessman, M. J., & Azad, A. F. (2002). The Rickettsia prowazekii invasion gene homolog (invA) encodes a Nudix hydrolase active on adenosine (5')-pentaphospho-(5')-adenosine. *Molecular & Cellular Proteomics : MCP*, *1*(3), 179–185. https://doi.org/10.1074/mcp.m100030-mcp200

Geisen, V., Stengel, C., Brem, S., Müller, W., Greene, C., & Hartmann, K. (2007). Canine leptospirosis infections - Clinical signs and outcome with different suspected Leptospira serogroups (42 cases). *Journal of Small Animal Practice*, *48*(6), 324–328. https://doi.org/10.1111/j.1748-5827.2007.00324.x

Ghazaei, C. (2018). Pathogenic <i>Leptospira</i>: Advances in understanding the molecular pathogenesis and virulence. *Open Veterinary Journal*, *8*(1), 13. https://doi.org/10.4314/ovj.v8i1.4

Goldstein, R. E. (2010). Canine leptospirosis. *The Veterinary Clinics of North America. Small Animal Practice*, *40*(6), 1091–1101. https://doi.org/10.1016/j.cvsm.2010.07.008

Gomard, Y., Dietrich, M., Wieseke, N., Ramasindrazana, B., Lagadec, E., Goodman, S. M., … Tortosa, P. (2016). Malagasy bats shelter a considerable genetic diversity of pathogenic Leptospira suggesting notable host-specificity patterns, *Infection and Immunity*, 1–12. https://doi.org/10.1093/femsec/fiw037

Gordon-Smith, C. E., Turner, L. H., Harrisson, J. L. & Brown, J. C. (1961). Animal leptospirosis in Malaya. *WHO Chronicle*, *15*, 343–345.

Goris, M. G. A., & Hartskeerl, R. A. (2014). Leptospirosis serodiagnosis by the microscopic agglutination test. *Current Protocols in Microbiology*, (SUPPL.32), 1–18. https://doi.org/10.1002/9780471729259.mc12e05s32

Greene. (2015). *Infectious Diseases of the Dog and Cat 4th Edition*. https://doi.org/10.1017/CBO9781107415324.004

Greenlee, J. J., Bolin, C. A., Alt, D. P., Cheville, N. F., & Andreasen, C. B. (2004). Clinical and pathologic comparison of acute leptospirosis in dogs caused by two strains of Leptospira kirschneri serovar grippotyphosa. *American Journal of Veterinary Research*, *65*(8), 1100–1107.

Guglielmini, J., Bourhy, P., Schiettekatte, O., Zinini, F., Brisse, S., & Picardeau, M. (2019). Genus-wide Leptospira core genome multilocus sequence typing for strain taxonomy and global surveillance. *PLoS Neglected Tropical Diseases*, *13*(4), 1–23. https://doi.org/10.1371/journal.pntd.0007374

Gulati, S., & Gulati, A. (2012). Pulmonary manifestations of leptospirosis. *Lung India*, *29*(4), 347–353. https://doi.org/10.4103/0970-2113.102822

Gupta, R. S., Mahmood, S., & Adeolu, M. (2013). A phylogenomic and molecular signature based approach for characterization of the phylum Spirochaetes and its major clades: proposal for a taxonomic revision of the phylum. *Frontiers in Microbiology*, *4*, 217. https://doi.org/10.3389/fmicb.2013.00217

Haake, D. A. (2009). Spirochaetal lipoproteins and pathogenesis. *Microbiol Immunol*, *146*(Pt 7), 1491–1504.

Haake, D. A., & Levett, P. N. (2015). Leptospirosis in humans. *Curr Top Microbiol Immunol*, *2015*, 65–97.

Haake, D. A., & Zückert, W. R. (2015). *The Leptospiral Outer Membrane*. *Curr Top Microbiol Immunol* (Vol. 25). https://doi.org/10.1080/00219266.1991.9655201

Haake, L. S. and D. A. (2006). Immunohistochemical Identification and Pathologic Findings in Natural Cases of Equine Abortion Caused by Leptospiral Infection. *Veterainry Pathology*, *6*(9), 2166–2171. https://doi.org/10.1021/nl061786n.Core-Shell

Haas, C. S., Lehne, W., Muck, P., Boehm, A., Rupp, J., Steinhoff, J., & Lehnert, H. (2013). Acute kidney injury and thrombocytopenic fever—consider the infrequent causes. *The American Journal of Emergency Medicine*, *31*(2), 441.e5-441.e9. https://doi.org/10.1016/j.ajem.2012.04.007

Habenicht, L. M., Webb, T. L., Clauss, L. A., Dow, S. W., & Quimby, J. M. (2013). Urinary cytokine levels in apparently healthy cats and cats with chronic kidney disease. *Journal of Feline Medicine and Surgery*, *15*(2), 99–104. https://doi.org/10.1177/1098612X12461007

Hagan, J. E., Costa, F., Calcagno, J., Kane, M., Torgerson, P., Martinez-Silveira, M. S., … Ko, A. (2013). Global morbidity and mortality of leptospirosis: a systematic review. *Scientific meeting of the International Leptospirosis Society. Fukuoka, Japan*.

Haines, D. M., & Clark, E. G. (1991). Enzyme immunohistochemical staining of formalin-fixed tissues for diagnosis in veterinary pathology. *The Canadian Veterinary Journal*, *32*(5), 295–302.

Harkin, K. R., Roshto, Y. M., & Sullivan, J. T. (2003). Clinical application of a polymerase chain reaction assay for diagnosis of leptospirosis in dogs. *Journal of the American Veterinary Medical Association*, *222*(9), 1224–1229.

Harkness, A. C., Smith, B. L., & Fowler, G. F. (1970). An isolation of leptospira serotype pomona from a domestic cat. *New Zealand Veterinary Journal*, *18*(8), 175–176. https://doi.org/10.1080/00480169.1970.33893

Hartmann, K., Egberink, H., Pennisi, M. G., Lloret, A., Addie, D., Belák, S., … Horzinek, M. C. (2013). Leptospira Species Infection in Cats: ABCD guidelines on prevention and management. *Journal of Feline Medicine and Surgery*, *15*(7), 576–581. https://doi.org/10.1177/1098612X13489217

Hartskeerl, R. A., Collares-Pereira, M., & Ellis, W. A. (2011). Emergence, control and re-emerging leptospirosis: Dynamics of infection in the changing world. *Clinical Microbiology and Infection*, *17*(4), 494–501. https://doi.org/10.1111/j.1469-0691.2011.03474.x

Hathaway, S. C., & Blackmore, D. K. (1981). Ecological aspects of the epidemiology of infection with leptospires of the Ballum serogroup in the black rat (Rattus rattus) and the brown rat (Rattus norvegicus) in New Zealand. *Journal of Hygiene*, *87*(3), 427–436. https://doi.org/10.1017/S0022172400069679

Herath, N. J., Kularatne, S. A. M., Weerakoon, K. G. A. D., Wazil, A., Subasinghe, N., & Ratnatunga, N. V. I. (2014). Long term outcome of acute kidney injury due to leptospirosis? A longitudinal study in Sri Lanka. *BMC Research Notes*, *25*, 2–5.

Isogai, E. (1996). Role of Platelet-Activating-Factor Responses after (PAF) on Cellular Leptospire Stimulation with. *Microbiology and Immunology*, *41*(3), 271–275.

J.E. Markovich, L. Ross, and E. M. (2012). The Prevalence of Leptospiral Antibodies in Free Roaming Cats in Worcester County, Massachusetts. *Journal of Veterinary Internal Medicine*, *26*, 688–689. https://doi.org/10.1002/em

Jamshidi, S., Akhavizadegan, M., Bokaie, S., Maazi, N., & Ghorban Ali, A. (2009). Serologic study of feline leptospirosis in Tehran , Iran. *Iranian Journal of Microbiology*, *1*(2), 32–36.

Johnson, R. C., & Rogers, P. (1964). Differentiation of Pathogenic And Saprophytic. *Journal of Bacteriology*, *88*(6), 1618–1623.

Jorge, S., Kremer, F. S., Oliveira, N. R. De, Oliveira, G. De, Valerio, S., Guimarães, A. M., … Dellagostin, O. A. (2018). Whole-genome sequencing of Leptospira interrogans from southern Brazil : genetic features of a highly virulent strain. *Memorias do Instituto Oswaldo Cruz*, *113*, 80–86. https://doi.org/10.1590/0074-02760170130

Khor, K. H., Tan, W. X., Lau, S. F., Mohd, A. R., Rozanaliza, R., Siti, K. B., & Abdul, R. B. (2016). Seroprevalence and molecular detection of leptospirosis from a dog shelter. *Tropical Biomedicine*, *33*(2), 276–284.

Kiernan, J. A. (2002). Silver staining for spirochetes in tissues: Rationale, difficulties, and troubleshooting. *Laboratory Medicine*, *33*(9), 705–708. https://doi.org/10.1093/labmed/33.9.705

King, A. M., Pretre, G., Bartpho, T., Sermswan, R. W., Toma, C., Suzuki, T., … Murray, L. (2014). High-Temperature Protein G Is an Essential Virulence Factor of Leptospira interrogans. *Infection and Immunity*, *82*(3), 1123–1131. https://doi.org/10.1128/IAI.01546-13

Klaasen, H. L. B. M., Molkenboer, M. J. C. H., Vrijenhoek, M. P., & Kaashoek, M. J. (2003). Duration of immunity in dogs vaccinated against leptospirosis with a bivalent inactivated vaccine. *Veterinary Microbiology*, *95*(1), 121–132. https://doi.org/https://doi.org/10.1016/S0378-1135(03)00152-4

Knight, L. L., Miller, N. G., & White, R. J. (1973). Cytotoxic factor in the blood and plasma of animals during leptospirosis. *Infection and Immunity*, *8*(3), 401–405.

Ko, A. I., Goarant, C., & Picardeau, M. (2009). Leptospira: the dawn of the molecular genetics era for an emerging zoonotic pathogen. *Nature Reviews. Microbiology*, *7*(10), 736.

Kohn, B., Steinicke, K., Arndt, G., Gruber, A. D., Guerra, B., Jansen, A., … Nockler, K. (2010). Pulmonary abnormalities in dogs with leptospirosis. *Journal of Veterinary Internal Medicine*, *24*(6), 1277–1282. https://doi.org/10.1111/j.1939-1676.2010.0585.x

Krajewska, J., Arent, Z., Zolkiewski, M., & Kędzierska-Mieszkowska, S. (2018). Isolation and identification of putative protein substrates of the AAA+ molecular chaperone ClpB from the pathogenic spirochaete Leptospira interrogans. *International Journal of Molecular Sciences*, *19*(4), 1–13. https://doi.org/10.3390/ijms19041234

Krulwich, T. A., Sachs, G., & Padan, E. (2011). Molecular aspects of bacterial pH sensing and homeostasis Terryess. *Nat Rev Microbiol*, *3*(3), 1–19. https://doi.org/10.1111/j.1751-9004.2009.00170.x.Experience

Kumar, K. V., Lall, C., Raj, R. V., Vedhagiri, K., & Vijayachari, P. (2015). Molecular detection of pathogenic leptospiral protein encoding gene (lipL32) in environmental aquatic biofilms. *Letters in Applied Microbiology*, 311–315. https://doi.org/10.1111/lam.12533

Kurilung, A., Chanchaithong, P., Lugsomya, K., Niyomtham, W., Wuthiekanun, V., & Prapasarakul, N. (2017). Molecular detection and isolation of pathogenic Leptospira from asymptomatic humans, domestic animals and water sources in Nan province, a rural area of Thailand. *Research in Veterinary Science*, *115*(February), 146–154. https://doi.org/10.1016/j.rvsc.2017.03.017

Lambert, A., Takahashi, N., Charon, N. W., & Picardeau, M. (2012). Chemotactic behavior of pathogenic and nonpathogenic Leptospira species. *Applied and Environmental Microbiology*, *78*(23), 8467–8469. https://doi.org/10.1128/AEM.02288-12

Lapointe, C., Plamondon, I., & Dunn, M. (2013). Feline leptospirosis serosurvey from a Quebec referral hospital. *Canadian Veterinary Journal*, *54*(5), 497–499.

Laras, K., Van, C. B., Bounlu, K., Tien, N. T. K., Olson, J. G., Thongchanh, S., … Corwin, A. L. (2002). The importance of leptospirosis in Southeast Asia. *American Journal of Tropical Medicine and Hygiene*, *67*(3), 278–286. https://doi.org/10.4269/ajtmh.2002.67.278

Larsson, C E, Santa Rosa, C. A., Hagiwara, M. K., Paim, G. V, & Guerra, J. L. (1984). Prevalence of feline leptospirosis: serologic survey and attempts of isolation and demonstration of the agent. *International Journal of Zoonoses*, *11*(2), 161–169.

Larsson, C E, Santa Rosa, C. A., Hagiwara, M. K., Paim, G. V, & Guerra, J. L. (1985). Laboratory and clinical features of experimental feline leptospirosis. *International Journal of Zoonoses*, *12*(2), 111–119. https://doi.org/10.1017/CBO9781107415324.004

Lau, S. F., Wong, J. Y., Khor, K. H., Roslan, M. A., Abdul Rahman, M. S., Bejo, S. K., … Bahaman, A. R. (2017). *Seroprevalence of Leptospirosis in Working Dogs*. *Topics in Companion Animal Medicine* (Vol. 32). https://doi.org/10.1053/j.tcam.2017.12.001

Lee, S. H., Kim, S., Park, S. C., Kim, M. J., Kim, K. A., Kim, Y. K., … Mmun, I. N. I. (2002). Cytotoxic Activities of Leptospira interrogans Hemolysin SphH as a Pore-Forming Protein on Mammalian Cells. *Infection and Immunity*, *70*(1), 315–322. https://doi.org/10.1128/IAI.70.1.315

Lee, Z. M.-P., Bussema 3rd, C., & Schmidt, T. M. (2009). rrnDB: documenting the number of rRNA and tRNA genes in bacteria and archaea. *Nucleic Acids Research*, *37*(Database issue), D489–D493. https://doi.org/10.1093/nar/gkn689

Lessa-Aquino, C., Borges Rodrigues, C., Pablo, J., Sasaki, R., Jasinskas, A., Liang, L., … Felgner, P. L. (2013). Identification of seroreactive proteins of Leptospira interrogans serovar copenhageni using a high-density protein microarray approach. *PLoS Neglected Tropical Diseases*, *7*(10), e2499. https://doi.org/10.1371/journal.pntd.0002499

Levett, P N. (2001a). Leptospirosis. *Clinical Microbiology*, *14*(2), 296–326. https://doi.org/10.1128/CMR.14.2.296-326.2001

Levett, P N. (2001b). Leptospirosis. *Clinical Microbiology*, *14*(2), 296–326. https://doi.org/10.1128/CMR.14.2.296

Levett, Paul N. (2004). Leptospirosis: A forgotten zoonosis? *Clinical and Applied Immunology Reviews*, *4*(6), 435–448. https://doi.org/10.1016/j.cair.2004.08.001

Levett, Paul N., Morey, R. E., Galloway, R. L., & Steigerwalt, A. G. (2006). Leptospira broomii sp. nov., isolated from humans with leptospirosis. *International Journal of Systematic and Evolutionary Microbiology*, *56*(3), 671–673. https://doi.org/10.1099/ijs.0.63783-0

Liao, S., Sun, A., Ojcius, D. M., Wu, S., Zhao, J., & Yan, J. (2009). Inactivation of the fliY gene encoding a flagellar motor switch protein attenuates mobility and virulence of Leptospira interrogansstrain Lai. *BMC Microbiology*, *9*(1), 253. https://doi.org/10.1186/1471-2180-9-253

Lilenbaum, W., Varges, R., Brandão, F. Z., Cortez, A., de Souza, S. O., Brandão, P. E., … Vasconcellos, S. A. (2008). Detection of Leptospira spp. in semen and vaginal fluids of goats and sheep by polymerase chain reaction. *Theriogenology*, *69*(7), 837–842. https://doi.org/https://doi.org/10.1016/j.theriogenology.2007.10.027

Lim, V. K. E. (2011). Leptospirosis: a re-emerging infection. *The Malaysian Journal of Pathology*, *33*(1), 1–5.

Lin, X., Zhao, J., Qian, J., Mao, Y., Pan, J., Li, L., … Yan, J. (2010). Identification of Immunodominant B- and T-Cell Combined Epitopes in Outer Membrane Lipoproteins LipL32 and LipL21 of Leptospira interrogans. *Clinical and Vaccine Immunology*, *17*(5), 778–783. https://doi.org/10.1128/CVI.00405-09

Llanes, A., Restrepo, C. M., & Rajeev, S. (2016). Whole genome sequencing allows better understanding of the evolutionary history of leptospira interrogans serovar hardjo. *PLoS ONE*, *11*(7), 1–12. https://doi.org/10.1371/journal.pone.0159387

Lo, M., Cordwell, S. J., Bulach, D. M., & Adler, B. (2009). Comparative Transcriptional and Translational Analysis of Leptospiral Outer Membrane Protein Expression in Response to Temperature. *PLOS Neglected Tropical Diseases*, *3*(12). https://doi.org/10.1371/journal.pntd.0000560

Louvel, H., Saint Girons, I., & Picardeau, M. (2005). Isolation and characterization of FecA- and FeoB-mediated iron acquisition systems of the spirochete Leptospira biflexa by random insertional mutagenesis. *Journal of Bacteriology*, *187*(9), 3249–3254. https://doi.org/10.1128/JB.187.9.3249-3254.2005

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., V., A., … B., H. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*, *380*(9859), 2095–2128. https://doi.org/10.1016/S0140-6736(12)61728-0

Luciani, O. (2004). Receptivité et sensibilité du chat aux leptospires [thesis]. *Nantes, France: École Nationale Vétérinaire de Nantes*.

Marotto, P. C., Nascimento, C. M., Eluf-Neto, J., Marotto, M. S., Andrade, L., Sztajnbok, J., & Seguro, A. C. (1999). Acute lung injury in leptospirosis: clinical and laboratory features, outcome, and factors associated with mortality. *Clinical Infectious Diseases : The Infectious Diseases Society of America*, *29*(6), 1561–1563. https://doi.org/10.1086/313501

Matthay, M. A., Folkesson, H. G., & Clerici, C. (2002). Lung epithelial fluid transport and the resolution of pulmonary edema. *Physiological Reviews*, *82*(3), 569–600. https://doi.org/10.1152/physrev.00003.2002

McBride, A. J. A., Athanazio, D. A., Reis, M. G., & Ko, A. I. (2005). Leptospirosis. *Current Opinion in Infectious Diseases*, *18*(5), 376–386.

McKeever, S., Gorman, G. W., Chapman, J. F., Galton, M. M., & Powers, D. K. (1958). Incidence of leptospirosis in wild mammals from Southwestern Georgia, with a report of new hosts for six serotypes of leptospires. *The American Journal of Tropical Medicine and Hygiene*, *7*(6), 646–655.

Merien, F., Truccolo, J., Baranton, G., & Perolat, P. (2000). Identi ¢ cation of a 36-kDa ¢ bronectin-binding protein expressed by a virulent variant of Leptospira interrogans serovar icterohaemorrhagiae. *FEMS Microbiology Letters*, *185*, 17–22.

Michna, S. W., & Campbell, R. S. F. (1970). Leptospirosis in wild animals. *Journal of Comparative Pathology*, *80*(1), 101–106.

Millán, J., Candela, M. G., López-Bao, J. V., Pereira, M., Jiménez, M. Á., & León-Vizcaíno, L. (2009). Leptospirosis in Wild and Domestic Carnivores in Natural Areas in Andalusia, Spain. *Vector-Borne and Zoonotic Diseases*, *9*(5), 549–554. https://doi.org/10.1089/vbz.2008.0081

Mineiro, A. L. B. B., Vieira, R. J., Costa, É. A., Santos, R. L., Gonçalves, L. M. F., Carvalho, S. M., … Costa, F. A. L. (2011). Serology, polymerase chain reaction and histopathology for leptospirosis in samples collected at slaughter from dairy cows of Parnaiba region, state of Piauí, Brazil. *Pesquisa Veterinaria Brasileira*, *31*(10), 859–866. https://doi.org/10.1590/S0100-736X2011001000005

Miotto, B. A., Gil, A., Guilloux, A., Tozzi, B. F., Moreno, Z., Santana, A., … Moreno, A. M. (2018). Prospective study of canine leptospirosis in shelter and stray dog populations : Identification of chronic carriers and different Leptospira species infecting dogs, 1–23.

Miyama, T., Watanabe, E., Ogata, Y., Urushiyama, Y., Kawahara, N., & Makita, K. (2018). Herd-level risk factors associated with Leptospira Hardjo infection in dairy herds in the southern Tohoku, Japan. *Preventive Veterinary Medicine*, *149*(August 2017), 15–20. https://doi.org/10.1016/j.prevetmed.2017.11.008

Monahan, A. M., Callanan, J. J., & Nally, J. E. (2009). Review paper: Host-pathogen interactions in the kidney during chronic leptospirosis. *Veterinary Pathology*, *46*(5), 792–799. https://doi.org/10.1354/vp.08-VP-0265-N-REV

Morey, R. E., Galloway, R. L., Bragg, S. L., Steigerwalt, A. G., Mayer, L. W., & Levett, P. N. (2006). Species-Specific Identification of Leptospiraceae by 16S rRNA Gene Sequencing. *Journal of Clinical Microbiology*, *44*(10), 3510–3516. https://doi.org/10.1128/JCM.00670-06

Mosallanejad, B., Ghorbanpoor najaf abadi, M., Avizeh, R., Abdollahpoor, G., & Abadi, K. (2011). A serological survey of Leptospiral infection of cats in Ahvaz, south-western of Iran. *Iranian Journal of Veterinary Medicine*, *5*(1), 49–52. https://doi.org/10.22059/ijvm.2011.22671

Murooka, Y., Higashiura, T., & Harada, T. (1978). Genetic mapping of tyramine oxidase and arylsulfatase genes and their regulation in intergeneric hybrids of enteric bacteria. *Journal of Bacteriology*, *136*(2), 714–722.

Murphy, L. C., Cardeilhac, P. T., & Carr, J. W. (1958). The prevalence of leptospiral agglutinins in sera of the domestic cat. *The Cornell Veterinarian*, *48*(1), 3—10.

Murray, G. L., Morel, V., Cerqueira, G. M., Croda, J., Srikram, A., Henry, R., … Picardeau, M. (2009). Genome-Wide Transposon Mutagenesis in Pathogenic Leptospira Species. *Infection and Immunity*, *77*(2), 810–816. https://doi.org/10.1128/IAI.01293-08

Murray, G. L., Srikram, A., Henry, R., Hartskeerl, R. A., Sermswan, R. W., & Adler, B. (2010). Mutations affecting Leptospira interrogans lipopolysaccharide attenuate virulence. *Molecular Microbiology*, *78*(3), 701–709. https://doi.org/10.1111/j.1365-2958.2010.07360.x

Musso, D., & La Scola, B. (2013). Laboratory diagnosis of leptospirosis: A challenge. *Journal of Microbiology, Immunology and Infection*, *46*(4), 245–252. https://doi.org/10.1016/j.jmii.2013.03.001

Mylonakis, M. E., Bourtzi-Hatzopoulou, E., Koutinas, A. F., Petridou, E., Saridomichelakis, M. N., Leontides, L., & Siochu, A. (2005). Leptospiral seroepidemiology in a feline hospital population in Greece. *Veterinary Record*, *156*(19), 615–616. https://doi.org/10.1136/vr.156.19.615

Mythri, B. A. (2015). Laboratory diagnosis of leptospirosis: a review. *Journal of Evolution of Medical and Dental Sciences*, *4*(50), 8759–8769. https://doi.org/10.14260/jemds/2015/1269

Nalam, K., Ahmed, A., Devi, S. M., Francalacci, P., Baig, M., Sechi, L. A., … Ahmed, N. (2010). Genetic Affinities within a Large Global Collection of Pathogenic Leptospira : Implications for Strain Identification and Molecular Epidemiology. *PLOS One*, *5*(8). https://doi.org/10.1371/journal.pone.0012637

Nally, J. E., Chantranuwat, C., Wu, X.-Y., Fishbein, M. C., Pereira, M. M., Da Silva, J. J. P., … Lovett, M. A. (2004). Alveolar septal deposition of immunoglobulin and complement parallels pulmonary hemorrhage in a guinea pig model of severe pulmonary leptospirosis. *The American Journal of Pathology*, *164*(3), 1115–1127. https://doi.org/10.1016/S0002-9440(10)63198-7

Natarajaseenivasan, K., Boopalan, M., Selvanayaki, K., Suresh, S. R., & Ratnam, S. (2002). Leptospirosis among rice mill workers of Salem, South India. *Japanese Journal of Infectious Diseases*, *55*(5), 170–173.

Nitipan, S., Sritrakul, T., Kunjantarachot, A., & Prapong, S. (2013). Infection , Genetics and Evolution Identification of epitopes in Leptospira borgpetersenii leucine-rich repeat proteins. *Infection, Genetics and Evolution*, *14*, 46–57. https://doi.org/10.1016/j.meegid.2012.10.014

Oliveira Filho, J. X., de Paula, D. A. J., Morés, N., Pescador, C. A., Ciacci-Zanella, J. R., Coldebella, A., … Nakazato, L. (2012). Interstitial nephritis of slaughtered pigs in the State of Mato Grosso, Brazil. *Pesquisa Veterinaria Brasileira*, *32*(4), 313–318. https://doi.org/10.1590/S0100-736X2012000400007

Ooteman, M. C., Vago, A. R., & Koury, M. C. (2006). Evaluation of MAT, IgM ELISA and PCR methods for the diagnosis of human leptospirosis. *Journal of Microbiological Methods*, *65*(2), 247–257. https://doi.org/10.1016/j.mimet.2005.07.015

Organization, W. H. (2010). Human leptospirosis: guidance for diagnosis, surveillance and control. 2003. *World Health Organization: Geneva, Switzerland*.

Ortega-Pacheco, A., Colin-Flores, R. F., Gutierrez-Blanco, E., & Jimenez-Coello, M. (2008). Frequency and type of renal lesions in dogs naturally infected with leptospira species. *Annals of the New York Academy of Sciences*, *1149*, 270–274. https://doi.org/10.1196/annals.1428.088

Pal, M., & Hadush, A. (2017). Leptospirosis: An Infectious Emerging Waterborne Zoonosis of Global Significance. *Air & Water Borne Diseases*, *06*(01), 1–4. https://doi.org/10.4172/2167-7719.1000133

Palaniappan, R. U. M., Ramanujam, S., & Chang, Y. F. (2007). Leptospirosis: Pathogenesis, immunity, and diagnosis. *Current Opinion in Infectious Diseases*, *20*(3), 284–292. https://doi.org/10.1097/QCO.0b013e32814a5729

Parreira, I. M., Jayme, V. de S., Buzin, E. J. W. K., Tomaz, L. A. G., & Delfino, A. A. D. (2010). Epidemiological features of infection through Leptospira spp in domestic cats (Felis catus) apparently healthy within the metropolitan area of Goiania, Brazil. *Enciclopédia Biosfera*, *6*, 1–5.

Peng, T., Ma, L., Feng, X., Tao, J., Nan, M., Liu, Y., … Zeng, W. (2017). Genomic and transcriptomic analyses reveal adaptation mechanisms of an Acidithiobacillus ferrivorans strain YL15 to alpine acid mine drainage. *PLoS ONE*, *12*(5), 1–17. https://doi.org/10.1371/journal.pone.0178008

Penna, D., DE Brito, T., Pupo, A. A., Machado, M. M., Ayroza, P. A., & DE Almeida, S. S. (1963). Kidney biopsy in human leptospirosis. *The American Journal of Tropical Medicine and Hygiene*, *12*, 896–901.

Petkanchanapong, W., Yasaeng, S., Chantapetch, P., & Bhudhilukul, N. (2011). The Cut-Off Values for Single Serum of Leptospirosis Detection. *PLOS Neglected Tropical Diseases*, *11(*2), e0005228.

Petrošová, H., & Mathieu, P. (2014). Screening of a Leptospira biflexa Mutant Library To Identify Genes Involved in Ethidium Bromide Tolerance. *Applied and Environmental Microbiology*, *80*(19), 6091–6103. https://doi.org/10.1128/AEM.01619-14

Picardeau, M. (2013). Diagnosis and epidemiology of leptospirosis. *Medecine et Maladies Infectieuses*, *43*(1), 1–9. https://doi.org/10.1016/j.medmal.2012.11.005

Picardeau, Mathieu, Bertherat, E., Jancloes, M., Skouloudis, A. N., Durski, K., & Hartskeerl, R. A. (2014). Rapid tests for diagnosis of leptospirosis: Current tools and emerging technologies. *Diagnostic Microbiology and Infectious Disease*, *78*(1), 1–8. https://doi.org/10.1016/j.diagmicrobio.2013.09.012

Picardeau, Mathieu, Bulach, D. M., Bouchier, C., Zuerner, R. L., Zidane, N., Wilson, P. J., … Adler, B. (2008). Genome Sequence of the Saprophyte Leptospira biflexa Provides Insights into the Evolution of Leptospira and the Pathogenesis of Leptospirosis. *PLoS ONE*, *3*(2), 1–9. https://doi.org/10.1371/journal.pone.0001607

Plank, R., & Dean, D. (2000). Overview of the epidemiology, microbiology, and pathogenesis of Leptospira spp. in humans. *Microbes and Infection*, *2*(10), 1265–1276. https://doi.org/https://doi.org/10.1016/S1286-4579(00)01280-6

Porcella, S. F., & Schwan, T. G. (2001). Borrelia burgdorferi and Treponema pallidum: a comparison of functional genomics, environmental adaptations, and pathogenic mechanisms. *The Journal of Clinical Investigation*, *107*(6), 651–656. https://doi.org/10.1172/JCI12484

Pratt, N., Conan, A., & Rajeev, S. (2017). Leptospira Seroprevalence in Domestic Dogs and Cats on the Caribbean Island of Saint Kitts. *Veterinary Medicine International*, *2017*. https://doi.org/10.1155/2017/5904757

Rafizah, A. A. N., Aziah, B. D., Azwany, Y. N., Imran, M. K., Rusli, A. M., Nazri, S. M., … Zaliha, I. (2013). A hospital-based study on seroprevalence of leptospirosis among febrile cases in northeastern Malaysia. *International Journal of Infectious Diseases*, *17*(6), e394–e397. https://doi.org/10.1016/j.ijid.2012.12.012

Rees, H. G. (1964). Leptospirosis in a cat. *New Zealand Veterinary Journal*, *12*(3), 64. https://doi.org/10.1080/00480169.1964.33553

Reilly, J. R., Hanson, L. E., & Ferris, D. H. (1970). Experimentally induced predator chain transmission of Leptospira grippotyphosa from rodents to wild marsupialia and carnivora. *American Journal of Veterinary Research*, *31*(8), 1443–1448.

Ren, S.-X., Fu, G., Jiang, X.-G., Zeng, R., Miao, Y.-G., Xu, H., … Zhao, G.-P. (2003). Unique physiological and pathogenic features of Leptospira interrogans revealed by whole-genome sequencing. *Nature*, *422*, 888.

Ren, S. X., Fu, G., Jiang, X. G., Zeng, R., Miao, Y. G., Xu, H., … Zhao, G. P. (2003). Unique physiological and pathogenic features of Leptospira interrogans revealed by whole-genome sequencing. *Nature*, *422*(6934), 888–893. https://doi.org/10.1038/nature01597

Reynolds, B. S., & Lefebvre, H. P. (2013). Feline CKD: Pathophysiology and risk factors - what do we know? *Journal of Feline Medicine and Surgery*, *15*(1), 3–14. https://doi.org/10.1177/1098612X13495234

Ricciotti, E., & FitzGerald, G. A. (2011). Prostaglandins and inflammation. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *31*(5), 986–1000. https://doi.org/10.1161/ATVBAHA.110.207449

Rissi, D. R., & Brown, C. A. (2014). Diagnostic features in 10 naturally occurring cases of acute fatal canine leptospirosis. *Journal of Veterinary Diagnostic Investigation*, *26*(6), 799–804. https://doi.org/10.1177/1040638714553293

Ristow, P., Bourhy, P., McBride, F. via W. da C., Figueira, C. P., Huerre, M., Ristow, P., … Picardeau, M. (2007). The OmpA-Like Protein Loa22 Is Essential for Leptospiral Virulence. *PLoS Pathogens*, *3*(7). https://doi.org/10.1371/journal.ppat.0030097

Ristow, P., Bourhy, P., McBride, F. W. D. C., Figueira, C. P., Huerre, M., Ave, P., … Picardeau, M. (2007). The OmpA-like protein Loa22 is essential for leptospiral virulence. *PLoS Pathogens*, *3*(7), 0894–0903. https://doi.org/10.1371/journal.ppat.0030097

Rodriguez, J., Blais, M. C., Lapointe, C., Arsenault, J., Carioto, L., & Harel, J. (2014). Serologic and urinary PCR survey of leptospirosis in healthy cats and in cats with kidney disease. *Journal of Veterinary Internal Medicine*, *28*(2), 284–293.

Rohrbach, B. W., Ward, D. A., Hendrix, D. V. H., Cawrse-Foss, M., & Moyers, T. D. (2005). Effect of vaccination against leptospirosis on the frequency, days to recurrence and progression of disease in horses with equine recurrent uveitis. *Veterinary Ophthalmology*, *8*(3), 171–179. https://doi.org/10.1111/j.1463-5224.2005.00367.x

Rojas, P., Monahan, A. M., Schuller, S., & Miller, I. S. (2010). Detection and quantification of leptospires in urine of dogs : a maintenance host for the zoonotic disease leptospirosis. *European Journal Of Clinical Microbiology & Infectious Diseases*, 1305–1309. https://doi.org/10.1007/s10096-010-0991-2

Romero, E. C., Billerbeck, A. E., Lando, V. S., Camargo, E. D., Souza, C. C., & Yasuda, P. H. (1998). Detection of Leptospira DNA in patients with aseptic meningitis by PCR. *Journal of Clinical Microbiology*, *36*(5), 1453–1455.

Saier Jr, M. H., & García-Lara, J. (2001). The spirochetes: molecular and cellular biology. *Horizon Scientific Press.*

Mason, R. W., King, S. J., Sc, B. V, & Mclachlan, N. M. (1972). Suspected leptospirosis in two cats, *Australian Veterinary Journal*. 48(11), 622-623.

Scanziani, E., Luini, M., Fabbi, M., & Pizzocaro, P. (1991). Comparison between specific immunoperoxidase staining and bacteriological culture in the diagnosis of renal leptospirosis of pigs. *Research in Veterinary Science*, *50*(2), 229–232.

Schrader, C., Schielke, A., Ellerbroek, L., & Johne, R. (2012). PCR inhibitors - occurrence, properties and removal. *Journal of Applied Microbiology*, *113*(5), 1014–1026. https://doi.org/10.1111/j.1365-2672.2012.05384.x

Schuller, S., Francey, T., Hartmann, K., Hugonnard, M., Kohn, B., Nally, J. E., & Sykes, J. (2015). European consensus statement on leptospirosis in dogs and cats. *Journal of Small Animal Practice*, *56*(3), 159–179. https://doi.org/10.1111/jsap.12328

Schuller, Simone, Sergeant, K., Renaut, J., Callanan, J. J., Scaife, C., & Nally, J. E. (2015). Comparative proteomic analysis of lung tissue from guinea pigs with leptospiral pulmonary haemorrhage syndrome (LPHS) reveals a decrease in abundance of host proteins involved in cytoskeletal and cellular organization. *Journal of Proteomics*. https://doi.org/10.1016/j.jprot.2015.03.021

Sebek, Z., Wallner, H., Sixl, W., Kaaserer, G., & Valova, M. (1976). Leptospiral antibodies in domestic animals in Tyrol. *Folia Parasitologica*, *23*(1), 15–23.

Seguro, A. C., & Andrade, L. (2013). Pathophysiology of leptospirosis. *Shock*, *39*(1), 17–23. https://doi.org/10.1097/SHK.0b013e31828fae49

Sehgal, S. C. (2006). Epidemiological patterns of leptospirosis. *Indian Journal of Medical Microbiology*, *24*(4), 310–311.

Sessions, J. K., & Greene, C. E. (2004). Canine leptospirosis: Epidemiology, pathogenesis, and diagnosis. *Compendium on Continuing Education for the Practicing Veterinarian*, *26*(August), 606–623.

Sethi, S., Sharma, N., Kakkar, N., Taneja, J., Chatterjee, S. S., Banga, S. S., & Sharma, M. (2010). Increasing trends of leptospirosis in Northern India: A clinico-epidemiological study. *PLoS Neglected Tropical Diseases*, *4*(1), 1–7. https://doi.org/10.1371/journal.pntd.0000579

Shafei, M. N., Sulong, M. R., Yaacob, N. A., Hassan, H., Wan Mohamad, W. M. Z., Daud, A., … Abdullah, M. R. (2012). Seroprevalence of Leptospirosis among Town Service Workers in Northeastern State of Malaysia. *International Journal of Collaborative Research on Internal Medicine & Public Health*, *4*(4), 395–403.

Sharma, M. and Yodav, A. R. (2008). Leptospirosis : Epidemiology , Diagnosis , and Control. *J Ournal of Infectious Disease and Antimicrobial Agents*, *25*(2), 93–103.

Shimizu, T., Matsusaka, E., Takayanagi, K., Masuzawa, T., Iwamoto, Y., Morita, T., … Yanagihara, Y. (1987). Biological activities of lipopolysaccharide-like substance (LLS) extracted from Leptospira interrogans serovar canicola strain Moulton. *Microbiology and Immunology*, *31*(8), 727–735.

Shophet, R. (1979a). A serological survey of leptospirosis in cats. *New Zealand Veterinary Journal*, *27*(11), 236–246. https://doi.org/10.1080/00480169.1979.34662

Shophet, R. (1979b). Feline leptospiral infection: with particular emphasis on Leptospira interrogans servor ballum: a thesis presented in partial fulfilment of the requirements for the degree of Master of Philosophy in Veterinary Pathology and Public Health. *Massey*. Massey University.

Shropshire, S. B., Veir, J. K., Morris, A. K., & Lappin, M. R. (2016). Evaluation of the Leptospira species microscopic agglutination test in experimentally vaccinated cats and Leptospira species seropositivity in aged azotemic client-owned cats. *Journal of Feline Medicine and Surgery*, *18*(10), 768–772. https://doi.org/10.1177/1098612X15593902.

Siqueira, G. H., Atzingen, M. V, Alves, I. J., Morais, Z. M. De, Vasconcellos, S. A., & Nascimento, A. L. T. O. (2013). Characterization of Three Novel Adhesins of Leptospira interrogans. *The American Journal of Tropical Medicine and Hygiene*, *89*(6), 1103–1116. https://doi.org/10.4269/ajtmh.13-0205

Skilbeck, N. ., & Miller, G. . (1986). A serological survey of leptospirosis in Gippslande dairy farmers. *Medical Journal Australia*, *144*(11), 565–567.

Slamti, L., Pedro, M. A. De, Guichet, E., & Picardeau, M. (2011). Deciphering Morphological Determinants. *Journal of Bacteriology*, *193*(22), 6266–6275. https://doi.org/10.1128/JB.05695-11.

Smythe, L., Adler, B., Levett, P. N., Turenne, C. Y., Hartskeerl, R. A., Smythe, L., & Galloway, R. L. (2012). Classification of Leptospira genomospecies 1, 3, 4 and 5 as Leptospira alstonii sp. nov., Leptospira vanthielii sp. nov., Leptospira terpstrae sp. nov. and Leptospira yanagawae sp. nov., respectively. *International Journal of Systematic and Evolutionary Microbiology*, *63*(Pt 5), 1859–1862. https://doi.org/10.1099/ijs.0.047324-0.

Socolovschi, C., Angelakis, E., Renvoisé, A., Fournier, P. E., Marié, J. Lou, Davoust, B., … Raoult, D. (2011). Strikes, flooding, rats, and leptospirosis in Marseille, France. *International Journal of Infectious Diseases*, *15*(10), 710–715. https://doi.org/10.1016/j.ijid.2011.05.017.

Sonja, O., Sonja, R., Nataša, S., Danica, B., Slobodanka, V., & Miroslav, V. (2014). Seroprevalence of cat leptospirosis in Belgrade (Serbia). *Acta Veterinaria*, *64*(4), 510–518. https://doi.org/10.2478/acve-2014-0047.

Spichler, A., Athanazio, D., Buzzar, M., Castro, B., Chapolla, E., Seguro, A., & Vinetz, J. M. (2007). Using death certificate reports to find severe leptospirosis cases, Brazil. *Emerging Infectious Diseases*, *13*(10), 1559–1561. https://doi.org/10.3201/eid1310.070150.

Sprissler, F., Jongwattanapisan, P., Luengyosluechakul, S., Pusoonthornthum, R., Prapasarakul, N., Kurilung, A., … Hartmann, K. (2019). Leptospira infection and shedding in cats in Thailand. *Transboundary and Emerging Diseases*, *66*(2), 948–956. https://doi.org/10.1111/tbed.13110.

Subharat, S, Wilson, P. R., Heuer, C., & Collins-Emerson, J. M. (2012). Growth response and shedding of Leptospira spp. in urine following vaccination for leptospirosis in young farmed deer. *New Zealand Veterinary Journal*, *60*(1), 14–20. https://doi.org/10.1080/00480169.2011.624985.

Subharat, Supatsak. (2010). Epidemiology, diagnosis and vaccination control of leptospirosis in farmed deer in New Zealand. *Institute of Veterinary Animal and Biomedical Sciences* (PhD Thesis).

Sykes, J. E., Hartmann, K., Lunn, K. F., Moore, G. E., Stoddard, R. A., & Goldstein, R. E. (2011). 2010 ACVIM Small Animal Consensus Statement on Leptospirosis: Diagnosis, Epidemiology, Treatment, and Prevention. *Journal of Veterinary Internal Medicine*, *25*(1), 1–13. https://doi.org/10.1111/j.1939-1676.2010.0654.x.

Talebkhan Garoussi, M., Mehravaran, M., Abdollahpour, G., & Khoshnegah, J. (2015). Seroprevalence of leptospiral infection in feline population in urban and dairy cattle herds in Mashhad, Iran. *Veterinary Research Forum : An International Quarterly Journal*, *6*(4), 301–304. https://doi.org/26973765.

Tanaka, K., Tanabe, K., Nishii, N., Takiue, K., Sugiyama, H., & Wada, J. (2017). Sustained Tubulointerstitial Inflammation in Kidney with Severe Leptospirosis. *Internal Medicine*, *56*(10), 1179–1184. https://doi.org/10.2169/internalmedicine.56.8084.

Thaipadunpanit, J., Chierakul, W., Wuthiekanun, V., Limmathurotsakul, D., Amornchai, P., Boonslip, S., … Peacock, S. J. (2011). Diagnostic accuracy of real-time PCR assays targeting 16S rRNA and lipl32 genes for human leptospirosis in Thailand: A case-control study. *PLoS ONE*, *6*(1), 1–6. https://doi.org/10.1371/journal.pone.0016236

Tochetto, C., Flores, M. M., Kommers, G. D., Barros, C. S. L., & Fighera*, e R. A. (2012). Aspectos anatomopatológicos da leptospirose em cães : *Pesquisa Veterinaria Brasileira*, *32*(5), 430–443.

Torres-Castro, M., Guillermo-Cordero, L., Hernández-Betancourt, S., Gutiérrez-Ruíz, E., Agudelo-Flórez, P., Peláez-Sánchez, R., … Puerto, F. I. (2016). First histopathological study in kidneys of rodents naturally infected with Leptospira pathogenic species from Yucatan, Mexico. *Asian Pacific Journal of Tropical Medicine*, *9*(2), 145–147. https://doi.org/https://doi.org/10.1016/j.apjtm.2016.01.018

Tulsiani, S. M., Lau, C. L., Graham, G. C., Van Den Hurk, A. F., Jansen, C. C., Smythe, L. D., … Craig, S. B. (2010). Emerging tropical diseases in Australia. Part 1. Leptospirosis. *Annals of Tropical Medicine & Parasitology*, *104*(7), 543–556. https://doi.org/10.1179/136485910X12851868779867

Turner, M. D., Nedjai, B., Hurst, T., & Pennington, D. J. (2014, November). Cytokines and chemokines: At the crossroads of cell signalling and inflammatory disease. *Biochimica et Biophysica Acta*. Netherlands. https://doi.org/10.1016/j.bbamcr.2014.05.014

Victoriano, B., Smythe, L. D., Gloriani-barzaga, N., Cavinta, L. L., Kasai, T., Limpakarnjanarat, K., … Adler, B. (2009). Leptospirosis in the Asia Pacific region. *BMC Infectious Diseases*, *9*, 1–9. https://doi.org/10.1186/1471-2334-9-147

Vieira, L., & Nascimento, A. L. T. O. (2015). Interaction of spirochetes with the host fibrinolytic system and potential roles in pathogenesis. *Critical Reviews in Microbiology*, *00*(00), 1–15. https://doi.org/10.3109/1040841X.2014.972336

Vinetz, J. M. (2000). Ten_Common_Questions_About_Leptospirosis.6.pdf. *Infectiois Diseases in Clinical Practice*, *9*(2), 59–65.

Vinh, T., Adler, B., & Faine, S. (1986). Ultrastructure and Chemical Composition of Lipopolysaccharide Extracted from Leptospira interrogans serovar copenhageni. *Microbiology*. https://doi.org/10.1099/00221287-132-1-103

Vinod, K., Lall, C., Vimal Raj, R., Vedhagiri, K., & Vijayachari, P. (2016). Molecular detection of pathogenic leptospiral protein encoding gene (lipL32) in environmental aquatic biofilms. *Letters in Applied Microbiology*, *62*(4), 311–315. https://doi.org/10.1111/lam.12533

Visith, S., & Kearkiat, P. (2005). Nephropathy in leptospirosis. *Journal of Postgraduate Medicine*, *51*(3), 184–188.

Volz, M. S., Moos, V., Allers, K., Luge, E., Mayer-scholl, A., Nöckler, K., … Jansen, A. (2015). Specific CD4 T-Cell Reactivity and Cytokine Release in Different Clinical Presentations of Leptospirosis. *Journal of Microbiology*, *22*(12), 1276–1284. https://doi.org/10.1128/CVI.00397-15.

Vysotskii, B. V, Malykh, F. S., & Prokof'ev, A. A. (1960). Leptospirosis in cats. *Journal of Microbiology*, *31*(2), 140-141.

Wasiński, B., & Dutkiewicz, J. (2013). Leptospirosis--current risk factors connected with human activity and the environment. *Annals of Agricultural and Environmental Medicine : AAEM*, *20*(2), 239–244. https://doi.org/1052323 [pii]

Webster, J. P., Macdonald, D. W., & Ellis, W. A. (1995). Prevalence of Leptospira species in wild brown rats (R. norvegicus) in UK farms. *Epedimiol Infec*, *114*(1), 195–201.

Weis, S., Rettinger, A., Bergmann, M., Llewellyn, J. R., Pantchev, N., Straubinger, R. K., & Hartmann, K. (2017). Detection of Leptospira DNA in urine and presence of specific antibodies in outdoor cats in Germany. *Journal of Feline Medicine and Surgery*, *19*(4), 470–476. https://doi.org/10.1177/1098612X16634389

Werts, C. (2010). Leptospirosis: a Toll road from B lymphocytes. *Chang Gung Medical Journal*, *33*(6), 591—601.

White, J. D., Malik, R., & Norris, J. M. (2011). Feline chronic kidney disease: Can we move from treatment to prevention? *Veterinary Journal*, *190*(3), 317–322. https://doi.org/10.1016/j.tvjl.2010.12.011.

Wu, M., Yang, C., Pan, M., Chang, C., & Chen, Y. (2004). Reduced renal Na þ – K þ – Cl - co-transporter activity and inhibited NKCC2 mRNA expression by Leptospira shermani : from bed-side to bench. *The European Dialysis and Transplant Association - European Renal Association*, *19*, 2472–2479. https://doi.org/10.1093/ndt/gfh452.

Wuichet, K., Alexander, R. P., & Zhulin, I. B. (2007). Comparative Genomic and Protein Sequence Analyses of a Complex System Controlling Bacterial Chemotaxis. *Methods in Enzymology*, *422*, 3. https://doi.org/10.1016/S0076-6879(06)22001-9.

Wysocki, J., Liu, Y., & Shores, N. (2014). Leptospirosis with acute liver injury. *Proceedings (Baylor University. Medical Center)*. United States.

Xu, Y., Zhu, Y., Wang, Y., Chang, Y. F., Zhang, Y., Jiang, X., … Wang, J. (2016). Whole genome sequencing revealed host adaptation-focused genomic plasticity of pathogenic Leptospira. *Scientific Reports*, *6*, 1–11. https://doi.org/10.1038/srep20020.

Yanagihara, Y., Kojima, T., & Mifuchi, I. (1982). Hemolytic activity of Leptospira interrogans serovar canicola cultured in protein-free medium. *Microbiology and Immunology*, *26*(7), 547–556.

Yang, C.-W., Wu, M.-S., Pan, M.-J., Hsieh, W.-J., Vandewalle, A., & Huang, C.-C. (2002). The Leptospira outer membrane protein LipL32 induces tubulointerstitial nephritis-mediated gene expression in mouse proximal tubule cells. *Journal of the American Society of Nephrology : JASN*, *13*(8), 2037–2045.

Yang, H. Y., Hung, C. C., Liu, S. H., Guo, Y. G., Chen, Y. C., Ko, Y. C., … Yang, C. W. (2015). Overlooked Risk for Chronic Kidney Disease after Leptospiral Infection: A Population-Based Survey and Epidemiological Cohort Evidence. *PLoS Neglected Tropical Diseases*, *9*(10), 1–15. https://doi.org/10.1371/journal.pntd.0004105.

Yener, Z., & Keles, H. (2001). Immunoperoxidase and histopathological examinations of leptospiral nephritis in cattle. *Transboundary and Emerging Diseases*, *48*(7), 441–447.

Yhee, J. Y., Yu, C. H., Kim, J. H., Im, K. S., Chon, S. K., & Sur, J. H. (2010). Histopathological retrospective study of canine renal disease in Korea, 2003~2008. *Journal of Veterinary Science*, *11*(4), 277–283. https://doi.org/10.4142/jvs.2010.11.4.277

Younes-Ibrahim, M., Burth, P., Faria, M. V, Buffin-Meyer, B., Marsy, S., Barlet-Bas, C., … Doucet, A. (1995). Inhibition of Na,K-ATPase by an endotoxin extracted from Leptospira interrogans: a possible mechanism for the physiopathology of leptospirosis. *Comptes Rendus de l'Academie Des Sciences. Serie III, Sciences de La Vie*, *318*(5), 619–625.

Zakeri, S., Khorami, N., Ganji, Z. F., Sepahian, N., Malmasi, A.-A., Gouya, M. M., & Djadid, N. D. (2010). Leptospira wolffii, a potential new pathogenic Leptospira species detected in human, sheep and dog. *Infection, Genetics and Evolution : Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases*, *10*(2), 273–277. https://doi.org/10.1016/j.meegid.2010.01.001

Zeng, L., Zhang, Y., Zhu, Y., Yin, H., Zhuang, X., Zhu, W., … Qin, J. (2013). Extracellular Proteome Analysis of Leptospira interrogans serovar Lai . *OMICS: A Journal of Integrative Biology*, *17*(10), 527–535. https://doi.org/10.1089/omi.2013.0043

Zhang, Y.-X., Geng, Y., Yang, J.-W., Guo, X.-K., & Zhao, G.-P. (2008). Cytotoxic activity and probable apoptotic effect of Sph2, a sphigomyelinase hemolysin from Leptospira interrogans strain Lai. *BMB Reports*, *41*(2), 119–125.

Zhang, Y., Geng, Y., Bi, B., He, J., Wu, C., Guo, X., & Zhao, G. (2005). Identification and classification of all potential hemolysin encoding genes and their products from Leptospira interrogans serogroup Icterohae-morrhagiae serovar Lai. *Acta Pharmacologica Sinica*, *26*(4), 453–461. https://doi.org/10.1111/j.1745-7254.2005.00075.x

Zilber, A. L., Belli, P., Artois, M., Kodjo, A., & Djelouadji, Z. (2016). First Observation of Leptospira interrogans in the Lungs of Rattus norvegicus. *BioMed Research International*. https://doi.org/10.1155/2016/9656274