Leptospirosis
A re-emerging zoonotic disease

Section I: Introduction
Leptospirosis is a serious infectious disease affecting domestic and wild animals. The disease has a worldwide distribution and has been reported in over 150 mammalian species. It is capable of causing mild to fatal disease in dogs and should be considered a differential diagnosis in any dog exhibiting signs of a non-specific illness or signs of haemorrhagic, renal, or hepatic disease.

Leptospirosis is recognized as an important zoonotic disease globally. The World Health Organization has recognised the disease as a re-emerging communicable disease that requires active surveillance.

Companion animal veterinarians play a vital role in the control of this disease by educating pet owners about the risks to their pets and themselves. Vaccination of dogs is an important method of disease control in this species and may reduce the zoonotic risk to humans.

Section II: Aetiology
Leptospirosis is a bacterial disease caused by pathogenic serovars of *Leptospira interrogans*, a member of the spirochaete family. Over 200 serovars have been identified, of which only a limited number have been demonstrated to cause disease in dogs. Based on serology, *Leptospira interrogans* serovars Copenhageni and Australis are the most frequently identified serovars infecting dogs in Australia.

**Section III: Epidemiology**

Leptospiral organisms are maintained in host-adapted species where they cause subclinical disease and prolonged shedding of the organism. Infection of incidental hosts such as dogs or humans can result in severe illness and mortality. In Australia, the maintenance host of serovar Copenhageni is the domestic rat. Serovar Australis is thought to be carried by the rat and some native marsupials in Australia.

Direct exposure can occur from urine, bite wounds or ingestion of infected tissue. Indirect exposure may be from contaminated water, food, soil or bedding. Leptospires do not replicate outside the host, but they may remain viable for several months in moist soil.

A serological survey of 956 shelter dogs in Australia revealed that infection is more widely spread than originally thought. An overall seroprevalence of 1.9% was found, with state-based variation. Serovar Copenhageni was the most prevalent serovar detected in this study. Interestingly, serovar Canicola, a canine adapted serovar, was identified for the first time in Australia in this study.

There is geographical variation in the predominant serovars affecting dogs in Australia. Serovar Copenhageni (of the icterohaemorrhagiae serogroup) is the most prevalent serovar in southern and eastern Australia, while serovar Australis is more prevalent in North Queensland. Canine fatality rates have been reported to be approximately 50% of hospitalised cases.

Given that indirect exposure to rodents is all that is needed to infect dogs, rural or urban dwelling dogs are both at risk of infection. In some studies working dogs

![Figure 1. Lifecycle of *L. interrogans* serovar Copenhageni](image-url)
have been shown to be at greatest risk. Additionally, the reported incidence in urban-dwelling dogs has increased.

Environmental and climatic conditions may affect the survival of leptospires in the environment, and thereby increase the risk of indirect transmission. Stagnant or slow moving warm water provides a suitable habitat and outbreaks often occur during periods of high rainfall or flooding.

Section IV: Pathogenesis

Leptospires enter the body through intact mucous membranes or wounds in the skin. Rapid replication in the blood leads to leptospiraemia and distribution throughout the body. Further replication occurs in many tissues, primarily the kidney and liver causing severe cell damage and inflammation. Experimentally the incubation period from infection to clinical signs was 7 days, however, this may vary due to infecting dose, strain and host immunity.

If the patient survives, antibodies are produced which eliminate the organism from all tissues except the kidneys, where it may persist for weeks resulting in urinary shedding and contamination of the environment.

Section V: Clinical Signs

Dogs with leptospirosis are often misdiagnosed as they can present with a wide range of clinical signs and varying levels of severity. Classically, infection results in acute to subacute haemorrhagic, renal and hepatic disease. Early on, dogs present with fever, shivering, muscle trembling and reluctance to move. Other cases may present with lethargy, inappetance, vomiting and diarrhoea. Jaundice on presentation is less common and associated with a poor prognosis. Leptospirosis should be considered a differential diagnosis in any dog exhibiting signs of a non-specific illness or signs of haemorrhagic, renal or hepatic disease.

### Table 1

| Clinical Signs of Leptospirosis
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<tbody>
<tr>
<td>Non-specific</td>
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<tr>
<td>Haemorrhagic</td>
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<td>Hepatic</td>
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<td>Renal</td>
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Section VI: Diagnosis

Diagnosis of leptospirosis is difficult with no perfect test available. Diagnosis is often dependent upon presence of relevant clinical signs combined with the detection of the organism or antibodies. Routine clinical pathology results may be mild or non-specific (see Table 2). Biochemical results indicating azotaemia and hepatopathy should always increase the suspicion of leptospirosis.

| Haematological Changes | Anaemia, leucocytosis, neutrophilia, lymphopenia, thrombocytopenia, prolonged clotting times |
| Biochemistry | Azotaemia, hyperphosphataemia, elevated ALKP, bilirubin and ALT, electrolyte disturbances |
| Urinalysis | Haematuria, isosthenuria, hyposthenuria, glucosuria |

Detection of antibodies using a microscopic agglutination test (MAT) was historically the most common method for diagnosing canine leptospirosis. There are challenges in interpreting antibody results as many infected dogs can present clinically ill up to 7 days prior to developing antibodies. Additionally, antibodies formed from vaccination or prior exposure cannot be distinguished from acute infection, thus paired and convalescent sera may be required for a serological diagnosis.

A real-time polymerase chain reaction (PCR) test is available to detect the presence of leptospires in blood and urine. Unlike serology, serovar specific results are not available, however, a positive or negative answer can be rapidly provided. In the first 10 days of infection, organism numbers are at their greatest in the blood, whilst after 10 days, numbers are at their highest concentration in the urine. Typically the time of infection is unknown, therefore, simultaneous testing of blood and urine can increase diagnostic sensitivity.
**Section VII: Treatment**

Treatment involves intensive supportive care and antimicrobial therapy. Early instigation of antimicrobial therapy is crucial for successful treatment. For that reason, antimicrobials should be instituted immediately upon suspicion of infection, prior to receiving test results.

The optimal treatment for leptospirosis is still unknown, with penicillins and doxycycline traditionally being the antibiotics of choice. The ACVIM Consensus panel recommends doxycycline, 5mg/kg PO or IV q12h for two weeks; with optimal duration of treatment still requiring further investigation. If vomiting or other reactions prevent doxycycline administration, ampicillin (IV only) or penicillin G may be used, however it is recommended that once gastrointestinal signs abate dogs should be treated with doxycycline for 2 weeks to ensure complete elimination of the organism from the renal tubules.

Supportive care for affected organ systems may require intravenous fluids, correction of acid-base imbalances, anti-emetics, gastroprotectants and plasma or blood transfusions. Urinary output should be monitored closely and haemodialysis can be life-saving for more than 80% of patients with severe anuric leptospirosis.
Section VIII: Zoonotic Risk

Leptospirosis is an important zoonotic disease with worldwide distribution. In Australia, 94 human cases were reported in 2010 and 189 were reported in 2011. Relative to the population this is significantly higher than in the US where 100 to 200 cases are seen annually, or, in the UK, where an average of 54 cases are reported annually. In these countries canine vaccination for leptospirosis is widespread.

Seasonal flooding can be a major risk factor for outbreaks in some countries. The number of human cases reported in Australia in 2011 was double those reported the previous year. Of these cases in 2011, 81.5% were in Queensland (see Figure 3). This was due to the extensive rain and flooding experienced in Queensland during December 2010 / January 2011, where notifications peaked in February 2011. Notifications then remained above the ten-year average during March and April.

The risk of zoonotic infection is highest for people that work outdoors (sugar cane harvesters, sewage workers) or with animals (farmers, abattoir workers and veterinary staff). Leptospirosis infection can also be a recreational hazard for campers and those involved in a range of water sports. One study found evidence for exposure by seroreactivity was 2.5% in a group of veterinarians attending a North American veterinary conference.

In most cases infection causes non-specific signs of illness such as flu-like signs, fever, headaches, muscle pain, nausea and vomiting. For this reason human cases are also thought to be underdiagnosed. About 10% of human patients will develop severe signs of hepatic and renal disease, and up to 15% of these patients die as a result. The serovar most commonly associated with fatal leptospirosis in humans belong to the icterohaemorrhagiae serogroup which includes serovar Copenhageni.

Veterinarians have an important role in reducing the incidence of this disease in animals and humans. Recommendations for the prevention of leptospirosis in dogs are to control and avoid rodent populations and to vaccinate at risk dogs against leptospirosis. Educating dog owners and children on basic hygiene as well as identifying and treating infected dogs will further reduce the zoonotic potential of dogs to humans.

Section IX: Vaccination

Protech® C2i is a cost effective bivalent vaccine containing *Leptospira interrogans* serovar Copenhageni, the most prevalent canine serovar in Australia. Protech® C2i also contains canine coronavirus, a potential cause of gastroenteritis, particularly in young dogs. It is conveniently packed in combination with Protech® C3 and C4. It can also be bought separately and used alone or as a diluent to reconstitute Protech® and Duramune Adult.

Vaccination is very effective at protecting dogs against disease and may be an important strategy to decrease the zoonotic risk to humans. The vaccine elicits serogroup-specific immunity and does not offer cross-protection against serovars not included in the vaccine.

In clinical trials for Protech® C2i, puppies were vaccinated at 6 and 9 weeks of age then challenged intra-peritoneally 3 weeks or 57 weeks later with virulent serovar Copenhageni. In both trials the vaccinated puppies showed a statistically significant reduction (p<0.05) in post-challenge thrombocytopenia, clinical scores and serologic responses versus controls. Challenge at 57 weeks resulted in 60% mortality of the control group.
whereas all vaccinated dogs survived. All Australian dogs, urban or rural dwelling, could be considered at risk of infection given the potential for exposure to infected rodents. As stated by the ACVIM consensus statement, “in geographic locations in which infection occurs in urban, backyard dogs, all dogs may be at risk, and the vaccine may be considered part of a core vaccination protocol”. Veterinarians should give serious consideration to vaccinating all dogs at risk with Protech® C2i to protect them against this serious disease.

“...in geographic locations in which infection occurs in urban, backyard dogs, all dogs may be at risk, and the vaccine may be considered part of a core vaccination protocol”.

![Efficacy of Protech® C2i. Total clinical score of pups challenged with virulent serovar Copenhageni (Protech® C2i vaccinates vs controls) 3 weeks post-vaccination.](Figure 4)
Section X: Protech® C2i Subunit Technology

To minimise the safety concerns commonly associated with the use of vaccines containing whole leptospiral organisms, Boehringer Ingelheim Animal Health uses an innovative process to manufacture Protech® C2i. This process is called subunit technology. Subunit manufacturing technology involves separating the surface immunogens, or bacterins, of the leptospira from extraneous cellular debris. These surface immunogens are involved in the induction of protective immunity. The extraneous cellular debris may be responsible for the undesired allergic reactions seen when a whole-bacterial vaccine is used. The final result of this process is a purified vaccine containing only the surface immunogens necessary for protection that is proven to be safe and efficacious under field conditions.

Figure 5

Purification of leptospiral antigens for Protech® C2i.
Summary

- Leptospirosis is a serious disease of dogs and humans
- Serovar Copenhageni is the most prevalent canine serovar in Australia
- Veterinarians play an important role in the zoonotic potential of leptospirosis
- Protech® C2i protects dogs against disease caused by serovar Copenhageni and aids in protection of disease caused by canine coronavirus
- Protech® C2i is available as a convenient and cost effective combination pack with Protech® C3 and C4, and can be used on its own or as a diluent for Protech® and Duramune Adult® C3 and C4

References: