LEPTOSPIRA INTERROGANS SSP.

Aetiology Epidemiology Diagnosis Prevention and Control
Potential Impacts of Disease Agent Beyond Clinical Illness References

AETIOLOGY

Classification of the causative agent

Leptospira interrogans, the causative agent of leptospirosis, consists of numerable serotypes capable of causing a variety of disease manifestations in a wide range of hosts. This motile and flagellated spirochete bacterium is recognizable via microscopy and earned its name from a characteristic hooked appearance that resembles a question mark. The taxonomic classifications within the *Leptospira* genus have been reorganized many times in accordance with new antigenic, genomic, and pathologic data. What was once over 250 serovars grouped into two *Leptospira* species is now 21 genomospecies of *Leptospira* with reclassified serovars. While the new taxonomic names are typically used in the scientific literature, historical names still circulate on product labels and in common use.

Not all serovars of *Leptospira* are pathogenic, and many are associated with a reservoir species in which little disease is apparent. Many serovars are highly prevalent within maintenance host populations and persist in the kidneys or genital tract. Small antibody responses and low tissue burdens are typical in these animals. Incidental hosts, however, typically develop serious disease with high tissue burdens and robust antibody responses. These classifications are not always entirely distinct and some overlap between presentations can exist.

Leptospirosis is a zoonotic disease but is typically associated with at-risk occupations (veterinarian, livestock owners, dairy workers, etc.) and exposure to contaminated water.

Resistance to physical and chemical action

Temperature: Generally fails to persist at <10°C or >34°C; pasteurization and moist heat at 121°C/15 minutes are effective methods of killing leptospires

pH: Prefers neutral to slightly alkaline conditions

Chemicals/Disinfectants: Inactivated by 1% sodium hypochlorite, 70% ethanol, formaldehyde, detergents, quaternary ammonium compounds, iodine based compounds, glutaraldehyde, and hydrogen peroxide

Survival: Warm, moist conditions greatly enhance survival; may persist up to 6 weeks under favorable conditions; freezing, dehydration, and UV radiation inactivate leptospires

EPIDEMIOLOGY

Hosts

- Virtually all mammals are vulnerable to pathogenic *Leptospira* serovars to varying degrees
    - Many serovars have specific maintenance hosts while others are more promiscuous
- *Leptospira* serovars known to cause disease in mammals have been isolated from amphibians
    - Some serovars have also been isolated from invertebrates, reptiles, and birds

Prominent host-serovar associations

- Armadillos (*Dasypus novemcinctus, Euphractus sexcinctus*) - Autumnalis, Cynopteri, Hebdomadis, Pomona
- Bandicoots (*Isoodon macrourus, Perameles* spp.) - numerous serovars have been associated with these species
- Brazilian tapir (*Tapirus terrestris*) - Pomona
- Canids (*Canis latrans, C. familiaris, C. lupus*) - Bratislava, Canicola, Grippotyphosa, Hardjo, Icterohaemorrhagiae, Pomona
- Cattle (*Bos taurus, Syncerus caffer*) - Hardjo and others
- Cervids - Bratislava, Canicola, Grippotyphosa, Hardjo, Icterohaemorrhagiae, Pomona
- European hedgehog (*Erinaceus europaeus*)
- Felids (*Felis silvestris silvestris, F. silvestris catus, Lynx* spp.)
- Flying foxes (*Pteropus* spp.) - a multitude of *Leptospira* serovars have been identified in various species of bat
- Foxes (*Vulpes lagopus, V. vulpes, Urocyon cinereoargenteus, Lycalopex griseus*) - Bratislava, Canicola, Grippotyphosa
- Giant anteater (*Myrmecophaga tridactyla*) - Djasiman
- Horses (*Equus ferus*) - Bratislava
- Lagomorphs (*Lepus europaeus, L. timidus, Oryctolagus cuniculus*) - Grippotyphosa
- Marine mammals (*Eubalaena australis,Trichechus manatus*) - Australis, Manaua
    - Sea lions (*Zalophus californianus, Z. wollebaeki*) and seals (*Callorhinus ursinus, Phoca vitulina, Mirounga angustirostris, Arctocephalus forsteri*) - Canicola, Hardjo, Pomona
    - There have been multiple mass-mortality events attributed to leptospirosis in California sea lions
- Marsupials - Australis, Autumnalis, Ballum, Bataviae, Celledoni, Cynopteri, Djasiman, Grippotyphosa, Hardjo, Hebdomadis, Icterohaemorrhagiae, Javanica, Mini, Panama, Pomona, Pyrogenes, Sejroe, Tarassov, Topaz
- Mongooses (*Herpestes auropunctatus, Mungos mungo, Paracynictis selousi*) - Bratislava, Hardjo
- Mustelids (*Meles meles, Martes fiona, M. martes, Mustela putorius, M. nivalis, M. ermine, Lutra lutra*)
- Platypus (*Ornithorhynchus anatinus*) - Autumnalis, Hardjo, Grippotyphosa
- Raccoons (*Procyon itor*) and skunks (*Mephitis mephitis*) - Bratislava, Canicola, Grippotyphosa, Hardjo, Icterohaemorrhagiae, Pomona
- Rodents and insectivores - Arborea, Australis, Ballum, Bindjei, Broomi, Canicola, Celledoni, Gryppotyphosa, Icterohaemorrhagiae, Javanica, Mini, Pomona, Pyrogenes, Sejroe, Tarrasovi, Zanoni
    - Rats are well-appreciated hosts for serotype Icterohaemorrhagiae
- Swine (*Sus scrofa* and other spp.) - Bratislava, Hardjo, Pomona
- Vervet monkey (*Cercopithecus aethiops sabaeus*) - Australis, Grippotyphosa, Javanica
- Multiple snake, turtle, toad, and frog species have also been identified as PCR and/or serologically positive

Transmission

- Ingestion
- Contact with mucous membranes or wet, abraded skin
- Some serovars can be transmitted venerally or transplacentally

Sources

- Urine
- Contaminated soil and water
- Placental fluids
- Genital secretions
- Milk
- Blood

Occurrence

Many wildlife species are reservoirs for *Leptospira* and subsequently maintain host-bacterium interactions that do not negatively impact the animal. Over time, selection pressures on the leptospires many change and drive reservoir species relationships to shift accordingly. Therefore, it is important to assess the epidemiology of leptospirosis on a more local level to understand transmission risks and disease impacts.

Leptospira is globally enzootic, but disease is more frequently seen in warm and moist environments. This may be seasonal (temperate zones) or more constant (tropical regions). Rainfall encourages persistence of the organism in the environment. Additionally, some serotypes are much more geographically dispersed and others are found in more limited regions.

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information System - Wild (WAHIS-Wild) Interface [http://www.oie.int/wahis_2/public/wahidwild.php/Index].

DIAGNOSIS

After invasion of mucous membranes or damaged skin, there is a 4-20 day incubation period followed by a 7-10 day period of circulation in the bloodstream. Clinical signs of acute leptospirosis depend on the tissues colonized during this period of bacteraemia, the host species, and infecting serovar. A robust antibody response follows and is associated with a declining bacteraemia. Tissues may recover slowly or not at all depending on the degree of damage. Death is possible in severe cases.

Incidental hosts maintain the bacterium in renal tubules for days to weeks and shed the organism in urine. Maintenance hosts, however, maintain the bacterium in the renal tubules, genital tract, and/or eyes and shed it in urine or genital secretions for months to years after infection.

Clinical diagnosis

Leptospirosis is a highly variable, systemic infection and the presentation depends on the infecting serovar, the host species, and the host's general health and immune status. Maintenance hosts typically do not develop significant clinical disease. Incidental hosts typically experience severe, acute disease secondary to bacterial toxins and inflammatory responses generated by the immune system. Initially, animals may be febrile and anorectic. They may quickly develop signs of haemorrhage and haemolytic anaemia secondary to endothelial damage such as mucosal petechiation, icterus, haemoglobinuria/haematuria, dehydration, vomiting, and colic. Acute renal injury develops rapidly and is a significant contributor to mortality. Pneumonia, meningitis, uveitis, corneal opacification, photosensitization, myalgia, and pancreatitis are also possible.

Reproductive disease is often characterised by abortion/stillbirth, mummified fetuses, infertility, blood in milk, or a cessation of milk production. If not aborted, neonates infected transplacentally are typically weak. Maintenance hosts do not develop reproductive disease acutely like incidental hosts, but instead remain subclinical for weeks to months.

Lesions

- Renal tubular necrosis and suppurative nephritis
    - Pale, oedematous parenchyma +/- pitting of the serosal surface and capsular adhesions
    - Subcapsular haemorrhage
    - Inflammation initially characterised by neutrophils but becomes lymphoplasmacytic
    - Mixed inflammatory processes are associated with higher mortality rates
- Hepatomegaly +/- necrotizing hepatitis
    - The liver is often friable and discolored in a lobular pattern
- Pulmonary haemorrhage
- Petechiae and ecchymoses on mucous membranes and internal organs
- Horses may develop uveitis with conjunctivitis, corneal oedema, synechia, or cataracts

Differential diagnoses

- Ocular disease
    - Equine recurrent uveitis
    - Traumatic uveitis/reflex uveitis
    - Infectious conjunctivitis
- Kidney disease
    - Toxin exposure (e.g., ethylene glycol)
    - Infectious nephritis, pyelonephritis, glomerulonephritis
    - Renal tubular acidosis
    - Nematodes (*Stephanurus dentatus, Dioctophyma renale*)
- Reproductive failure or compromise
    - Brucellosis
    - Bovine viral diarrhea virus (BVDV)
    - Porcine reproductive and respiratory syndrome (PRRS)
    - Q-Fever (*Coxiella burnetii*)
    - *Neospora* spp.
    - *Tritrichomonas foetus*
    - Mastitis, metritis
- Liver disease, icterus, and haemolytic anaemia
    - Viral hepatitis
    - Toxin exposure (e.g., heavy metals, anticoagulant rodenticides)
    - Rickettsial infection
    - *Clostridium haemolyticum, C. perfringens* A
    - Neonatal isoerythrolysis
- Bacterial septicaemia

Laboratory diagnosis

Samples

For isolation of agent

- Kidney
- Blood
- Urine
- Other grossly affected tissue such as liver

Serological tests

- Serum
- Whole blood

Procedures

Identification of the agent

- Silver-stained histopathology slides allow for direct visualization of the organism in renal tubules
- Immunohistochemistry (IHC)
- Bacterial culture
    - Because the organism is low-growing, this may take 12-26 weeks
    - Best available method to determine infecting serovar
- Polymerase chain reaction (PCR)
    - Widely variable protocols
    - Does not provide serovar-specific results

Serological tests

- Microscopic agglutination test (MAT)
    - Uses live, regionally common serovars of *Leptospira*
    - Requires diagnostic laboratory to maintain live cultures of serovars
    - Provides quantitative titre level
- Antibody capture enzyme-linked immunosorbent assay (ELISA)
    - Currently used for domestic canines; detects antibodies to LipL32 protein
    - Results are qualitative (positive/negative) and may yield false positives in the event of prior vaccination
- Immunofluorescence assay (IFA)
- There is not yet a consensus on what a diagnostic titre for *Leptospira* should be, therefore paired acute and convalescent sera are recommended for testing
- Caution should be taken when interpreting serology data; antibody titre does not always correspond with disease state

For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 3.1.12 *Leptospirosis* in the latest edition of the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.

PREVENTION AND CONTROL

Sanitary prophylaxis

- Extra precautions should be taken when cleaning areas frequented by potential *Leptospira* hosts. Wear gowns, shoe covers, and gloves to prevent contamination of personal clothing. Face shields are recommended to protect mucous membranes from aerosols.

Medical prophylaxis

- There are a variety of *Leptospira* vaccines available for domestic animals, including livestock
    - Vaccine intent may vary from prevention of infection to reduction of renal colonization and urine shedding
    - Read vaccine labels to determine which serovars are targeted, as immunity is believed to be serovar-specific

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Leptospirosis is a zoonotic disease. Because clinical signs can be vague and maintenance hosts can be asymptomatic carriers, basic protective measures are suggested for at-risk populations (veterinarians, livestock owners, dairy workers, etc.): protect eyes with safety glasses, wear gloves especially if there are openings in the skin, thoroughly wash hands after interacting with animals of unknown status and before consuming food or water, etc.
    - Pregnant individuals within at-risk populations are particularly advised to utilise protective measures.
- Many domestic animal species, including dogs, horses, and livestock, are susceptible to leptospirosis and could potentially transmit it to humans. Individuals should speak with local veterinarians to determine risk and appropriate prevention strategies, including animal vaccines.

Risks to agriculture

- If livestock or working animals (horses, dogs) develop clinical disease due to *Leptospira*, decreased thrift and reproductive compromise can significantly impact production. Working animals may not be

able to do their jobs as efficiently, and livestock may demand increased resources for treatment while producing less.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated 2020. Written by Samantha Gieger and Erin Furmaga with assistance from the USGS National Wildlife Health Center.