Canine Leptospirosis: Diagnostic and vaccination controversies.

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INTRODUCTION.
• A systemic bacterial infection of dogs (and very rarely, cats) causing mainly acute nephritis and hepatitis, vasculitis, and chronic carrier states.

CAUSE/PATHOGENESIS
• Pathogenic members of the genus Leptospira – main serovars causing disease in dogs include L. pomona, L. grippotyphosa (about the same incidence although perhaps more cases of L. pomona in Northeast, more L. grippotyphosa in mid-west), occasionally L. autumnalis and L. bratislava, and rarely, L. canicola, L. hardjo, and L. icterohaemorrhagiae – these results mainly based on serologic data.
• In fact, if you try to infect young beagle puppies with L. bratislava, none become infected raising the issue as to whether this serovar is pathogenic or merely a serologic phenomenon.
• Direct transmission – host-to-host contact via infected urine, postabortion discharge, infected fetus/discharge, and sexual contact (semen).
• Indirect transmission – exposure (via urine) to a contaminated environment (vegetation, soil, food, water, and bedding) under conditions in which Leptospira can survive.
• Wildlife reservoirs in Northeast – about a third of raccoons (mainly L. icterohaemorrhagiae), 15% of skunks (virtually all L. grippotyphosa) show exposure to serovars that infect dogs.
• Leptospira – penetrate intact or cut skin or mucous membranes; rapidly invade bloodstream (4-7 days); spread to all parts of the body (2-4 days).
• Invasion leads to transient fever, leukocytosis, transitory anemia (hemolysis), mild hemoglobinuria, and albuminuria; capillary and endothelial cell damage (occasionally results in petechial hemorrhages); liver necrosis and jaundice; acute nephritis with leptospiuria (organism replicates readily in tubular epithelial cell).
• Vasculitis – may cause interstitial pneumonia, anterior uveitis, myocardial damage and meningitis (rare), abortions.
• Death – usually a result of interstitial nephritis, vascular damage, and renal failure; may result from acute septicemia or DIC.
• Usually one or more serovars account for endemic disease in a geographic area – overall reported incidence probably falsely low as most infections are inapparent (undiagnosed).
• Worldwide distribution – especially in warm, wet climates or seasons.
• Standing water and neutral or slightly alkaline soil – promote presence in environment.
• Most cases occur during late summer/fall in Northeastern USA.

SIGNALMENT
• Dogs in rural habitat, more males affected, 4 to 7 yr-olds more at risk than dogs < 1 yr.
• Dogs in that walk or swim in a rural area, or drinking outdoor water are 8 and 12 times, respectively, more likely to get infected.
• Young dogs – without passive maternal antibody-more likely to exhibit severe disease.
• Old dogs – with adequate antibody titer levels-seldom exhibit clinical disease unless exposed to a serovar not in the vaccine.
• Dense animal population (kennels and urban settings) – increases chances of urine exposure, exposure to rodents, and other wildlife (hunting dogs).

CLINICAL SIGNS
• Lethargy, depression, anorexia and vomiting are the most common clinical signs.
  o Peracute/Acute – fever, sore muscles, stiffness, weakness, anorexia, depression, acute onset of vomiting, rapid dehydration, diarrhea (occasional bloody), occasionally icterus, cough with mild respiratory distress if respiratory component severe, Pu/Pd progressing to
anuria.
- Chronic – usually no apparent illness, Pu/Pd if chronic renal failure, hepatic signs.

**DIFFERENTIAL DIAGNOSIS**
- Subacute/acute disease – any severe systemic disease involving mainly the liver or kidneys alone, or together: heartworm disease; immune mediated hemolytic anemia; bacteremia/septicemia (bite wound, prostatitis, endocarditis, dental disease); infectious canine hepatitis virus; canine herpesvirus; hepatic neoplasia; trauma; lupus; Rocky Mountain spotted fever; ehrlichiosis; toxoplasmosis; acute nephritis, renal neoplasia; renal calculi.
- Reproductive failure – brucellosis; distemper; herpes.

**DIAGNOSIS**
- CBC – signs of dehydration (PCV and total plasma solids elevated); anemia, and thrombocytopenia are the main findings. Leukocytosis with left shift also.
- Serum biochemistry profile – Elevated BUN, creatine, phosphate, liver enzymes are main changes.
- Other changes due to dehydration, renal failure (electrolyte changes include hyponatremia, hypochloremia, hyperkalemia, hyperphosphatemia, hypoalbuminemia).
- Although Dogs infected with *L. pomona* are more likely to suffer from vomiting, thrombocytopenia, severe azotemia, and hyperphosphatemia (i.e., the most severe cause of renal disease), and are less likely to survive infection, there are few differences in clinical signs and lab data from dogs infected with different serovars.
- Urinalysis – proteinuria, isosthenuria usually, casts.
- In chronic carrier states – may only see isosthenuria with few granular casts in urine.
- Serology – MAT; test in acute stage and 3-4 weeks later (convalescent serum); in unvaccinated patients, titers may be low initially (1:100-1:200), then rise during convalescents (1:800 - 1:1600 or higher); several serovars usually show elevated titer but make serovars diagnosis based on highest titer.
- MAT titers in vaccinated dogs – vaccination causes elevation of MAT titer in most cases but usually only to serovars vaccinated against (no cross reactivity); do get MAT titer elevations to *L. autumnalis* after vaccination with subunit vaccines against *L. grippotyphosa* and *L. pomona* (Fort Dodge).
- Dogs vaccinated with whole cell bacteria – usually develop higher MAT titers (up to 1:800) than subunit vaccines (negative to 1:400).
- MAT titers induced by vaccination - usually only last up to 4 months.
- Darkfield Microscopy of Urine – often inconclusive as difficult to read and requires fresh urine.
- Fluorescent Antibody Test of Urine – more conclusive as leptospires do not need to be viable; submit urine to laboratory on ice by overnight courier; pretreatment with furosemide (2 mg/kg, SC) 15 min before urine collection will increase success rate.
- PCR on urine – offered by some commercial laboratories; shown in 1 dog out of 8 to detect organisms in urine before development of serologic titer; needs more work in experimentally infected dogs before being well validated.
- Culture – usually unrewarding.
- Tissue diagnosis (kidney biopsy) – FA, immunohistochemistry, Warthin-Starry silver stain, PCR, all effective.

**TREATMENT/PREVENTION**
- Inpatient for acute severe disease – extent of supportive therapy depends on severity; renal failure requires closely monitored diuresis, attention to DIC development; care must be taken not to over-hydrate as vasculitis of respiratory endothelium can lead to pulmonary edema during diuresis.
- Vaccines – bacterin and subunit vaccines available against *L. canicola* and *L. icterohaemorrhagiae*, and subunit vaccine available against *L. pomona*, *L. grippotyphosa*; most
claim year efficacy except those subunit vaccines covering *L. pomona* and *L. grippotyphosa* (protect for 2 to 2 ½ weeks post-booster); no cross-protection outside of the serovars used in vaccine serogroup); revaccination at least yearly; Data suggests to vaccinate at-risk groups (middle aged dogs actively visiting /muddy areas, ponds, low-lying areas with stagnant surface water, heavily irrigated pastures, and access to wildlife) every 4-6 months, or at least yearly just before at-risk period of infection (late summer – fall); reports on earlier bacterin vaccines suggested there was no protection against carrier state but some studies do show that urine shedding is prevented in dogs infected 2 – 3 weeks post vaccination with most vaccines, and up to a year in certain vaccines (not available in the US); vaccination is associated with a high incidence of anaphylaxis (particularly bacterin vaccines) after booster doses occurring within 1 hour of booster.

- There is still considerable controversy about the efficacy of some vaccines with little data. Some vaccines show efficacy out to a year post-booster; others are ineffective after 7 weeks post-booster (shed organisms in urine when challenged). Kennels - strict sanitation to avoid contact with infected urine; control rodents; monitor and remove carrier dogs until treated; isolate affected animals during treatment; disinfection of premises, use iodine-based disinfectant or stabilized bleach solutions.

**DRUGS USED IN TREATMENT**

- Doxycycline – use alone to clear leptospiremia and leptospiruria, as well as carrier state. [Dose: 5 mg/kg, PO or IV, q12h, for 2 weeks. IV doxycycline may induce vomiting].
- If doxycycline to be used, unnecessary to use penicillin.
- Penicillin compounds – may be used during acute leptospiremic phase if unable to administer doxycycline.
- Streptomycin – will clear organisms from kidneys but difficult to obtain and may potentiate renal insufficiency.

**PUBLIC HEALTH CONCERNS**

- Inform client of zoonotic potential from contaminated urine of affected dogs and their environment; after doxycycline, risk of shedding is greatly reduced.

**REFERENCES**