LEPTOSPIROSIS:
CASE STUDIES, DIAGNOSTIC OPTIONS
AND TREATMENT RECOMMENDATIONS

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LEPTOSPIRA

- Spirochetal bacterium.
- Highly motile.
- Obligate aerobe with features of gram-negative and gram-positive bacterium.
- Thin, flexible, filamentous bacteria.
- Stagnant or slow-moving water, neutral or alkaline pH, 0 - 30°.
- Preference is for ~30°.
LEPTOSPIRA

- Saprophytic and pathogenic species.
- Serovars are adapted to different wild or domestic reservoir hosts; approximately 250 serovars exist.
- Serovars are grouped into antigenically related serogroups.

<table>
<thead>
<tr>
<th>Species</th>
<th>Serogroup</th>
<th>Serovar</th>
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<tbody>
<tr>
<td><em>L. interrogans</em></td>
<td>Icterohaemorrhagiae</td>
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<tr>
<td>Canicola</td>
<td>Canicola</td>
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<tr>
<td>Pomona</td>
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<tr>
<td>Australis</td>
<td>Bratislava</td>
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<tr>
<td>Autumnalis</td>
<td>Autumnalis</td>
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<tr>
<td><em>L. kirschneri</em></td>
<td>Grippotyphosa</td>
<td>Grippotyphosa</td>
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</tbody>
</table>
COMPARISON OF Leptospira spp. Serovars identified in Ontario dogs 2010-2017 by percentage (AHL data)
LEPTOSPIRA - AUTUMNALIS

- Controversy over pathogenicity of serovar Autumnalis.
- Increased incidence of this serovar noted however only recently added to testing panel of many labs.
- Cross-reactivity in the past blamed for increased titres to Autumnalis.
- Now thought to be a potential cause of renal and non-renal leptospirosis.
### Leptospira spp. Serovar Reservoirs (AHL data)

<table>
<thead>
<tr>
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<td><em>L. kirschneri</em></td>
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<td>Raccoons, skunks, voles</td>
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<td>Dogs</td>
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**Leptospira in Ontario wildlife (2014 CVJ data)**

<table>
<thead>
<tr>
<th>Species</th>
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<th>% positive</th>
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<tr>
<td>Coyote</td>
<td>0/5</td>
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<tr>
<td>Deer</td>
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<tr>
<td>Opossum</td>
<td>3/53</td>
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<td>Fox</td>
<td>6/73</td>
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<tr>
<td>Beaver</td>
<td>1/11</td>
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<tr>
<td>Raccoon</td>
<td>82/245</td>
<td>33%</td>
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<tr>
<td>Skunk</td>
<td>14/33</td>
<td>42%</td>
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CVJ 2014, Shearer et al
DISTRIBUTION IN WILDLIFE, ONTARIO

CVJ 2014, Shearer et al
Welcome to the Real-Time Pet Disease Reporting Site

Prevention, early detection and timely response are key when dealing with emerging infectious diseases affecting animals and humans alike.

The Real-Time Pet Disease Reporting website has been designed to offer the Canadian public and the veterinary healthcare profession timely, crucial data, helping to manage the potential spread of infectious diseases. By consistently recording and reporting test results, Pet Disease Reporting aims to reduce the risk of future disease outbreaks and protect public safety.

Now Tracking Leptospirosis

Veterinarians can report and share their Leptospirosis test results.

Leptospirosis is a deadly bacterial disease that can cause acute kidney failure in dogs when coming into contact with contaminated wet grass, soil, puddles, streams or ponds.

Learn more >

View Positive Test Results on Maps

New! Print 2014 Maps

2014 Reported Positive SNAP® 4Dx® Plus Test Results

Lyme, Anaplasmosis, Ehrlichiosis, Heartworm

www.petdiseasereport.com
REAL TIME PET DISEASE REPORTING

Leptospirosis

Search by Postal Code
Enter Postal Code

Select Disease
Leptospirosis

Select Year
2017

Results

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<td>Nu</td>
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</table>

View/Print Test Results Analysis

Map data ©2018 Google, INEGI, 1:500 km | Terms of Use
REAL TIME PET DISEASE REPORTING

Instructions: Click a report's marker to learn more. Use the Report Filters on the left to filter the mapped reports.

www.wormsandgermsmap.com
INCIDENCE

- Appears to be increasing, and not just an effect of increased testing.
- Most ideal climate: 0-30\(^\circ\)C, with rainfall, so spring and fall are favoured. Poor survival with freezing.
- Southern, semi-tropical belt of USA.
- Strongly correlated with high rainfall and flooding.
- Example of triathletes in Illinois competing just after heavy rainfall.
- Spikes of incidence seen in certain years.
INCIDENCE

Why has leptospirosis in dogs increased?

- Increase in infection in wildlife vectors in both urban and suburban areas
- Climatic factors and the impact on the survival of vectors
- Awareness by vets, increased testing
- Possible increase in shedding – dogs and cats
INCIDENCE

- Raccoon study performed at the Toronto Zoo, 2007
- 19/61 animals (31%) MAT positive for *Leptospira*
- Little evidence they were persistently infected
- Seroprevalence ↑ from 5% in June to 38% in October
  - 15/19 Grippotyphosa
  - 4/19 Pomona
  - 1/19 Australis
  - 0/19 Autumnalis, Canicola, Icterohaemorrhagiae
- Bottom line – we are likely over-estimating raccoons as a source of *Leptospira* carriers
Large active breeds:
- 2000 AHL data >6 times more likely if:
  - Mixed breeds, Labrador/Retriever, Miniature Schnauzer, Bichon Frise, Doberman, German Shepherd, Alaskan Malamute, (Siberian Huskies, Standard Poodles)
- Shift to increased prevalence of dogs <15 pounds or Terriers since 2000 (JVIM 2014 USA data)
- Males > females in some studies
- Suburban(urban) >> rural
RISK FACTORS

- Spending time outdoors
- Exposure to wild animals
  - Enhanced by urbanization of environment
- Exposure to water, especially areas with flooding
- Lower socioeconomic areas
- Living within 2.5 km of a university/college or park/forest
- Global warming, years with high rainfall
- Housing in kennels or shelters
- Ages 4-10 years old
- Lack of vaccination
  - Are small breeds less vaccinated due to a perceived lower risk and perceived higher incidence of vaccine reactions?
Typical signalment

- Roaming dogs, those exposed to standing water
- Some studies support increased incidence in male dogs
- Wildlife in area
- Geographic region and season
- However
  - Small dogs
  - Urban centres
  - Numerous cases in suburban and metropolitan centers in Southern Ontario
- European Consensus Statement 2015:
  “Practitioners should consider leptospirosis as a possible diagnosis regardless of the signalment of the patient”
**Incidence, Ontario**

- Ontario
  - Seroprevalence has increased since 1990.
  - Incidence rates are stabilizing (due to vaccination?).
  - All breeds and ages, regardless of gender.
  - Urban > rural dogs.
  - Late fall and winter.
  - Serovars: Autumnalis, Bratislava and Grippotyphosa.

![Graph 1](linear_increase_proportion_positive_dogs.png)
**Linear increase in the proportion of positive tested dogs in Ontario 1998 – 2006.**

![Graph 2](annual_submission_samples_MAT_pos_neg.png)
**Annual submission of samples for MAT and counts of positive and negative from 1998 to 2006.**

![Graph 3](monthly_percentage_cases.png)
**Monthly percentages of annual canine leptospirosis cases averaged over 1998 – 2006.**
TRENDS, USA 1970-2009

SEASONALITY, USA 2000-2010

JVIM 2014, Regional and Temporal Variations of Leptospirosis
PATHOPHYSIOLOGY

- Bacteria are maintained in the renal tubules of reservoir hosts and excreted in the urine.
- Hosts are not typically ill and can shed bacteria their whole life. Unsure if this occurs in dogs.
- Direct transmission via urine, venereal routes, placental transfer, bites, ingestion of infected tissue.
- Indirect transmission via exposure to a contaminated environment.
- Most commonly from water (also soil, food, bedding).
- The organism invades through skin wounds or intact mucous membranes.
PATHOPHYSIOLOGY

- May begin multiplying within 1 day of exposure
- Leptospiremic phase lasts a few days (~7 days)
- Then enters organs such as kidneys, liver, spleen, CNS, eyes, and genital tract
- Damage to organ is due to replication causing cytokine production and inflammation
- Initial damage is to liver and kidneys.
- Extent of damage based on serovar, virulence and host susceptibility.
- Recovery based on production of antibodies.
- Without antibiotic therapy, colonization of kidneys usually occurs which allows long term shedding.
ORGAN DAMAGE

- Liver: necrosis and subcellular damage, intrahepatic cholestasis consistent with acute hepatitis.
- Vascular: *Leptospira* LPS results in stimulation of coagulation system and vascular inflammation, leading to endothelial damage and DIC.
- Other organ damage:
  - Uveitis
  - Meningitis
  - Abortion and infertility
  - Interstitial pneumonia
  - Immune-mediated disease?
Clinical Syndromes

- Dependent on: infecting strain, geographical location and host immunity.
- **Acute renal failure** – PU / PD (can progress to oliguria and anuria), dehydration, vomiting, diarrhea, inappetence, lethargy or abdominal pain.
- **Hepatic failure** – Icterus, dehydration, vomiting, diarrhea, inappetence, lethargy or abdominal pain.
- Acute respiratory distress syndrome or leptospiral pulmonary hemorrhage syndrome (LPHS) – Tachypnea or dyspnea.
- Conjunctivitis, uveitis, pyrexia, pancreatitis, bleeding tendencies.
CLINICAL SYNDROMES

- Does a chronic form of leptospirosis exist?
- Evidence for PU/PD with no azotemia; proven cases of leptospirosis, often with hyposthenuria
  - Nephrogenic diabetes insipidus?
- Chronic active hepatitis – suspected in two dogs due to Gripphothyphosa (1) and Australis (1)
- Chronic renal disease as a sequel to recovery from acute renal failure due to leptospirosis
CLINICOPATHOLOGY

- Azotemia with dilute urine
- Increased hepatic parameters (ALT, ALP, bilirubin)
- Electrolyte disturbances
- Leukocytosis
- Thrombocytopenia +/- anemia
- Glucosuria
- Granular casts
- Mild to moderate proteinuria
IMAGING

- Renal ultrasound (retrospective, uncontrolled study)
  - Renomegaly, pyelectasia, increased cortical echogenicity, perinephric fluids, and a medullary band of increased echogenicity
  - Lymphadenopathy, pancreatitis, thickened GI walls, hepatomegaly, splenomegaly

- Thoracic radiographs (retrospective, uncontrolled study)
  - Reticulonodular pulmonary opacity (focal or diffuse)
  - Likely pulmonary hemorrhage due to vasculitis
  - May be misinterpreted as neoplasia, pneumonia, edema, or pulmonary thromboembolism.
CASE EXAMPLES
TISSUE

- 10 yo FS Shih Tzu
- Vomiting and anorexia 2 days prior to presentation
- Lives in Burlington, leash walks only
- Does like to eat feces of wild animals
Tissue

Initial blood work

- ALT $\uparrow$ 177 (5-95)
- ALP $\uparrow$ 206 (24-141)
- Bilirubin $\uparrow\uparrow$ 103 (0-5)
- Albumin $\downarrow$ 27 (31-43)
- Urea $\uparrow\uparrow$ 34 (3-10)
- Creatinine $\uparrow\uparrow$ 640 (30-130)

- Abdominal ultrasound mildly mottled liver, mild loss of renal CM definition
TISSUE

Differential diagnoses:
- Toxin exposure
- Leptospirosis
- Neoplasia (lymphoma, histiocytic sarcoma)

Additional diagnostics
- Leptospirosis titres
- FNA or biopsy of liver and kidneys (declined)

Initial therapy:
- Ampicillin, enrofloxacin, metronidazole
- Metoclopramide, famotidine
- IV fluid therapy
After 7 days of hospitalization in the ICU, all values were markedly improved.

- Amoxicillin, enrofloxacin, metronidazole
- Metoclopramide, omeprazole
- Zentonil

**Leptospirosis titres:**

- *Leptospira canicola* 1:400
- *Leptospira pomona* 1:100
- *Leptospira grippotyphosa* 1:200
- *Leptospira icterohaemo* Negative
- *Leptospira bratislava* 1:800
- *Leptospira autumnalis* 1:1600
TISSUE

- Final diagnosis – acute leptospirosis affecting the liver and kidneys

- Therapy:
  - Two weeks of amoxicillin followed by two weeks of doxycycline
  - Continue Zentonil until normalization of liver values
HOWIE

- 4 yo MI Chihuahua
- On and off NSAIDs for a few weeks for soft tissue injury
- Polyuria/polydipsia 7 days prior to presentation
- Anorexia and lethargy for 2 days
- Lives in Etobicoke, leash walks only
- No travel history, no history of vaccination for leptospirosis
HOWIE

Initial blood work

- ALT N
- ALP N
- Bilirubin N
- Albumin N
- Urea ↑↑ 34 (3-10)
- Creatinine ↑↑ 319 (30-130)

- Abdominal ultrasound normal liver, mild loss of renal CM definition
HOWIE

- **Differential diagnoses:**
  - NSAID side effect
  - Toxin exposure
  - Leptospirosis
  - Pyelonephritis
  - Neoplasia (lymphoma)

- **Additional diagnostics**
  - Leptospirosis titres
  - Urine culture
  - FNA or biopsy of kidneys if values did not improve with therapy
  - Monitor blood pressure, renal values etc
HOWIE

- Initial therapy:
  - Ampicillin, enrofloxacin
  - Famotidine (reduced frequency)
  - Sucralfate
  - IV fluid therapy at high rate
  - Cerenia added in on day 2 due to vomiting

- After 4 days of hospitalization in the ICU, all values were markedly improved.
  - Urine culture negative
  - UPC 4.0 – Benazepril added
HOWIE

- Discharged on day 6 with stable azotemia, eating well
  - Clavamox, Benazepril and Ranitidine
  - Renal diet

- Leptospirosis titres:
  - Leptospira canicola: Negative
  - Leptospira pomona: 1:400
  - Leptospira grippotyphosa: 1:1200
  - Leptospira icterohaemo: Negative
  - Leptospira bratislava: 1:800
  - Leptospira autumnalis: Negative
HOWIE

- Doxycycline to be started after 2-week course of Clavamox
- Day 20 renal parameters almost normalized
- Day 28 renal parameters normal
- All medications discontinued

- Leptospirosis titres:
  - Leptospira canicola: Negative
  - Leptospira pomona: 1:6400
  - Leptospira grippotyphosa: 1:6400
  - Leptospira icterohaemo: Negative
  - Leptospira bratislava: 1:6400
  - Leptospira autumnalis: Negative
Final diagnosis – acute leptospirosis affecting the kidneys (NSAID use also exacerbated?)
OSCAR

- 13 yo MN Shih Tzu
- Presented last summer for routine wellness, comment on drinking/urinating more
- Blood work showed mild azotemia
- Treated for chronic renal failure by transition to renal diet, monitoring renal parameters and blood pressure
Oscar

- Acute inappetence and vomiting in October. Owners spent the next few weeks enticing Oscar to eat, clinical signs would wax and wane.
- Increased urination and drinking during this time.
- Visiting family in Florida in December, progressed to complete anorexia.
**OSCAR**

- Seen by ER clinic in Florida, severe azotemia. Owners declined treatment and drove back to Ontario.
- Seen by family veterinarian when they arrived home, now markedly dehydrated.
- Transferred to MOVEH, ultrasound revealed mild renal changes consistent with CRF.
Oscar

- Seen by ER clinic in Florida, severe azotemia. Owners declined treatment and drove back to Ontario.
- Seen by family veterinarian when they arrived home, now markedly dehydrated.
- Transferred to MOVEH, ultrasound revealed mild renal changes consistent with CRF.
OSCAR

- Not vaccinated for leptospirosis.
- Leptospira Panel performed:
  - PCR negative (urine and blood)
  - ELISA positive
- Leptospirosis diagnosed, suspect present since October.
- Treatment with doxycycline.
- Improved azotemia at recheck.
  - Creatinine from ~900 to 450.
PETER

- 5 yo MN Samoyed
- Vaccinated for leptospirosis 1 week prior to presentation
- Vomiting and anorexia 5 days prior to presentation
- Blood work at rDVM revealed moderate elevation in ALT, ALP and bilirubin
- Amoxicillin, enrofloxacin, metronidazole, Zentonil and famotidine started
Peter

Presented for further evaluation:

- **ALT**: ↑↑ 644 (5-95)
- **ALP**: ↑ 440 (24-141)
- **Bilirubin**: ↑↑ 100
- **Albumin**: ↓ 27
- **Urea**: ↓ 2.9
- **Creatinine**: N 70

Abdominal ultrasound mildly mottled liver, normal biliary system, rest wnl
Differential diagnoses:
- Toxin exposure
- Acute bacterial hepatitis
- Acute on chronic immune-mediated hepatitis
- Leptospirosis
- Neoplasia (lymphoma, histiocytic sarcoma)
- Vaccine reaction (unlikely)

Initial therapy:
- Ampicillin, enrofloxacin, metronidazole
- Metoclopramide, omeprazole
- Zentonil
Histopathology of liver:
- Combination of interstitial fibrosis, ongoing hepatocellular necrosis, impaired regeneration and parenchymal collapse

Aerobic/anaerobic culture negative

Leptospirosis titres:
- Leptospira canicola: 1:800
- Leptospira pomona: 1:200
- Leptospira grippotyphosa: 1:6400
- Leptospira icterohaemo: 1:200
- Leptospira bratislava: Negative
- Leptospira autumnalis: 1:400
CAUSE OF ILLNESS?

- Clinical leptospirosis with exposure prior to vaccination
  - Titres would be more consistent with this due to high titre to grippotyphosa, which typically causes acute hepatitis
  - Histopathology was consistent with an acute on chronic condition, which is not consistent with acute leptospirosis
  - No response to amoxicillin, with clinical deterioration and increased liver enzymes
CAUSE OF ILLNESS?

- Acute flare-up of chronic hepatitis (immune-mediated hepatitis)
  - Histopathology would fit with this
  - Lack of response to amoxicillin would fit with this
  - High titre can occur with vaccination

- Recommended to start prednisone therapy, and perform convalescent leptospirosis titres
COURSE OF ILLNESS?

- Convalescent leptospirosis titres:
  - Leptospira canicola: Negative
  - Leptospira pomona: 1:200
  - Leptospira grippotyphosa: 1:100
  - Leptospira icterohaemo: Negative
  - Leptospira bratislava: Negative
  - Leptospira autumnalis: Negative
Cause of Illness?

- Partial response to prednisone, final regime:
  - Prednisone
  - Cyclosporine
  - Ursodiol
  - Hepatosupport
  - Zentonil
  - Omeprazole
OBTAINING A DIAGNOSIS

- Microscopic Agglutination Test (MAT):
  - Detection of antibodies in blood.
  - Limitations
    - Cross-reactivity (correct in 46% of cases in human study)
    - Positive reaction with vaccinal antibodies
    - Persistence of antibodies
    - Negative results early in the disease course.
    - Cross-reactivity to other spirochetes (*Borrelia*, oral spirochetes)
  - Increasing diagnostic utility: Convalescent sample (two to four weeks) demonstrating a four-fold increase in MAT titers differentiate current infection from previous infection or vaccinations (consider timing of vaccination).
Obtaining a Diagnosis

- **Take Home Message:** A single positive titer does not confirm the diagnosis, especially if vaccinated; a convalescent titer should be performed. The predicted infecting serovar should be considered in light of the clinical syndrome and geographical location.
Titres achieved with vaccines

- It is often cited to use <800 indicative of vaccinal titres
- Reports of post-vaccinal titres >4000 in one study, rare reports of >6400 with vaccination
- Insufficient data available on specific vaccines over a long time period to determine a set cut off point
- Always consider vaccine history and clinical data when interpreting titres
## Titres Achieved with Vaccines

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- Vaccine used was Duramune LGP, Fort Dodge (L. pomona and L. grippotyphosa).
- Interesting to note cross-reactivity by L. autumnalis
- No titres measured in puppies against grippotyphosa
TITRES ACHIEVED WITH VACCINES

- Recent study assessing titres after receiving 1 of 4 major leptospirosis vaccines
  - 32 healthy dogs
  - Vaccinated at 0, 3 and 52 weeks
  - Received Boehringer-Ingelheim, Merck, Merial or Pfizer vaccine
    - canicola, grippotyphosa, icterohemorrhagiae and pomona
  - Measured titres at 0, 3, 4, 7, 15, 29, 52 and 56 weeks
Titres achieved with vaccines

JVIM 2014 Martin et al
Titres achieved with vaccines

JVIM 2014 Martin et al
CONCLUSIONS OF STUDY

- Vaccination can result in no measurable titres, to very high titres
- Due to variability of titres after vaccination and over time, measurement of titres cannot be used to predict protection and need for re-vaccination
- Increase in titres after vaccination will complicate the diagnosis of clinical leptospirosis
- Titres against serovars not contained within vaccine can be seen
Obtaining a Diagnosis

- Polymerase Chain Reaction (PCR):
  - Detection of DNA in blood, urine, CSF and aqueous humor.
  - Blood sample is recommended in the first 10 days.
  - Thereafter, urine assessment is the most accurate.
  - Paired samples (blood and urine) should be submitted if duration of infection is unknown.
  - Limitations: Antimicrobial administration can result in false negatives, negative results do not rule out disease, limited information regarding sensitivity, specificity and PPV.
  - Very recent vaccination will NOT cause a false positive.
  - Increasing diagnostic utility: Use early in the course of disease, prior to treatment administration and interpret in conjunction with other diagnostic tests.
LEPTO ELISA AT IDEXX

- Detects antibodies to LipL32 (most abundant outer membrane protein found in pathogenic species of *Leptospira*)
- Qualitative test – obtain either a negative or a positive
- Does not give information on infecting serovar
- The test is affected by vaccination
- Published data
  - Performed similarly to the MAT Curtis et al, Goldstein et al, Winzelberg et al
  - Performance not as good to MAT/Witness Lizer et al
Witness Lepto Test

Witness Canine Leptospira Antibody Test Kit

- Only canine test offered bedside in Canada
- IgM based, study has indicated that IgM antibodies are formed within 4-6 days of infection
- These antibodies likely exist for a few weeks after infection or vaccination
- Qualitative test – either a negative or a positive
- Tests for Canicola, Grippotyphosa, Pomona and Icterohaemorrhagiae
- Likely detects other serovars
- Does not give information on infecting serovar
Witness Lepto

• How does it compare to other testing? A study looked at 4 serovars in experimentally infected beagles:

<table>
<thead>
<tr>
<th>Day</th>
<th>Witness</th>
<th>MAT</th>
<th>IDEXX SNAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>87.5%</td>
<td>65.6%</td>
<td>3.1%</td>
</tr>
<tr>
<td>10</td>
<td>100%</td>
<td>93.5%</td>
<td>9.7%</td>
</tr>
<tr>
<td>14</td>
<td>100%</td>
<td>95.8%</td>
<td>0%</td>
</tr>
</tbody>
</table>

• Another study indicated that 76% of client-owned dogs with clinical leptospirosis had a positive Witness lepto test within 2-4 days of showing clinical signs.
What about vaccination? Lizer et al, Vet Record 2018

% Positive on Witness Lepto after Vaccination

Days Since Vaccination
**Witness Lepto**

- Zoetis data – 23 laboratory dogs

% Positive on Witness Lepto after Vaccination

![Graph showing % Positive on Witness Lepto after Vaccination](image)

- Additional study with 48 dogs – all negative at 3-4 weeks after vaccination
**Witness Lepto Test**

Witness Canine Leptospira Antibody Test Kit

Using whole blood, plasma or serum
WITNESS LEPTO

Take home from this information:

• The Witness Lepto test is likely your best test for diagnosis, however prepare owners that a repeat test may be required a few days later if a negative if obtained and high suspicion remains

• Possibility of a false positive if vaccinated less than 6 months ago, so consider other tests in these cases

• For other tests, you need to consider vaccination and antibiotic use in order to select the appropriate test
Suspected leptospirosis
History, physical examination, clinical signs
CBC, chemistry panel, urinalysis

Confirm not vaccinated in last 4-6 months

Witness Lepto

Negative

High suspicion remains

PCR or re-test

Negative

Leptospirosis unlikely

Investigate other causes of illness
Consider Lepto MAT if chronic disease or high suspicion remains

Positive

Leptospirosis diagnosed

Confirm no recent vaccination (<6mos)

Leptospirosis diagnosed

Continue treatment

Ensure blood and urine samples collected prior to treatment. Treat with doxycycline or penicillin derivative if you have to wait for PCR/ELISA/MAT diagnostic results.

Positive

Continue treatment
How can we best use Leptospira testing?

- Dog that has NOT received antibiotics and NOT vaccinated:
  - Start with Witness Lepto if you have it in clinic
  - Otherwise Leptospira spp. Panel (ELISA and PCR)
  - If positive on any you have your diagnosis
  - If negative and clinical suspicion remains high, repeat testing or do MAT, administer appropriate antibiotics in case of false negative

- Dog that has NOT received antibiotics and IS vaccinated in last 4-6 months:
  - Leptospira spp. PCR
  - If positive you have your diagnosis
  - If negative and clinical suspicion remains high, do MAT, administer appropriate antibiotics in case of false negative
HOW CAN WE BEST USE LEPTOSPIRA TESTING?

- Dog that has received antibiotics and NOT vaccinated:
  - Start with Witness Lepto if you have it in clinic
  - Otherwise Leptospira spp. ELISA
  - If positive on any you have your diagnosis
  - If negative and clinical suspicion remains high, repeat testing or do MAT

- Dog that has received antibiotics and IS vaccinated in last 4-6 months:
  - Acute and convalescent MAT titres

- Dog that has received antibiotics and IS vaccinated but not in the last 4-6 months:
  - Start with Witness Lepto if you have it in clinic
  - Acute and convalescent MAT titres
OBTAINING A DIAGNOSIS

Culture
- Limitation: Sample fragility, special culture media, three to six month incubation, overgrowth with contaminate bacteria.
- Utility: Epidemiological data.
OBTAINING A DIAGNOSIS

- Tissue samples (antemortem or postmortem)
  - PCR
  - Special stains
  - IHC

- Testing not always readily available
- Tissue sample collection often not performed in critical patients with coagulopathies
TREATMENT — FIRST STAGE

Antimicrobial therapy:

- Essential!
- Initiate prior to confirmation of the diagnosis but after submission of PCR testing.
- Goal: Immediately inhibit multiplication of the organism, terminate leptospiremia and rapidly reduce fatal complications.
- Doxycycline (5mg/kg PO q12hr) or Penicillin (and its derivatives; ampicillin 22mg/kg IV q8hr).
- Prevent shedding and transmission of organisms within 24 hours of initiation (72 hours?)
- Does not necessarily clear infection or prevent carrier state
TREATMENT – FIRST STAGE

- Supportive therapy:
  - Depends on the severity of clinical signs.
  - Usually requires hospitalization and diuresis.
    - Renal function, serum protein concentration and electrolyte / acid-base status monitored every 24 hours
    - Complete blood count/hepatic parameters monitored every 48 hours.
  - Indwelling urinary catheter?
  - Gastroprotection (reduce dose if ARF), anti-emetics (avoid Cerenia if liver failure), analgesia if indicated (no NSAIDs).
  - Renal replacement therapy (hemodialysis or CRRT).
    - Not widely available, can consider peritoneal dialysis at a center with an ICU if no RRT available.
TREATMENT – SECOND STAGE

Antimicrobial therapy:
- Goal: Eliminate the carrier state.
- Doxycycline (do not need to reduce dose in ARF), current recommendation is 3 weeks (some sources say 2 weeks)
- Can use ampicillin then doxycycline
- Other dogs in the household should be treated.
- Discuss zoonosis with owners.

Follow up:
- Will vary from patient to patient.
- Re-examination one week after discharge.
- Serum biochemical panel, CBC, urinalysis.
- Prognosis is good; > 80% survival. Prognosis highly dependent on conservation of renal function.
Zoonosis

- Transmission from pet dogs to humans has not been substantiated.
  - Study of 91 personnel/dog owners involved in cases diagnosed with acute leptospirosis – 0% positive
  - Higher titres in Trinidad/Tobago veterinary students than general population
  - Possible case in Quebec involving a veterinary student?
- Have documented simultaneous exposure of humans and dogs.
- Human exposure usually due to water-related activities, either work or leisure based
Zoonosis

- Viable organisms in blood or urine within the first 72 hours of treatment.

- Minimizing risk at the hospital:
  - Minimize movement around the hospital.
  - Floor-level cages.
  - Disinfect areas of contact.
  - Warning labels on cages.
  - Pregnant or immunocompromised individuals avoid contact.
  - Gloves, disposable gown, face mask.
  - Urinary catheter versus frequent walking.
  - Bathe dog after 72 hours of treatment before reducing precautions.
Minimizing the risk at home:

- Treated dogs represent a low risk.
- Avoid contact with urine.
- Wash hands.
- Bathe the dog after 72 hours of therapy.
- Routine household disinfectants to clean areas of urine contamination.
- Dogs should be walked and should urinate away from standing water and where other pets and people do not have access.
- Encourage contact with the family physician.
PREVENTION: VACCINATION

- Initial vaccines were protective against icterohaemorrhagiae and canicola infection ("bivalent")
- These were chemically inactivated whole cell bacterins; potentially a higher reaction to vaccine
- Vaccination resulted in a reduction in the highly virulent forms of infection
- Believed no cross protection with other strains
- Variable increase in titre with vaccination including very high titres, but typically back to <100 to 200 beyond 16 weeks after vaccination
- Believed increase should be to serovar in vaccine
Prevention: Vaccination

- Newer vaccines protect against canicola, pomona, grippotyphosa and icterohaemorrhagiae (“quadrivalent”)
- Either whole cell bacterin or subunit vaccines (only the surface immunogens)
- More purified vaccines
- Apparent reduction in reactions
- Serogroup-specific immunity and possible partial immunity to other serogroups – more study needed
- Must be given yearly
- Do not use titres to assess protection!!
**PREVENTION: VACCINATION**

- **Adverse vaccination reaction:**
  - Anaphylactoid reactions.
  - Small breeds (Pugs, Mini. Dachshunds) over-represented?
  - Anecdotal evidence that prevalence of reactions is decreasing.

- **Moore study (JAVMA 2005)**
  - Studied rate of adverse events after vaccination in 1.2 million dogs – overall rate of 38.2/10,000 dogs
  - Reaction more common in young adult, small breed neutered pets
  - Reaction increased with the number of vaccines given at one visit
Adverse Events - Vaccination

Moore study (JAVMA 2005)
When should vaccination be recommended?
- At-risk dogs, regardless of breed.
- Definition of at-risk varies with geography.
- Dogs that have recovered from leptospirosis.
  - At risk of ongoing exposure
  - Unknown if life-long immunity results after natural infection
- Dogs in contact with immunocompromised individuals.

European Consensus Statement 2015:
“Practitioners should consider leptospirosis as a possible diagnosis regardless of the signalment of the patient”
**Prevention: Vaccination**

- Measured titres does not equate to protection
- Challenge studies indicate protection for about a year
- Recommended annually; two-injection initial series in puppies (> 12 weeks) or unvaccinated dogs.
- Titre increases typically are a small rise but occasionally a transiently high titre (>1:4000)
- Elevated titre therefore does not indicate which serovar caused disease, or in the case of vaccination, does not indicate protection against a specific serovar
- Importance of convalescent titres if using MAT titres in suspected infection in vaccinated dog
PREVENTION: OTHER

- Decreased access to potential sources of infection.
  - Marshy areas, standing water, isolate infected animals.
- Minimizing wild animal contact.
  - Fencing, rodent control.
- Maintenance of environmental conditions.
  - Discourage bacterial survival.
- Some sources recommend treating all dogs in household where pet was diagnosed with leptospirosis.
WHAT ABOUT CATS?

- Serologic evidence of exposure exists.
- Clinical disease is rarely reported.
- Experimental infection results in leptospiruria and leptospiremia.
- Extent to which cats contaminate the environment is unknown.
QUEBEC STUDIES

- 10/40 cats (25%) presented to VTH were positive
  - Other studies have shown 4.8 to 16.9% prevalence

- Follow up study with 239 cats
  - Healthy cats 7.2% (9/125)
  - Renal disease 14.9% (17/114)

- 3 cats (2001-2009) presented to VTH for varying stages of renal insufficiency were confirmed to be carrying leptospirosis; all indoor/outdoor
  - Two cases had mild azotemia with recent clinical signs, both recovered with therapy
  - One cat presented with severe, acute renal failure that was fatal despite peritoneal dialysis in an ICU
  - Two cats had ocular symptoms as well
JFMS – GUIDELINES FOR CATS

- Transmission likely due to rodent consumption
- Antibody prevalence 0-35%
  - *icterohemorrhagiae, canicola, grippotyphosa, pomona, hardjo, autumnalis, ballum* titres
- No association with breed or sex, but more prevalent in older cats
- Prevalence of shedding in healthy cats in one shelter similar to dogs (10/85; 12%)
- Clinical signs rare; still unclear, but most likely renal impairment. Have been cases of acute hepatitis.
- Diagnosis via MAT; no vaccinal interference
- Treatment as per dogs. Treat asymptomatic carrier with doxycycline as per dogs.
Bottom line - cats

- European Consensus Statement 2015 “The role of healthy cats as reservoir hosts and the role of leptospirosis as a clinical disease in cats might have been underestimated in the past and deserves further study”

- We need more data!

- For indoor/outdoor cats, or indoor cats that eat mice:
  - Consider testing cats presenting with recent polyuria/polydipsia, even with no azotemia
  - Consider testing cats presenting with acute renal failure

- Should we be testing chronic renal failure patients???

- Should we be vaccinating cats??? Then cat specific vaccines will need to be developed.