



April 2012

Focus this Month: Leptospirosis

We hope you enjoy this issue of ANTECH Insights. Please pass it along!

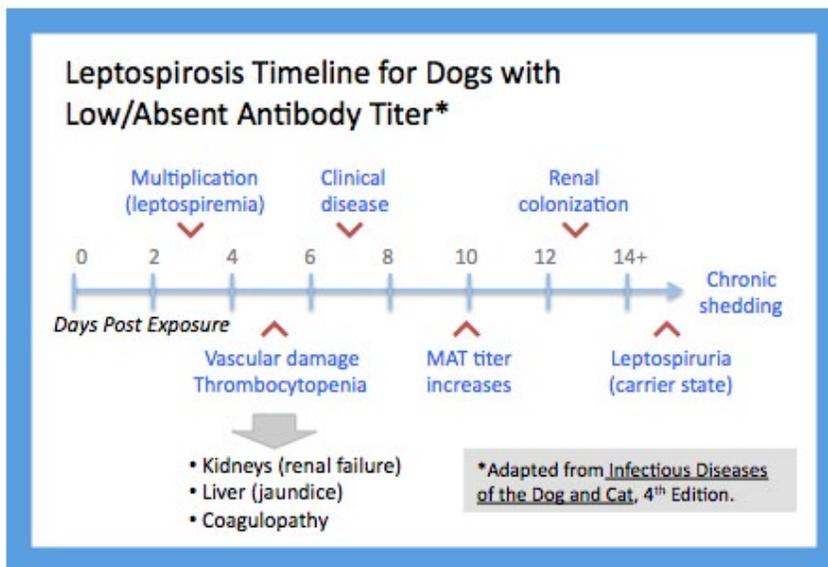
NEW! Canine Leptospirosis PCR Test Available



Real-time PCR panel provides for earlier detection in acute cases

ANTECH's most recent addition to its menu of real-time PCR profiles is the FastPanel® PCR Canine Leptospirosis Profile. With a **turnaround time of just 1-3 days**, the profile enables earlier and more specific diagnosis of leptospirosis compared to serology (microscopic agglutination test or MAT).

With the increasing prevalence of canine leptospirosis across the United States and its deadly zoonotic potential, the disease is an important consideration in dogs with kidney disease with or without hepatic disease, uveitis, acute febrile illness, myalgia, unexplained polyuria/polydipsia, neutrophilia & thrombocytopenia, acute pulmonary disease, or abortion. The FastPanel PCR Canine Leptospirosis Profile detects the presence of *Leptospira* spp. in a patient's blood or urine **several days prior to the development of antibodies** measurable by MAT, enabling a specific diagnosis to be made in the earliest stages of illness.



At a Glance

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Real-time PCR panel provides for earlier detection in acute cases

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Important reminders for your hospital staff

PCR testing for leptospirosis can also aid clinicians in two situations that are likely to confound MAT interpretation: (1) subclinical or previous infections; and (2) recently vaccinated animals (within the last 3 months). In both situations, PCR results can clarify the patient's current infection status.

The FastPanel PCR Canine Leptospirosis profile is an important diagnostic tool for dogs presenting with clinical signs of acute or chronic leptospirosis. The table below details ordering information and specimen requirements, including recommendations on when to submit blood versus urine samples.

**FastPanel® PCR Canine Leptospirosis Profile:
Ordering Information**

Indications:	Kidney disease with or without hepatic disease, uveitis, acute febrile illness, myalgia, unexplained polyuria/polydipsia, neutrophilia & thrombocytopenia, acute pulmonary disease, or abortion.
Test Codes:	T974 - Blood Only; T976 - Urine Only; T978 - Blood and Urine.
Turnaround Time:	1-3 days
Sample Recommendations:	Blood PCR in first week of illness; Urine PCR after first week; Blood and Urine PCR recommended if timing uncertain.
Specimen Requirements:	Whole blood (EDTA, heparinized, or citrated); sample volume: 0.5 ml Urine sample volume: 2 ml
Tests for:	DNA from the following pathogenic <i>Leptospira</i> serovars: <i>Leptospira interrogans</i> serovars Icterohaemorrhagiae, Canicola, Pomona, Australis, Bratislava, Autumnalis, Ballum and Pyrogenes; <i>L. kirschneri</i> serovar Grippotyphosa; <i>L. interrogans/borgpetersenii</i> serovar Sejroe
Results:	Positive or Negative for pathogenic <i>Leptospira</i> serovars (the specific serovar is not reported).
Limitations:	A negative PCR test may be due to acute disease (prior to urine shedding if only urine is tested), intermittent shedding of organisms, or prior use of antibiotic therapy.

NOTE: The FastPanel PCR Canine Leptospirosis test is canine specific. For other species, please order UC S16514.

Common Questions about Canine Leptospirosis

Interview with **George Moore, DVM, PhD, DACVIM, DACVPM**

Co-author, 2010 ACVIM Small Animal Consensus Statement on Leptospirosis: Diagnosis, Epidemiology, Treatment, and Prevention



Q: What are the most common questions you hear from general practitioners about diagnosing canine leptospirosis?

A: It's a two-part question: first, "What is the best diagnostic test?" followed by, "How do I interpret the results?" Early in the course of disease, it's most important to determine whether or not leptospirosis is the cause of disease, i.e., the infecting serovar is not so important. If it's a very early stage infection, I'm going to lean toward recommending PCR. At a later stage, I would recommend the MAT (microscopic agglutination test), or MAT combined with PCR if there is some concern about previous vaccination or previous natural exposure confounding the MAT result.

Later in the course of disease, identifying the infecting *Leptospira* serovar is valuable from an epidemiological standpoint, so the clinician and dog owner will be better informed about how and where the pet might have been exposed, and whether there was vaccine failure.

Regarding the interpretation of MAT results, the 2nd or convalescent titer is very important to help identify the infecting serovar. If there is a four-fold rise in titer for a particular serovar, that serovar is most likely the one responsible for disease. We know the MAT has its limitations but it's the best readily available tool we have today for predicting the infecting serovar.

Q: What are some recent trends you've seen in the prevalence of canine leptospirosis in the U.S.?

A: The regional shift of leptospirosis from a disease formerly identified primarily in the Midwest to more of a **pan-regional disease** seen in Hawaii, the West coast, the upper Midwest, the northeast and mid-Atlantic regions, as well as the Southeast and some parts of Texas and Colorado is well documented.



We're also seeing leptospirosis **more frequently diagnosed in small breed dogs** – it was previously thought to be limited to mid-to-large breeds. And most recently, because of our very mild winter, we saw leptospirosis cases **as early as February**, because the ground didn't freeze and kill the organisms. We saw some decline, but not the usual seasonal cessation that is typical in the Midwest due to weather and wildlife migration.

Q: What is the best sample type to submit for Leptospira PCR testing?

A: Blood is preferred during the first seven to ten days of illness; urine is preferred after that. If the timing of infection is uncertain, it is best to submit both blood and urine. If the animal has begun to receive antibiotic treatment,

a blood sample is unlikely to be positive but non-viable organisms may be detected in urine for several days after therapy has started.

Q: Based on what is now known about the various pathogenic serovars infecting dogs in the U.S., do you believe the four-way *Leptospira* vaccines are providing good coverage of the circulating pathogenic serovars?

A: We believe the serovars that would be covered by today's four-way leptovaccines -- *L. icterohaemorrhagiae*, *L. canicola*, *L. grippityphosa* and *L. Pomona* -- are responsible for over 90% of today's canine leptospirosis cases. There are over 250 pathogenic *Leptospira* serovars in existence, however, so vaccine coverage may need to continue to evolve over time.

The *L. autumnalis* and *L. bratislava* serovars are frequently identified in positive canine MAT results, but we believe the results are very likely due to cross-reactivity with other pathogenic serovars.

Q: Is *Lepto* PCR testing useful to confirm that an infected dog has cleared the organism after treatment?

A: Yes, PCR testing would be a useful follow-up if that is a concern, for example in a household with multiple dogs or dogs maintaining a persistently high MAT titer -- with the caveat that PCR can pick up non-viable (dead) organisms as well as live ones.

Q: Any other suggestions or reminders you would like to share with our readers related to utilizing *Leptospira* PCR testing?

A: Yes, remember that it is important to **submit samples that were obtained prior to antimicrobial therapy**. In general, it is a good practice to reserve a sample from any patient coming in with primary renal and/or liver disease for subsequent follow-up serology, PCR or other testing.

Rule-Outs for Renal and Hepatic Disease: A Sequential Diagnostic Approach

Contributed by ANTECH Internal Medicine Consultants Stephanie Lifton, DVM, DACVIM and Edward Fleming, DVM, DACVIM

Leptospirosis is an important consideration when evaluating canine patients with kidney or liver irregularities because of its zoonotic potential. According to ANTECH Internal Medicine Specialist Dr. Stephanie Lifton, "When we see both liver and renal changes on the laboratory findings, leptospirosis becomes our biggest concern. Leptospirosis can present with just liver changes or just renal changes alone and should therefore be on our differential list whenever we see these changes. However, it is important to keep an open mind when pursuing these differentials so that we don't miss other diseases."

Other more common causes of renal and hepatic disease that should be investigated as well include:

- Kidney infection
- Chronic renal failure
- Pancreatitis
- Toxins/poisoning (in particular, lilies, raisins and antifreeze)
- Chronic hepatitis

When you discover evidence of liver and/or kidney disease based on physical examination and initial laboratory findings (CBC, chemistry panel and urinalysis), **which diagnostic tests should you consider next to work through your list of differentials?**

While every case is unique based on the patient's breed, signalment and history, Dr. Lifton and fellow ANTECH Internal Medicine Specialist Dr. Edward Fleming offer the following step-wise approach to group follow-up tests in a rational, cost-effective fashion.

Round:	Test(s):	Looking for:
1	<ul style="list-style-type: none"> • CBC • Serum Chemistry • Urinalysis • Fecal flotation (if GI signs) 	<p>Indicators of kidney/liver disease: Anemia, elevated liver enzymes (ALP, ALT, AST, GGT), total bilirubin.</p> <p>Elevated BUN and/or creatinine, low USG, ammonia biurate crystals, proteinuria, casts.</p>
2	<ul style="list-style-type: none"> • Urine Culture • Lepto MAT/PCR • Serum Bile Acids (if bilirubin not elevated) • Liver fluke test (Baerman) if endemic 	<ul style="list-style-type: none"> • Urinary Tract Infection • Leptospirosis • Liver dysfunction • Acute or chronic hepatitis, reactive hepatopathy
3	<ul style="list-style-type: none"> • Imaging: • Radiographs • Ultrasound (followed in some cases by abdominocentesis) <p><i>Note: Ultrasound may reveal liver morphology in general or reveal focal or multifocal lesions. Renal changes may suggest acute or chronic inflammation or perhaps focal/multifocal lesions compatible with neoplasia. Abdominal fluid accumulation may be sampled for cytologic evaluation and culture. Ultrasound evaluation of the abdomen may also reveal changes consistent with pancreatitis.</i></p>	<ul style="list-style-type: none"> • Urinary calculi • Evidence of pyelonephritis • Choleliths • Neoplasia of the urinary tract or liver • Evaluate size and texture of liver & kidneys
4	<p>Biopsy (coag panel prior) & bile culture</p> <p><i>Depending on previous findings, liver biopsy for histopathology, culture and in some cases quantitative copper determination may be indicated. Aspiration of focal/multifocal lesions in the kidneys may be performed.</i></p>	<ul style="list-style-type: none"> • Chronic active hepatitis or cholangiohepatitis • Cholangitis • Neoplasia
5	<p>Other Infectious Disease Tests</p>	<p>Depending on history of pet's tick and environmental exposure, may include Bartonella, Toxoplasma, FIP (feline), Salmonella, or Fungal infections such as Histoplasma</p>

“Every round of testing described above represents a fork in the road, where you’re going to head down a different branch in your decision tree depending on the outcome,” commented Dr. Fleming. “This chart is not meant to be all-inclusive, given the tremendously large list of differentials for liver and kidney disease, but it includes important steps or considerations we frequently review with general practitioners in our daily case consultations.”

If you have perplexing liver/kidney disease case, don’t hesitate to call ANTECH’s Consult Line and request one of our boarded Internal Medicine experts.

ANTECH® Leptospirosis Testing Do’s & Don’ts!

DO :	DON'T :
Consider leptospirosis in each patient with PU/PD, renal failure or liver disease.	Don't rely solely on MAT testing for diagnosing leptospirosis, especially in acutely ill patients.
Obtain sample(s) for PCR testing prior to initiating antimicrobial therapy	Don't rely on single MAT titers for recently vaccinated patients, since MAT baseline titers may be significantly elevated for several months post vaccination.
Consider PCR testing in any acute to subacute suspected leptospirosis case even with low to negative MAT titers (titers can lag in some patients)	Don't delay 2nd/convalescent MAT titer too long when patient is put on antibiotics (target 2-3 weeks after initial titer)
Submit blood samples for early-stage PCR testing (7-10 days post infection); submit urine samples if later.	Don't forget to have your staff and the pet owner take precautions (e.g., latex gloves, face mask and goggles) when handling the dog's urine or urine-contaminated areas if Leptospirosis is a possibility!

