Leptospiroses are thin, flexible, motile, filamentous spirochete bacteria. All cases of canine leptospirosis are caused by infection with the parasitic species *Leptospira interrogans sensu lato*, of which eight are most important to dogs and cats. The disease, which is caused by serovars most commonly incriminated (icterohaemorrhagiae and canicola) with cases of “classic” canine leptospirosis, has decreased greatly in prevalence with the development of commercial vaccines containing antigens from these serovars. However, reported clinical cases associated with other pathogenic serovars (particularly pomona, grippotyphosa, and bratislava) not included in these vaccines have seen a dramatic increase over the past 10 to 15 years. Serovars pomona and grippotyphosa have been associated with numerous cases of acute renal failure, and serovars bratislava, hardjo, and bataviae have been implicated in both hepatic and renal disease as well. Recent advances in diagnosing leptospirosis by using polymerase chain reaction have been described and may allow quicker, more accurate diagnosis of dogs affected with leptospirosis.
ban areas, along with improved recognition of these serovars with broader serologic testing.

**EPIDEMIOLOGY**

Leptospires are transmitted among animals by direct contact (i.e., infected urine, venereal secretions, animal bites, ingestion of infected tissue) and indirect contact (i.e., contaminated water, soil, food, bedding)\(^1\) (see boxes on page 608). Once outside their host, leptospires do not replicate. The occurrence of spread via infected insects is unknown.

Stagnant or slow moving warm water provides a suitable habitat for spirochetes. Outbreaks of human and canine leptospirosis have been associated with periods of heavy rainfall and flooding\(^1,11,12\). A seasonal distribution (i.e., late summer to early fall) for clinical disease in dogs has been reported, along with a significant correlation between leptospirosis cases and the average rainfall recorded 3 months before diagnosis.\(^1,11,13\) Optimal survival in soil is more likely with a neutral or slightly alkaline pH.\(^1\) In humans, most cases reported in the United States are in the warmer climates of the South Atlantic, Gulf, and Pacific coastal states, with Hawaii reporting the most cases.\(^2,12,14\)

**ROUTES OF INFECTION**

Pathogenic leptospires penetrate a host’s mucous membranes or abraded skin after the host has been exposed to contaminated urine, water, or infected animal tissues.\(^1-3\) Leptospires may be able to invade intact skin if exposure is prolonged (i.e., through the “pruned” or “wrinkled” wet skin of human hands). The duration of immersion in contaminated water is probably important regarding transmission of infection, especially if immersion results in skin maceration and exposure of the conjunctivae.\(^12\)

**PATHOGENESIS**

After entering the body, leptospires rapidly invade the bloodstream and spread to multiple sites, including the liver, spleen, kidneys, eyes, central nervous system, and urogenital tract (Figure 1). The extent of damage to internal organs is variable and may depend on the virulence of the organism and host susceptibility.\(^1\)

### Table 1. Range of Common Serovars of *L. interrogans sensu lato* That Infect Animals and Humans\(^a\)

<table>
<thead>
<tr>
<th>Species-Selected Serovars</th>
<th>Known Primary Reservoir Hosts</th>
<th>Domesticated Animals and Humans</th>
<th>Wild Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. interrogans sensu strictu</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bratislava</td>
<td>Rat, pig, horse</td>
<td>Dog, human, cow, horse</td>
<td>Mouse, raccoon, opossum, vole, fox, skunk, weasel, nutria</td>
</tr>
<tr>
<td>autumnalis</td>
<td>Mouse</td>
<td>Dog, human, cow</td>
<td>Rat, raccoon, opossum</td>
</tr>
<tr>
<td>icterohaemorrhagiae</td>
<td>Rat</td>
<td>Dog, cat, human, cow, horse, pig</td>
<td>Mouse, raccoon, opossum, fox, woodchuck, ape, skunk</td>
</tr>
<tr>
<td>pomona</td>
<td>Cow, pig, skunk, opossum</td>
<td>Dog, cat, human, horse, sheep, goat, rabbit</td>
<td>Mouse, raccoon, wolf, fox, sea lion, deer</td>
</tr>
<tr>
<td>canicola</td>
<td>Dog</td>
<td>Dog, cat, human, cow, horse, pig</td>
<td>Rat, raccoon, armadillo, mongoose, nutria, vole, jackal, skunk</td>
</tr>
<tr>
<td>bataviae</td>
<td>Dog, rat, mouse</td>
<td>Dog, cat, human, cow</td>
<td>Hedgehog, vole, armadillo, shrew, leopard</td>
</tr>
<tr>
<td>hardjo</td>
<td>Cow</td>
<td>Dog, human, pig, horse, sheep</td>
<td>Wild Bovida</td>
</tr>
<tr>
<td><em>Leptospira kirschneri</em></td>
<td>Vole, raccoon, skunk, opossum</td>
<td>Dog, cat, human, cow, pig, sheep, goat, rabbit, gerbil</td>
<td>Mouse, rat, fox, squirrel, bobcat, shrew, hedgehog, muskrat, weasel, mole, leopard</td>
</tr>
</tbody>
</table>

**Leptospirosis Research in Other Species**

The question of why some animals become ill and others do not after exposure to leptospires remains unanswered. As with Lyme disease, there appear to be many more animals with evidence of exposure than there are animals that become diseased.

In a 1998 human leptospirosis outbreak among triathletes, contaminated lake water was the source of infection. A study by Lingappa et al. examined the association between leptospirosis and gene polymorphism. The report concluded that triathletes who tested positive for HLA-DQ6 had increased risk of contracting leptospirosis after swallowing contaminated lake water compared with triathletes who tested negative for DQ6. The authors claim that this is the first documented gene–environment interaction affecting infectious disease susceptibility, which underscores the potential importance of gene–environment interactions in all species.

Of 109 small wild mammals sampled in a Connecticut study, evidence of exposure to leptospirosis was detected in 36% of raccoons, 13% of skunks, and 5% of squirrels. All opossums tested negative. In order of prevalence, serovars icterohaemorrhagiae, grippotyphosa, and canicola were found. Results suggest that common backyard wildlife species should be considered potential sources of leptospirosis in humans and dogs.

Two recently published studies have added more information on the epidemiology of leptospirosis in dogs. In the first study, 90 cases of serologically confirmed leptospirosis were evaluated retrospectively to identify the most likely infecting serovar as well as pertinent risk factors associated with infection. This study identified grippotyphosa as the most commonly incriminated serovar associated with clinical leptospirosis. In addition, male dogs were found to be at significantly greater risk of leptospirosis than were females. In the second study, 36 cases of serologically confirmed leptospirosis, along with 138 seronegative cases, were evaluated retrospectively to identify environmental risk factors for leptospirosis. This study also identified grippotyphosa as the most commonly identified infecting serovar. In addition, dogs in periurban areas were found to be at greater risk of leptospirosis, as urbanization was the most important environmental factor influencing leptospirosis occurrence. Based on the results of these studies, the authors advised consideration of leptospirosis vaccination in dogs in periurban areas, especially with vaccines including the grippotyphosa serovar.

lipopolysaccharide-like substance produced by some leptospires has been isolated that may represent an endotoxin, but its presence does not contribute to the pathogenesis of leptospirosis. The hemorrhagic phenomena seen in acute cases of leptospirosis have generally been attributed to severe vasculitis with endothelial damage rather than to consumption of coagulation factors or to thrombocytopenia. However, tissue edema and disseminated intravascular coagulation (DIC) may occur in the most severe infections.

Renal colonization occurs in most infected animals because the organism preferentially replicates and persists in renal tubular epithelial cells. Renal insufficiency and failure are the result of tubular damage, often without histopathologically significant interstitial inflammation. Renal failure develops in the subacute stage of leptospirosis as invading organisms colonize and destroy the renal epithelial cells in the convoluted tubules. Acute interstitial nephritis and parenchymal swelling ensues, decreasing renal perfusion and the glomerular filtration rate. Acute impairment of renal function may result from a decreased glomerular filtration rate caused by kidney swelling that impairs renal blood perfusion. Hypoxia secondary to renal ischemia may be the fundamental alteration causing nephropathy in patients with leptospirosis. Hence, renal function may rapidly and dramatically improve when therapy is instituted early in the course of infection. Hypovolemia and hypotension may occur in severe cases as a result of dehydration, massive hemorrhage, or altered capillary permeability secondary to vasculitis.

In dogs exhibiting hepatic involvement, profound hepatic dysfunction may occur without major histologic abnormalities because of subcellular damage caused by leptospiral toxins. The degree of icterus usually corresponds to the severity of hepatic necrosis. Chronic

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**Update in Dogs**


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active hepatitis has been a sequela of grippotyphosa infection in dogs. Extensive hepatic fibrosis and failure may result from long-standing infections.

Other body systems damaged during the acute phase of infection include the central nervous system and eyes. Infection and tissue damage in these body systems have not been well documented in dogs, but infection in these body systems can be a major sequela in humans with leptospirosis.

**CLINICAL FINDINGS**

Clinical signs of canine leptospirosis depend on the age and immunity of the host, environmental factors affecting the organisms, and virulence of the infecting serovar. A recent study showed that male dogs were at significantly higher risk of leptospirosis than were female dogs. In addition, dogs in age groups of 4 to 7 and 7 to 10 years of age were at significantly greater risk than were dogs younger than 1 year of age. Herding dogs, hounds, working dogs, and mixed-breed dogs were also at higher risk than were companion dogs, presumably because of increased outdoor exposure to contaminated water and thus higher concentrations of infective leptospiral organisms. Another study investigated clustering of reported cases of leptospirosis in the midwestern United States over the past 15 years but did not identify risk factors associated with the observed clustering.

Infection with the serovar icterohaemorrhagiae has classically been associated with either acute hemorrhagic disease or subacute liver failure and uremia. Affected dogs may be initially examined for icterus, depression, and pyrexia and exhibit signs of muscle pain. Patients with classic infections with serovar canicola are more likely to exhibit acute interstitial nephritis with less hepatic involvement. Table 2 outlines the most commonly reported historical and physical examination findings in dogs with leptospirosis.

The prevalence of leptospirosis associated with serovars icterohaemorrhagiae and canicola has decreased significantly with the development of a bivalent vaccine.
containing antigens from those serovars. Renal failure (and less commonly hepatic failure) associated with infection with serovars not present in this bivalent vaccine has become the predominant clinical syndrome in both vaccinated and unvaccinated animals. Most recent reports have described infection with serovars pomona, grippotyphosa, and bratislava.

Adin and Cowgill described 36 cases of dogs infected predominantly with serovars pomona and bratislava in which the dogs presented almost exclusively with acute renal failure without concomitant hepatic insufficiency, despite elevated liver enzyme activity in many of those cases. Birnbaum et al. reported 36 cases from New York State in which serovars pomona and grippotyphosa predominated; they also reported predominant renal involvement with less consistent hepatic involvement. Brown et al. reported 11 dogs infected with serovar grippotyphosa; 90% of these cases presented for evaluation of acute renal failure with only minor hepatic involvement. However, selection bias may be present in these studies because dogs selected for serotesting were primarily evaluated at referral institutions where leptospirosis may have been given more consideration after documentation of renal failure.

### Renal Disease

In animals presenting with renal failure secondary to leptospirosis, lethargy, depression, anorexia, dehydration, and vomiting are common historical complaints, with polyuria, polydipsia, and abdominal pain noted less commonly. Other significant physical examination findings may include fever, renomegaly, muscle pain, and icterus. Progressive renal deterioration may manifest as oliguria or anuria. Renal function in some untreated dogs that survive subacute infections may return to normal in 2 to 3 weeks, or chronic compensated polyuric renal failure may develop.
Hepatic Disease

Hepatic disease may be seen in the acute phase of infection with serovars icterohaemorrhagiae and canicola. Dogs with chronic active hepatitis or hepatic fibrosis as a sequela to leptospiral infection may eventually demonstrate overt signs of hepatic failure, including decreased appetite, weight loss, icterus, ascites, or hepatic encephalopathy. Chronic hepatitis caused by the *Leptospira australis* serovar has been documented despite vaccination with the bivalent *L. interrogans* vaccinc (containing serovars canicola and icterohaemorrhagiae) in a breeding colony of beagles.

Neurologic and Ocular Disease

The prevalence of neurologic and ocular disease in dogs with leptospirosis has not been well documented. Possible signs that could be associated with central nervous system infection (including leptospiral meningitis) include cervical and neck pain, ataxia, and seizures in severe cases. Because leptospirosis is an acute disease characterized by vasculitis, uveitis could reasonably be expected to be present in acute infection. However, in experimental canine leptospirosis, there is not much evidence for the occurrence of uveitis. Conjunctivitis and scleral injection have occasionally been reported in experimental infections.

**DIAGNOSIS**

**Clinical Laboratory Findings**

Common hematologic abnormalities in dogs with leptospirosis include leukocytosis and thrombocytopenia, with 55% of affected dogs thrombocytopenic at admission in a recent report. Leukopenia (common in the leptospiresemic phase) usually develops into leukocytosis with a left shift, with leukocyte counts of 15,000 to 45,000/µl. Platelet counts of 25,000 to 150,000/µl have been reported.

Most dogs have evidence of renal insufficiency during initial examination. Increases in serum urea and creatinine of varying severity are seen in dogs with renal failure. Electrolyte abnormalities (i.e., hyponatremia, hypochloremia, hypokalemia, hyperphosphatemia) typically parallel the degree of renal and gastrointestinal (GI) dysfunction in most cases, and hyperkalemia may be seen in terminal renal failure. Blood pH and serum total carbon dioxide are reduced in the severely ill, reflecting metabolic acidosis. Evidence of hepatic dysfunction may be seen in some dogs but is usually less apparent than renal dysfunction. Hepatic damage occurs with elevated serum alanine aminotransferase (ALT), aspartate aminotransferase, lactic acid dehydrogenase, and alkaline phosphatase (ALP), along with elevated total bilirubin concentration. Marked bilirubinuria may precede increased

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**Table 3. Reported Hematologic and Serum Biochemical Abnormalities in Dogs with Serologically Confirmed Leptospirosis**

<table>
<thead>
<tr>
<th>Hematologic/Biochemical Abnormality</th>
<th>Predominantly Serovar grippotyphosa (n = 11)</th>
<th>Predominantly Serovars pomona and grippotyphosa (n = 36)</th>
<th>Predominantly Serovars pomona, grippotyphosa, or autumnalis (n = 17)</th>
<th>Predominantly Serovar autumnalis (n = 31)</th>
<th>Predominantly Serovars pomona and bratislava (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>NR</td>
<td>33</td>
<td>18</td>
<td>45</td>
<td>NR</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>NR</td>
<td>31</td>
<td>53</td>
<td>58</td>
<td>55</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>NR</td>
<td>14</td>
<td>24</td>
<td>35</td>
<td>55</td>
</tr>
<tr>
<td>Increased creatinine</td>
<td>90</td>
<td>83</td>
<td>82</td>
<td>87</td>
<td>100</td>
</tr>
<tr>
<td>Increased BUN</td>
<td>100</td>
<td>81</td>
<td>82</td>
<td>94</td>
<td>100</td>
</tr>
<tr>
<td>High ALP</td>
<td>30</td>
<td>56</td>
<td>65</td>
<td>58</td>
<td>NR</td>
</tr>
<tr>
<td>High ALT</td>
<td>10</td>
<td>33</td>
<td>35</td>
<td>26</td>
<td>NR</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>20</td>
<td>17</td>
<td>41</td>
<td>68</td>
<td>22</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>86</td>
<td>50</td>
<td>47</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR = not reported.
Canine Leptospirosis: Epidemiology, Pathogenesis, and Diagnosis

The microscopic agglutination test remains the most common serologic method of diagnosing leptospirosis in dogs.

Serologic Testing

Microscopic Agglutination Test

The microscopic agglutination test (MAT) remains the standard, most frequently evaluated and used serologic test for canine leptospirosis. This test detects serum antibodies to leptospiral antigens. Because it requires darkfield microscopy, samples must be sent to a commercial laboratory for analysis. Leptospiral organisms grown in a liquid medium are exposed to serial dilutions of a patient’s sera; the endpoint is the highest serum dilution that causes 50% of the organisms to agglutinate. It is somewhat serovar-specific, so numerous antigens must be used to identify the serovars causing disease. Thus it is important to determine the MAT for multiple serovars common in a geographic region because there is some cross-reactivity of antibodies to leptospiral serovars and because dogs may become infected by any of the many serovars of Leptospira spp. In general, the MAT should typically include serovars canicola, grippotyphosa, hardjo, icterohaemorrhagiae, pomona, bratislava, and (potentially) autumnalis. Dogs with positive titers generally have sera that cross-react to numerous serovars; in this case, the serovar with the highest titer is interpreted as the infecting one, with the lower titers likely representing antibody cross-reaction between serovars. Brown et al. reported that in dogs naturally and experimentally infected with serovar grippotyphosa, the highest titer is usually against this
Canine Leptospirosis: Epidemiology, Pathogenesis, and Diagnosis

serovar, with lower titers to serovars bratislava and pomona. Cross-reactivity usually occurs within 6 weeks of disease onset, after which the titer of the infecting serovar predominates. A single high titer (i.e., >1:800) in an animal with compatible clinical and laboratory abnormalities is considered diagnostic, assuming recent vaccination for leptospirosis has not occurred. In this case, a diagnosis cannot be made based solely on MAT results.

Because titers can be negative in the first week to 10 days of acute illness, a second and (occasionally) third serum sample should be obtained at 2- to 4-week intervals. The magnitude of rise in titer does not always equal the severity of clinical illness. Antimicrobial therapy early in the course of disease can decrease the magnitude of rise in the antibody titer. Antibody titers often reduce fourfold over weeks to months after successful antimicrobial therapy for established infections. A convalescent titer that does not change from the initial titer suggests previous or chronic infection.

Postvaccinal titers are usually low (1:100 to 1:400), although they can occasionally rise as high as 1:3,200. The antibodies produced by vaccination (typically serovars canicola and icterohaemorrhagiae) can cross-react with other serovars, but at a low titer (<1:100) and usually for less than 3 months. Cross-reactivity between antibodies of Leptospira and Borrelia spp have been suspected but never confirmed.

ELISA
ELISAs have been used to detect IgM or IgG antibodies to leptospires. The primary advantage associated with using a single-use “screening” test such as ELISA is avoiding the need for paired serum samples (as commonly needed with the MAT) and the expertise required to conduct the MAT. IgM ELISA levels rise within 1 week of initial infection, with the maximum titer seen 14 days after infection. Increased IgG levels can be seen within 2 to 3 weeks of initial infection, with a maximal titer seen at approximately 1 month. Ribotta et al reported development of a sensitive initial screening test to detect leptospiral antibodies in canine sera while awaiting confirmation with the MAT, but it has not been made commercially available. Indirect hemagglutination assays have also been described for early diagnosis, but they, like most ELISA tests for leptospirosis, are not commercially available to practicing veterinarians.

Ancillary Diagnostics
Organism Isolation
Leptospires are very fastidious organisms; thus proper timing and technique are essential to their successful bacteriologic recovery. Organism isolation is indicated when investigating an outbreak, but it is not typically clinically practical. Samples for isolation should be obtained before initiating antibiotic therapy. Infected dogs are leptospiremic during the first 7 to 10 days of infection, but the numbers of circulating organisms decrease as serum antibody titers increase. Urine is the best fluid to culture once leptospiremia decreases, but numerous samples must be collected because of intermittent shedding of organisms. Media used for leptospiral isolation include EMJH (Ellinghausen, McCullough, Johnson, Harris), a liquid or semisolid medium containing polysorbate 80 and fetal calf serum. Culture of spirochetes from body fluids and tissues is not diagnostic when used alone because non-
pathogenic leptospires can be recovered from both fluids and tissues, including skin, of healthy dogs.\(^8\)

**Darkfield Microscopy**

Although often cited as a tool for early diagnosis of leptospirosis, directly visualizing leptospires in urine by darkfield microscopy (Figure 2) is no longer recommended because of its technical difficulty and low specificity.\(^10\) Other spirochetes (such as *Borrelia* spp) may also appear in urine. In addition, darkfield microscopy can fail to detect active infections because approximately \(10^5\) organisms/ml are required.\(^25\) Likewise, demonstrating leptospires by silver staining of renal biopsy specimens (Figure 3) has been recommended but has also lost favor because of low sensitivity and specificity.\(^10\) Immunohistochemical stains (e.g., peroxidase staining) can be used to identify spirochetes in biopsy samples. However, despite the high specificity of this method, organisms are usually present in such low numbers that this technique is considered insensitive.\(^1\)

**Fluorescent Antibody**

Fluorescent antibody (FA) techniques have been developed to identify leptospiral serovars in infected liver and kidney tissue imprints and in body fluids such as blood and urine (Figure 4). FA test results must be interpreted in light of the fact that leptospires may not be shed into urine until 4 to 10 days after the onset of clinical signs and that appropriate antibiotic therapy eliminates leptospiruria rapidly.\(^10\) Also, well-trained laboratory personnel who have access to specialized microscopy equipment must conduct these tests.

**Polymerase Chain Reaction**

Amplification of leptospiral DNA by several polymerase chain reaction (PCR) techniques has been described recently in dogs, cattle, and humans.\(^26–30\) Identifying the infective serovar is occasionally possible, and the technique is very sensitive and specific. Clinical samples that can be tested include blood, urine, aqueous humor, semen, and cerebrospinal fluid. PCR assays may have the advantage of identifying infection earlier than routine serologic testing, although the high sensitivity of the assay may result in occasional false-positive diagnoses.\(^27\) PCR testing may be a more suitable tool compared with serology in identifying subclinical shedders.\(^31\)

**Thoracic Radiography**

Although not always conducted as part of the routine workup for leptospirosis, a small review of thoracic
radiograph findings in dogs with leptospirosis has been reported. This review revealed that in all dogs, a reticulonodular pulmonary opacity was noted, affecting the entire lung in 60% of cases and mostly the caudodorsal lung field in 40%. These patterns were likely associated with pulmonary hemorrhage due to endothelial damage and vasculitis. Therefore, such findings could be misinterpreted and attributed to neoplasia, pneumonia, edema, hemorrhage secondary to DIC, and pulmonary thromboembolism. In humans with leptospirosis, pulmonary lesions are primarily hemorrhagic rather than inflammatory, with the inflammatory changes most likely due to secondary pyogenic infection. Pulmonary involvement with leptospirosis infection is reported in 20% to 70% of humans, with cough, hemoptysis, and chest pain representing the most common respiratory signs. If a dog with suspected leptospirosis exhibits respiratory signs (e.g., cough, tachypnea), thoracic radiographs should be included as part of the diagnostic evaluation while awaiting results of serologic testing.

Abdominal Ultrasound

Ultrasonographic renal findings in 20 dogs with confirmed leptospirosis have recently been reported as well. This review revealed renal abnormalities in 85% of dogs examined, with increased cortical echogenicity (75%), renomegaly (50%), and pyelectasia (45%) representing the most common abnormalities detected. In addition, a medullary band of increased echogenicity was seen in 30% of the cases, a finding reportedly seen by the authors only in dogs with leptospirosis. Thus this may be a specific sonographic finding for this disease. However, a larger group of affected dogs may need to be evaluated with abdominal ultrasound before this finding can be considered truly specific for leptospirosis.

Look for an upcoming companion article on treatment, prevention, and zoonosis.

REFERENCES

c. Changes seen on thoracic radiography may be associated with pulmonary hemorrhage.
d. Decreased cortical echogenicity is commonly noted on renal ultrasonography.
e. Renal ultrasonography may identify findings potentially specific for leptospirosis.

2. Which statement regarding the epidemiology of leptospiral organisms is incorrect?
   a. Stagnant water is a suitable habitat for spirochetes.
   b. Optimal survival in soil is more likely with a slightly acidic pH.
   c. Outbreaks of human leptospirosis have been associated with flooding.
   d. A seasonal distribution (i.e., late summer) for clinical disease in dogs has been reported.
   e. Once outside their host, leptospires do not replicate.

3. Icterus is most commonly seen with infection from serovars
   a. pomona and grippotyphosa.
   b. grippotyphosa and bratislava.
   c. autumnalis and bratislava.
   d. hardjo and pomona.
   e. canicola and icterohaemorrhagiae.
4. Which statement regarding diagnosis of leptospirosis is incorrect?
   a. Darkfield microscopy of urine is highly sensitive and specific.
   b. Clotting parameters are usually normal in affected dogs.
   c. Thrombocytopenia is not uncommon at initial presentation in affected dogs.
   d. Anorexia is a common presenting complaint in affected dogs.
   e. Many dogs present with USGs in the isosthenuric range.

5. Which statement regarding the MAT is incorrect?
   a. Postvaccinal titers are usually low (i.e., 1:100 to 1:400).
   b. The magnitude of rise in titer in paired samples does not always equal the severity of clinical illness.
   c. A single high titer (i.e., >1:800) in a dog with compatible clinical signs is usually considered diagnostic.
   d. Titer can be negative in the first 7 to 10 days of acute illness.
   e. Antimicrobial therapy early in the course of disease does not decrease the magnitude of rise in antibody titer.

6. Which statement regarding leptospiral organism isolation is correct?
   a. Samples for isolation can be obtained after initiating antibiotic therapy.
   b. The numbers of circulating organisms in bacteremic dogs increase as serum antibody titers increase.
   c. When used alone, culture of spirochetes from tissues is diagnostic for leptospirosis.
   d. Infected dogs are leptospiremic during the first 7 to 10 days of infection.
   e. A single urine sample is typically sufficient to culture leptospires from urine.

7. Which statement regarding transmission of leptospiral infection is correct?
   a. The duration of immersion in contaminated water is not important.
   b. Infected animal tissue is not a possible source of infection.
   c. Leptospires may be able to invade intact skin.
   d. Mucous membranes are not a common portal of entry for leptospires.
   e. Exposure of the conjunctivae plays no role in disease transmission.

8. Which statement regarding the pathogenesis of leptospiral infection is incorrect?
   a. The degree of organ damage may depend on host susceptibility.
   b. DIC may occur in dogs with severe infections.
   c. After leptospires enter the body, they rapidly invade the bloodstream.
   d. Renal colonization rarely occurs in infected animals.
   e. Leptospires may spread to the eyes, spleen, and central nervous system after entering the body.

9. Which statement regarding the clinical findings associated with leptospiral infection is incorrect?
   a. Outdoor dogs are at higher risk of infection than are companion dogs.
   b. Clinical signs depend on the age and immunity of the host.
   c. The virulence of the infecting serovar is of little importance.
   d. Muscle pain and fever may be present during physical examination.
   e. Conjunctivitis has been reported in experimental infections.

10. Which statement regarding renal disease associated with leptospirosis is correct?
    a. Vomiting and dehydration are extremely uncommon historical complaints.
    b. Progressive disease may manifest as anuria.
    c. Renal function never returns to normal in untreated dogs with subacute infections.
    d. Histopathologically significant inflammation must be present for renal failure to occur.
    e. Hypoxia plays no role in nephropathy associated with leptospirosis.