Practical Guide to Tick-Borne Disease

Stephen C. Barr, BVSc, MVS, PhD, Diplomate ACVIM (Small Animal), Cornell University

Profile

DEFINITION

Tick-borne diseases are caused by etiologic agents that are transmitted from ticks to dogs; such agents include *Ehrlichia, Anaplasma, Babesia, Rickettsia*, hemotropic *Mycoplasma, Francisella, Hepatozoon americanum*, and *Borrelia* species.

SYSTEMS

- Ticks cause multisystemic disease in dogs.
- Hematologic changes are common and sometimes typical (e.g., thrombocytopenia)
- Multiorgan dysfunction with associated clinical signs and clinicopathologic changes are common (*Ehrlichia, Anaplasma, Rickettsia, H. americanum*).
- Single organ dysfunction can occur (arthropathy in borreliosis).

INCIDENCE/PREVALENCE/ GEOGRAPHIC DISTRIBUTION

- Incidence and geographic distribution are dependent on distribution of the tick vector throughout the United States (**Table 1**).
- Prevalence within a geographic region is usually dependent on season and ecology of the tick vector (**Table 1**).

BREED PREDILECTION

- All dogs are susceptible to tick-borne disease.
- *Babesia gibsoni* has shown an increased incidence of infection in American Staffordshire and American pit bull terriers; disease is believed to be acquired during fighting.
- German shepherds and Doberman pinschers develop more chronic and severe forms of rickettsial diseases.

RISK FACTORS

- Major factor is exposure to ticks (young hunting dogs with extensive outdoor activity).
- Exposure depends on ecology of the tick, including the season during which it is most prevalent, infection rate of the disease in the tick species, attachment requirements of tick to transmit disease—American dog tick requires attachment > 5 hours to transmit *R. rickettsii*; ticks of the *Ixodes* species require 24 hours of attachment to transmit *Borrelia burgdorferi*; *Amblyomma maculatum* requires ingestion to transmit *H. americanum*.
- Blood transfusion—receiving blood from unscreened donors from enzootic regions is a high risk factor.
- Splenectomy predisposes dogs to clinical disease with *M. hemocanis*; a milder form of *E. canis* infection also occurs in splenectomized dogs.
- Concomitant infection with tick-borne or other diseases or a weakened immune system (from age, immunosuppressive drug therapy, or congenital defects) predisposes to more severe disease.

PATHOPHYSIOLOGY

- Depends on the disease.
  - **Rickettsials**—Vasculitis and immune mechanisms lead to endothelial damage in multiple organs, thrombocytopenia, hyperglobulinemia, and eventual bone marrow depletion with pancytopenia. Different organisms manifest with different organ involvement—for example, *E. ewingii* mainly centers on joints and the central nervous system, *A. platys* mainly affects platelets, *R. rickettsii* mainly affects endothelial cells of small arteries and venules. Incubation period is 8 to 20 days.
  - ***Babesia***—Intravascular and extravascular hemolysis with anemia. Transplacental transmission occurs.
  - ***Mycoplasma***—Splenectomy, immunosuppression from concomitant infectious diseases, or drug therapy can precipitate anemia in which immune mechanisms are also involved. Transplacental transmission does not occur.
  - ***Francisella***—Macrophages become infected and spread the organism to lungs, spleen, liver, lymph nodes, and skin where microabscess formation occurs.
  - ***Borrelia***—Few infected dogs develop clinical signs; immune mechanisms against borrelial proteins and cytokine responses are implicated in pathologic conditions of the joint. Transplacental transmission rare but can occur.
  - ***Hepatozoon***—Infected ticks are ingested; sporozoites enter blood and

continues

Ticks of Pathogenic Importance in the United States

Unengorged female of *Amblyomma americanum* (bar = 1 mm)

Unengorged female of *Amblyomma maculatum* (bar = 2 mm)

Unengorged female of *Dermacentor andersoni* (bar = 1 mm)

Unengorged female of *Dermacentor variabilis* (bar = 1 mm)

Unengorged female of *Ixodes scapularis* (bar = 1 mm)

Table 1. Geographic and Seasonal Distribution of Tick Vectors in the United States*

Tick	Etiologic Agent	Geographic Area	Season
Rhipicephalus sanguineus (brown dog tick)	*B. canis vogeli, B. gibsoni,*† *E. canis, Mycoplasma hemocanis, E. ewingii,*† *A. platys*†	Widely distributed throughout United States	Throughout year but especially spring
Dermacentor variabilis (American dog tick)	*E. canis, E. chaffeensis, Rickettsia rickettsii, Francisella tularensis, E. ewingii*†	East from ND, SD, NE, KS, OK, and mid TX; coastal CA, southwestern OR, southern WA, ID	Spring through early fall
Dermacentor andersoni (wood tick)	*Rickettsia rickettsii, Francisella tularensis*	Northwestern states (WY, ID, UT, NV, western MT and CO, eastern WA and OR)	Spring through early summer
Amblyomma americanum (Lone Star tick)	*E. ewingii, E. chaffeensis, Francisella tularensis*	Southern, southeastern, and Atlantic coastal states; moving northward (OK, KS, KY)	Spring to late fall
Amblyomma maculatum (Gulf Coast tick)	*Hepatozoon americanum*	Mainly southern states of TX, LA, MS, AL, GA, and FL but expanding north into OK, KS, and KY	Summer through early fall
Ixodes scapularis (eastern black-legged tick) *Ixodes pacificus* (western black-legged tick)	*A. phagocytophilum, Borrelia burgdorferi, Babesia* species†	Most cases occur in New England and Northeastern and Atlantic states; fewer cases occur in Midwest (WI, MI, MN, IL, MS, IA) and on West Coast	Nymphs feed during the spring; adults in early fall

**A = Anaplasma; B = Babesia; E = Ehrlichia*
†Suspected

Unengorged female of *Rhipicephalus sanguineus* (bar = 2 mm)

lymphatics via stomach mucosa then target lymphatic tissue, bone marrow, or other organs (liver, lungs, kidneys), causing hepatitis, pneumonitis, and glomerulonephritis. Transplacental transmission occurs.

SIGNS

- There is no one clinical sign typical of tick-borne diseases (**Table 2**).
- Travel history should be carefully considered (**Table 1**).
- Many infections, such as those caused by *Borrelia, Babesia, Rickettsia, Anaplasma,* and *Mycoplasma*, are asymptomatic, but may manifest with clinical signs if they occur concomitantly with other infections or immunosuppression.
- Clinical signs usually indicate multisystemic involvement, which should always prompt the clinician to place tick-borne diseases high on the differential diagnosis list.
- Some tick-borne diseases do show more specific signs, such as severe debilitation, intermittent antibiotic–nonresponsive fever, weight loss, muscle atrophy, and hyperesthesia; mucopurulent ocular discharge occurs in most dogs infected with *H. americanum*.

Diagnosis

- Identification of a tick removed from a patient with specific clinical signs can provide direction in diagnosing the specific pathogen (**Table 1, Figures**).
- Clinical signs should be correlated within the geographic area in which the patient resides or has traveled. For example, a dog from New Jersey that presents with joint pain (polyarthritis) is likely to have borreliosis; a dog from Oklahoma with joint pain probably has *E. ewingii* infection.
- Important and common clinical signs often associated with tick-borne diseases include fever, chronic weight loss, petechiae/ecchymoses, and lymphadenopathy.
- Clinicopathologic findings (**Table 2**) in conjunction with clinical signs should prompt a more specific search (serologic evaluation) for certain pathogens.
- Important and common clinicopathologic findings that should trigger the clinician to think of tick-borne diseases include thrombocytopenia (rickettsial diseases, *Babesia, Francisella*), regenerative anemia (*Babesia, Mycoplasma*), hyperglobulinemia (*Ehrlichia, H. americanum*), and profound leukocytosis (*H. americanum*).
- Many tick-borne diseases cause visible intracellular inclusions that, although rare for some agents, are definitively diagnostic if found:
  - ***Ehrlichia***—Morulae within leukocytes (*E. canis, E. chaffeensis, E. ewingii, A. phagocytophilum*) or platelets (*A. platys*).
  - ***Babesia***—Large, often in doubles, piriform organisms (*B. canis*) or smaller, single organisms (*B. gibsoni*) within red blood cells.
  - ***Mycoplasma***—Chains of organisms on red blood cell surfaces.
  - ***H. americanum***—Gamonts within neutrophils or monocytes.
- Tick-borne diseases can occur concomitantly, so use serologic testing and other pathogen-specific assays to search widely; the finding of one disease should prompt a search for others transmitted by the same tick species or others that are enzootic to a specific geographic area.
- Results of serologic tests need to be assessed in the context of prevalence, which affects the predictive value of a test.
- Cross-reaction with other pathogens is often common, especially within the rickettsial group (**Table 3**).

Treatment

- Most dogs can be treated as outpatients.
- The sooner treatment is initiated, the more favorable will be the prognosis.
- Dogs with chronic tick-borne diseases are rarely curable.
- Supportive therapy with fluids for dehydration (rickettsial diseases, *Francisella*), and blood transfusion (*Babesia, Mycoplasma*) may be indicated but will not appreciably increase platelet or leukocyte counts.

Medications

- Although there is a range of drugs for rickettsial agents, doxycycline is the most commonly used agent (**Tx at a Glance**).
- Imidocarb may be a first choice for rickettsial diseases as well at *Babesia canis* if a definitive diagnosis has not yet been made.
- Whether dogs that are serologically positive for *Borrelia* but clinically normal should be treated with doxycycline or other antibiotics is controversial. Because fewer than 5% of *Borrelia*-positive dogs ever develop clinical signs and treatment does not guarantee removal of the organism, there seems to be little rationale for antibiotic treatment in these dogs at this time.
- Early use of glucocorticoids in diseases with an immune-mediated component (rickettsial diseases, *Babesia*, *Mycoplasma*) may improve the outcome as long as they are used in conjunction with appropriate antibiotic therapy.
- Glucocorticoids used for immunosuppression in suspected cases of immune-mediated thrombocytopenia will

continues

Table 2. Clinical Signs Associated with Tick-Borne Diseases*

Etiologic Agent	Main Clinical/Clinicopathologic Findings
Ehrlichia ewingii	Lameness (polyarthritis) Fever, neurologic abnormalities (ataxia, paresis, conscious proprioceptive deficits, anisocoria, vestibular dysfunction) Mild thrombocytopenia and anemia Neutrophils in joint fluid and CSF
Ehrlichia canis	Fever, anorexia, weight loss Hemorrhagic diathesis, CNS signs, lymphadenopathy Thrombocytopenia, leukopenia, anemia Hyperglobulinemia, proteinuria
Ehrlichia chaffeensis	Anterior uveitis, lymphadenopathy, vomiting, epistaxis, erythema multiforme Thrombocytopenia, lymphocytic pleocytosis
Anaplasma phagocytophilum	Fever, anorexia Splenomegaly, hepatomegaly, CNS signs Lameness (polyarthritis) Thrombocytopenia, mild ↓ serum albumin, ↑ ALP, neutrophils in joint fluid and CSF
Babesia canis vogeli	Often asymptomatic Mild fever, uveitis, petechiae Thrombocytopenia
Anaplasma platys	Often asymptomatic Young animals: fever, lethargy, anemia, icterus, splenomegaly, lymphadenopathy, pigmenturia Anemia (regenerative), thrombocytopenia, ↑ bilirubinemia (if RBC lysis rapid), large piroplasms in RBC
Babesia gibsoni	Hemolytic regenerative anemia, weight loss, debilitation Chronic form more common—lethargy, mild fever, anemia, splenomegaly, hepatomegaly, lymphadenopathy Thrombocytopenia (variable), small single annular bodies in RBC
Mycoplasma hemocanis	Asymptomatic (nonsplenectomized dogs) Splenectomized dogs—listless but normal appetites, pale mucous membranes, regenerative anemia, chains of organisms on RBC surface
Rickettsia rickettsii	Fever, lethargy, weight loss, vomiting, diarrhea Edema/hyperemia: lips, scrotum, pinnae, prepuce, cutaneous necrosis Petechial hemorrhage: ocular, oral, genital; mucosal (epistaxis rarely) Ocular signs: scleral congestion, conjunctivitis, anterior uveitis Lymphadenopathy, joint swelling, arthralgia CNS signs: hyperesthesia, tetraparesis, ataxia, seizures Thrombocytopenia, leukocytosis + left shift, ↓ serum albumin, ↑ ALP, ↑ coagulation times, neutrophils in joint fluid and CSF
Francisella tularensis	Anorexia, listlessness, low-grade fever Subcutaneous abscesses Ocular signs: uveitis, conjunctivitis Sudden death Thrombocytopenia, leukocytosis + left shift, ↑ ALT, ↑ serum bilirubin
Hepatozoon americanum	Fever, anorexia, diarrhea, paraparesis, ataxia Bloody diarrhea (dogs in Tx) Generalized muscle atrophy, cervical/trunk rigidity (periosteal pain), chronic weight loss, hyperesthesia, stiffness, neck guarding (radiographically apparent periosteal bone proliferation) Ocular: low tear production, focal retinal scarring, hyperpigmentation, papilledema, uveitis Prolonged course: periods of remission interspersed with fever and pain Profound leukocytosis (sometimes up to 200,000 cells/µl blood) + left shift; sometimes eosinophilia (up to 20%); mild normocytic, normochromic regenerative anemia Thrombocytosis ↓ serum albumin, ↑ ALP, ↑ globulin, ↓ glucose (artifact due to high neutrophil counts), ↑ urine protein-creatine ratio (glomerulopathy)
Borrelia burgdorferi	Recurrent acute arthritis with lameness in 1 or more joints (3–4 days; responds well to antibiotic treatment) Fever, anorexia, depression, lymphadenopathy (superficial cervical and/or popliteal), complete heart block—rare CNS signs—rare Glomerulonephritis progressing to fatal renal failure Joint fluid: ↑ neutrophils in multiple joints Renal failure: uremia, proteinuria, ↑ cholesterol and phosphate levels, ↓ albumin

* ALP = alkaline phosphatase
ALT = alanine transaminase
CNS = central nervous system
CSF = cerebrospinal fluid
RBC = red blood cell
Tx = treatment

not negatively affect concurrent treatment of rickettsial agents.

Follow-up

- Response to therapy during acute stages of disease caused by rickettsial agents, *Babesia, Mycoplasma*, and *Borrelia* should occur within 24 to 48 hours.
- Most follow-up should consist of physical examination, CBC, biochemistry panel (globulins, liver enzymes, renal function), and urinalysis rather than serologic testing.
- Platelet counts should return to normal within 5 to 8 days. If not, seek another cause.
- Repeat platelet counts at the end of therapy and again in 6 months.
- Serologic testing and blood polymerase chain reaction are not effective methods of assessing the efficacy of therapy with ehrlichial diseases; reinfection is possible.
- Long-term immunity does develop after successful treatment of *R. rickettsii*.
- Therapy is seldom effective in removing the organism in most cases of tick-borne disease, so lifelong monitoring for return of clinical signs is essential. The exception is that a single dose of imidocarb is believed to eliminate the carrier state of *B. canis*.

PREVENTION

- Vaccines are only available for *Borrelia* and should only be used in enzootic areas.
- Whole-cell vaccines and recombinant

continues

Table 3. Preferred Serologic Tests for Tick-Borne Diseases*

Etiologic Agent	Serologic Diagnostic Technique of Choice
Ehrlichia ewingii	Specific serology unavailable; IFA using other rickettsial antigens (e.g., *E. canis, E. chaffeensis*) that cross-react with *E. ewingii* Western blot (rarely clinically available)—differentiates between *E. canis* and *E. ewingii*
Ehrlichia canis	Specific IFA; cross-reaction with *E. chaffeensis, E. ewingii* (not pathogenic *Anaplasma* species); titers reliable 3 wk postinfection (reliable in clinically affected dogs) SNAP-3Dx (IDEXX; an in-house ELISA antibody test)—excellent specificity and good sensitivity
Ehrlichia chaffeensis	Specific IFA; cross-reaction with *E. canis, E. ewingii* (not pathogenic *Anaplasma* spp.); titers reliable 3 wk postinfection (reliable in clinically affected dogs)
Anaplasma phagocytophilum	Specific IFA; very low cross-reaction with *E. canis, E. ewingii*, and *A. platys*; titers reliable 3 wk postinfection (reliable in clinically affected dogs)
Anaplasma platys	Specific IFA; very low cross-reaction with *A. phagocytophilum*; titers reliable 3 wk postinfection (reliable in clinically affected dogs) Polymerase chain reaction
Babesia canis vogeli	IFA; cross-reaction with other *Babesia* species Microscopic exam of stained (modified Wright's stain) blood smear; capillary blood will ↑ sensitivity
Babesia gibsoni	IFA; cross-reaction with other *Babesia* species Microscopic examination of blood smear stained with modified Wright's stain; capillary blood may ↑ sensitivity
Mycoplasma hemocanis	Microscopic examination of blood smear stained with modified Wright's stain; capillary blood may ↑ sensitivity Organisms usually present in clinically affected dogs
Rickettsia rickettsii	Micro-IFA most commonly used; may take 2–3 wk for IgG titers to increase; if first test negative in highly suspect case, repeat in 3 wk
Francisella tularensis	Microscopic agglutination Titers of 1:140 to 1:160 = recent infection
Hepatozoon americanum	Muscle biopsy (most definitive method) Gamonts in neutrophils or monocytes in blood smears (rare) ELISA is 93% as sensitive and 96% as specific as muscle biopsy
Borrelia burgdorferi	SNAP-3Dx (in house) or ELISA followed by Western blot to differentiate infected vs vaccinated

*ELISA = enzyme-linked immunosorbent assay
IFA = indirect fluorescent antibody assay

OspA vaccines induce antiOspA antibodies to develop in the host; these antibodies are passed to the tick while feeding and incapacitate the *Borrelia* organisms within the tick, thereby preventing transmission.

- Vaccination of an already infected dog is not indicated.
- Tick control is essential.
- Effective products include fipronil (Frontline—Merial), imidocloprid/permethrin combination (K9 Advantix—Bayer), and amitraz (Preventic—Virbac). Use of spot-on or oral flea control products combined with pyrethrum-based collars is also effective.
- Daily body checks for attached ticks is likely to be effective in preventing infection with tick-borne diseases, although it requires considerable effort for the owner, who must wear gloves and use tweezers to remove the ticks. Ticks need to be disposed of carefully (incinerated) to prevent dogs from eating them.
- Some have advocated the use of tetracycline (6.6 mg/kg, PO Q 24 H) as chemoprophylaxis against the rickettsial agents, *Borrelia,* and *Mycoplasma,* for dogs entering enzootic areas, although this approach may not be practical.
- Screening of blood donors or blood used for transfusion and limiting fighting behavior in pit bull terriers are important.

PROGNOSIS/FUTURE CONSIDERATIONS

- It is often difficult to separate recrudescence from reinfection in most tick-borne diseases.
- Response to therapy for cases of definitively diagnosed rickettsial agents can be expected to be approximately 70%.
- All *Borrelia* cases showing clinical signs of polyarthropathy should improve dramatically after 3 days of antibiotics—failure to do so should prompt further investigation of the joints for other causes, especially immune-mediated.
- Dogs treated for babesiosis clinically improve within 24 hours but few drugs eliminate the parasites. However, because of the balance between low parasite numbers and host immune response, hemolytic crises during recurring infection are rare.
- The long-term prognosis for dogs infected with *H. americanum* is good (**Tx at a Glance**). Relapses do occur, but a 2-year survival rate of 84% can be expected. Some dogs live for more than 5 years after diagnosis. Death usually results from glomerulonephritis and amyloidosis.
- Few reports of diagnosed *Francisella* or survival of *Francisella* have been documented in dogs.

See Aids & Resources, back page, for references, contacts, and appendices.

Tx at a glance

Etiologic Agent	Treatment of Choice
Ehrlichia ewingii, E. canis, E. chaffeensis, Anaplasma platys, A. phagocytophilum, Mycoplasma hemocanis	Doxycycline: 5 mg/kg PO Q 12 H × 28 days
Rickettsia rickettsii	Doxycycline: 10 mg/kg PO Q 12 H × 14 days
Borrelia burgdorferi	Doxycycline: 10 mg/kg PO Q 12 H × 28 days
Babesia canis vogeli	Imidocarb dipropionate: 6.6 mg/kg IM once; then repeat × 14 days
Babesia gibsoni	Atovaquone: 13.3 mg/kg PO Q 8 H *together with* Azithromycin: 10 mg/kg PO Q 24 H × 10 days
Francisella tularensis	Gentamicin: 5 mg/kg SC Q 24 H *together with* Enrofloxacin: 5 mg/kg PO Q 24 H × 10 days
Hepatozoon americanum	TMS: 15 mg/kg PO Q 12 H *together with* Clindamycin: 10 mg/kg PO Q 8 H *and* Pyrimethamine: 0.25 mg/kg PO Q 12 H × 2 weeks Maintain remission with decoquinate: 15 mg/kg PO Q 12 H for life

*TMS = trimethoprim-sulfadiazine