Babesiosis

OVERVIEW
- Babesiosis is the disease caused by the protozoal parasites of the genus Babesia. Merozoites or pirolasms are the stage that infects mammalian red blood cells.
- B. canis—a large (4–7 μm) pirolasm that infects dogs; B. canis is distributed worldwide, and there are three subspecies based on genetic, biologic, and geographic data. B. canis vogelii has been reported in the United States, Africa, Asia, and Australia. B. canis rossi is the most virulent and is present in Africa. B. canis canis has been reported in Europe.
- Some have proposed that these organisms are indeed three distinct species: B. vogelii, B. rossi, and B. canis.
- Recent studies have identified at least three genetically distinct small (2–5 μm) pirolasms that can infect dogs:
  - B. gibsoni (a.k.a. B. gibsoni [Asia])—small pirolasm that infects dogs; worldwide distribution; emerging disease in the United States.
  - B. canis (a.k.a. B. gibsoni [United States/California])—small pirolasm that infects dogs; only reported in California.
  - Babesia Theileria anae (a.k.a. Spanish dog pirolasm and B. microti-like parasite)—small pirolasm that infects dogs; reported in Spain, other parts of Europe, and most recently in the United States.
- Babesia sp. (Coco)—large pirolasm identified in spleenectomized and immune-suppressed dogs in the United States.
- Several other single-case reports of novel Babesia sp. and other pirolasms (i.e., T. equi) have been published.
- B. felis—small (2–5 μm) pirolasm that infects cats; reported in Africa.
- Cytotauxozoon felis—small pirolasm that infects cats; reported in the United States.
- Infection may occur either by tick transmission, direct transmission via blood transfer during dog bites, blood transfusions, or transplacental transmission.
- Incubation period averages about 2 weeks, but some cases are not clinically diagnosed for months to years.
- Pirolasms infect and replicate in red blood cells, resulting in both direct and immune-mediated hemolytic anemia.
- Immune-mediated hemolytic anemia is likely to be more clinically important than parasite-induced RBC destruction, since the severity of signs does not depend on the degree of parasitemia.

SYSTEMS AFFECTED
- Hemat/Lymphatic/Immune—anemia, thrombocytopenia (bleeding tendencies appear rare), fever, splenomegaly, lymphadenomegaly, vasculitis (experimental only).
- Hepatobiliary—increased liver enzymes (mild-moderate, not the sole abnormality detected).
- Neuromuscular/bone—babesiosis, weakness, disorientation, collapse (most common with B. canis rossi).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
- Any cause of immune-mediated hemolytic anemia or thrombocytopenia, including idiopathic immune-mediated hemolytic anemia or thrombocytopenia, ehrlichiosis, Rocky Mountain spotted fever, systemic lupus erythematosus, neoplasia, endocarditis, hemolytic mycoplasmosis (haemobartonellosis), and cytotauxozoonosis.
- A positive Coombs’ test does not rule out babesiosis since many animals with babesiosis are also Coombs’ positive.
- Non-immune-mediated hemolytic anemia, including microangiopathic anemia, caval syndrome, splenic torsion, DIC, Heinz body anemia, pyruvate kinase deficiency, phosphofructokinase deficiency.
- Hepatic and post-hepatic jaundice.

CBC/BIOCHEMISTRY/URINALYSIS
- Anemia—absent to severe; usually regenerative (reticulocytosis) unless signs are very acute; anemia can be severe in some cases (PCV < 10%), anemia is not present in all cases.
- Thrombocytopenia—usually moderate to severe; some animals have thrombocytopenia without anemia. Thrombocytopenia is the most common hematologic abnormality.
- Leukocyte responses are variable, with both leukocytosis and leukopenia reported.
- Hyperbilirubinemia may be present depending on the rate of hemolysis.
- Hyperglobulinemia is common in chronic infections and may be the only biochemical abnormality in some animals.
- Mildly elevated enzyme levels from anemia/hypoxia.
- Proteinuria and hypoalbuminemia (protein-losing nephropathy) may occur.
- Azotemia and metabolic acidosis secondary to renal failure have been reported with B. canis rossi and B. annae.
- Bilirubinuria is common.
- Hemoglobinuria is detected less commonly in the United States than in Africa.

OTHER LABORATORY TESTS
- Microscopic examination of stained thin or thick blood smears—can provide a definitive diagnosis; sensitivity depends on microscopic experience and staining technique; most success using a quick modified Wright stain; capillary blood may enhance sensitivity; microscopy may not accurately differentiate the species or subspecies.
- IFA—tests for antibodies in serum that react with Babesia organisms; cross-reactive antibodies can prevent the differentiation of species and subspecies; some infected animals, particularly young dogs, may have no detectable antibodies.
- PCR—tests for the presence of Babesia DNA in a biologic sample (usually EDTA anticoagulated whole blood); can differentiate subspecies and species; more sensitive than microscopy.

TREATMENT
- May require inpatient or outpatient care, depending on the severity of disease.
- Hypovolemic animals should receive aggressive fluid therapy.
- Severely anemic animals may require blood transfusion.
**Babesiosis**

**PREVENTION/AVOIDANCE**
Vaccines for *B. canis canis* and *B. canis rossi* are available in Europe, but these vaccines may not confer protection against other *Babesia* spp.

Tick control is important for disease prevention. Some recent studies suggest that using acaricides can prevent infection with *Babesia* spp. All attached ticks should be removed as soon as possible.

**MISCELLANEOUS**
All potential blood donors should test negative for the disease (preferably by 2–3 consecutive PCR tests) prior to use as a donor animal.

**ZOONOTIC POTENTIAL**
N/A

**PREGNANCY/FERTILITY/BREEDING**
Transplacental transmission

**ABBREVIATIONS**
- DIC = disseminated intravascular coagulation
- EDTA = ethylenediaminetetra-acetic acid
- FDA = US Food and Drug Administration
- IFA = indirect fluorescent antibody
- PCR = polymerase chain reaction
- PCV = packed cell volume
- RBC = red blood cell

*Suggested Reading*


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**FOLLOW-UP**

- Recheck the CBC and biochemistry as needed to monitor for resolution of anemia, thombocytopenia, icterus, and other signs.
- Most patients have a clinical response within 1–2 weeks of treatment.
- 2–3 consecutive negative PCR tests beginning 2 months post-treatment should be performed to rule out treatment failure and persistent parasitemia. IFA titers are not recommended for follow-up because titers may persist for years.
- Long-term follow-up of *B. conraze*ae, *B. microti*, or *B. felis* after treatment has not been reported.
- When a dog housed in a multi-dog kennel is diagnosed with babesiosis, all dogs in that kennel should be screened since there is a high percentage of carrier animals in kennel situations.
- Co-infection with other vector-transmitted pathogens (e.g., *Ehrlichia*, hemotropic *Mycoplasma, Leishmania*) should be considered, especially in animals that fail to respond to treatment.

**CONTRAINDICATIONS**
High doses of antibacterial drugs (imidocarb and diminazene) have resulted in liver and kidney failure.

**DRUG(S) OF CHOICE**
- Imidocarb dipropionate (FDA approved; 6.6 mg/kg SC or IM every 1–2 weeks) and diminazine aceturate (not FDA approved; 3.5–7 mg/kg SC or IM every 1–2 weeks) decrease morbidity and mortality in affected animals. They may completely clear *B. canis* infections but not *B. gibsoni* (Asia).
- Combination therapy of azithromycin (10 mg/kg PO q48h for 10 days) and atovaquone (15 mg/kg PO q8h for 10 days) is the treatment of choice and the only treatment that can potentially clear *B. gibsoni* infections in dogs. In a controlled study, 85% of dogs cleared the infection after treatment.
- A combination of clindamycin (25 mg/kg PO q12h), metronidazole (5 mg/kg PO q12h), and doxycycline (5 mg/kg PO q12h) has been associated with elimination or reduction of the parasite below the limit of detection of PCR testing. Unfortunately a defined treatment course has not been established, with treatment times ranging from 24 to 92 days.
- A combination of doxycycline (7–10 mg/kg PO q24h), enrofloxacin (2–2.5 mg/kg PO q24h), and metronidazole (5–15 mg/kg PO q24h) for 6 weeks was associated with clinical resolution in 85% of dogs but PCR was not performed to assess its effect on parasitemia.
- Metronidazole (25–50 mg/kg PO q24h for 7 days), clindamycin (12.5–25 mg/kg PO q12h for 7–10 days), or doxycycline (100 mg/kg PO q12h for 7–10 days) alone each have been reported to decrease clinical signs but not to clear infections.
- Primidapine phosphate (1 mg/kg IM, single injection) is the treatment of choice for *B. felis*.

**MEDICATIONS**

- Since the anemia and thombocytopenia are often immune mediated, immunosuppressive agents, such as prednisone (2.2 mg/kg/day PO), may be indicated in some cases that are not responding to anti-protozoal treatments alone. Prolonged immune suppressive therapy BEFORE specific antiprotozoal therapy is contraindicated.
- Antibabesial drugs (imidocarb and diminazene) can cause cholestatic signs that can be minimized by administering atropine (0.02 mg/kg SC, 30 minutes prior to imidocarb or diminazene administration).

**INTERPRETATION OF RESULTS**

- Infection: Detection of *Babesia* DNA is diagnostic.
- Indeterminate: Positive or negative results may indicate a false-negative or false-positive, respectively.
- Cure: PCR negative and no clinical signs.
- Treatment failure: Presence of *Babesia* DNA in a patient receiving treatment without clinical signs.

**OTHER LABORATORY TESTS**

- Microscopic examination of blood (peripheral smear).

**DIAGNOSIS**

- Detection of *Babesia* DNA in a peripheral smear.

**DIFFERENTIAL DIAGNOSES**

- Anemia: other causes (hemolytic, aplastic, neoplastic).
- Thrombocytopenia: other causes (immune, sequestration, bone marrow failure).
- Icterus: other causes (congenital, hepatic, obstructive).

**PROGNOSIS**

- Generally good with appropriate treatment. Recurrence within a month suggests treatment failure.

**REFERENCES**


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