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# CANINE BABESIOSIS IN THE DEVELOPED WORLD

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VECTOR BORNE DISEASE

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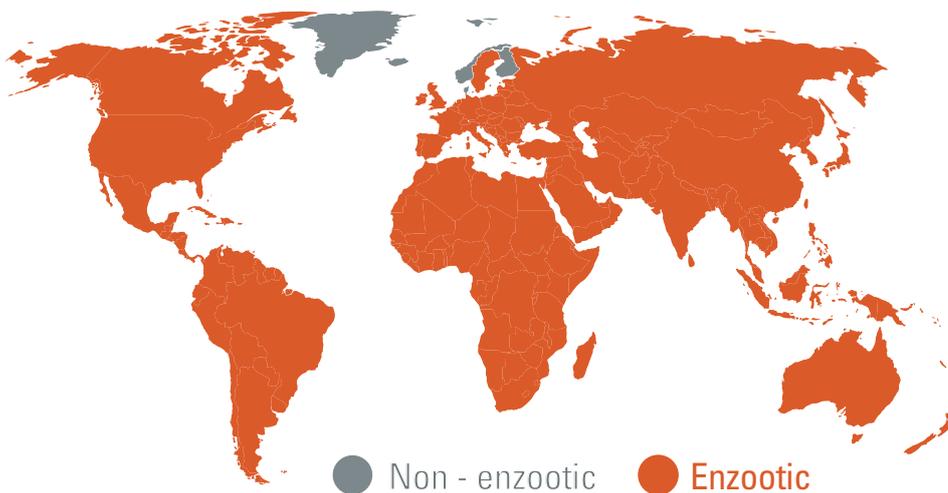
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# WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Babesiosis occurs in domesticated dogs and wild canids on every continent on earth, with the exception of Antarctica. It is generally considered the most common and widespread of all the canine vector-borne diseases. Canine babesiosis is also called piroplasmosis, when species of *Theileria* parasites are included.

**Geography, climate** and socioeconomic factors play pivotal roles in delineating the distribution and clinical picture of babesiosis in dogs.

## BABESIOSIS



### Geography

The distribution of the various clinical forms of canine babesiosis, caused by different species of *Babesia* parasites, follows closely that of their respective tick vectors, and **therefore most have well defined geographic ranges**. For example, *Babesia rossi* is confined to sub-Saharan Africa and *Babesia canis* to Europe, as a direct consequence of the enzootic distributions of their vector ticks *Haemaphysalis elliptica* and *Dermacentor reticulatus*, respectively.

### Climate

In some cases a much wider geographic distribution is recognized, as is the case with *Babesia vogeli*, transmitted by the ubiquitous brown dog tick (*Rhipicephalus sanguineus sensu lato*), which occurs worldwide in tropical, sub-tropical, and some temperate regions of developed and developing countries, and *Babesia gibsoni*, whose spread internationally is attributed to **global travel of certain breeds of dogs**, combined with a non-vectorial mode of transmission.



## WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Local transmission of *Babesia* parasites requires a susceptible mammalian host population and a competent tick vector. Clinical disease risk is greatly increased where high densities of dogs are in close contact with all tick life-cycle stages, such as in **kennels, shelters and breeding establishments**.

Ticks have evolved within distinct **climatic regions**, influenced predominately by the effects of temperature and relative humidity, underpinning the geographic distribution of the various *Babesia* species they transmit.

Studies investigating canine babesiosis epidemiology report a **seasonality** to babesiosis in dogs, coinciding with periods of tick activity and greater likelihood of exposure to infected ticks.

### Local environment

*Rhipicephalus sanguineus* (referred to as the 'brown dog tick' or 'kennel tick') is well adapted to such environments and unless stringent acaricidal strategies are employed, babesiosis (*B. vogeli*) can quickly become a problem, especially when there are large numbers of young dogs that are susceptible.



### Favorable climatic conditions

*Dermacentor reticulatus*, the vector for *Babesia canis* in Europe prefers cool and wet climates, whereas *R. sanguineus* prefers warm and humid conditions, however, this latter tick is also very adaptable, capable of establishing within centrally-heated homes in colder climates. Favorable climatic conditions may exist outside the current vector tick ranges (including in non-endemic countries), and populations of ticks may establish unexpectedly in such regions.



### Seasonality to babesiosis in dogs

Recent data from Europe investigating meteorological conditions and acute babesiosis suggested a bimodal seasonal distribution of cases, in spring and autumn. Cases in cooler climates and seasons have increased, with northward expansion of babesiosis.

- ▶ *D. reticulatus* adults are most active during winter months, from October to March if the weather is not too severe.
- ▶ *R. sanguineus* is active all year in the tropics, but with a peak of activity from May to August in temperate climates and around the Mediterranean basin.

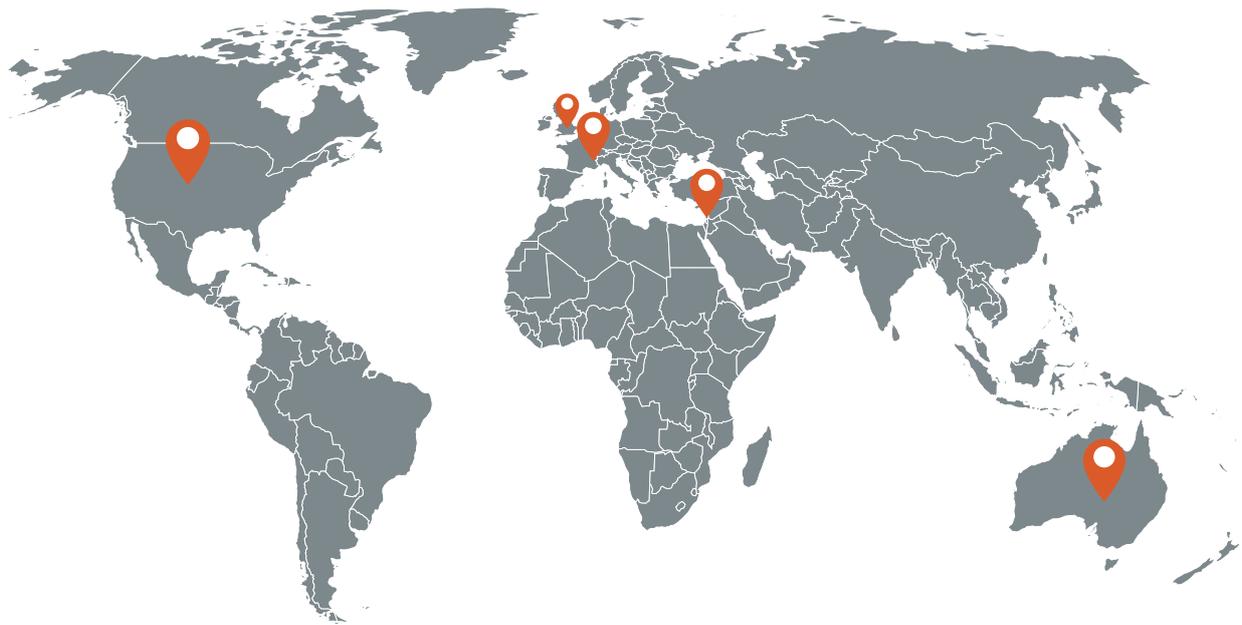


## WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Reports in recent years have described the **emergence of canine babesiosis** around the world. Possible explanations for the apparent spread of canine babesiosis include: expansion in the ranges of vector

ticks as a result of their spread by travelling dogs returning from endemic areas; climate change; increased veterinarian awareness of exotic disease; and improved availability and sensitivity of diagnostic tests.

## BABESIOSIS



### Reports in recent years

In most cases this was discovery of a known pathogen in a new area (region, country or continent), but some entirely new parasites have been described, as is the case with *Babesia vulpes* (*Babesia microti*-like) infections in Europe and North America and *Babesia negevi* in Israel.

New cases of canine babesiosis occurring well beyond previously documented ranges have been reported from Northern Europe (Northern Germany, Poland, Scandinavia), Russia, and Romania.

The first autochthonous (locally acquired infection) cases of *B. canis* infections were reported in southern parts of the United Kingdom in 2015 / 2016 and were traced to foci of infected ticks (*D. reticulatus*) in popular dog exercising areas and walking trails.

*Babesia gibsoni*, originally endemic to central and eastern Asia, especially Japan and Korea, has spread to many countries including Australia by the international movement of dogs used illegally for fighting.



# HOW DOES A DOG BECOME INFECTED?

## An introduction to the causative agent

Canine babesiosis is a tick-borne, hemotropic disease with the majority of dogs becoming infected as a consequence of a tick bite, however, dog-to-dog transmission (i.e. bypassing the tick) occurs when the blood of one individual is mixed directly with that of another, as can occur through blood exchanged **during fighting** (*B. conradae*, *B. gibsoni*), via blood transfusions and transplacentally during gestation in an infected dam.

There are currently eleven **piroplasm species** recorded in dogs. *Babesia canis*, *B. rossi*, *B. vogeli*, *B. vulpes*, *B. conradae* and *B. gibsoni*, are the best recognised and most comprehensively studied forms of canine babesiosis, however, be aware that other species may arise unexpectedly in your area, or present in dogs with travel history.

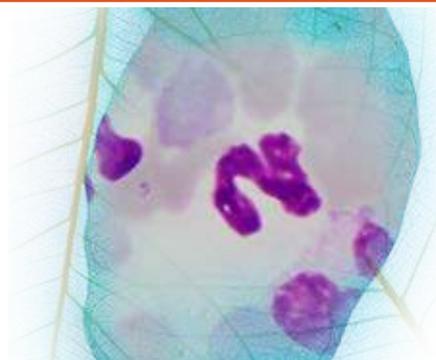
**Piroplasm species in dogs together with their tick vectors and reservoir hosts**

Size	Species	Synonyms	Vector in dog	Geographic Distribution	Comments and Reservoir (if known)
<b>Large</b>	<i>Babesia vogeli</i>	<i>Babesia canis vogeli</i>	<i>Rhipicephalus sanguineus</i>	Wide range: Tropical, subtropical, some temperate and Mediterranean regions	
	<i>Babesia canis</i>	<i>Babesia canis canis</i>	<i>Dermacentor reticulatus</i>	Europe	
	<i>Babesia rossi</i>	<i>Babesia canis rossi</i>	<i>Haemaphysalis elliptica</i> (formerly <i>H. leachi</i> )	Sub-Saharan Africa, South Africa	Jackals and other wild canids act as reservoirs
	<i>Babesia</i> spp.	Un-named <i>Babesia</i> spp., North Carolina isolate	Unknown	North Carolina, USA	
<b>Small to Intermediate</b>	<i>Babesia gibsoni</i>	<i>Babesia gibsoni</i> Asia strain	<i>Haemaphysalis longicornis</i> <i>Haemaphysalis hystricis</i>	Asia including Japan, sporadic occurrence worldwide	Outside Asia this infection is often associated with Pit Bull Terriers and other fighting dogs
	<i>Babesia conradae</i>	Originally described as <i>B. gibsoni</i>	<i>R. sanguineus</i> ? <i>Ornithodoros</i> spp.?	Western and Southern United States	Coyotes and other wild canids act as reservoirs
	<i>Babesia vulpes</i>	<i>Theileria annae</i> , <i>Babesia annae</i> , <i>Babesia microti</i> -like isolate / piroplasm / agent and the Spanish dog isolate	<i>Ixodes hexagonus</i> (putative)	Spain, Portugal, other parts of Europe and North America	Foxes are the reservoir
	<i>Babesia negevi</i>		Unknown, the argasid tick <i>Ornithodoros tholozani</i> is suspected.	Israel	First reported in 2020. Some forms are of intermediate size, larger than typical 'small' forms
	<i>Theileria</i> spp.	Un-named <i>Theileria</i> spp., South African <i>Theileria</i> spp.	Unknown	South Africa	Molecular detection only
	<i>Theileria annulata</i>		Unknown	Africa, Europe, Asia	Molecular detection only
	<i>Theileria equi</i>	<i>Babesia equi</i>	Unknown	Africa, Europe, Asia	Molecular detection only

## HOW DOES A DOG **BECOME INFECTED?**

### Piroplasm species

The application of molecular techniques (PCR & Sanger sequencing) has contributed to the identification of novel species of *Babesia* and *Theileria* in dogs globally, however, in some cases there is no concurrent clinical data, making it difficult to understand their true significance.



**Veterinarians should keep an open mind and remain vigilant as some disease syndromes and laboratory abnormalities (e.g. hemolytic anemia, thrombocytopenia) assigned an idiopathic or primary immune-mediated etiology, have actually been associated with infections. The pathogenicity and consequences of these so-called 'stealth' organisms need further investigation.**



## Vector

Canine babesiosis is vectored by hard ticks (Ixodidae) of the genera *Ixodes*, *Rhipicephalus*, *Haemaphysalis* and *Dermacentor*, although for some newly described species the vector, life cycle and reservoir hosts are unknown, and in the case of *B. negevi* the vector is suspected to be a soft tick.



## HOW DOES A DOG **BECOME INFECTED?**

### Proportion of vectors infected

The prevalence of infected ticks varies considerably between locations and tick species, as well as the method of collection. In general, the prevalence of piroplasm DNA is lower in unfed (questing) ticks collected in the environment compared with ticks that were removed from dogs:

- 🍃 In a survey conducted in Russia, 20.3% of *D. reticulatus* ticks (n = 404) removed from dogs contained *Babesia canis* DNA.
- 🍃 Yet just 1.5% ticks removed from dogs in the UK were positive for babesial DNA, and only 10% of these were of a species known to cause disease in dogs.
- 🍃 In Malaysia 1.4% of *R. sanguineus* removed from dogs contained both *B. vogeli* or *B. gibsoni* DNA.

### Reservoirs

The mammalian reservoir for *Babesia vogeli*, *B. canis* and *B. gibsoni* is the domestic dog, and these three parasites appear to have evolved and fully adapted to canine companion animals, however, transmission of these piroplasms to wild canids may occur from time to time (e.g. *B. vogeli* to dingoes in Australia).

For other ***Babesia* (and *Theileria*) species** the reverse is true – wild animals maintain the parasite within sylvatic life cycles, and ‘spill-over’ (i.e. accidental infection) occurs from time to time, presumably when domestic dogs encounter the native tick vector. This situation is analogous to the way that people become infected with zoonotic tick-borne infections.



#### ***Babesia* spp. are transovarially transmitted**

A recent study of the larvae of *Haemaphysalis hystricis* in Taiwan revealed 16.2% of larval pools were infected, confirming this tick as a competent invertebrate host and likely vector of canine babesiosis in the north of the island.

#### ***Babesia* (and *Theileria*) species**

Piroplasms whose primary (reservoir) hosts are wild canids are recognized (e.g. the red fox for *Babesia vulpes* in Europe, the red and grey foxes in North America, coyotes for *B. conradae* in North America, and the Black Backed Jackal for *B. rossi* in Africa), and for the most part these hosts do not show clinical illness when infected.



## HOW DOES A DOG **BECOME INFECTED?**

### Probability of transmission

Probability of vector-borne transmission increases with:

#### High densities of dogs and ticks in the same environment

The time from tick attachment to transmission of infectious agents is longer for *Babesia* than for some other organisms such as viruses and bacteria; it takes 48 -72 hours for *Babesia* parasites to be transmitted after tick attachment.

#### Activities that facilitate the exchange of blood between dogs

In several studies the prevalence of *B. gibsoni*, *B. conradae* and *B. vulpes* was significantly higher in American Pit Bull Terrier and related breeds than other dogs; veterinarians should consider babesiosis when presented with a dog possibly involved in fighting.

### Transmission mechanics

Tick bite is the common way that dogs become infected and transmission dynamics align with tick life cycles. For the most part, canine babesiosis vectors are 'three-host' ticks, meaning that each life cycle stage (larvae, nymphs and adults) feed on a different individual mammalian host, detaching and molting prior to their next feed.

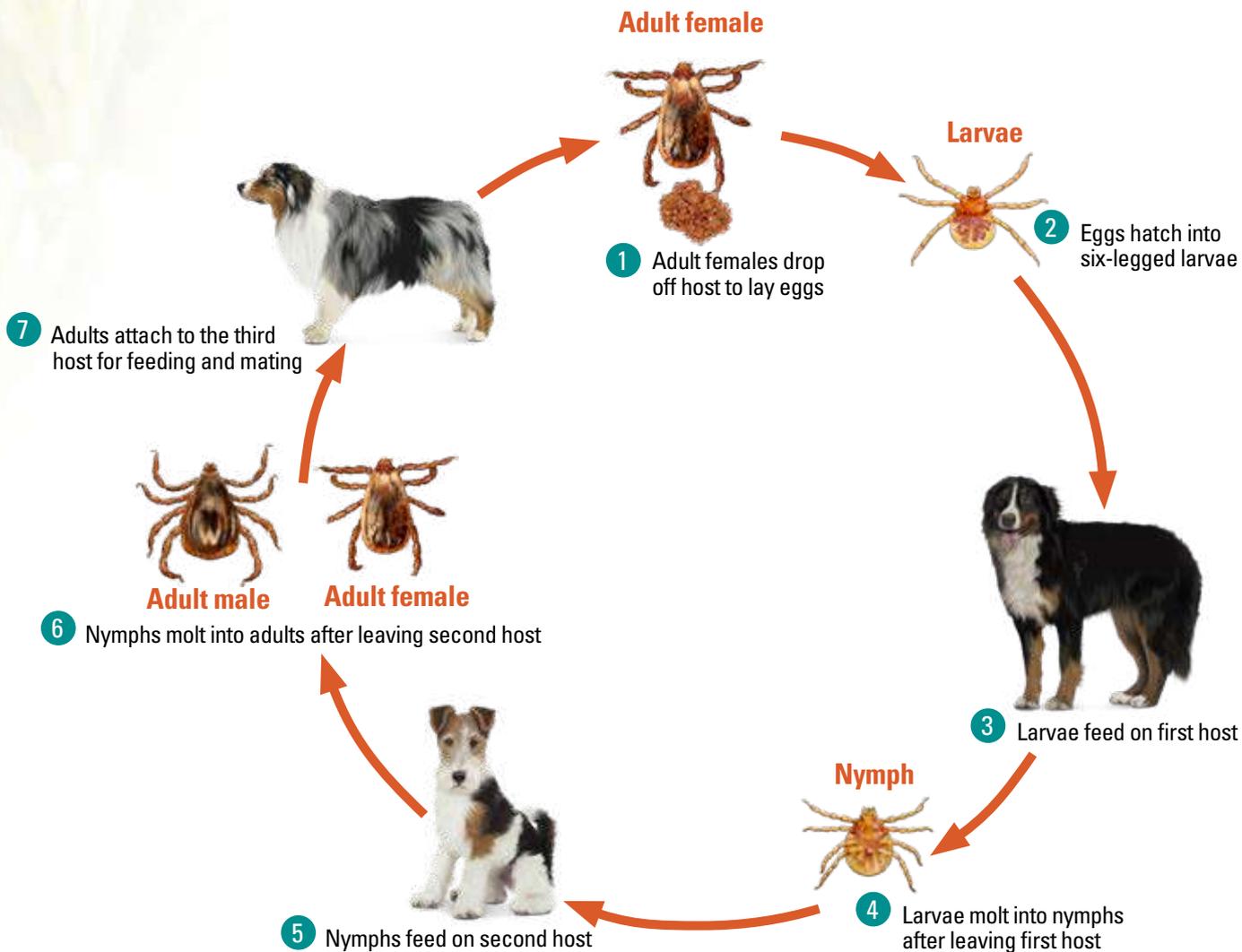
*Babesia* parasites can be transmitted in blood from an infected dog, either through bite wounds or blood transfusions, or **transplacentally**, although the documented evidence for this varies between species.



A recent case series reported that eight dogs with *B. conradae* infection were descended from a single infected dam, suggesting that transplacental transmission may be the main route of infection for this species in North America.

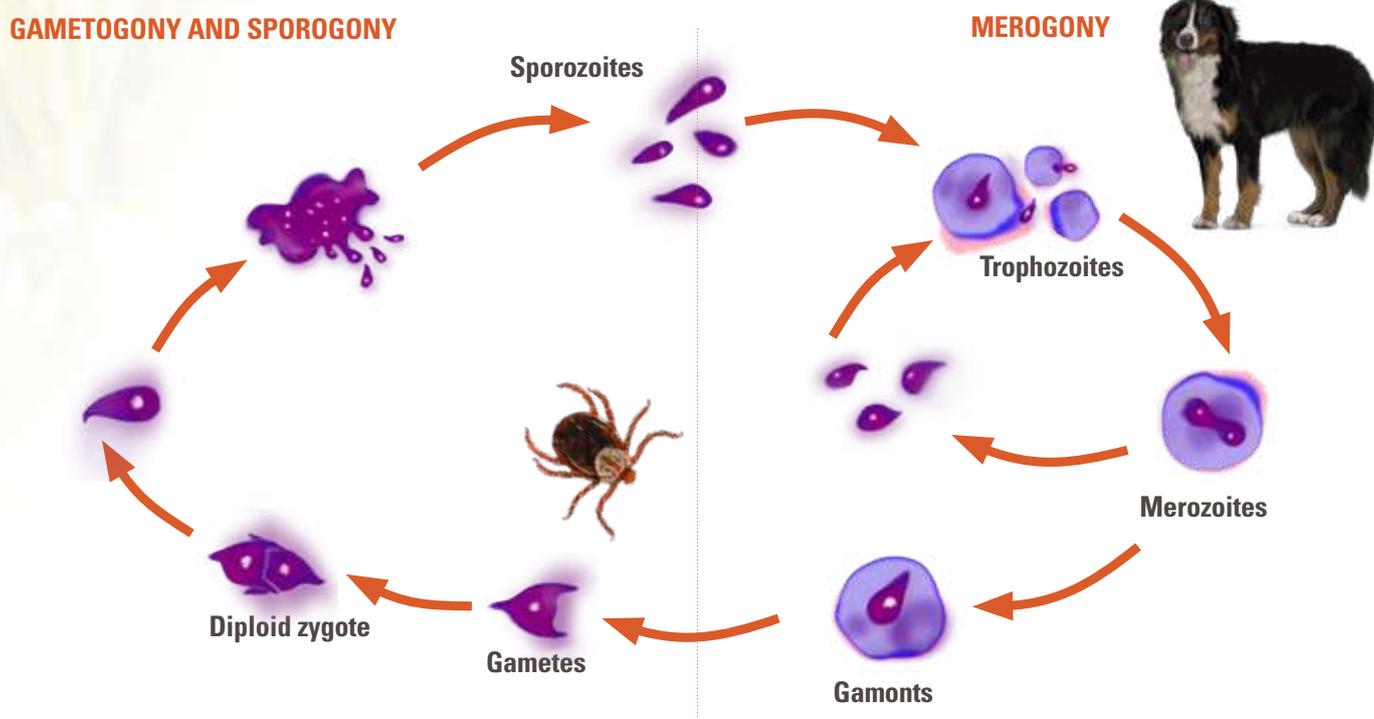
# HOW DOES A DOG BECOME INFECTED?

## Life cycle of the global tick *Rhipicephalus sanguineus*



# HOW DOES A DOG BECOME INFECTED?

## Life cycle of *Babesia canis* in the tick and dog



1

Ticks become infected when ingesting blood from a parasitemic dog.

2

The parasites then undergo sexual reproduction (sporogony) and migrate from the tick's gut prior to developing in the tick's salivary glands.

3

Sporozoites are injected into the bloodstream of a vertebrate host during the blood meal of an infected tick.

4

After invading erythrocytes they differentiate into trophozoites and divide asexually into merozoites. A few merozoites stop division and transform into gamonts.

# WHAT BEHAVIORS PUT A DOG AT RISK FOR THE DISEASE?



## Activities

Activities and environments which bring dogs into contact with ticks will provide opportunities for infection. Kennels, shelters and breeding establishments, and places where ectoparasite control is poor (e.g. in low socioeconomic locations) potentially increase tick burdens and the risk of infection.

Fighting also puts dogs at risk of contracting babesiosis, and there are occasional reports of non-fighting dogs becoming infected after being attacked by infected dogs.



**Veterinarians should ask about the potential for tick exposure and about possible recent fights when presented with dogs showing signs or laboratory abnormalities consistent with babesiosis.**



## Time of day for increased exposure

Ticks remain attached for many days and transmit *Babesia* parasites throughout the later period of engorgement and therefore there is **no known increased risk based on time of day.**



## WHAT BEHAVIORS PUT A DOG AT RISK FOR THE DISEASE?



### Breed-related risks

Entire male dogs are more at risk of babesiosis than neutered males or females, possibly as a result of increased roaming and potential exposure to ticks.

Increased prevalence of *B. gibsoni* and *B. vulpes* have been reported in breeds such as Pit Bull Terriers, Staffordshire Terriers and their crosses, and the Tosa (Japanese Mastiff) due to their use in fighting, and of *B. conradae* in coyote hunting dogs in the US.

### Diet

Diet is unlikely to play a role in this disease.



### Contact with other animals

Inter-dog aggression and blood exchange may result in babesiosis and situations where there are dense populations of dogs, together with the presence of ticks, potentially increase the risk of tick-transmitted disease.

Babesiosis is infectious but not contagious, so epidemics of the disease do not occur. In cases where the *Babesia* species reservoir host is not a pet dog, either exposure to the natural habitats of the reservoir host's ticks (e.g. for *B. vulpes*) or the other animal itself (e.g. *B. conradae*) poses a risk of infection for domestic dogs.



# CAN A DOG BE INFECTED AND **NOT SHOW SIGNS?**

## Infection vs disease

Subclinical infections occur with canine babesiosis, so potential infection in a patient without obvious disease is an important consideration, especially in endemic regions, and one that should be foremost in the veterinarian's mind. This is especially relevant for blood donation programs and the updated 2015 ACVIM Consensus Statement about canine and feline blood donor screening for infectious disease includes *Babesia* amongst organisms to test for.

### Risk of subclinical disease (frequency in the population)

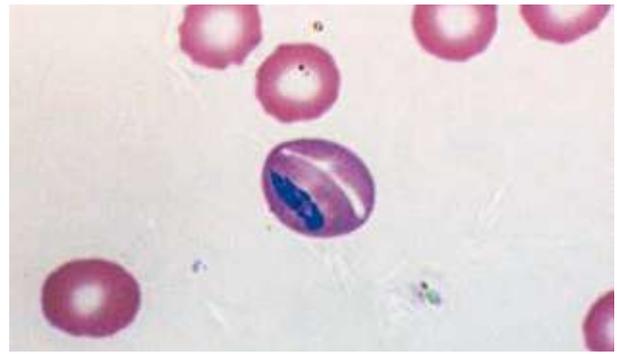
The prevalence of subclinical infections of canine babesiosis has not been studied extensively, however, dogs recovered from acute babesial infection usually become carriers, thus contributing to a population of subclinically infected dogs.

A recent report indicated a prevalence of 15.1% for *Babesia vulpes* and 2.2% for *B. canis* in clinically normal (healthy) dogs in Northwest Spain, with the prevalence even higher in dogs used for hunting.



### Risk to the population from subclinically diseased dogs

Subclinically infected dogs generally maintain a low level of parasitemia throughout their lives, in a state sometimes referred to as 'premunition'. These individuals remain capable of transmitting *Babesia* parasites to ticks, thus maintaining infection within the invertebrate reservoir population. Providing they are parasitemic, direct dog-to-dog transmission of babesiosis may also occur, despite no apparent illness in the infected dog.



### Tests that reveal a subclinically infected dog

Very low parasitemias are typically associated with subclinically infected dogs and highly sensitive tests are required to identify these infected carriers. The combination of a serological test, usually IFAT, and PCR is recommended for canine babesiosis.

For some infectious agents, a positive titer cannot distinguish between active and past infection, but most dogs infected with *Babesia* remain infected for life despite treatment, suggesting that **the presence of anti-*Babesia* antibodies most likely means the dog is infected.**

Some of these dogs are negative on a single PCR test (presumably due to very low numbers of parasites in circulation) but that the sensitivity for detection improves with subsequent PCR tests.

# WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

## Pathogenesis

The severity of babesiosis ranges from subclinical infections to widespread organ failure and death.

Infected animals develop some level of **anemia** and some develop specific organ pathologies.

Anemia occurs as a result of direct erythrocyte injury and anti-erythrocytic immune-mediated mechanisms; most dogs are also moderately to severely thrombocytopenic.

The pathogenicity of canine babesiosis depends on several factors:

- 🍃 It is primarily a function of the infecting species, with some forms of babesiosis (*B. canis* and *B. gibsoni*) considered more pathogenic than others (e.g. *B. vogeli*).
- 🍃 Other factors such as **dog age and immune status**, the presence or absence of co-morbidities (e.g. immunosuppressive states), and presence of other tick-borne infections all contribute to the clinical outcome.

Young dogs tend to be more severely affected than adults, and immunocompromised individuals may be more susceptible to babesiosis than dogs with normal immune systems.



## Early signs

Clinical signs of babesiosis are variable in the early (acute) stages of infection, however, most dogs will develop lethargy, inappetence, weakness (progressing to collapse and death in some cases), and pallor (pale mucous membranes).



Pallor (pale mucous membranes) with icterus (jaundice) in the conjunctiva and sclera of a dog with acute hemolysis caused by babesiosis.



Pallor (pale mucous membranes) with icterus (jaundice) in the oral mucosa and gums of a dog with acute hemolysis caused by babesiosis.

## WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

### Progression

Depending on the virulence of the organism and its pathogenicity, progression of the clinical picture in dogs that survive the first few days may be mild (i.e. towards recovery) or associated with worsening signs:

- 👉 Epistaxis in some dogs
- 👉 Extreme pallor usually with jaundice (icterus) observed in areas of pale skin, in the mucous membranes, and in the sclera of the eyes
- 👉 Discolored urine (hemoglobinuria or bilirubinuria)

Other dogs, especially with *B. vulpes* and *B. gibsoni* infections, may develop acute renal disease signs characterized by polyuria and polydipsia, and later oliguria. Diarrhea, effusions and weight loss can be seen as the disease progresses.

Clinicians should consider the potential for co-infections (e.g. ehrlichiosis) also contributing to the development of clinical signs in their patients.



Hemoglobinuria (shown in a collecting bag); typical of dogs with severe intravascular hemolysis associated with acute babesiosis.



Necropsy of a 9-week old pup that died of acute babesiosis (*B. vogeli*). Note hepatosplenomegaly, icterus of the tissues, dark discoloration of the renal capsule and thin watery blood in the thoracic cavity.



Dark discoloration of the renal cortex (hemoglobinuric nephrosis) in a 9-week old pup that died of acute babesiosis (*B. vogeli*).

## WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

### Prognostic factors

Severe babesiosis is characterized by a high mortality, but the prognosis is not necessarily correlated with clinical signs or parasitemia.

#### Clinicopathologic markers

There is little evidence for reliable clinical or clinicopathologic markers of prognosis in most forms of canine babesiosis, despite this being an active research area.

Non-survivors of *B. canis* infections in Europe showed significantly higher concentrations of serum lactate, triglycerides and phosphate and lower PCV, leukocyte counts, total serum protein concentrations, and thrombocyte counts compared with survivors.

Multiple laboratory analytes change significantly during severe babesiosis (notably with *B. canis* and *B. rossi* infections), including lipid profiles, biomarkers of endothelial injury and fibrinolysis, other acute phase proteins, and cardiac markers (e.g. troponins and creatinine kinase; CK).

Results from a larger number of dogs are required to provide clarity about specific values for prognostication.

#### Acute infections

From a pragmatic perspective, the prognosis for acute infections with *Babesia* spp. of high virulence (*B. canis*, *B. gibsoni*, *B. rossi*) is guarded, as complications may develop quickly.

Pups with acute *B. vogeli* infections also have a guarded prognosis as they quickly develop life-threatening anemia as their hematocrit is lower to start with than in adults.



### Recovery indications

Uncomplicated babesiosis, that is dogs without severe metabolic derangements, tend to recover quickly (within 24-48 hours) once their hematocrit is restored to normal through blood transfusion and anti-babesial drug therapy.

Signs that indicate recovery include a **brighter demeanor**, **return of appetite**, **fever reduction (if present)**, and **return of strength**.



# WHAT DIAGNOSTIC TESTS SHOULD BE RUN IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

## Rapid, table-side

Highly sensitive and regionally-appropriate molecular (PCR-based) tests can be requested at local pathology laboratories and have significantly improved the diagnostic options available to practitioners.

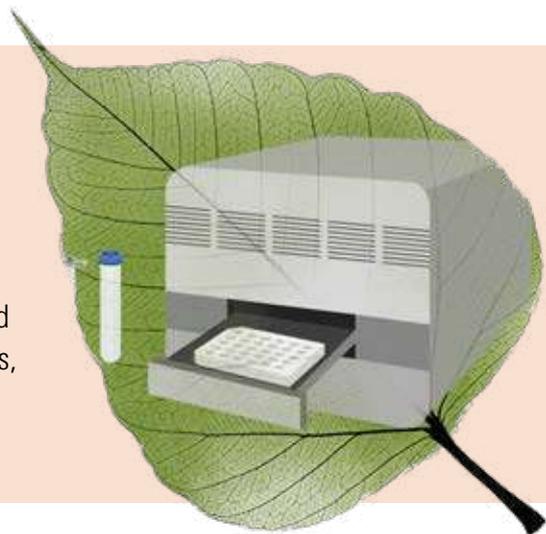
A **thorough history** is essential. The physical examination should document the associated clinical signs

Emphasize questions that raise the clinical suspicion of babesiosis: travel history (to tick endemic areas), previous tick attachments, regular use (or otherwise) of acaricidal drugs, and recent dog bite or fighting history are pertinent.

## Diagnostic laboratories

Samples should be collected for **hematology, serum biochemistry** and **urinalysis** in all cases of suspected babesiosis.

Specific vector-borne disease panels, which include PCR and serological tests, are available from some commercial laboratories, and babesiosis is usually one of the diseases tested.



## In hospital using microscope or similar equipment

Intra-erythrocytic inclusions can be seen in blood smears of dogs with **acute babesiosis**.

Microscopic evaluation of blood smears from dogs with chronic babesiosis is less likely to be successful given few parasites in the blood, however, other important blood cell characteristics may be seen, and this diagnostic step should always be performed.

Large piroplasms (i.e. *B. canis* and *B. vogeli*) accumulate in large numbers in the microvasculature of infected dogs and parasitized erythrocytes tend to be observed in higher concentrations in capillaries and in the feather area of the blood smear.

However, all piroplasms, even in acute cases, are present in the peripheral blood in relatively low numbers (parasitemias < 1-2%) and smaller piroplasms may require careful and prolonged microscope time to be seen.

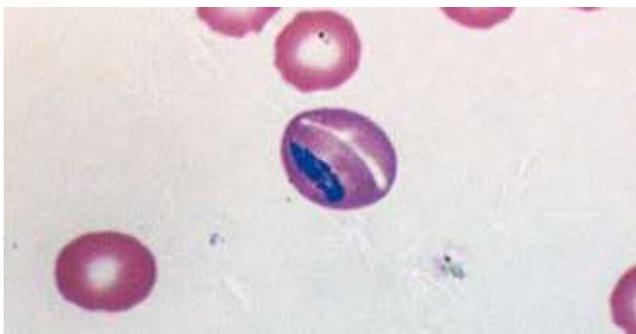
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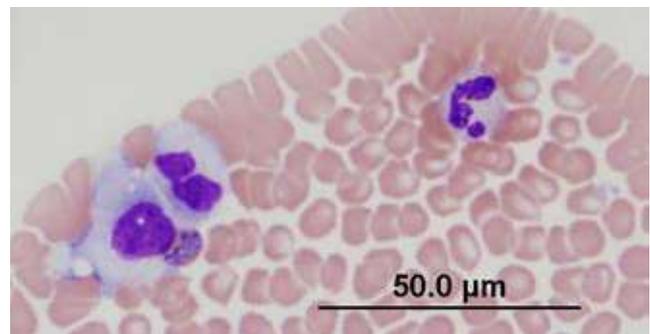
Variable morphology of large *Babesia* trophozoites (*Babesia vogeli*).



Large *Babesia* in another blood smear showing the variable morphology of *Babesia vogeli* trophozoites.



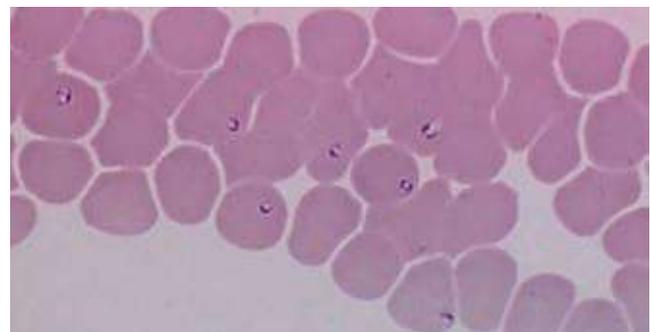
A single trophozoite of a large *Babesia* (*Babesia vogeli*).



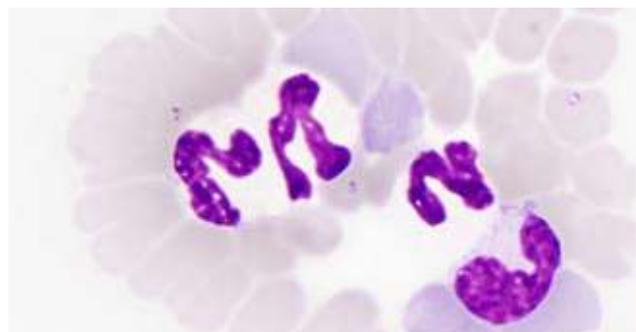
Four intraerythrocytic trophozoites of a large *Babesia* phagocytosed by a mononuclear cell.



A mononuclear cell phagocytosing an erythrocyte containing two large *Babesia* trophozoites.



Small *Babesia* (*Babesia gibsoni*) seen in flattened red blood cells in a blood smear.

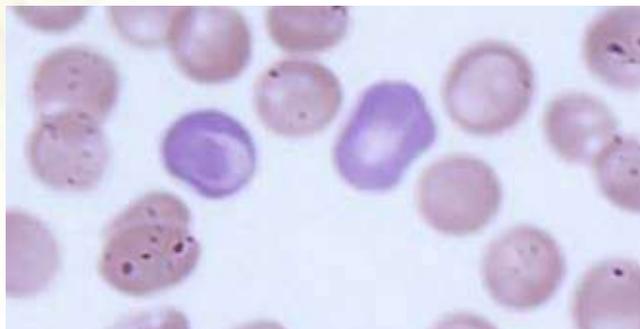


In this photo, small *Babesia* (*Babesia gibsoni*) are present in blood cells and these can also be contrasted with the size of white blood cell nuclei.

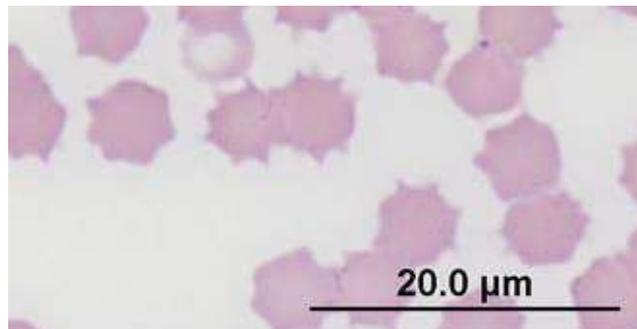
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### In hospital using microscope or similar equipment

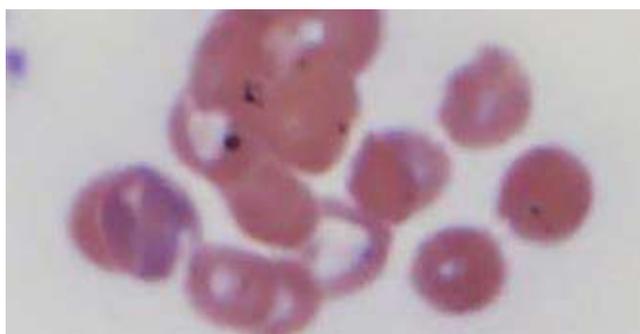
A good blood smear with minimal artefact (e.g. stain precipitate, contamination) is critical.



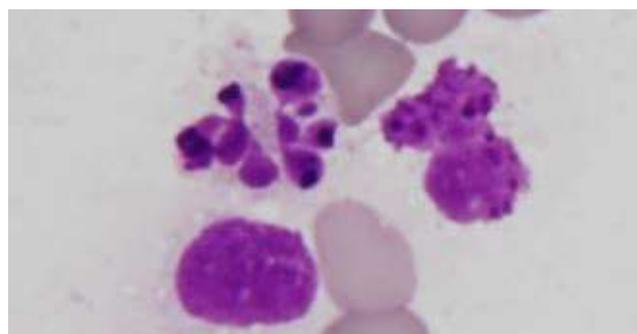
This image shows a refractile artefact that could be mistaken for *Babesia* organisms. This most commonly occurs as a result of insufficient drying time of the blood smear prior to fixing and staining.



This image shows an artefact as a result of drying that could be mistaken for *Babesia* organisms. Erythrocytes in the photo are crenated perhaps because of prolonged storage or excess EDTA.



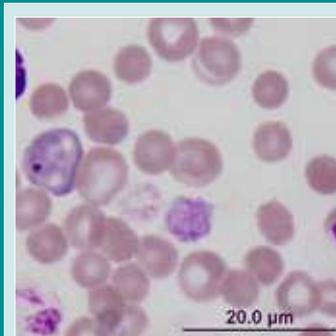
This is another image of a water drying related artefact that could be mistaken for *Babesia* organisms.



This photo shows an artefact from ageing of the slide. The leukocytes are degenerating and their pyknotic nuclei, particularly in the middle cell, could be mistaken for organisms. This blood sample was stored at room temperature for several hours before the smear was made.



**Dogs with acute hemolysis will have anisocytosis, polychromasia and plentiful Howell-Jolly bodies, which could be mistaken for parasites, but if organisms are present, they will have distinct cytological characteristics (i.e. nucleus and cytoplasm) despite a polymorphic appearance.**



This photo shows a polychromatophil (large blue-staining erythrocyte) containing a Howell-Jolly body. These are a common finding, especially in regenerative anemias, and should not be mistaken for intraerythrocytic parasites, especially *Babesia*.

## WHAT DIAGNOSTIC TESTS SHOULD BE RUN IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

### Test interpretation

Depending on the species of *Babesia* (and therefore the predominant pathophysiology), one or more organ systems may be affected during acute infection and this will be reflected in the laboratory results. Additionally, secondary injury associated with the inflammatory response, hypoxemia and shock may result in numerous metabolic derangements.

▶▶▶ The hemogram usually includes hemolytic anemia, thrombocytopenia and inflammatory leukogram in cases of acute babesiosis.

#### Anemia

Anemia severity, as measured by hematocrit or PCV, ranges from life-threatening (HCT < 20%) to moderate or mild. In severe, acute babesiosis, the hematocrit may be < 10% at presentation. Non-regenerative (normochromic, normocytic) anemia may occur with *B. canis* infections in Europe and with other forms of babesiosis (*B. gibsoni*, *B. vulpes*, *B. vogeli*) the hematological picture is usually regeneration (e.g. polychromasia, anisocytosis) in the presence of red (or icteric) plasma (hemoglobinemia or hyperbilirubinemia).

#### Thrombocytopenia and inflammatory leukogram

The degree of thrombocytopenia and white cell change varies considerably, and generalizations are difficult. Moderate to severe thrombocytopenia is reported in all forms of canine babesiosis, associated with immune-mediated injury to platelets and exacerbated clinically in some cases by a generalized vasculitis, often resulting in signs of a primary hemostatic disorder. Leukopenia with neutropenia and/or lymphopenia occurs mostly with *B. canis* yet in other forms there may be a leukocytosis with neutrophilia and monocytosis reported.

▶▶▶ Plasma total solids/protein measurements are variable; hypoalbuminemia is reported with *B. canis*, *B. gibsoni* and *B. vulpes*, and a polyclonal gammopathy has been recorded in some cases, associated with hyperglobulinemia.

▶▶▶ Serum biochemistry abnormalities reflect respective organ pathologies and acid-base disturbances associated with acute infections.

#### Serum biochemistry

Most patients have elevations in the activities of ALT, AST and ALP, and acute *B. canis* infections are associated with hypokalemia, hyponatremia, hypochloremia, hyperlactatemia and hypoglycemia. *B. gibsoni*, *B. vulpes* and *B. canis* infections frequently result in pre-renal or renal azotemia, hyperphosphatemia and proteinuria.

## WHAT DIAGNOSTIC TESTS SHOULD BE RUN IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

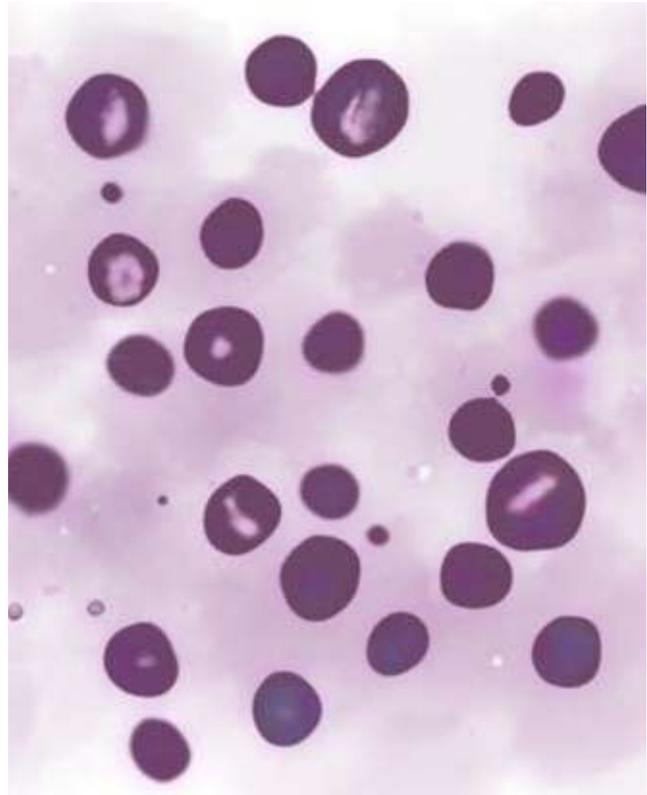
### Differential diagnoses

Differential diagnoses should include other causes of **acute hemolysis** and other causes of systemic inflammatory response syndrome (SIRS) such as acute septicemia.

#### Causes of acute hemolysis

Immune-mediated hemolytic anemia (IMHA), Heinz-body anemia (e.g. onion or garlic ingestion, drug toxicities), macro- and microangiopathies [including heartworm caval syndrome, disseminated intravascular coagulation (DIC)], and neoplastic disease (e.g. hemangiosarcoma).

Differentiation between primary IMHA and babesiosis-induced secondary IMHA can be challenging because both may demonstrate morphological characteristics of immune-mediated pathology (e.g. spherocytosis) and most cases will be Coombs' test positive. In such cases the visual presence of parasites or a positive PCR confirms the diagnosis.



### Acute vs convalescent

Death in complicated cases of babesiosis generally occurs within 24-48 hours after admission, but most cases start to recover soon after the administration of a blood transfusion, supportive fluid therapy, and anti-babesial drugs.

A rapid improvement in hematocrit is observed in dogs starting to recover, and other analytes, except for bilirubin, also quickly return to reference intervals in survivors.

Some dogs remain icteric for a week or more, and this is reflected in elevated bilirubin and orange urine for several days.



# WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

## Classes of drugs to use

Acute canine babesiosis treatment requires specific management of the metabolic derangements, with blood transfusion(s) and specific **anti-babesial drugs**.

Drugs used to treat Canine Babesiosis (Note: drugs and doses may include off-label recommendations)			
Drug Name	Recommended Dose	Susceptible <i>Babesia</i> species	Comments
Imidocarb dipropionate	5-7mg/kg SC or IM once and repeat in 14 days	<i>Babesia canis</i> <i>Babesia vogeli</i> <i>Babesia rossi</i> Large unnamed <i>Babesia</i> spp.	Pain at site of injection and nodule may develop at site of injection. Cholinergic signs controlled with atropine (0.05mg/kg SC)
Trypan blue	10mg/kg IV once	<i>Babesia rossi</i>	Tissue irritant, use as 1% solution Reversible staining of body tissues occurs
Phenamidine isethionate	15mg/kg SC once, or repeat in 24h	<i>Babesia rossi</i>	Nausea, vomiting and CNS signs are common side-effects
Pentamidine isethionate	16.5mg/kg IM repeat 24h	<i>Babesia rossi</i>	
Diminazine aceturate	3.5mg/kg IM once	<i>Babesia gibsoni</i> <i>Babesia rossi</i>	Variable and unpredictable toxicity CNS signs may be severe May contain antipyrone
Atovaquone and Azithromycin combination	13.3mg/kg PO q8h (atovaquone) and 10mg/kg PO q24h (azithromycin), together for 10 days	<i>Babesia gibsoni</i> <i>Babesia vulpes</i> <i>Babesia conradae</i>	May contain proguanil in addition to atovaquone which may induce vomiting in dogs
Buparvaquone and azithromycin combination	5mg/kg IM twice 48h apart (buparvaquone) and 10mg/kg PO q24h (azithromycin), together for 10 days	<i>Babesia vulpes</i>	

- Anti-babesial drugs encompass aromatic diamidines, naphthoquinones, artemisinin derivatives and antibiotic classes. There are dissimilar drug susceptibilities, and an important consideration for the appropriate treatment of canine babesiosis is **early identification of the *Babesia* species**.
- Despite the worldwide importance of this disease there are relatively few robust studies on anti-babesial drug efficacy. Treatment protocols for canine babesiosis should not be expected to eliminate the pathogen.
- Combinations of tetracyclines (minocycline and doxycycline), metronidazole, clindamycin and enrofloxacin are used for atovaquone/azithromycin-resistant *B. gibsoni* infections, with variable efficacy. Without further data these combinations cannot be recommended.

### Identification of the *Babesia* species

*Babesia* species identification is achieved accurately through PCR and sequencing, however, local knowledge will guide the veterinarian in endemic regions.

The morphological appearance of the parasites can inform therapeutic decisions, because most large species (*B. canis*, *B. vogeli*, the unnamed large *Babesia* spp. in the USA, and *B. rossi*) respond favorably to imidocarb dipropionate, whereas smaller species (*B. gibsoni*, *B. vulpes*, *B. conradae*) are often treated with atovaquone and azithromycin.

## WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

### Monotherapy or combination therapy

The efficacy of mono-versus combination drug therapy for canine babesiosis needs further investigation.

**Atovaquone/Buparvaquone +  
Azithromycin**



The best-recognized therapeutic combinations are atovaquone or buparvaquone with the macrolide antibiotic azithromycin for the treatment of *B. gibsoni* and *B. vulpes*, respectively.

**Diminazine aceturate +  
Imidocarb dipropionate/  
Clindamycin/Metronidazole**



Other combinations such as diminazine aceturate with imidocarb dipropionate, with clindamycin and/or metronidazole have shown efficacy in a few cases in uncontrolled studies.

### Management of co-infections

Co-infections such as monocytic ehrlichiosis and anaplasmosis (*A. platys*) are common, especially with *B. vogeli* and should be treated with doxycycline (10 mg/kg q24h PO x 28 days).



### Supportive treatment strategies

Supportive treatment restores adequate tissue oxygenation by correcting anemia, dehydration and electrolyte disturbances, if present.

#### Blood transfusions

Blood transfusions restore and maintain the PCV while anti-protozoal drug(s) start to take effect.

#### Fluid therapy

As with all anemic animals, fluid therapy should be used judiciously and is primarily indicated if the patient is also dehydrated or anorectic.

## WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

### Oxygen therapy

Oxygen therapy in anemic patients is of questionable benefit unless concurrent lung pathology is affecting respiratory function and oxygen exchange.

### Good nursing support

Good nursing support (warmth, nutrition) should also be provided.

### Treating tick infestations

In addition, dogs with tick infestations should be treated immediately with a rapid-acting acaricidal agent and individual ticks removed and destroyed to reduce the risk of ticks contaminating the hospital environment.



## Monitoring for response to treatment

Hematocrit, blood gases, electrolytes and renal function should be assessed at least daily during acute infection.



# ARE OTHER PETS OR PEOPLE IN THE HOUSE AT RISK?

## The risks to people from an infected/sick dog

Babesiosis is not contagious, in the sense that it is not readily transmitted between dogs although parasites may be transmitted through bite wounds (blood exchange). The presence of an infected dog indicates there is a risk to other dogs in the household from tick bite transmission.

## Can cats get this infection/disease?

No currently recognized agent of canine babesiosis infects cats.

- A *Babesia* parasite closely related to *B. canis* (sensu lato) may infect cats but is a distinct sub-species named *B. canis* subsp. *presentii*

## Other public health considerations

Canine babesiosis is not known to be zoonotic; although, dog owners can face other risks from tick bites.



# WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

## How to avoid the vector

There are recent remarkable advances in the types and range of acaricidal drugs available, with **new compounds** replacing earlier generations of drugs that were potentially more toxic to the mammalian host.

The isoxazoline family of drugs, a class of parasiticides that are potent inhibitors of gamma-aminobutyric acid-gated chloride channels (GABACs), are available for companion animal markets worldwide. These drugs induce a spastic paralysis in parasites leading to starvation and death.

Increasing owner compliance with treatment recommendations is an important goal in acaricide treatment.

## General thoughts on preventive treatments

Regular acaricidal and tick prophylactic treatment is recommended in endemic areas, together with avoidance of dog fighting and pre-screening of blood donors.

Ensuring owner compliance is a key goal for preventive treatment.

## Is there a vaccine?

A vaccine for *B. canis* is available in Europe and appears to have reasonable **efficacy for preventing** infection with this form of babesiosis.

The protective effect is not transferable to other species of *Babesia*.

## Is routine testing recommended?

### Blood donors



Routine testing for the safety and suitability of dogs to act as blood donors is recommended.

### Other animals



Routine testing of other apparently healthy dogs is of no value and chronically infected dogs are difficult to detect, even using PCR. Treatment is not generally curative, therefore routine testing may not offer much value.



# WHAT DOES THE FUTURE LOOK LIKE?

## What are the changes being seen with the disease?

The geographic range of canine babesiosis appears to be expanding into new regions, including northward extension into cooler climates of Europe and North America.

Autochthonous *B. canis* cases are now present in the United Kingdom and veterinarians everywhere need to be ever-vigilant for the unexpected appearance of vector-borne diseases in day-to-day clinical practice.

Wide application of molecular diagnostic techniques makes it inevitable that new species will be discovered, and some could be significant pathogens. Countering this increasing disease burden of disease is the availability of novel and highly effective acaricidal drugs.

## Is the risk of disease increasing?

The disease risk is increasing and canine babesiosis is being diagnosed in areas thought to be disease free.

## Has resistance to prevention or reduced treatment effect been seen?

Resistance to atovaquone associated with cytochrome b gene mutations is reported for *B. gibsoni* and may occur with other forms of 'small' *Babesia* parasite. There are insufficient reports to be confident of this, or whether resistance occurs with other anti-babesial drugs.

Cure (organism elimination) is rarely achieved, and it is likely that a degree of innate resistance exists in most *Babesia* spp. for the drugs that are prescribed. Tick resistance is reported for older acaricidal drugs; however, newer generations of tick treatments are delivering a high level of efficacy.

# FURTHER READING

## Bibliography

- 🍃 Baneth G, *et al.* 2004. Infection with a Proposed New Subspecies of *Babesia canis*, *Babesia canis* subsp. *presentii*, in Domestic Cats. *Journal of Clinical Microbiology*. 42: 99-105.
- 🍃 Baneth G. 2018. Antiprotozoal treatment of canine babesiosis. *Veterinary Parasitology*. 254:58-63.
- 🍃 Baneth G, *et al.* 2020. A new piroplasmid species infecting dogs: morphological and molecular characterization and pathogeny of *Babesia negevi* n. sp. *Parasites and Vectors*. 13:130.
- 🍃 Barash NR, *et al.* 2019. Prevalence of *Babesia* spp. and clinical characteristics of *Babesia vulpes* in infection in North American dogs. *Journal of Veterinary Internal Medicine*. 33: 2075-2081.
- 🍃 Dear JD, *et al.* 2017. *Babesia conradae* infection in coyote hunting dogs infected with multiple blood-borne pathogens. *Journal of Veterinary Internal Medicine*. 32:1609-1617.
- 🍃 Irwin PJ. 2009. Canine babesiosis: from molecular taxonomy to control. *Parasites and Vectors*. 2 Supplement 1 S4.
- 🍃 Schnittger L, *et al.* 2012. *Babesia*: a world emerging. *Infection, Genetics and Evolution*. 1:1788-1809.
- 🍃 Solano-Gallego L, Baneth G. 2011. Babesiosis in dogs and cats – expanding parasitological and clinical spectra. *Veterinary Parasitology*. 181:48-60.
- 🍃 Solano-Gallego L, *et al.* 2016. A review of canine babesiosis: the European perspective. *Parasites and Vectors*. 9:336.
- 🍃 Wardrop KJ, *et al.* 2016. Update on Canine and Feline Blood Donor Screening for Blood-Borne Pathogens. *Journal of Veterinary Internal Medicine*. 30:15-35.
- 🍃 Wright I. 2018. Babesiosis in Essex: monitoring and learning lessons from a novel disease outbreak. *Parasites and Vectors*. 11:132.



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VECTOR BORNE DISEASE

