# TICK-BORNE RICKETTSIAL DISEASES

VECTOR BORNE DISEASE

MSD Animal Health

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She is past-president of both the American Association of Veterinary Parasitologists and the Companion Animal Parasite Council and currently serves as Co-Director of the National Center for Veterinary Parasitology. Susan is an outstanding teacher and has received numerous class, college, and national teaching awards, including two Excellence in Teaching – Basic Sciences awards from the Student American Veterinary Medical Association. In 2017 she received the Distinguished Veterinary Parasitologist Award from the American Association of Veterinary Parasitologists.

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# WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

## Geography

A variety of rickettsial agents cause disease in dogs and the distribution of the group is worldwide. The geographic distribution of each individual pathogen generally follows that of the key tick vectors and reservoir hosts, with greater infection risk found in areas with more intense vector tick populations.

## Local environment

### Domestic cycles

Rickettsial tick-borne pathogens supported by domestic cycles use dogs as the principal reservoir host and are primarily transmitted by **brown dog ticks (*Rhipicephalus* spp.),** which prefer to feed on dogs as larvae, nymphs, and adults. Accordingly, disease caused by **these agents** is often identified in kennels or seen in areas with dog overpopulation and a failure of tick control on dogs.

- *Anaplasma platys*
- *Ehrlichia canis*
- *Rickettsia conorii*
- *Rickettsia rickettsii* (dog-associated)
- Other spotted fever group *Rickettsia* spp.

### Sylvatic cycles

**Rickettsial pathogens** harboured by sylvatic cycles are more often found infecting and causing disease in dogs that have contact with natural areas with ample populations of both wildlife reservoir hosts and wildlife-associated tick vectors.

- *Anaplasma phagocytophilum*
- *Ehrlichia chaffeensis*
- *Ehrlichia ewingii*
- *Rickettsia rickettsii* (wildlife-associated)
- Other spotted fever group *Rickettsia* spp.

## Favourable climate conditions

Maintenance cycles for various tick-borne rickettsial agents are found in many different climates around the world **(Table 1a and 1b).**

- Brown dog ticks thrive in high temperatures and may be found in both tropical, humid regions and more arid environs, and pathogens transmitted by brown dog ticks are often more common in warmer regions.
- In contrast, the sylvatic cycles which support other rickettsial pathogens vary more widely, from warmer climates where *Amblyomma* spp. thrive to the more temperate areas favoured by *Ixodes* spp. and *Dermacentor* spp. ticks.

# WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

**Table 1a. Maintenance cycles of common tick-borne rickettsial pathogens: DOMESTIC CYCLE**

| Pathogen | Disease name | Primary tick vector(s) | Proportion of ticks infected | Reservoir host(s) | Region found |
|---|---|---|---|---|---|
| *Anaplasma platys* | Anaplasmosis | *Rhipicephalus* spp. | <1% to >10%[A] | Dogs | Worldwide, but more common in warmer areas that support large numbers of brown dog ticks |
| *Ehrlichia canis* | Canine monocytic ehrlichiosis, tropical canine pancytopenia | *Rhipicephalus* spp. | <1% to >10%[A] | Dogs | Worldwide, but more common in warmer areas that support large numbers of brown dog ticks |
| *Rickettsia conorii* | Mediterranean spotted fever; also known as Boutonneuse fever, Marseilles fever, Israeli spotted fever | *Rhipicephalus* spp. | <1%[B] | Dogs | Mediterranean countries, sub- Saharan Africa, Asia |
| *Rickettsia massiliae* | Rickettsiosis | *Rhipicephalus* spp. | <1% to >10%[A] | Dogs | Worldwide, but more common in warmer areas that support large numbers of brown dog ticks |
| *Rickettsia rickettsii* | Rocky Mountain spotted fever, Brazilian spotted fever | *Rhipicephalus* spp. | <1% [B] | Dogs | Southwestern USA, Mexico, Central and South America |

**Table 1b. Maintenance cycles of common tick-borne rickettsial pathogens: SYLVATIC CYCLE**

| Pathogen | Disease name | Primary tick vector(s) | Proportion of ticks infected | Reservoir host(s) | Region found |
|---|---|---|---|---|---|
| *Anaplasma phagocytophilum* | Granulocytic anaplasmosis | *Ixodes* spp. | 2–5% | Small mammals | Northeast, upper Midwest, and West Coast of USA; Canada; Northern Europe |
| *Ehrlichia chaffeensis* | Monocytic ehrlichiosis | *Amblyomma americanum* | 2–5% | White-tailed deer | Southern and Eastern USA |
| *Ehrlichia ewingii* | Granulocytic ehrlichiosis | *Amblyomma americanum* | 2–5% | White-tailed deer, wild canids | Southern and Eastern USA |
| *Rickettsia rickettsii* | Rocky Mountain spotted fever, Brazilian spotted fever | *Dermacentor* spp. *Amblyomma sculptum* *Amblyomma aureolatum* | <1%[B] | Small mammals | North, Central, and South America |

[A] Prevalence is usually low in the absence of active infection in dogs in the area. However, when actively feeding ticks are removed from infected dogs, prevalence of infection in ticks is higher either due to the presence of infected blood in feeding ticks or due to ongoing transmission on the premise.

[B] High prevalence of infection (up to 100%) has been noted during an outbreak and may be supported, in part, by transovarial transmission in tick populations. However, *R. rickettsii* and *R. conorii* have been shown to reduce tick fitness and survival and prevalence in the overall tick population is generally very low.

## Evidence of disease spread

Changes in climate and habitat in recent decades, as well as increases in wildlife populations and point-source introduction of infested animals, are together resulting in the spread of both domestic and sylvatic maintenance cycles to new areas and an overall increase in both infection prevalence in dogs and cases of disease.

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

## An introduction to the causative agent(s)

Tick-borne rickettsial agents important for canine health are minute, obligately intracellular Alphaproteobacteria in the order Rickettsiales.

The genomes of members of the Rickettsiales are reduced (~ 1.1–1.3 Mb) and almost all these organisms are adapted to arthropod vectors for transmission between hosts.

Important pathogens are found in two main families:

- The Rickettsiaceae, which includes the genus *Rickettsia*.
- The Anaplasmataceae, which includes the genera *Anaplasma* and *Ehrlichia*.

## Vector (life cycle)

Those pathogens maintained in domestic, dog-focused maintenance cycles use brown dog ticks as the primary vector and domestic dogs as the principal reservoir host.

Pathogens maintained in wildlife that only occasionally spill over to infect and cause disease in dogs have more varied maintenance cycles.

Although ticks provide the natural means of infection, rickettsial agents are occasionally transmitted by blood transfusion or direct contact with blood contaminated materials. Important tick vectors, prevalence of infection in ticks, and key reservoir hosts are listed in **Table 1a and 1b**.

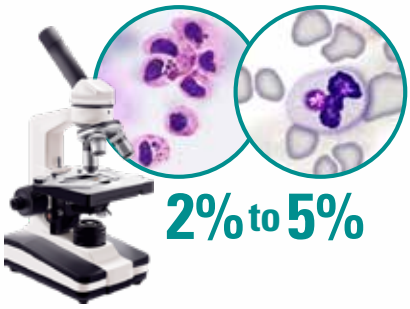
## Proportion of infected vectors

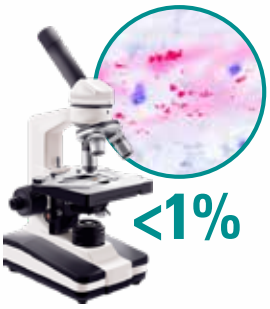
**Prevalence** of rickettsial infection **in brown dog ticks** is usually low **(not detected or <1%)** in the absence of active infection in dogs in the area **(Table 1a and 1b).**

However, when feeding *Rhipicephalus* spp. ticks are removed from infected dogs, particularly **when active transmission** is ongoing in the area, prevalence of tick infection can be much higher **(5% to >20%)**.

For rickettsial pathogens maintained in sylvatic cycles:

- Prevalence of ***A. phagocytophilum*** or ***E. ewingii infection*** in questing ticks removed from vegetation is usually **2% to 5%** although higher percentages have been reported in some areas with intense transmission pressure.
- The prevalence of ***R. rickettsii* infection** in wildlife-associated ticks is usually very low **(<1%)** although non-pathogenic or **less pathogenic *Rickettsia* spp.** (e.g. *R. amblyommatis, R. andeanae, R. montanensis*) may be commonly found, with 20% to >50% of ticks infected. Transovarial maintenance of *Rickettsia* spp. in tick populations contributes to the high prevalence seen in some areas.




## Reservoirs

For those rickettsial agents that cycle primarily between brown dog ticks and domestic dogs, asymptomatic or symptomatic rickettsemic dogs can be a key reservoir host to support continued infection of the local tick population.

Pathogens are maintained in wildlife for the sylvatic cycles **(Table 1a and 1b).** Common wildlife reservoir hosts include:

### Small mammals:

*R. rickettsii, A. phagocytophilum*

### White-tailed deer:

*E. chaffeensis, E. ewingii*

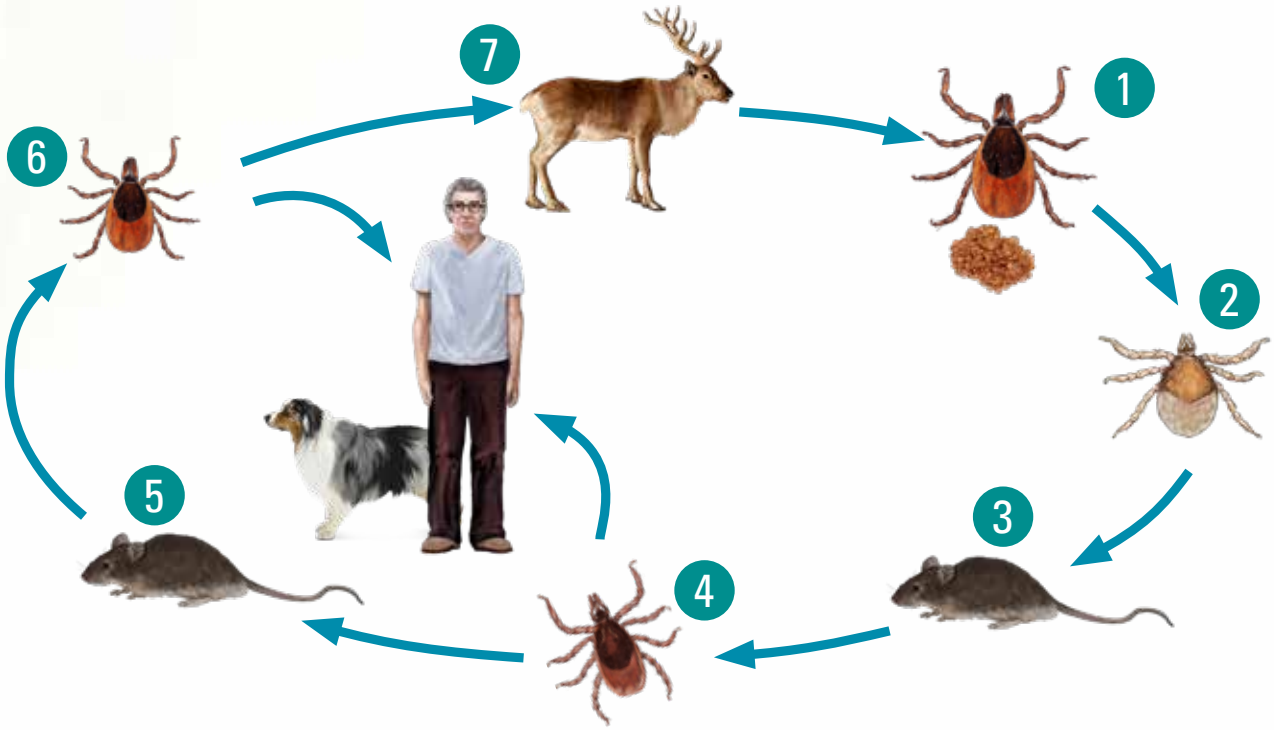
### Wild canids:

*E. ewingii*

Deer and other wild ruminants also may be important reservoirs for supporting adult stages of ticks that transmit rickettsial infections even though the pathogens themselves are maintained primarily in the small mammal hosts that support the immature tick stages.

# Sylvatic life cycles of example **rickettsial agents**

## Transmission cycle for maintenance of *Anaplasma phagocytophilum*




**1** Adult females drop off the host to lay eggs.

**2** Eggs hatch into six-legged larvae.

**3** Larvae attach to and feed on the first host and may acquire *A. phagocytophilum.*

**4** Larvae molt into nymphs after leaving the first host.

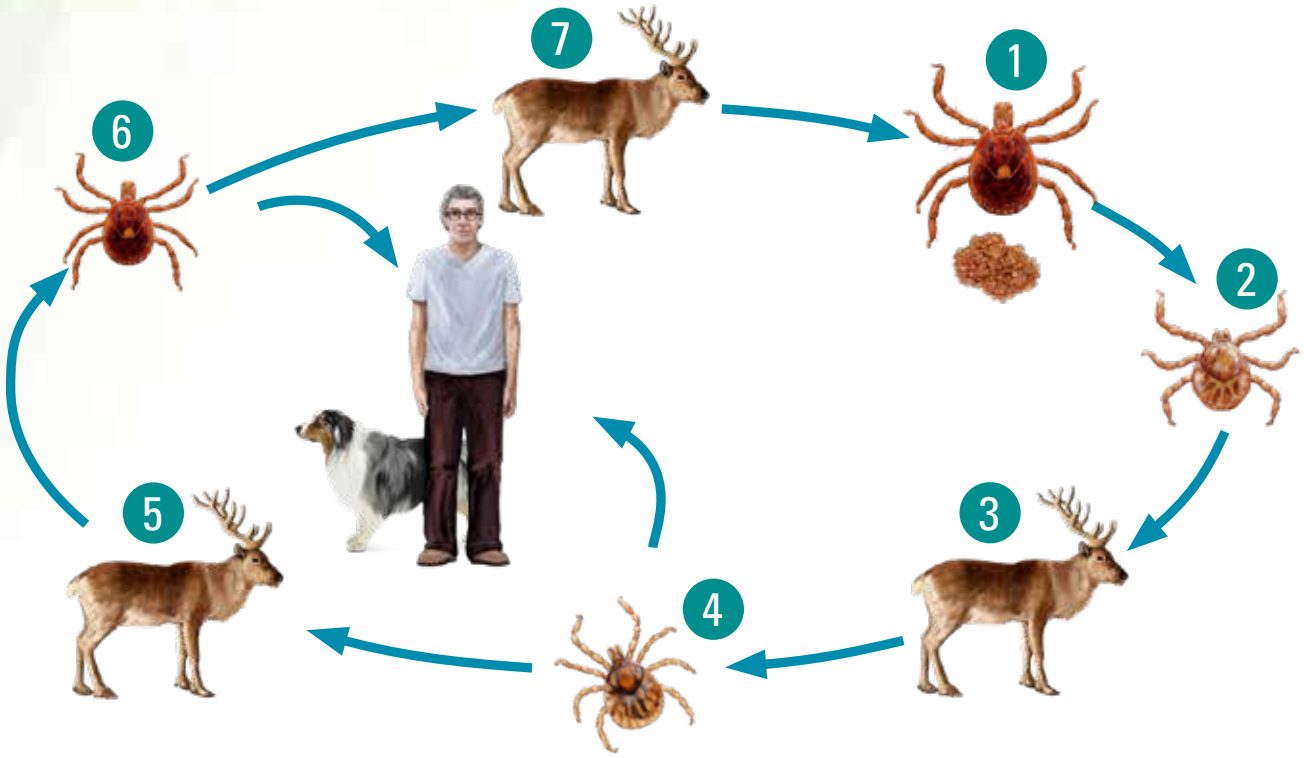
**5** Nymphs attach to and feed on the second host and may acquire *A. phagocytophilum.*

**6** Nymphs molt into adults after leaving the second host.

**7** Adults attach to the third host for feeding and mating.

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

## Transmission cycle for maintenance of *Ehrlichia chaffeensis*




**1** Adult females drop off the host to lay eggs.

**2** Eggs hatch into six-legged larvae.

**3** Larvae attach to and feed on the first host and may acquire *E. chaffeensis.*

**4** Larvae molt into nymphs after leaving the first host.

**5** Nymphs attach to and feed on the second host and may acquire *E. chaffeensis.*

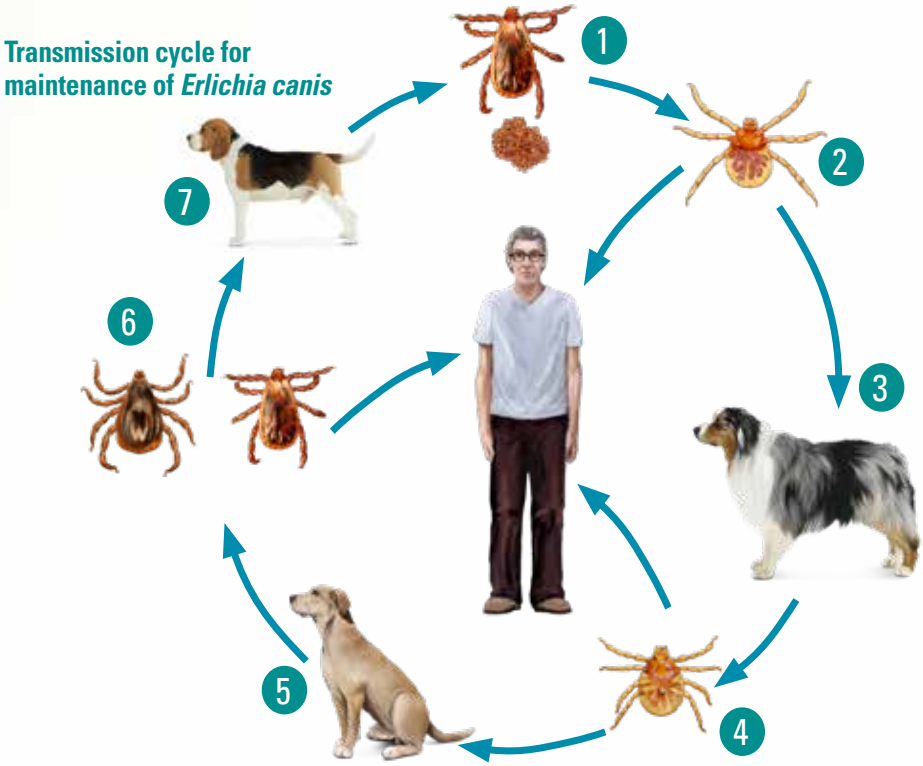
**6** Nymphs molt into adults after leaving the second host.

**7** Adults attach to the third host for feeding and mating.

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

## Domestic life cycle

### Transmission cycle for maintenance of *Erlichia canis*



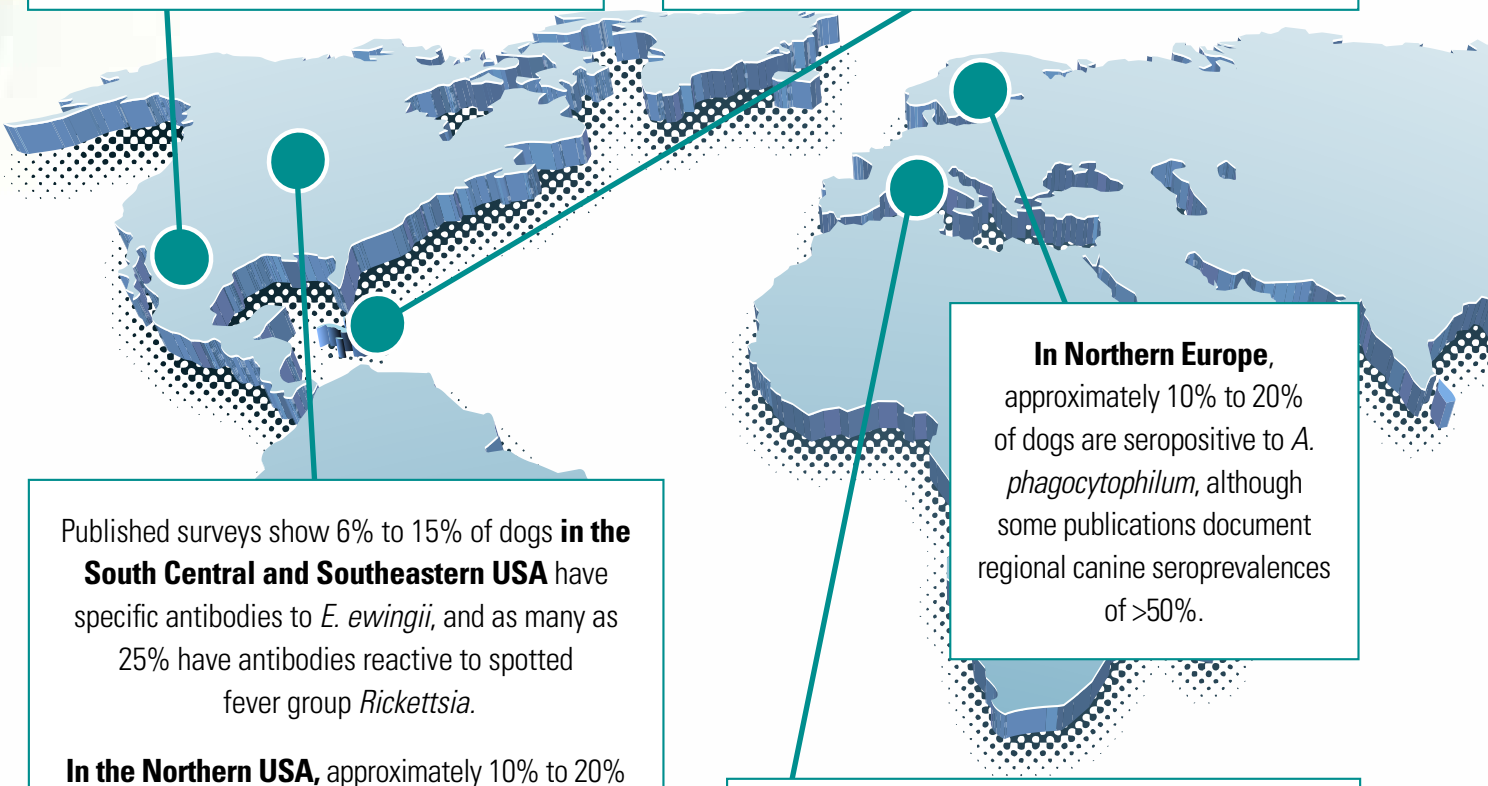

1. Adult females drop off the host to lay eggs.
2. Eggs hatch into six-legged larvae.
3. Larvae attach to and feed on the first host and may acquire *Erlichia canis.*
4. Larvae molt into nymphs after leaving the first host.
5. Nymphs attach to and feed on the second host and may acquire *Erlichia canis.*
6. Nymphs molt into adults after leaving the second host.
7. Adults attach to the third host for feeding and mating.

## Probability of transmission and routes of transmission

Dogs in homes, kennels, or free-roaming in communities where **brown dog tick** populations are intense and pathogens are present have a high probability of infection.

In the Southwestern USA, Mexico, and Central America, 6% to 12% of dogs tested have antibodies reactive to *R. rickettsii,* indicating past or current infection with spotted fever group *Rickettsia* spp.

Similarly, serological surveys of dogs in the Caribbean, where brown dog ticks are common, show 30% to almost 50% have antibodies to *Ehrlichia* and 15% to 25% have antibodies to *Anaplasma*, with PCR confirming the infections as *E. canis* and *A. platys*, respectively.



**In Northern Europe**, approximately 10% to 20% of dogs are seropositive to *A. phagocytophilum*, although some publications document regional canine seroprevalences of >50%.

Published surveys show 6% to 15% of dogs **in the South Central and Southeastern USA** have specific antibodies to *E. ewingii*, and as many as 25% have antibodies reactive to spotted fever group *Rickettsia.*

**In the Northern USA,** approximately 10% to 20% of dogs are seropositive to *A. phagocytophilum*, although some publications document regional canine seroprevalences of >50%.

In some surveys in **Mediterranean countries**, more than 50% of dogs have antibodies to *R. conorii.*

The sylvatic cycles supporting transmission of *E. ewingii, R. rickettsii,* and *A. phagocytophilum* are similarly robust, and dogs with outdoor access allowing tick exposure are often seropositive.

Estimates of infection vary according to the age and health status of the dog population considered as well as **the assays used.** For many rickettsial agents, cross-reactivity, particularly on immunofluorescent antibody tests, can lead to overestimation of seroprevalence, while highly specific assays that only detect antibodies generated at a certain time point following infection may underestimate the risk.

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

## Transmission mechanisms

Rickettsial agents are transmitted from infected ticks to dogs via tick saliva introduced to the host during tick feeding. Transmission of rickettsial agents can occur within the first 24 hours of tick attachment:

- Infection from 3 hours to 12 hours of tick feeding with *Ehrlichia canis* and *Rickettsia rickettsii*.
- *Anaplasma phagocytophilum* transmission also may occur in less than 24 hours of tick feeding, although estimates vary.

Both efficiency of transmission and the percent of dogs that become infected increase with longer feeding times for all rickettsial agents.

*Rickettsia* spp. can be aerosolised when attached ticks are removed, leading to potential infection by inhalation, and organisms present within engorged ticks may be directly introduced into the bite wound if ticks are damaged at removal.

**Blood transfusion** also serves as a potential route of infection, particularly for *Ehrlichia* spp. and *Anaplasma* spp.

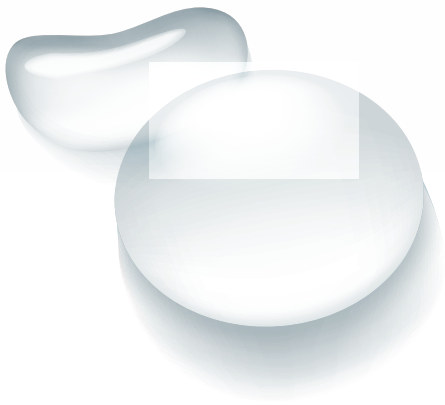
# WHAT BEHAVIOURS
## PUT A DOG AT RISK FOR THE DISEASE?

### Activities

All dogs are at risk of infection and disease with these agents, although tick-borne rickettsial infections are more common in dogs that share an environment with numerous other dogs and well-established brown dog tick populations (domestic cycles) and in dogs that have an active, outdoor lifestyle that allows frequent excursions into natural environments harbouring ticks (sylvatic cycles). Failure of consistent use of tick control products is associated with a higher risk of both infestation and infection. Allowing dogs to roam further exacerbates risk of rickettsial diseases in that wildlife ticks are acquired by dogs with frequent access to wooded areas, brown dog ticks readily spread between premises with dogs, and canine reproduction often continues unabated. Dog overpopulation can lead to dramatic increases in brown dog tick populations in a given community.

### Time of day for increased exposure

Ticks quest throughout the day, but activity of ticks in the environment peaks when temperature and humidity conditions are ideal to allow survival of a given species in the environment or to facilitate longer periods of questing on vegetation.



# **WHAT BEHAVIOURS** PUT A DOG AT RISK FOR THE DISEASE?

## Breed-related risks

Large breed dogs in general, including sporting and herding breeds, are over-represented in some case series evaluating dogs presented with rickettsial infections, a difference that may be due, in part, to risk of tick infestation.

Some tick surveys have shown that **sexually intact** dogs, as well as **sporting, terrier,** and **herding breeds,** are more likely to present with ticks.

While lifestyle and outdoor access may account for some of the differences seen, variations in breed-related susceptibility to ticks has also been documented.

- Five-times as many brown dog ticks attached to **Cocker Spaniel dogs** compared to Beagles in a co-housed group of dogs in an infested kennel, a difference apparently due to innate repellency of the Beagles.
- Once infected, ehrlichiosis due to *E. canis* can be particularly severe in **German shepherd and Siberian Husky dogs.**
- Both **German shepherd dogs and English Springer Spaniel** dogs with phosphofructokinase deficiency are reported to develop more severe disease following *R. rickettsii* infection.

### Diet

Diet has not been shown to affect tick infestation or susceptibility to rickettsial infection.

### Contact with other animals

The risk of tick exposure is likely to increase with dense populations; however, there is no risk for direct dog to dog transmission of rickettsial pathogens.

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

## Infection *vs* disease

Rickettsial infections are potentially fatal, although many dogs infected with common tick-borne rickettsial agents do not develop any evidence of clinical disease.

These asymptomatic infections are often identified when dogs are routinely screened in-clinic for antibodies to *Ehrlichia* spp. and *Anaplasma* spp. at annual examination or may be identified when **serological panel testing** for tick-borne infections is performed.

A positive antibody test confirms a history of tick infestation that resulted in an infection, and in many dogs the immune system appears to have managed that infection without leading to clinical signs or pathology.

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

One study in the central United States found that all healthy dogs (10 of 10) exposed to ticks on weekly walks seroconverted to both *Ehrlichia* spp. and *Rickettsia* spp., and PCR confirmed rickettsemia, indicating active infection, in 9 of 10, but none developed clinical disease or evidence of pathology on weekly complete blood counts and serum chemistry panels.

National summaries reporting serological results from testing millions of dogs around the world confirm that many dogs harbour antibodies indicating evidence of past or current infection with rickettsial agents.

Complete health records to evaluate clinical disease are not available in most wide-scale surveys, but as many as 5% to 40% of dogs **test positive for antibodies** to these agents, with reported canine seroprevalence in a region under intense transmission pressure sometimes exceeding 50%.

### Positive antibody test

Seroprevalence of clinically normal dogs and ill (e.g. febrile) dogs is often not significantly different, supporting the interpretation that many of these infections are self-limiting, and thus resolve, or cause only subclinical disease. When antibodies are the only evidence of infection, and in the absence of any evidence of disease or clinical pathologic changes, many internal medicine advisory groups do not recommend treatment.

## Risk to the population from subclinically diseased dogs

Domestic dogs are not considered a significant source of infection for tick-borne rickettsial pathogens maintained **in sylvatic cycles** as most of these agents use wildlife reservoir hosts and wildlife-associated tick vectors.

However, for those organisms that cycle primarily between **brown dog ticks and domestic dogs**, asymptomatic, **rickettsemic dogs** can be a key reservoir host to support continued infection of the local tick population.

### Source of infected ticks

Dogs may be necessary to provide an ongoing source of infection to ticks because pathogens (*Ehrlichia* spp., *Anaplasma* spp.) are not maintained transovarially in tick populations.

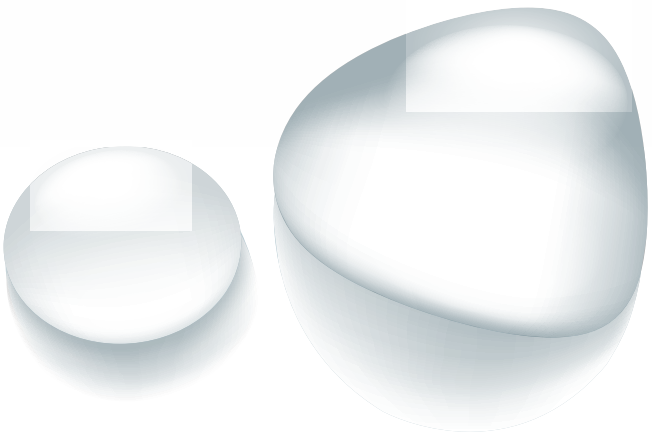
For those organisms maintained transovarially in tick populations *(Rickettsia* spp.), brown dog ticks may also be considered a reservoir of infection.

However, *Rickettsia* spp. infection often compromises tick fitness and survival, and thus infected dogs are important to maintain a continued source of infected ticks.

## Tests that reveal a subclinically infected dog

Subclinically but actively infected canine reservoir hosts can be identified by PCR of whole blood, PCR of tissues, or by **xenodiagnosis**.

Negative ticks are fed on dogs and then assayed to evaluate if pathogens were acquired; this approach has been shown experimentally to confirm persistence of a rickettsial infection in some dogs that are consistently negative on PCR of whole blood.



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

## Pathogenesis

After inoculation during tick feeding, rickettsial organisms enter **endothelial cells** (*Rickettsia* spp.) or **leucocytes** (*Ehrlichia* spp., *Anaplasma* spp.).

***R. rickettsii* infection**

Damage to endothelial cells:

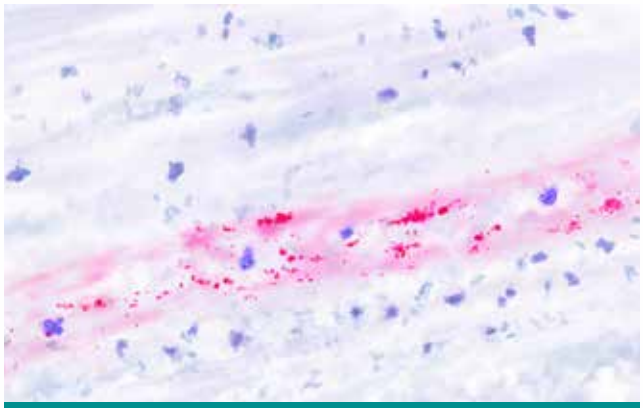
- Inflammation
- Vasculitis
- Increased vascular permeability
- Oedema with associated tissue damage

***Ehrlichia* spp. and *Anaplasma* spp.** exhibit species-specific affinities for different cell types:

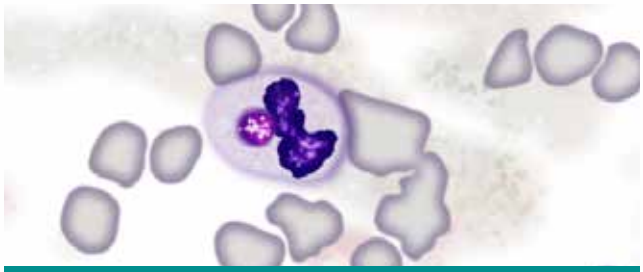
- *E. canis* most commonly found infecting monocytes
- *E. ewingii* and *A. phagocytophilum* in neutrophils and, occasionally, eosinophils
- *A. platys* in platelets

Megakaryocytes are commonly infected and most rickettsial infections induce moderate to severe **thrombocytopenia** as well as impaired platelet function. Anti-platelet antibodies have been described in several rickettsial disease systems, suggesting immune-mediated mechanisms.

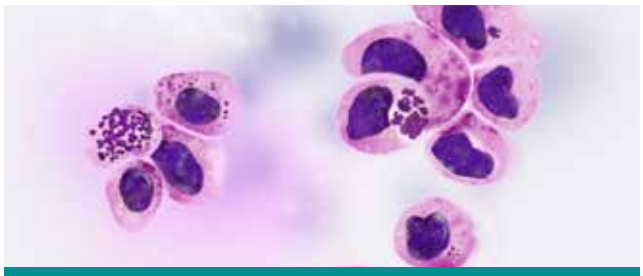
Other **cytopenias** are also commonly seen. In *E. canis* infection, dogs may develop profound neutropenia, lymphopenia, and mild anaemia as well as evidence of large granular lymphocytosis. Serum chemistry profiles may show elevated liver enzymes, decreased albumin/globulin ratio, and hypokalaemia.



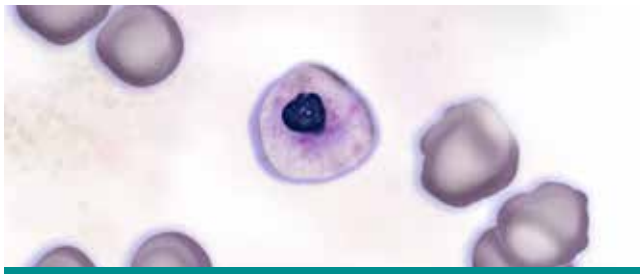
*R. rickettsii*



*A. phagocytophilum*



*E. canis*



*A. platys*

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

## Early signs

Dogs with clinical disease due to rickettsial infection often present with:

- Lethargy
- Myalgia
- Anorexia
- Fever is common

***R. rickettsii*** **and** ***E. canis*** have been associated with severe disease, including neurologic signs such as seizures and ataxia. Bleeding diatheses are described, and dogs may present with epistaxis or petechial and ecchymotic hemorrhages; when cutaneous lesions are widespread, hyperaemia, oedema, and necrosis may be evident. Fatalities can occur early in the course of infection.

## Progression

### Severe cases of ehrlichiosis due to *E. canis*

- Lymphadenopathy and splenomegaly may develop as infection progresses.
- When infections become chronic, anorexia, myalgia, neurologic disease, and ocular lesions are often seen.

### *E. ewingii* and *A. phagocytophilum* infection

- Neutrophilic polyarthritis.
- Infections are sometimes persistent, but chronic disease due to infection with these two agents has not been described.

## Prognostic factors

When identified and treated promptly, most dogs with clinical disease due to rickettsial infection respond well. Fatalities most often occur in dogs infected with ***R. rickettsii*** or ***E. canis,*** particularly when treatment is delayed, or co-morbidities are present.

In the absence of co-infection, fatalities are not known to occur in dogs due to *R. conorii, R. massiliae, A. platys, A. phagocytophilum,* or *E. ewingii* infection.

### *Rickettsia rickettsii*

Dogs with *R. rickettsii* that develop neurologic signs, evidence of vestibular disease (e.g. nystagmus, circling), or dyspnea are less likely to recover.

### *Ehrlichia canis*

In *E. canis* infection, prognosis is more guarded in dogs that present with pale mucous membranes and bleeding tendencies, as well as those with more severe pancytopenia and hypokalaemia.

## Recovery indications

If marked clinical improvement, as evidenced by resolution of improvement in activity and appetite, is not evident within 24 to 48 hours of instituting appropriate antibiotics and supportive care, the diagnostic evaluation should be carefully reviewed and co-infection with another aetiologic agent considered.

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

## Rapid, table-side

Rapid, patient-side assays are widely available to detect antibodies to *Ehrlichia* spp. or *Anaplasma* spp. in patient whole blood, plasma, or serum. Serological assays for *Rickettsia* spp. are only available through diagnostic laboratories.

Serological assays should always be interpreted with caution and awareness of the full spectrum of rickettsial agents likely infecting dogs in a given region **(Table 2)**:

- Samples may test negative during acute infection, even in the presence of clinical signs, if antibodies have not yet developed.
- Many clinically-normal dogs harbour antibodies to these organisms and serological cross-reactivity within genera is common in rickettsial agents.

**Table 2. Diagnostic strategies for tick-borne rickettsial infections of dogs**

| Pathogen | Acute infection | Established infection | Tick vector identification* |
|---|---|---|---|
| *Anaplasma platys* | Clinical impression<br>PCR, Blood smear<br>Antibody test | Antibody test<br>+/- PCR |  |
| *Ehrlichia canis* | Clinical impression<br>PCR, Blood smear<br>Antibody test | Antibody test<br>+/- PCR | |
| *Rickettsia conorii* | Clinical impression<br>PCR, Antibody test | Antibody test | |
| *Rickettsia massiliae* | Clinical impression<br>PCR, Antibody test | Antibody test | |
| *Rickettsia rickettsii* | Clinical impression<br>PCR, Antibody test | Antibody test | |
| *Anaplasma phagocytophilum* | Clinical impression<br>PCR, Blood smear,<br>Antibody test | Antibody test<br>+/- PCR |  |
| *Ehrlichia ewingii* | Clinical impression<br>PCR, Blood smear,<br>Antibody test | Antibody test<br>+/- PCR |  |
| *Rickettsia rickettsii* | Clinical impression<br>PCR, Antibody test | Antibody test |  |

* Ticks may not be found when dogs present for clinical disease. Images show dorsal (left) and ventral (right) views of unengorged adult female (A) and male (B) ticks. For identification of immature ticks or engorged or damaged specimens, consult with a diagnostic parasitology laboratory.

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

## In hospital using microscope or similar equipment

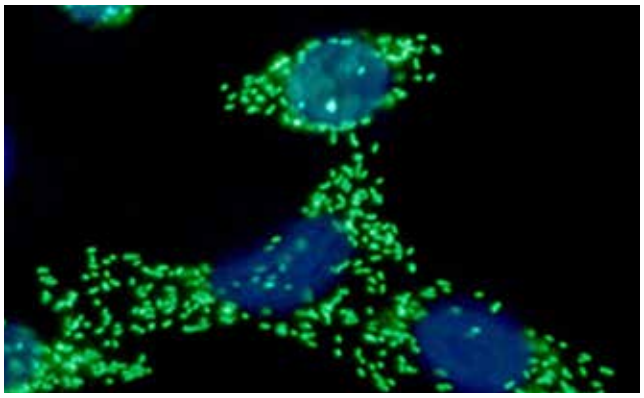
Morulae of *Ehrlichia* spp. and *Anaplasma* spp. may occasionally be identified by microscopic examination of stained blood smears or buffy coat preparations, and appear as cytoplasmic inclusions in granulocytes (*E. ewingii* and *A. phagocytophilum*), monocytes (*E. canis*), or platelets (*A. platys*).

## Laboratory testing

Diagnostic laboratories offer **indirect immunofluorescent antibody (IFA)** assays that detect antibodies to *Rickettsia* spp., *Ehrlichia* spp., and *Anaplasma* spp. **Antibody-based tests** may detect cross-reactive antibodies among related organisms.

> If serology alone is used for diagnosis, clinical confirmation of active infection can be made based on a four-fold rise in IgG antibody titre from two samples collected 2 to 4 weeks apart, or a single, elevated titre (≥ 1:1,024) from a sample evaluated at least one week after the onset of clinical signs.

**For example** positive IFA titres for *E. canis* or *R. rickettsii* may indicate past or current infection with other, less pathogenic agents, such as *E. chaffeensis* or *R. amblyommatis*, which are not known to cause canine disease or require treatment.



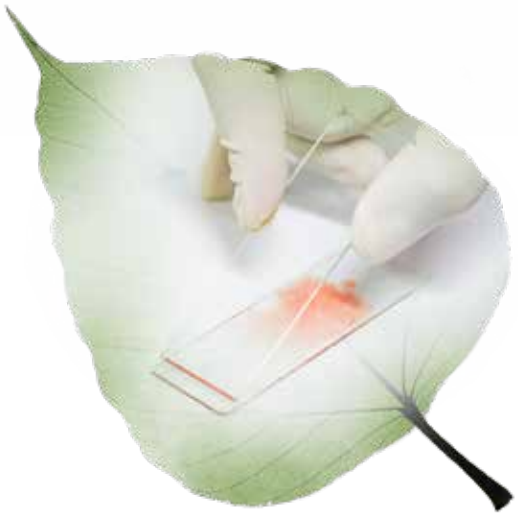
Appearance of a positive SFGR IFA test for *Rickettsia montanensis*.

Diagnostic laboratories also offer specific PCR assays to detect nucleic acid of *Ehrlichia* spp., *Anaplasma* spp., and ***Rickettsia* spp.** in whole blood. Members of the Anaplasmatacea are readily detected by PCR during active rickettsemia, particularly when samples are collected before instituting antibiotic therapy.

However, *Rickettsia* spp. primarily infect endothelial cells and PCR of whole blood is much less rewarding for confirming active infection with spotted fever group *Rickettsia* spp.

## Test interpretation

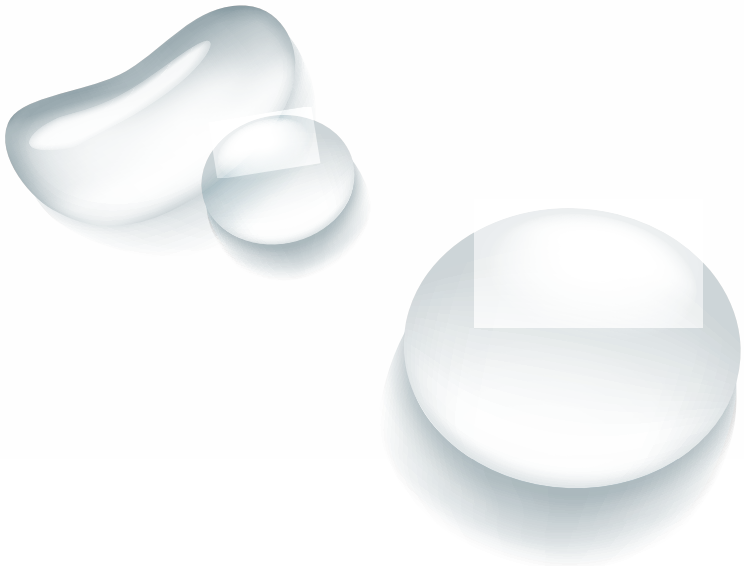
The decision to treat should be made primarily on clinical impression, regardless of the test used (antibody, stained blood smear, or PCR), and a negative test should not be taken as evidence of absence of infection.



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

## Acute *vs* convalescent

Dogs with clinical disease due to rickettsial infection often present before seroconversion has occurred; organisms may not be detected on blood smears, and molecular assays often require 1–2 days to obtain results which, depending on the test used, sometimes can be a false negative. The clinical presentation of many rickettsial infections is nonspecific and co-infections are common. Accordingly, when tick-borne rickettsial disease is suspected, both whole blood and serum should be submitted for comprehensive evaluation using both PCR and serological assays that detect a panel of vector-borne pathogens. During acute infection, PCR is usually preferred, and in more established, chronic infections, serology will be of greater value. However, when a dog presents with clinical illness the exact time of infection is rarely known.



# WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

## Types of drugs to use

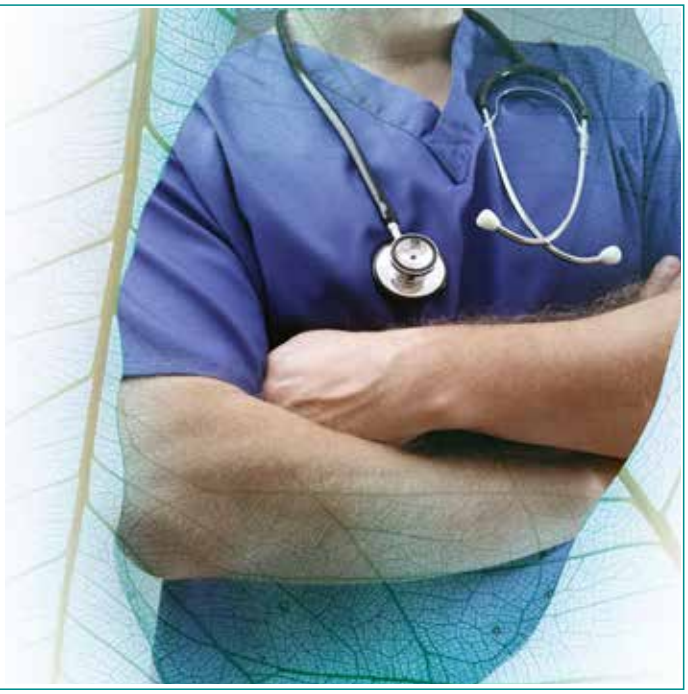
Doxycycline, a tetracycline antibiotic, is considered the **treatment of choice for all tick-borne rickettsial infections.**

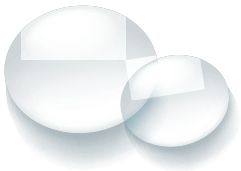
Veterinary consensus statements from Europe and North America recommend doxycycline at either 5 mg/kg every 12 hours or 10 mg/kg every 24 hours for 28 days.

Some suggest shorter courses (2–3 weeks) of doxycycline may be effective against *A. phagocytophilum* and *A. platys,* but concern about incomplete efficacy in some patients or the potential for co-infection leads many to recommend a full 28-day course of therapy for all rickettisal infections.

### Doxycycline

- Tooth discolouration is not seen with doxycycline, and gastrointestinal side effects can be managed by using the split-dose regimen (5 mg/kg every 12 hours) and administering with food.
- Doxycycline use should proceed with caution and under close veterinary supervision if hepatic disease is present.
- Persistent infection following treatment with doxycycline, recrudescence of infection, and re-infection have been reported. When this occurs, a second, 4-week course of doxycycline and a thorough diagnostic evaluation for potential co-infections and co-morbidities are recommended.





# WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

## Monotherapy or combination therapy

Most patients with mild to moderate disease due to rickettsial infection can be treated with doxycycline alone.

## Monitoring for response to treatment

In uncomplicated cases, clinical improvement is usually seen within the first two days of antibiotic therapy and blood values (complete blood count, serum chemistry profile) return to normal in 1–2 weeks.

## Supportive treatment strategies

For some patients with moderate to severe disease, more intensive supportive care may be indicated, including blood transfusion, fluid therapy, and pain management. While not appropriate for routine treatment, a short course of glucocorticoid therapy (e.g. prednisone) may be helpful in some patients to manage immune-mediated complications such as haemolytic anaemia, glomerulonephritis, uveitis, or vasculitis.

## Management of co-infections

Dogs that do not respond to doxycycline treatment should be carefully re-evaluated for co-infections, including protozoal tick-borne disease agents that require different antimicrobial therapy.

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

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

Most canine rickettsial pathogens are zoonotic, but infections are transmitted by ticks, not through direct contact with infected dogs.

## Can cats get this infection/disease?

Although less well-studied, disease due to rickettsial infection has been described in cats, particularly *A. phagocytophilum* and, less commonly, *Ehrlichia* spp. Ticks are occasionally identified on cats even when owners report that the cats live entirely indoors. Clinical disease, diagnosis, and treatment strategies for cats are similar to those used in dogs. When treating cats with doxycycline, liquid formulations should be used to avoid oesophageal stricture.

## Other public health considerations

Diagnoses in dogs will often alert the community that a public health risk also exists because people and dogs that share the same environment also share a risk of exposure to infected ticks.

For the diseases vectored by brown dog ticks and maintained in **domestic cycles**, dogs may also serve as an important reservoir host supporting both the tick population and the rickettsial pathogens.

Controlling canine overpopulation and brown dog tick infestations are important aspects of limiting human disease due to ***R. conorii, R. massiliae,*** **and** ***R. rickettsii*** in areas where these infections occur.

For infections maintained in **sylvatic cycles (*A. phagocytophilum, E. chaffeensis, E. ewingii, R. rickettsii*)**, humans are also at risk of developing severe, life-threatening disease when bitten by a tick, but wildlife serve as the main source of infection to ticks and reservoir for ticks.

Human infection with *R. rickettsii* has been reported due to apparent aerosolisation during mechanical tick removal.

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

**Tick-borne rickettsial infections in people** usually present as an acute, flu-like, febrile illness. Myalgia and severe headache are commonly described.

With spotted fever group *Rickettsia* spp. infection, cutaneous lesions such as an eschar at the tick bite site or a maculopapular rash may be evident. If left untreated, neurological disease or disseminated involvement of multiple organs may develop.

Fatality rates vary with the pathogen, region, and case population evaluated but are usually approximately 2% to 5%. However, most human patients respond well to prompt institution of antibiotic therapy (doxycycline treatment).

Ticks may be carried into the home on the clothing of people that encounter questing ticks while outdoors as well as on untreated dogs allowed outside. For this reason, veterinary advisory groups like the Companion Animal Parasite Council and the European Scientific Counsel on Companion Animal Parasites recommend that pet owners limit pet access to areas of high tick density, inspect pets daily for ticks, and use tick control products with persistent activity.

# WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

## How to avoid the vector

Different species and stages of ticks are active in various habitats and at different times of the year, creating a near-constant risk of tick infestation and infection with tick-borne rickettsial pathogens. Avoiding wooded or grassy natural areas at times of the year when tick questing is at its peak will reduce the number of ticks encountered and thus the risk of infection.

Requiring persistent tick control in all dogs that use shared animal facilities, such as dog day care, boarding kennels, or dog parks, reduces the likelihood of establishing brown dog ticks on these premises.

# WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

Because it is difficult to precisely predict when sylvatic ticks will be questing in the future, and because domestic brown dog tick populations can establish inside homes and kennels, veterinary advisory boards in many countries recommend routine use of year-round **persistent tick control products.**

While consistent acaricide use is important, breakthrough infections can still occur, particularly when tick questing in the environment is intense; no tick control product should be considered 100% effective at preventing rickettsial infections. If attached ticks are identified on dogs, prompt removal using gloved fingers or forceps is advised.

Environmental management strategies, such as landscaping to impede tick survival and discourage wildlife, as well as careful use of acaricides in targeted areas may also be helpful at reducing tick numbers around homes and kennels.

## Is routine testing recommended?

Routine (annual) testing for tick-borne diseases is widely recommended. Early detection of infection alerts the vet about the risk for clinical disease, allowing more thorough work-up for evidence of clinical pathologic changes and, if indicated, appropriate antibiotic treatment. Uncovering antibody evidence of past or current rickettsial infection also enhances awareness about the risk posed by ticks to that patient and encourages consistent use of tick control products to address the concern.

## General thoughts on preventive treatments

Consistent use of tick control has been shown to reduce transmission of many tick-borne infections, including rickettsial agents. Prophylactic daily administration of doxycycline has been used to protect canine health when ticks cannot be avoided, such as in a kennel or home where an active brown dog tick infestation is not yet under control, but this approach is not practical or advisable as a long-term solution.

## Is there a vaccine?

Commercial vaccines are not currently available for canine tick-borne rickettsial pathogens in most countries.

# WHAT DOES THE FUTURE LOOK LIKE?

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

The geographic ranges of several tick species have increased in recent decades, leading to concomitant spread of areas with autochthonous transmission of canine rickettsial infections. Populations of *Ixodes* spp. that transmit *A. phagocytophilum* are now established at higher latitudes and higher altitudes in both North America and Europe, and the *Amblyomma* spp. that transmit *E. ewingii* and spotted fever group *Rickettsia* spp. have moved northward in North America.

Increased average temperatures are making a broader region suitable for supporting large populations of tropical brown dog ticks; increased prevalences of *E. canis, A. platys*, and spotted fever group *Rickettsia* spp. are likely to follow. Recent introductions of tick species have also been identified, including *Haemaphysalis longicornis* into the Americas and *Rhipicephalus sanguineus* in Northern European households, and these tick vectors may play a future role in increasing the risk of rickettsial infections in a given region.

## Is the risk of disease increasing?

The geographic spread of tick populations and increased intensity of ticks in areas where they have long been present are both contributing to an increasing risk of canine infection and disease due to rickettsial agents. The prevalence of dogs testing positive to *A. phagocytophilum* in several states in the Northeastern USA increased by 50% (e.g. from 5% to 7.5%) to more than 100% (e.g. from 5% to >10%) in the past decade. Similar increases in prevalence of antibodies to *Ehrlichia* spp. in dogs in the USA over the past 10 years are thought to be due to a combination of a shift in analytes to allow detection of antibodies to *E. ewingii,* in addition to antibodies to *E. canis*, on commonly used patient-side assays, as well as increases in vector tick populations and thus risk of infection. Human cases of ehrlichiosis, anaplasmosis, and spotted fever group rickettsioses are also increasing in many regions.

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

Resistance of these organisms to doxycycline has not been documented, but some populations of brown dog ticks have been shown to be resistant to topical acaricides (e.g. permethrin, amitraz). Continued efforts by vets to protect dogs from ticks and identify and treat rickettsial infections early are necessary to protect canine health in the face of increasing risk of tick-borne rickettsial infections.

# FURTHER READING

## References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VECTOR BORNE DISEASE

MSD Animal Health