TICK-BORNE RICKETTSIAL DISEASES

START

VECTOR BORNE DISEASE

MSD Animal Health

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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.

Sylvatic cycles

Rickettsial pathogens harbored 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.

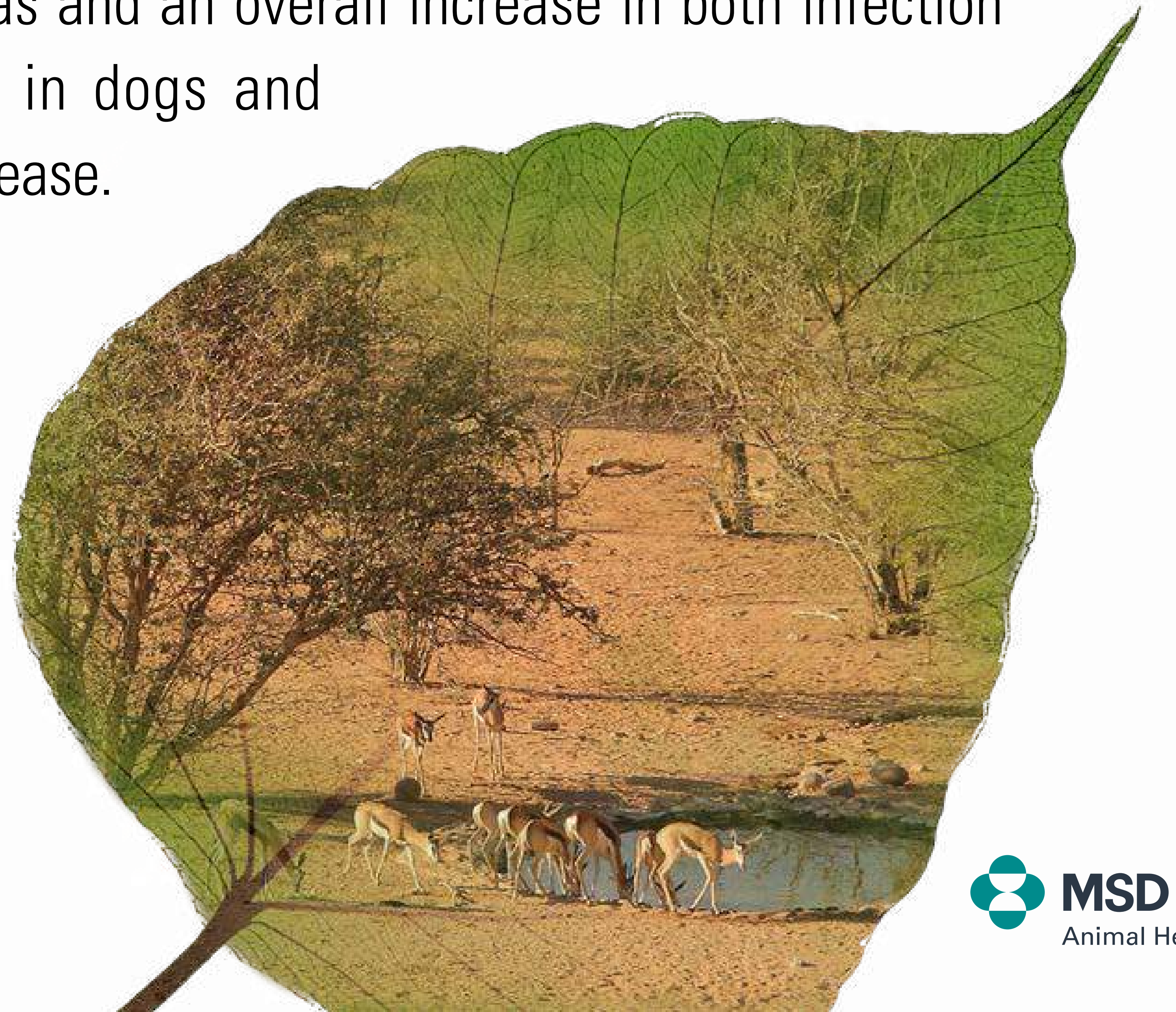
Favorable climate conditions

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

- 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 favored by *Ixodes* spp. and *Dermacentor* spp. ticks.

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:

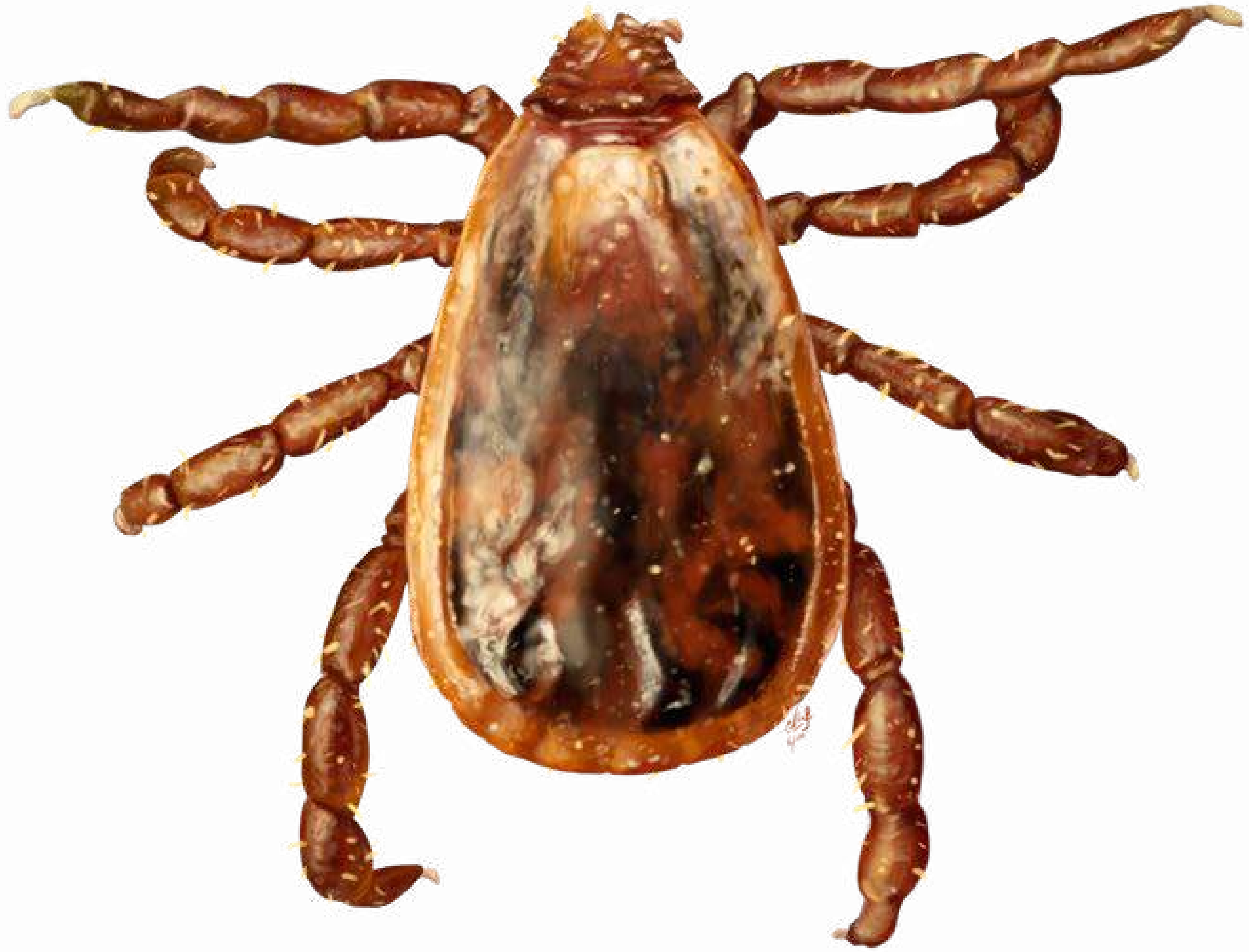
- The Rickettsiaceae, which includes the genus *Rickettsia.*
- The Anaplasmataceae, which includes the genera *Anaplasma* and *Ehrlichia*.

Vector (lifecycle)

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.**



Proportion of infected vectors

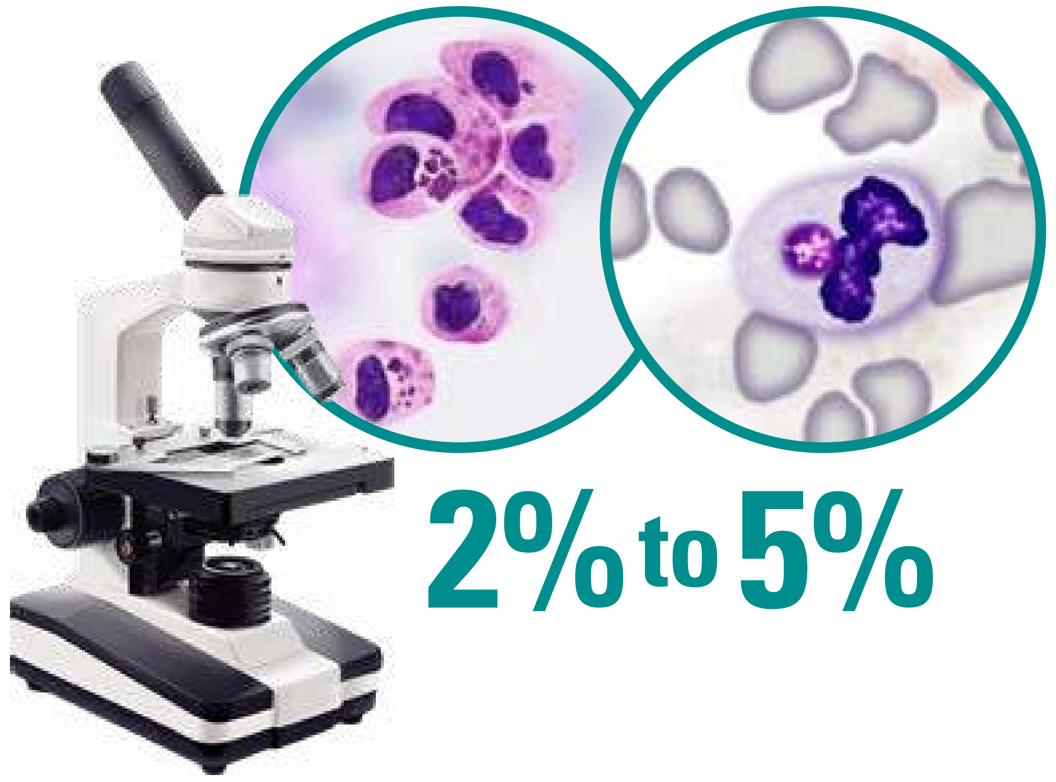
Prevalence of rickettsial infection **in brown dog ticks** is usually low **(not detected or <1%)** in the absence of active infection in dogs in the area **(Table).**

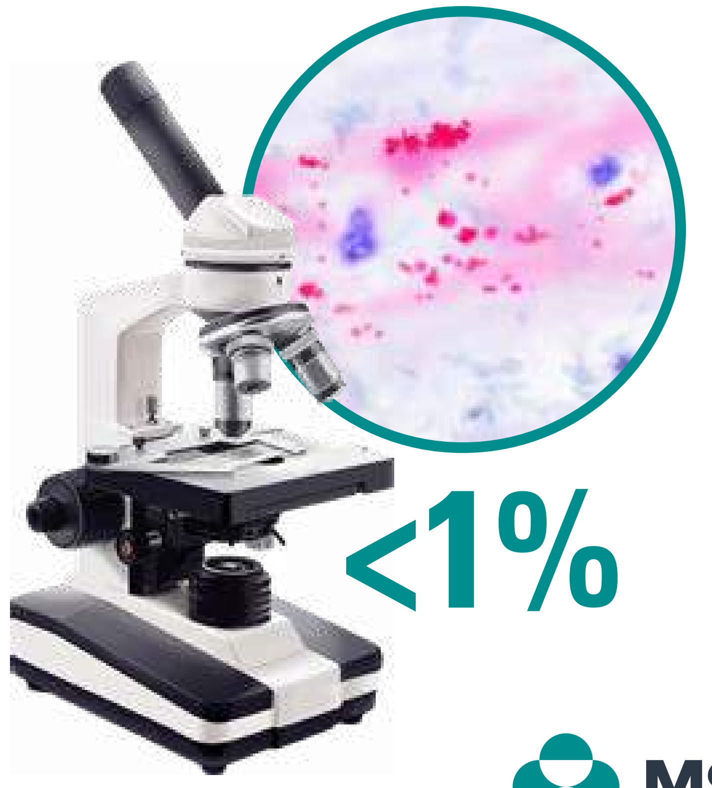
However, when feeding Rhipicephalus spp. ticks are removed from infected dogs, particularly **when active transmission** is ongoing in the area, prevalence of tick infection can be much higher **(5% to >20%).**

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).** Common wildlife reservoir hosts include:

Small mammals:

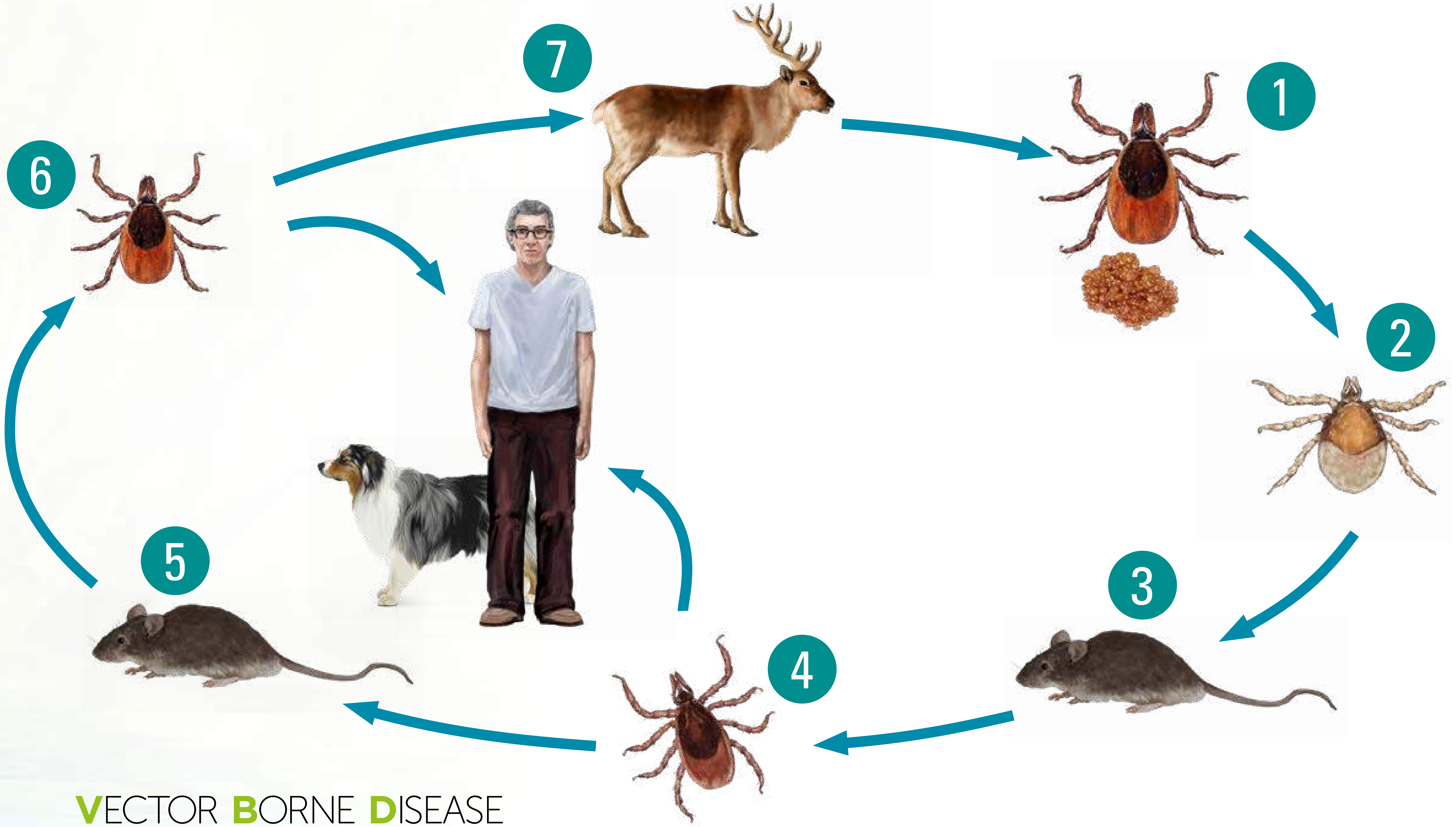
White-tailed deer:

Wild canids:

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*



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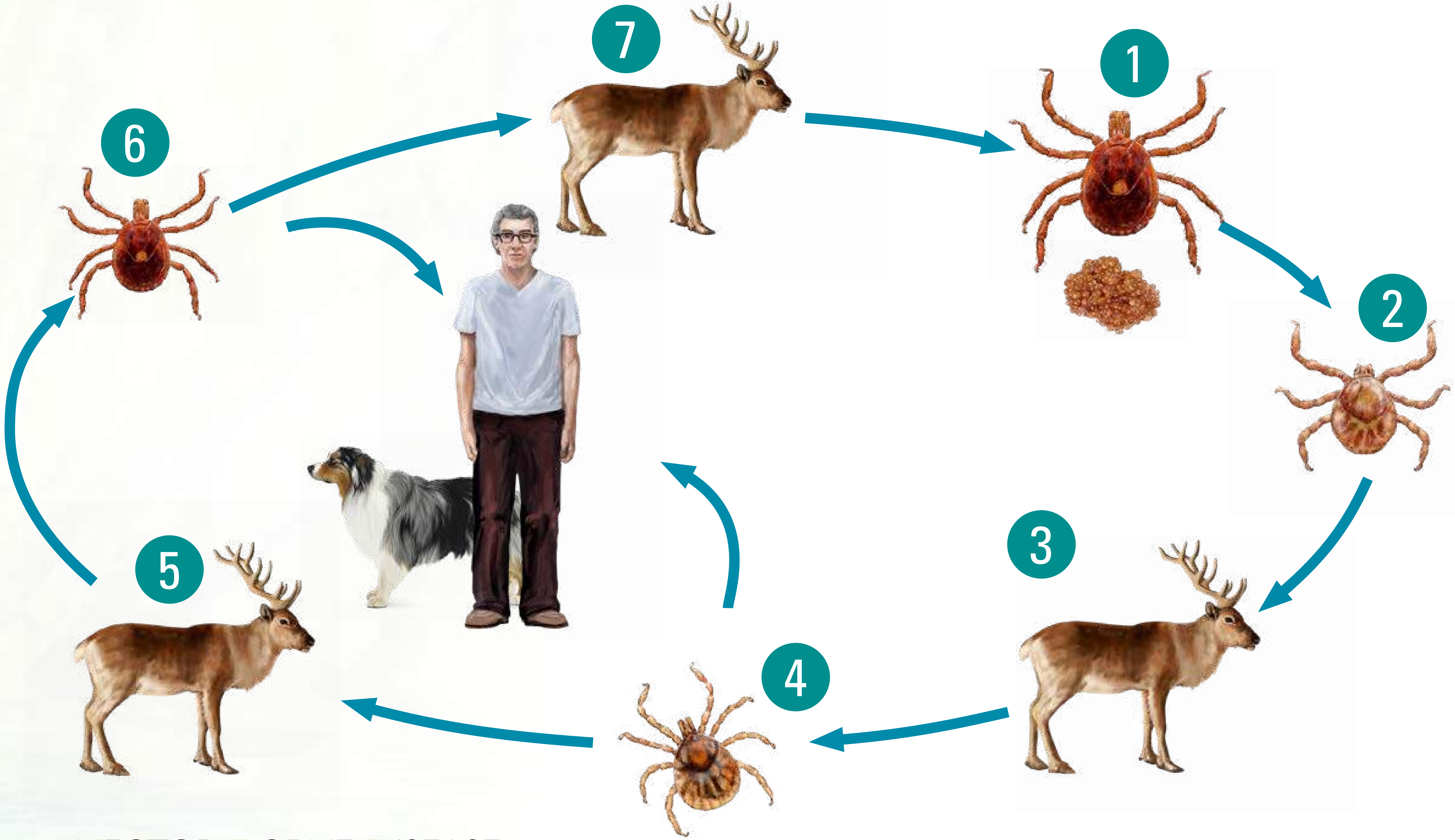
HOW DOES A DOG **BECOME INFECTED?**

Transmission cycle for maintenance of *Ehrlichia chaffeensis*



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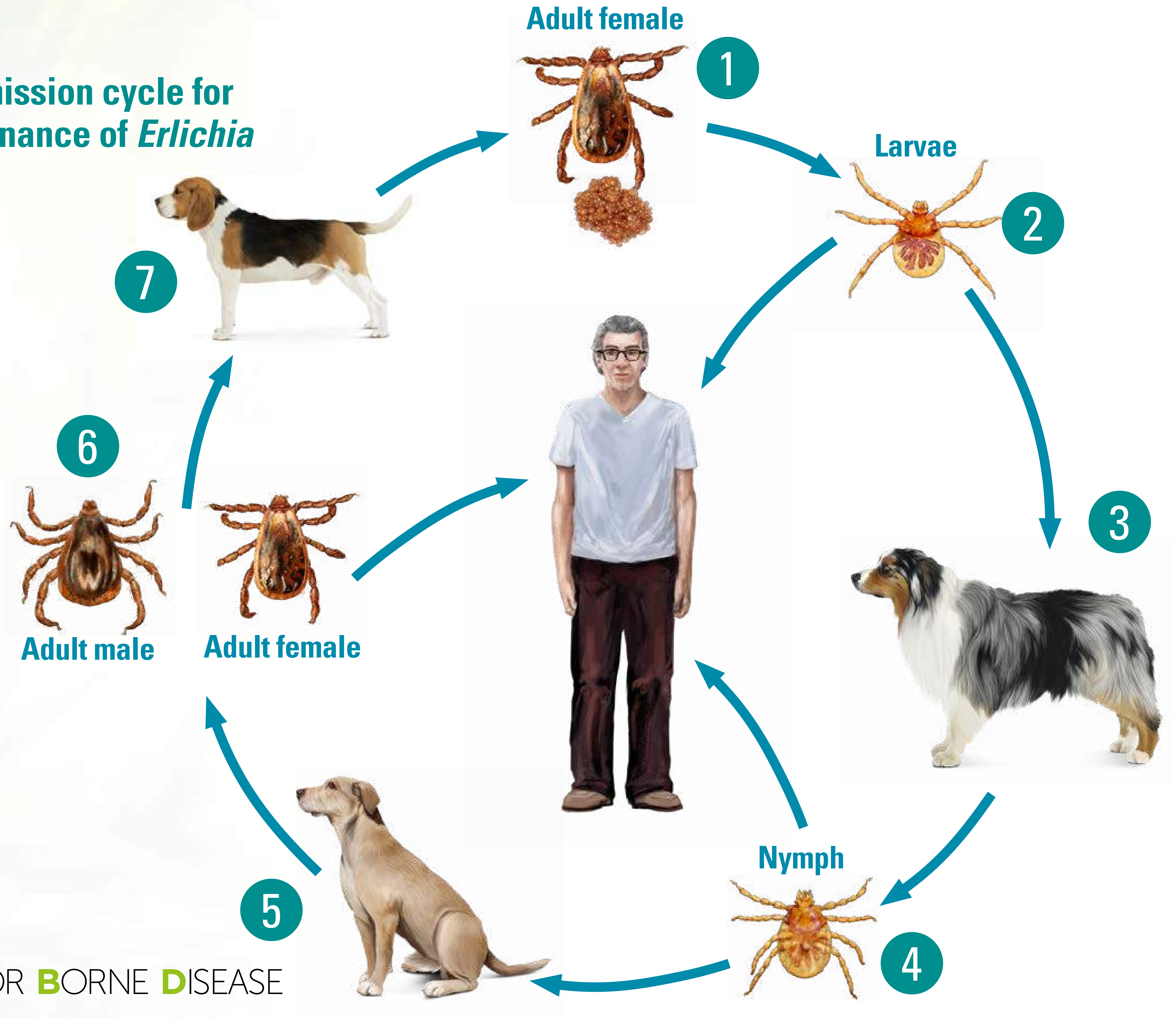
HOW DOES A DOG **BECOME INFECTED?**

Transmission cycle for maintenance of *Erlichia canis*



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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.

HOW DOES A DOG **BECOME INFECTED?**

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.**

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 aerosolized 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.

WHAT BEHAVIORS
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 harboring 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.

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 **serologic panel testing** for tick-borne infections is performed.

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 serologic results from testing millions of dogs around the world confirm that many dogs harbor 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%.

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.

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.**

WHAT CLINICAL SIGNS
DOES A SICK DOG SHOW AND WHY?

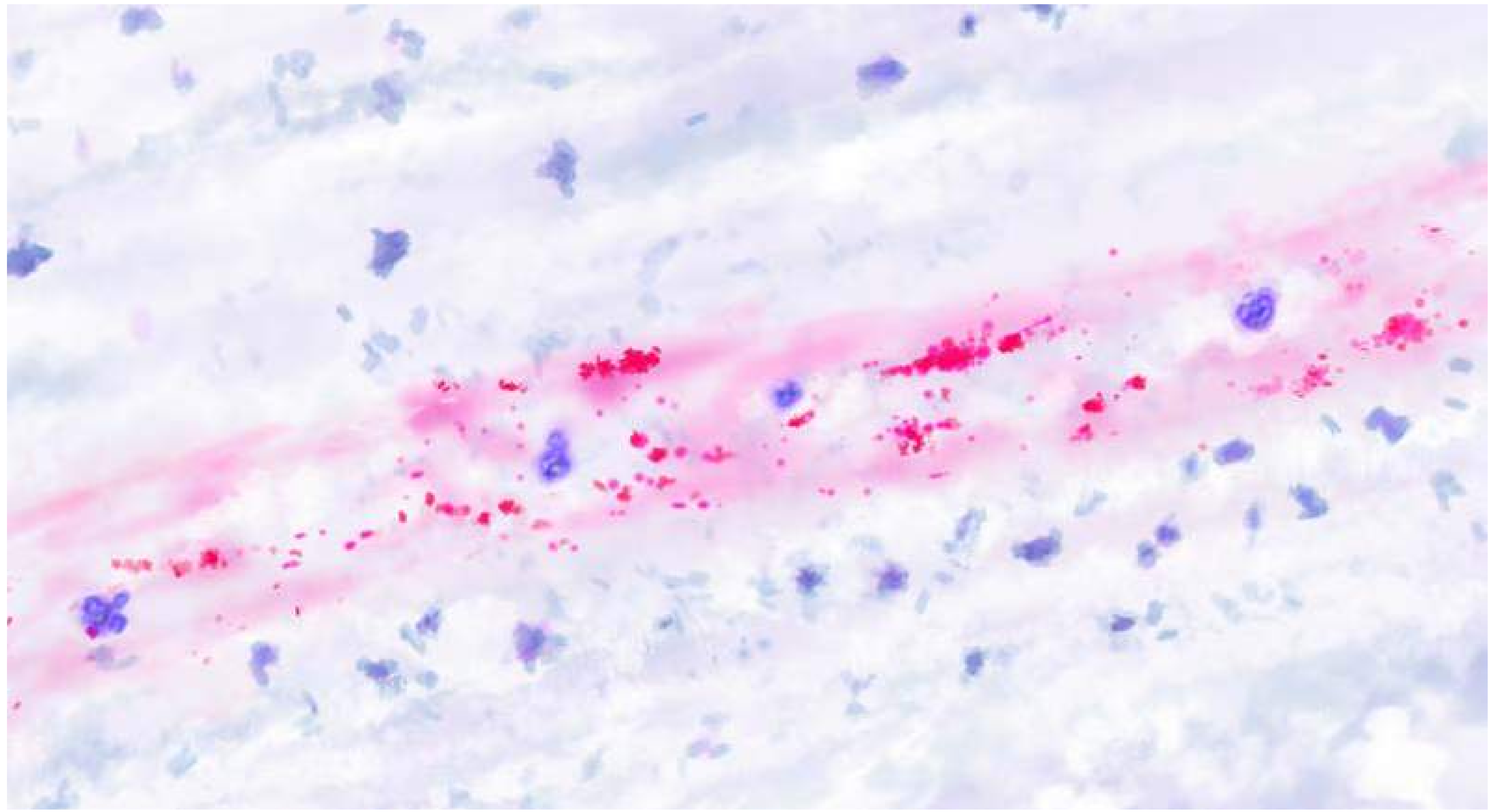
Pathogenesis

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

R. rickettsii infection

Damage to endothelial cells:

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



WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

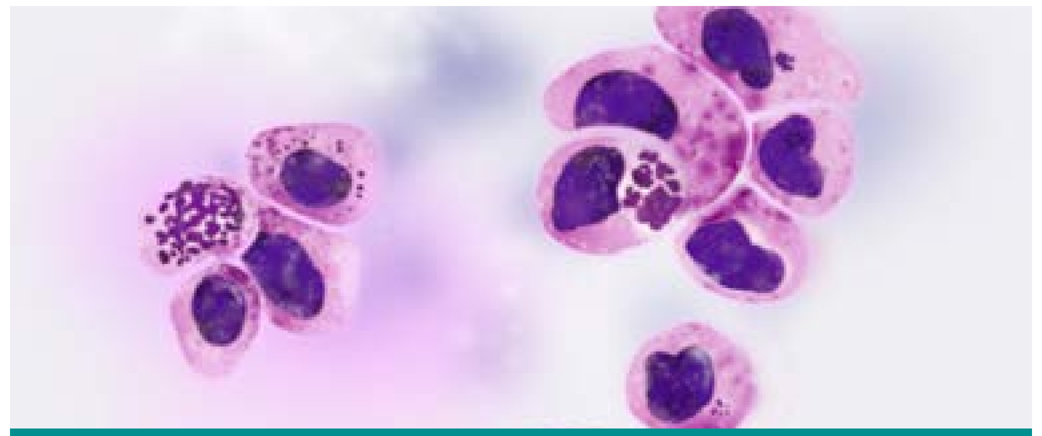
***Ehrlichia* spp. and *Anaplasma* spp.** exhibit species-specific affinities for different cell types:

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

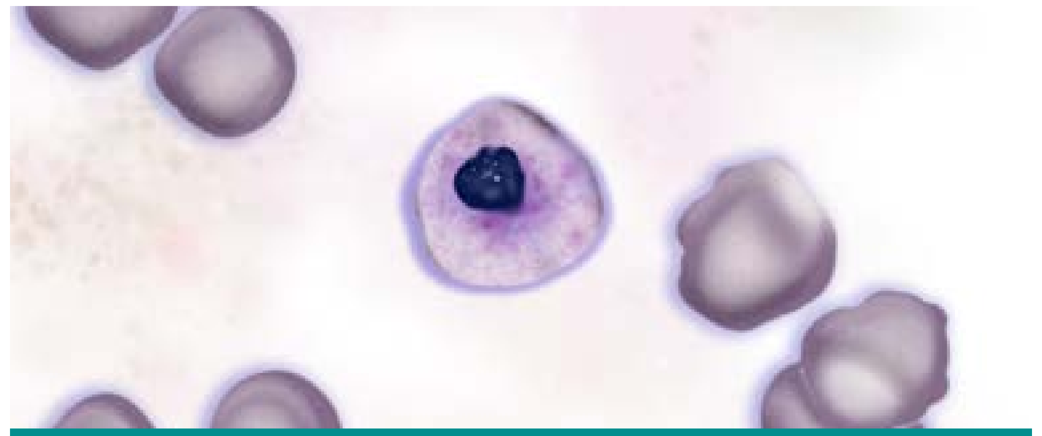
Megakaryocytes are commonly infected and most rickettsial infections induce moderate to severe **thrombocytopenia** as well as impaired platelet function.

Other **cytopenias** are also commonly seen.

A. phagocytophilum



E. canis



A. platys

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, hyperemia, edema, 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.

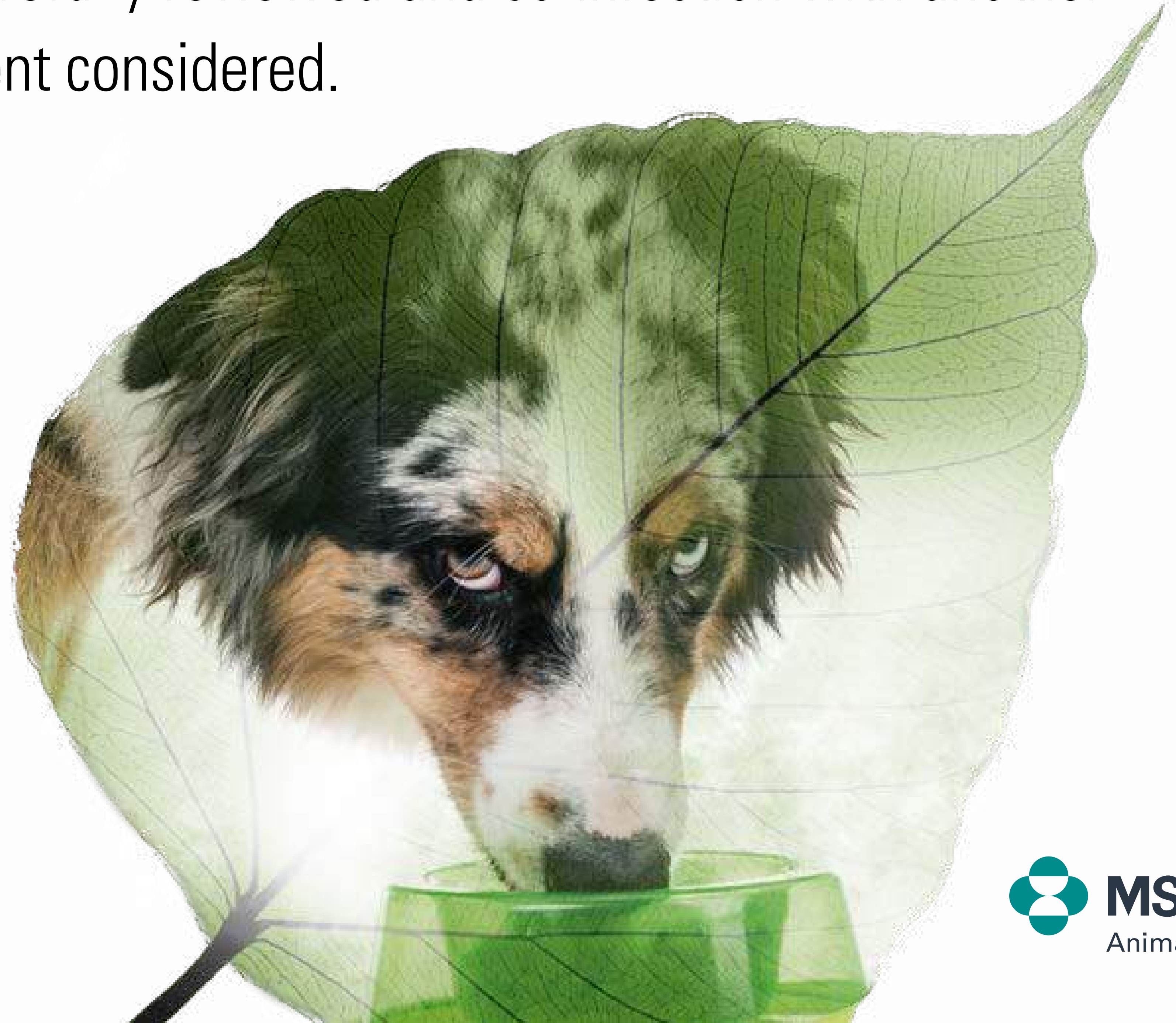
Prognostic factors

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 comorbidities 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.

Recovery indications

If marked clinical improvement, as evidenced by resolution of fever and 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 etiologic 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. Serologic assays for *Rickettsia* spp. are only available through diagnostic laboratories.

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

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

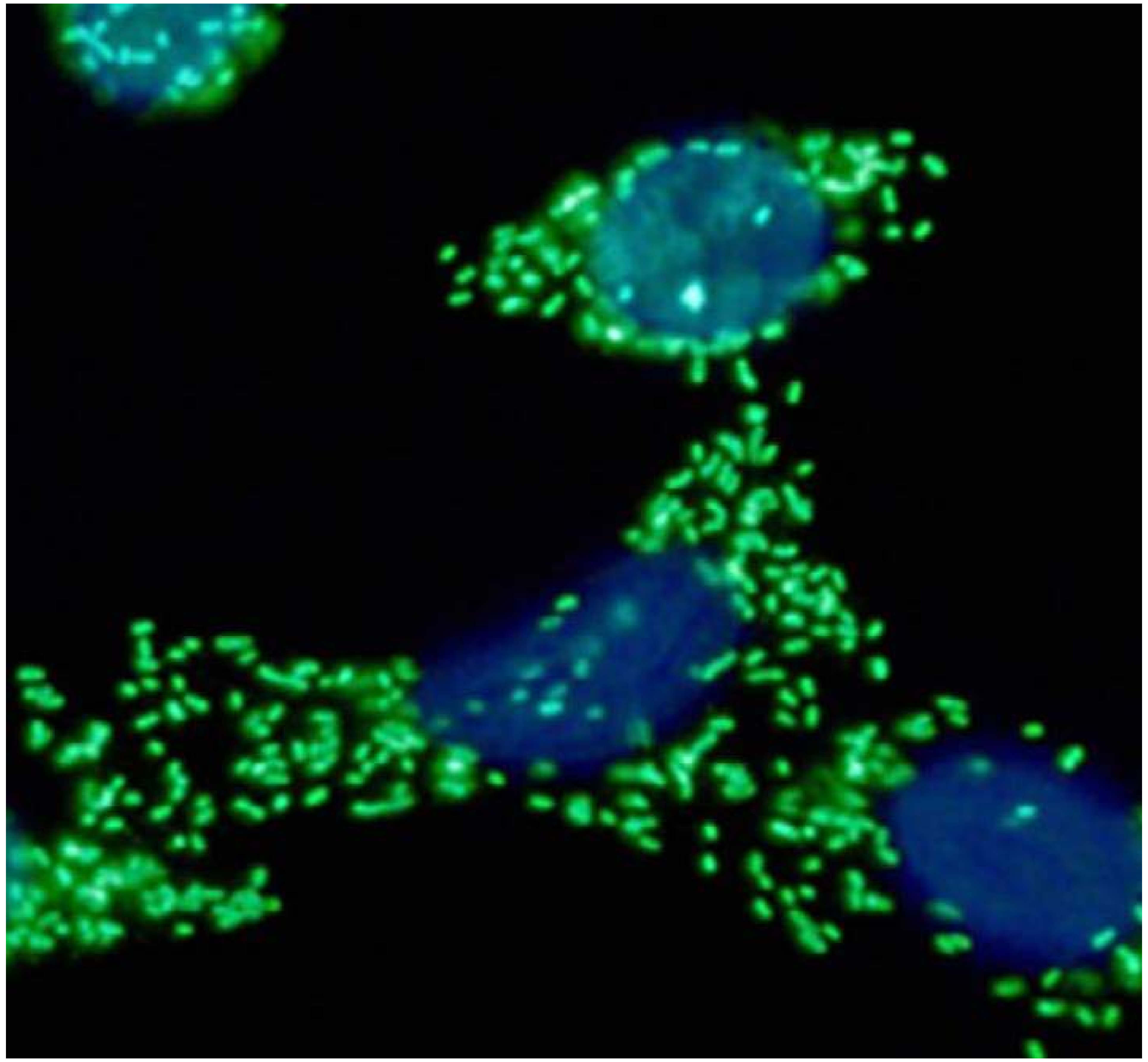
In hospital using microscope or similar equipment

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.

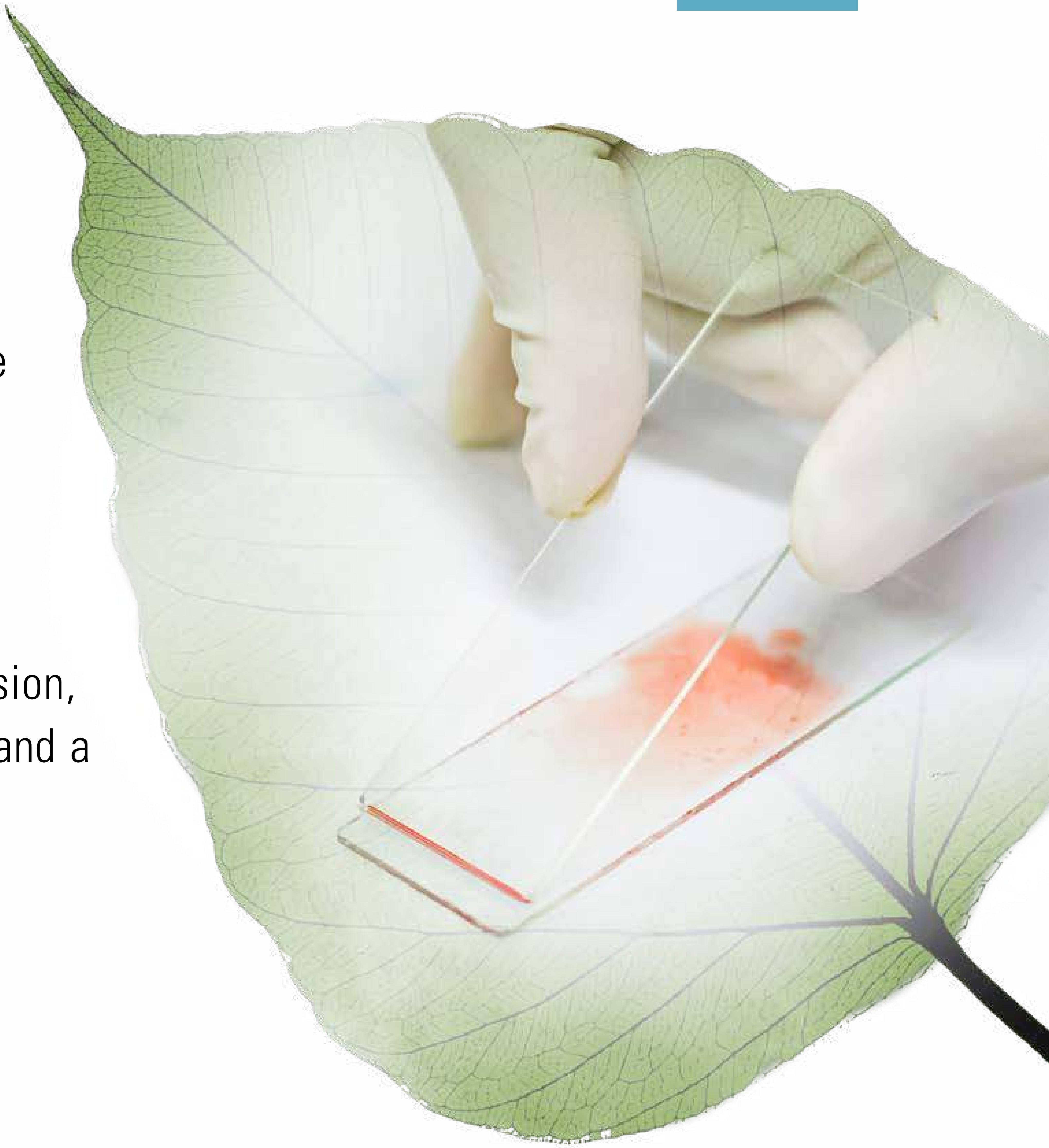
For example...



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

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

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.



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.

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 serologic 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.** Minocycline can also be used if doxycycline is not available although fewer published reports support its efficacy and associated outcomes in dogs.

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 rickettsial infections.

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.

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 esophageal 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.

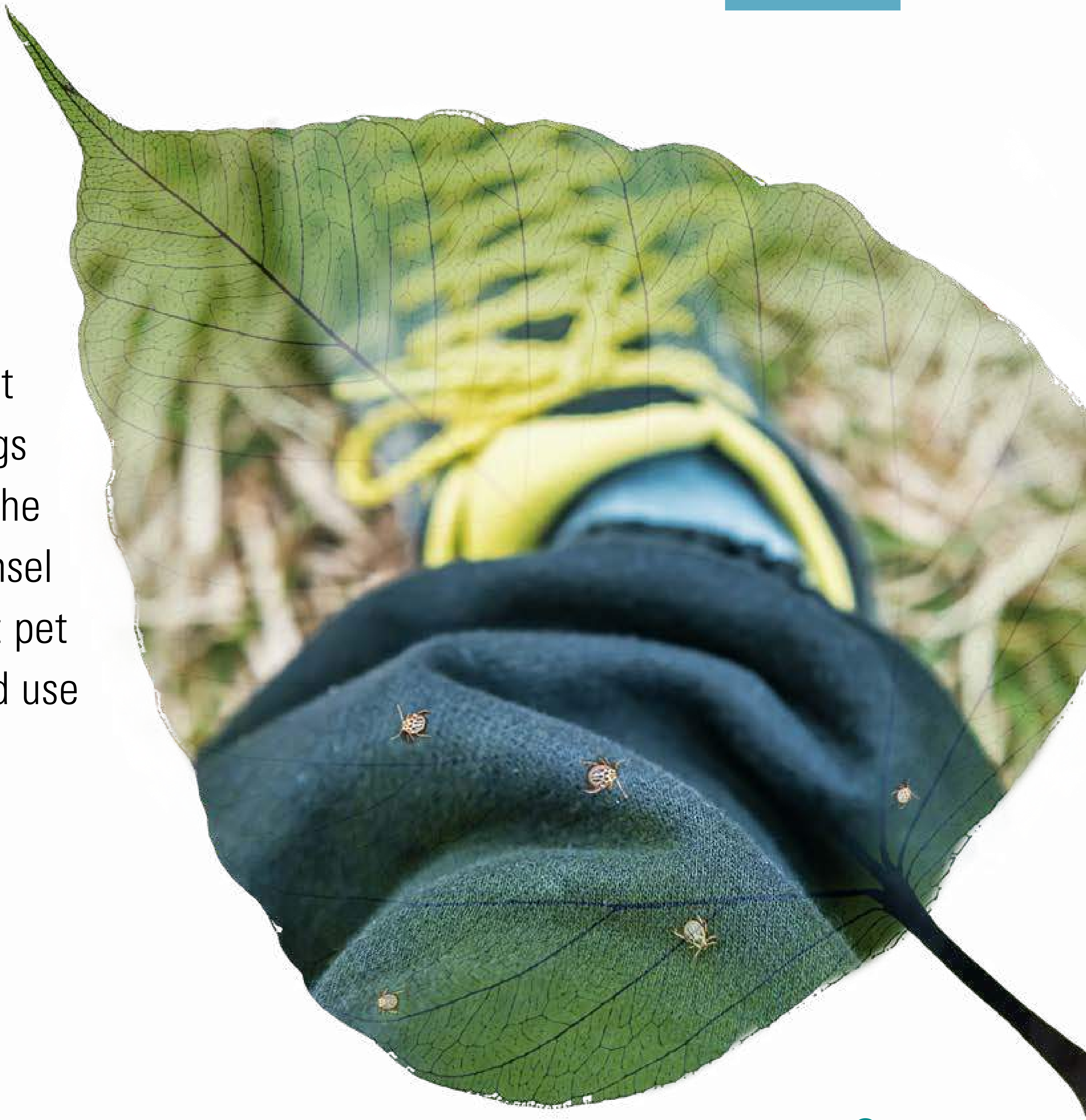
For infections maintained in **sylvatic cycles (*A. phagocytophilum, E. chaffeensis, E. ewingii, R. rickettsii*)**, humans are also at risk of developing severe, life-threatening disease when bitten by a tick, but wildlife serve as the main source of infection to ticks and reservoir for ticks.

Human infection with *R. rickettsii* has been reported due to apparent aerosolization 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.

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?

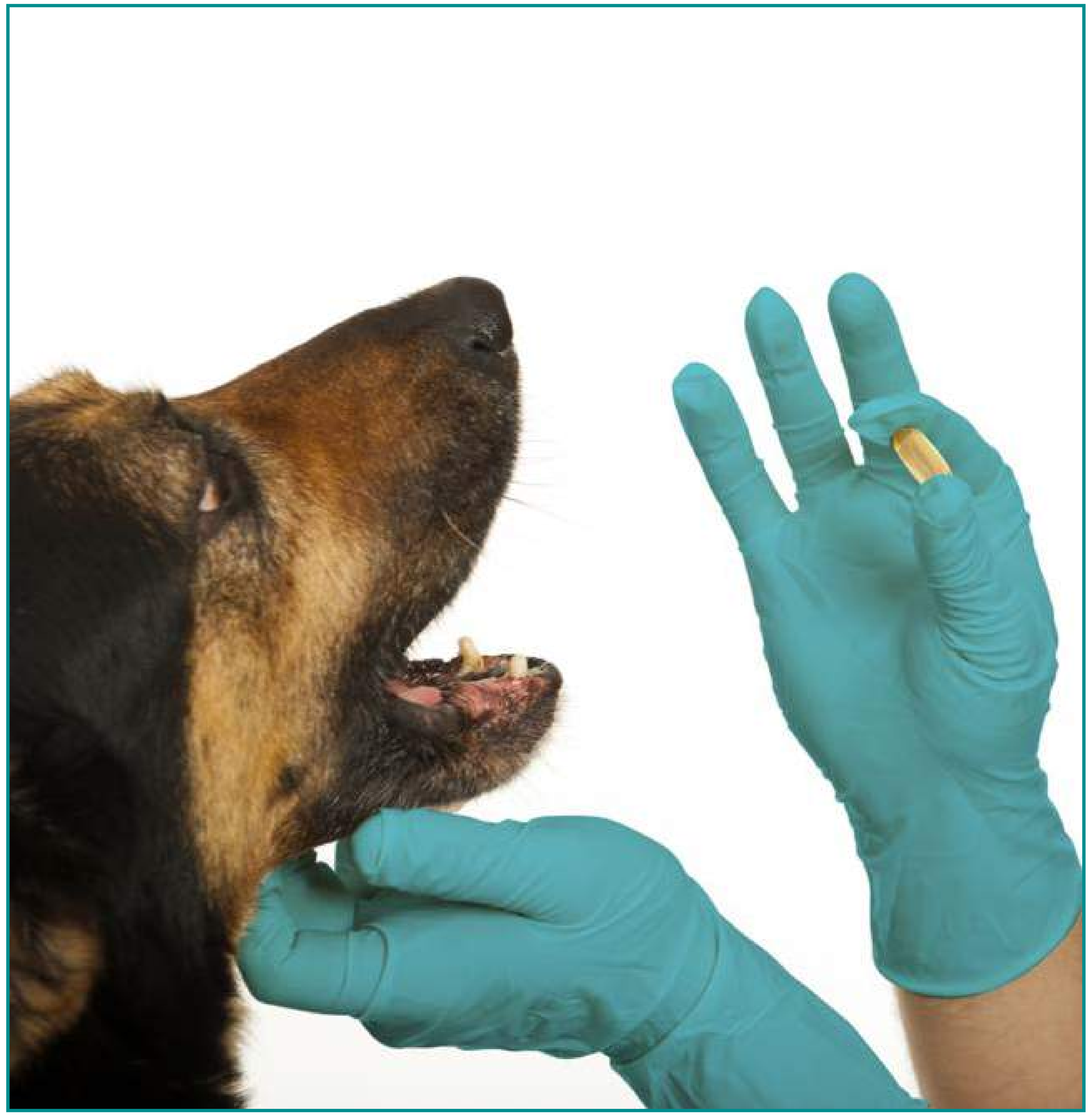
Because it is difficult to precisely predict when sylvatic ticks will be questing in the future, and because domestic brown dog tick populations can establish inside homes and kennels, veterinary advisory boards in many countries recommend routine use of year-round **persistent tick control products.**

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.

WHAT ARE SOME RECOMMENDATIONS
AROUND PREVENTION STRATEGIES?

Is routine testing recommended?

Routine (annual) testing for tick-borne diseases is widely recommended. Early detection of infection alerts the veterinarian 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.



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.

FURTHER READING

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