

# Ehrlichia and Anaplasma<sup>1</sup>

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## Synopsis

*Ehrlichia* and *Anaplasma* are bacteria that cause diseases, known as ehrlichiosis and anaplasmosis, in humans and other animals. *Ehrlichia* and *Anaplasma* are primarily transmitted through the bites of infected hard ticks, such as the lone star tick, the blacklegged tick, and the American dog tick. In the United States, four *Ehrlichia* species and a single *Anaplasma* species are known to cause disease in humans (*Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris euclairensis*, Panola Mountain *Ehrlichia* and *Anaplasma phagocytophilum*). However, human ehrlichiosis and anaplasmosis have not been a severe problem in Florida with no more than 40 confirmed cases every year for each disease. In addition to humans, multiple *Ehrlichia* and *Anaplasma* species cause disease in domestic animals and livestock, resulting in veterinary costs and potentially significant economic losses. Heartwater in domestic ruminants and canine ehrlichiosis in dogs are two significant diseases in animals caused by *Ehrlichia*. Tick prevention and management are the best ways to reduce ehrlichiosis and anaplasmosis in humans and animals.

## Introduction

*Ehrlichia* (Figure 1a) and *Anaplasma* (Figure 1b) are related bacterial genera in the Order Rickettsiales, Family Anaplasmataceae. Species in *Ehrlichia* and *Anaplasma* are obligate intracellular bacteria that are responsible for diseases known as ehrlichiosis and anaplasmosis, respectively, in humans and other animals. Because of the lack of

specific symptoms, diagnostic of these two species relies on serological and/or molecular techniques.

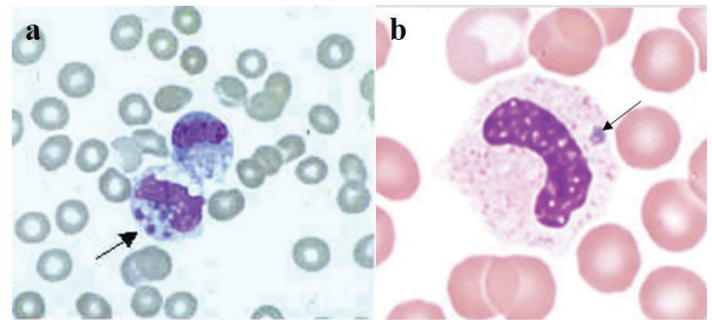


Figure 1. (a) Stained blood showing *Ehrlichia chaffeensis* (arrow) in a white blood cell. (b) Stained blood smear showing *Anaplasma phagocytophilum* (arrow) in a white blood cell.

Credits: (a) Centers for Disease Control and Prevention; (b) Bobbi S. Pritt, Mayo Clinic

Hard ticks (Figure 2), such as *Amblyomma americanum* Linnaeus, the lone star tick; *Ixodes scapularis* Say, the blacklegged tick; and *Dermacentor variabilis* Say, the American dog tick, are the primary biological vectors of both *Ehrlichia* and *Anaplasma* bacteria to humans and other animals. The majority of these bacteria are biologically transmitted (with pathogen reproduction within the host) to human through the bite of infected ticks. In ticks, certain *Ehrlichia* and *Anaplasma* bacterial species can be transmitted through transstadial transmission (from one life stage to the next, i.e., from larva to nymph and from nymph to adult) and transovarial transmission (from female to offspring). Lastly, in addition to biological transmission via ticks, mechanical transmission (without pathogen reproduction within

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the host) by biting flies, particularly horse flies, has been reported (Yunik et al. 2016).

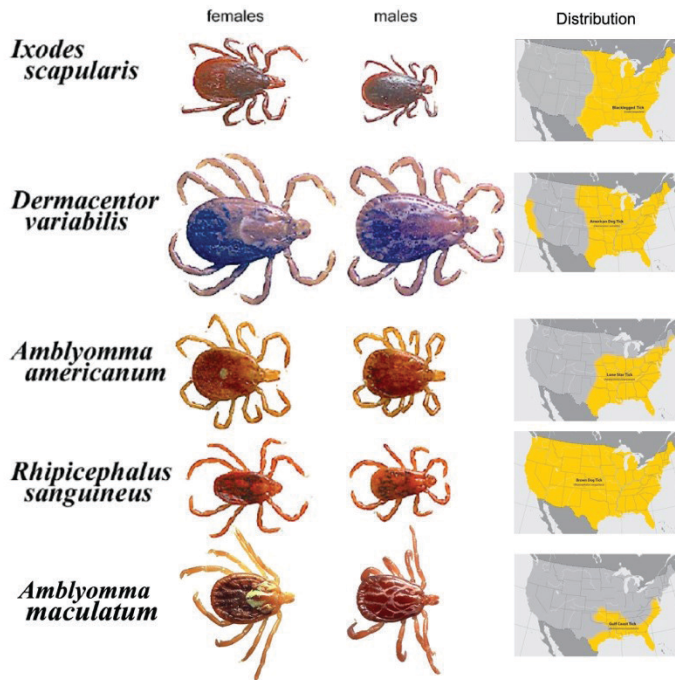


Figure 2. Female and male of *Ixodes scapularis* (blacklegged tick), *Dermacentor variabilis* (American dog tick), *Amblyomma americanum* (lone star tick), *Rhipicephalus sanguineus* (brown dog tick), and *Amblyomma maculatum* (Gulf Coast tick) and their geographical distributions in the United States.

Credits: James Newman, University of Florida

This publication provides an in-depth description of *Ehrlichia* and *Anaplasma* species that cause diseases in humans and/or other animals. Its intended audience is professionals in the fields of acarology, medical entomology, medicine, public health, veterinary medicine, and livestock production, as well as anyone interested in learning more about potential pathogens transmitted by ticks. One thing worth noting is that, due to an improved understanding of these organisms, the names for some *Ehrlichia* and *Anaplasma* species have been revised. Thus, you may find different names in old and new literature that are referring to the same organism.

## Human Disease-Causing *Ehrlichia* and *Anaplasma* in the United States

Currently in the United States, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris euclairensis* (formerly *Ehrlichia muris*-like agent), and Panola Mountain *Ehrlichia* species (Reeves et al. 2008, CDC 2020a) as well as *Anaplasma phagocytophilum* (formerly known as *E. equi* and *E. phagocytophilum*), have been found to cause disease in humans (CDC 2020b). However, other species may be

identified in the future as detection methods are improved. These five pathogens are transmitted transstadially in ticks but not transovarially. The early symptoms of the diseases usually start within 7–14 days after exposure, can be similar for the two diseases, and include malaise (feeling unwell), fever, chills, myalgia (muscle pain), headache, nausea, and rash. Early symptoms in ehrlichiosis cases can sometimes progress to symptoms associated with severe, late-stage illness, such as respiratory failure, uncontrolled bleeding, brain or nervous system damage, organ failure, and death. Severe illness is more likely in those with delayed antibiotic treatment or weakened immune systems and/or the elderly or very young (CDC 2020a).

*Ehrlichia chaffeensis* is the most common bacterium reported in human ehrlichiosis cases and was first described as a human pathogen in 1986 (Dumler et al. 2007). The lone star tick (*Amblyomma americanum*), which is distributed mainly in the south-central and eastern United States but is moving into the Midwest, is the main vector (Figure 2). White-tailed deer (*Odocoileus virginianus*) are recognized as reservoirs in the transmission cycle of *Ehrlichia chaffeensis*. Domestic dogs (Paddock and Childs 2003), raccoons (Ganguly and Mukhopadhyay 2008), and coyotes (Kocan et al. 2000) are also possible reservoirs. Lone star ticks can become infected with *Ehrlichia chaffeensis* when they feed on infected hosts (Long et al. 2003). The pathogen remains in the infected tick and can be transmitted to reservoir species or to human hosts through feeding during the subsequent tick nymphal and adult stages.

*Ehrlichia chaffeensis* is the causative agent responsible for human monocytic ehrlichiosis (HME), mainly by infecting monocytic cells (a type of white blood cell) as well as other cells such as lymphocytes (Ganguly and Mukhopadhyay 2008). According to CDC statistics, the number of reported HME cases has increased from 200 in the year 2000 to more than 1,799 in 2018. However, the fatality rate has decreased. Both of these trends may be, in part, due to increased recognition and diagnosis of cases based on clinical suspicion. Also, early treatment with the antibiotic doxycycline can prevent death and severe illness (CDC 2020a). Although HME cases have been reported throughout the year, summer (June and July) is the peak period, that corresponds to the peak abundance of lone star tick nymphs (Figure 3) and adults (Figure 2) (from April to September) (Holderman and Kaufman 2013). HME is most common in the southeastern United States but human cases have been diagnosed in most US states. This is likely a

result of human travel, considering that the vector does not occur in every state.



Figure 3. Lone star tick nymph.  
Credits: James Newman, University of Florida

### ***Ehrlichia ewingii***

*Ehrlichia ewingii*, which was first described as a human pathogen in 1996 (Dumler et al. 2007), is also vectored by the lone star tick and therefore shares a distribution similar to that of *Ehrlichia chaffeensis*. It also displays a similar transmission cycle and human symptoms, which contributes to the difficulty in distinguishing between infections caused by the two species. These two bacteria can be distinguished by genetic methods that are used in research but not clinical diagnostic tools (based on medical tests and reported symptoms). However, the presence of a rash is rare in *E. ewingii* cases compared to *E. chaffeensis* (Heitman et al. 2016). From 2008–2018, a total of 218 cases of *E. ewingii* ehrlichiosis were reported to CDC, and no fatal cases of *E. ewingii* ehrlichiosis have been reported (CDC 2020a).

### ***Ehrlichia muris euclairensis***

*Ehrlichia muris euclairensis* was known formerly as *Ehrlichia muris*-like agent. It is a human ehrlichiosis-causing pathogen that was first identified in patients from Minnesota and Wisconsin in 2009 (Pritt et al. 2011) and is transmitted by the blacklegged tick (*Ixodes scapularis*) that can be found primarily in the eastern half of the United States (Figure 2). Since its first detection, more than 115 cases of ehrlichiosis caused by *Ehrlichia muris euclairensis* have been identified in the upper midwestern region of the United States. No deaths have been described. The white-footed mouse plays an important role in maintaining

*Ehrlichia muris euclairensis* in nature (Karpathy et al. 2016). Blacklegged ticks (Figure 4) can be infected by *Ehrlichia muris euclairensis* when they feed on infected hosts or co-feed on uninfected hosts with infected ticks (Karpathy et al. 2016). However, the complete ecology of *Ehrlichia muris euclairensis* is not understood at present.

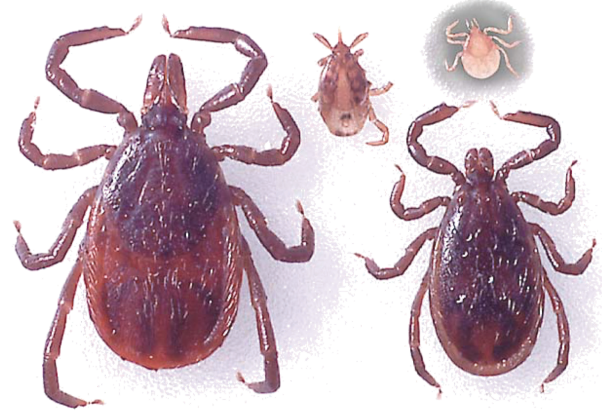


Figure 4. The three life stages of a blacklegged tick: larva, nymph, and adult female and male.

Credits: James Newman, University of Florida

## **Panola Mountain *Ehrlichia* Species**

The Panola Mountain *Ehrlichia* species (PMES) was described as a disease-causing pathogen following its detection from a goat after being exposed to lone star ticks collected at Panola Mountain State Park, Georgia, in 2005. The goat developed a fever at 19 days after the tick fed on it (Loftis et al. 2006). The first human disease caused by PMES was reported in 2008. PMES was detected in blood from a patient after a bite from a nymphal lone star tick (Reeves et al. 2008). Cases of human infection with this pathogen are not as common as infection with the other three *Ehrlichia* species. Genetically, PMES is more closely related to *Ehrlichia ruminantium* (a bacterium that causes the disease heartwater in domestic and wild ruminants—see below) (Reeves et al. 2008). Quantitative polymerase chain reaction (PCR) assays can be used to differentiate PMES and *Ehrlichia ruminantium* (Sayler et al. 2016). The lone star tick is the recognized vector of PMES. However, this pathogen has been detected in wild-caught adult Gulf Coast ticks (*Amblyomma maculatum* Koch) (Figure 2) from the United States and tropical bont ticks (*Amblyomma variegatum* Fabricius) (Figure 5) from the Caribbean and Africa (Loftis et al. 2016). Diagnosis of PMES in patients can be accomplished using PCR and serological tests (Reeves et al. 2008).

*Anaplasma phagocytophilum* was formerly referred to as *E. equi* or *E. phagocytophilum* before taxonomic revision in 2001 (Dumler et al. 2001) and is responsible for human

granulocytic anaplasmosis (HGA), previously known as human granulocytic ehrlichiosis (CDC 2020b). The white-footed mouse is the major mammal reservoir of *Anaplasma phagocytophilum* in nature, although other small mammals, white-tailed deer, other ruminants, and birds can be infected (Dumler et al. 2005, Keesing et al. 2012). Humans acquire the pathogen through infected tick bites (black-legged ticks and western blacklegged ticks, *I. pacificus*, in the United States) and begin to show symptoms within one to two weeks after the tick bite (CDC 2020b). *Anaplasma phagocytophilum* in vertebrates can be detected by PCR assay and serologic testing (Sanchez et al. 2016).



Figure 5. Male (left) and female (right) tropical bont ticks.  
Credits: Alan Walker, University of Edinburgh, UK

## Ehrlichiosis and Anaplasmosis in Other Vertebrates

### *Ehrlichia canis*

*Ehrlichia canis* is one of the common *Ehrlichia* bacteria that causes ehrlichiosis in canine species. It infects mononuclear cells (types of white blood cells) and causes canine monocytic ehrlichiosis (CME) (Harrus and Waner 2011), which also is referred to as canine tropical pancytopenia (condition in which there is a reduction of red and white blood cells and platelets) due to the reduction of all blood cell types observed in this disease (Nicholson et al. 2019). CME caused by *Ehrlichia canis* was first identified in Algeria in 1935 and is now found worldwide. *Ehrlichia canis* is transmitted by the brown dog tick (*Rhipicephalus sanguineus* Latreille) (Figure 2) and can be maintained between tick stages and transmitted to susceptible dogs during nymph or adult blood feeding (Nicholson et al. 2019). All dog breeds can be infected with this species, but German shepherds and Siberian huskies are more susceptible to acute severe illness (Gahalot et al. 2017). Dogs infected with *Ehrlichia canis* usually experience high fever, low appetite, and abdominal pain (Moreira et al 2003). Some infections may progress to a chronic phase with less severe symptoms after the acute infection (Harrus and Waner 2011, Nicholson

et al. 2019). Diagnosis of *Ehrlichia canis* can be made by examining platelet counts and through serological tests. However, co-infections with other tick-borne pathogens can affect the clinical symptoms. PCR and genetic sequencing can be used to provide a definitive confirmatory result (Harrus and Waner 2011).

### *Ehrlichia ewingii* and *Ehrlichia chaffeensis*

*Ehrlichia ewingii* and *Ehrlichia chaffeensis*, transmitted by the lone star tick, are also responsible for canine ehrlichiosis. Based on serological studies of preserved canine serum samples, *Ehrlichia ewingii* is the most prevalent species that causes canine ehrlichiosis in North America, especially in the central and southeastern United States (Beall et al. 2012). This bacterium infects granulocytes (a granulocyte is a type of white blood cell) and causes canine granulocytic ehrlichiosis (CGE). Dogs can acquire *Ehrlichia ewingii* through bites from infected ticks, are able to maintain the pathogen for over two years without developing clinical signs, and serve as reservoir hosts of the pathogen (Starkey et al. 2015). White-tailed deer may serve as reservoir hosts as well (Nicholson et al. 2019). Dogs infected with *Ehrlichia ewingii* usually exhibit kidney disease, anemia, and increased liver enzyme activities (Quorollo et al. 2019). *Ehrlichia ewingii* cannot be distinguished morphologically from *Anaplasma phagocytophilum* in blood smears. Molecular assays must be conducted to provide accurate diagnosis (Nicholson et al. 2019). Dogs in the southcentral and southeastern United States can be infected with *Ehrlichia chaffeensis*. *Ehrlichia chaffeensis* rarely causes clinical disease in dogs by itself with more severe disease symptoms developing with other *Ehrlichia* species co-infections (Nicholson et al. 2019).

### *Ehrlichia ruminantium*

*Ehrlichia ruminantium*, formerly known as *Cowdria ruminantium*, is the agent that causes heartwater disease in domestic ruminants, especially cattle, sheep, and goats, as well as some wild animals such as white-tailed deer (Peter et al. 2002). *Ehrlichia ruminantium* is transmitted by at least 10 *Amblyomma* species, with the tropical bont tick and the bont tick (*Amblyomma hebraeum* Koch) (Figure 6) serving as the primary vectors. Heartwater occurs mainly in sub-Saharan Africa and surrounding islands, such as Madagascar. It is also found in the Caribbean islands after its 19th century introduction through cattle imported from West Africa carrying infected ticks (Allsopp 2015, Nicholson et al. 2019). Infected animals usually develop a fever and loss of appetite, and demonstrate behavioral signs such as abnormal walking. Diarrhea has been observed in cattle. However, age, species, breed of the infected animal, and the

*Ehrlichia ruminantium* genotype may alter clinical signs, making diagnosis difficult (Allsopp 2015). An animal's age, species, breed, and previous exposures also influence its disease outcome. Mortality rates in susceptible livestock can range from <10% to 90% (Spickler 2015). Animals that survive infection acquire immunity. Examination of dead animals often reveals massive fluid accumulation in the heart, lungs, and other organs (Nicholson et al. 2019) (Figure 7). Healthy ruminant hosts can carry the pathogen and transmit infection to feeding ticks for almost one year (Allsopp 2010). Serological tests can diagnose this pathogen in ruminants, while molecular tests can identify the pathogen in both ruminants and infected ticks (Allsopp 2015). Heartwater management can be carried out using tick control, selection of resistant breeds of livestock, antibiotic treatment of infected animals, application of acaricides, and a preventative vaccination.



Figure 6. Male (left) and female (right) bont ticks from South Africa. Credits: James Occi. Rutgers University

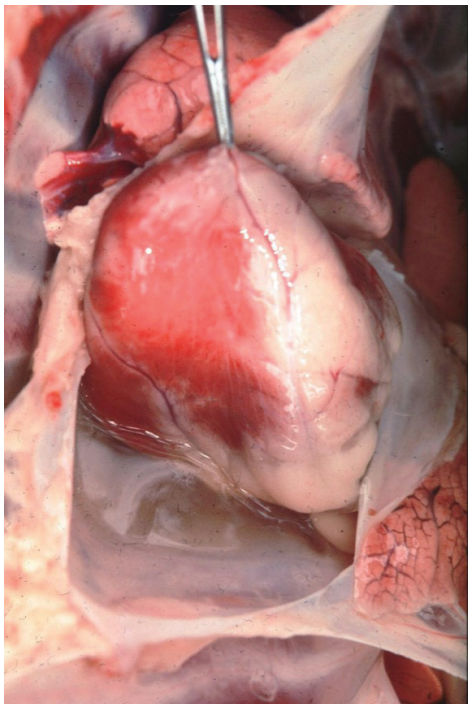


Figure 7. Heart of a goat that died of heartwater disease. Credits: Wikimedia Commons. Alan Walker, University of Edinburgh, UK

Heartwater is one of the most important diseases of livestock in Africa and has caused significant economic losses in Africa and the Caribbean due to livestock death and difficulty in introducing high-yielding livestock breeds, which are more susceptible to *Ehrlichia ruminantium* (Allsopp 2015). The average animal product losses caused by heartwater in southern Africa were estimated to be \$48 million annually (Minjauw et al. 2000) and \$5.6 million in Zimbabwe (Mukhebi et al. 1999). With increased animal trade in the global market, heartwater has posed a potential threat to wildlife and to the livestock industry in the United States (Introduction risk is discussed below), and the United States Department of Agriculture projects an estimated \$762 million in annual losses should a US outbreak occur.

### **Anaplasma phagocytophilum**

*Anaplasma phagocytophilum* is a disease-causing pathogen in livestock and other animals (Dugat et al. 2017) in addition to humans. The vectors of *Anaplasma phagocytophilum* are ticks in the genus *Ixodes*; however, vector species vary based on geographic distribution. Vectors include: castor bean ticks (*Ixodes ricinus* Linnaeus) in Europe, blacklegged ticks in the eastern United States, western blacklegged ticks and *Ixodes spinipalpis* Hadwen and Nuttall in the western United States, and taiga ticks (*Ixodes persulcatus* Schulze) in Asia (Dugat et al. 2015). *Anaplasma phagocytophilum* can be transmitted between tick stages but not through trans-ovarial transmission (Nicholson et al. 2019). Rodents and white-tailed deer serve as reservoir hosts in the transmission cycle (Dugat et al. 2015). The most common symptoms in ruminants are high fever (>41°C), loss of appetite, and sudden milk yield reduction (dairy cattle), which causes significant economic impacts in Europe (Stuen et al. 2013). However, the severity of symptoms is affected by multiple factors including the animal's age, immunity, and species, as well as pathogen variants (Stuen et al. 2013). *Anaplasma phagocytophilum* can infect horses and cause equine granulocytic anaplasmosis (EGA) with symptoms of fever, weakness, anemia, and reduction of white blood cells (Dugat et al. 2015). EGA is an endemic disease, and its prevalence varies in different regions (Saleem et al. 2018). During the initial fever period, diagnosis can be accomplished by microscopy of a blood smear, while PCR and serological tests can be used during the later stages after infection (Stuen et al. 2013).

### **Anaplasma marginale**

*Anaplasma marginale* infects red blood cells and causes anaplasmosis in cattle and sheep throughout most the world (Nicholson et al. 2019). Bovine anaplasmosis, caused

by *Anaplasma marginale*, is considered the most important rickettsial disease in cattle and results in significant economic loss in livestock production (Quiroz-Castañeda et al. 2016).

This pathogen can be transmitted biologically by approximately 20 hard tick species. Rocky Mountain wood ticks (*Dermacentor andersoni* Stiles) (Figure 8) and American dog ticks serve as primary vectors in the United States (Kocan et al. 2010). In particular, male Rocky Mountain wood ticks are important vectors due to multiple-host feeding, the shorter extrinsic incubation period (pathogen cycle in the tick), and shorter feeding periods on hosts compared to female ticks (Nicholson et al. 2019). For American dog ticks, white-tailed deer are an important host for these tick species and can be infected, but are not a competent reservoir of *Anaplasma marginale*, which means uninfected ticks cannot acquire this pathogen from white-tailed deer. Mule deer serve as primary hosts and competent reservoirs in the western United States (Nicholson et al. 2019).



Figure 8. Male (left) and female (right) Rocky Mountain wood ticks. Credits: Centers for Disease Control and Prevention

Blood-sucking flies, such as the [stable fly \(\*Stomoxys calcitrans\* Linnaeus\)](#) and Tabanidae species (such as the horse fly and the deer fly), and blood-contaminated fomites, such as re-used needles and ear tag application tools, can also serve as mechanical transmission vectors of *Anaplasma marginale* (Kocan et al. 2010). While mechanical transmission may not be as effective as biological transmission via ticks (Scoles et al. 2005), mechanical transmission seems to be the primary route when *Anaplasma marginale* strains (a genetic variant or subtype of the bacteria) are not infective for ticks and in areas without tick populations (Kocan et al. 2004).

The severity of symptoms in infected animals increases with age. Without adequate treatments, recovered animals maintain low-level parasitemia and develop lifelong immunity to clinical disease (Eriks et al. 1989). However, they can serve as reservoirs by providing infective blood sources for both mechanical and biological transmission (Kocan et al. 2003). Diagnosis of bovine anaplasmosis may be made based on animal location, season, and clinical signs, but requires laboratory tests, such as microscopic evaluation of

stained blood smears and serological tests, to confirm the infection (Kocan et al. 2010).

## Florida Situation

Several tick species that transmit *Ehrlichia* or *Anaplasma* bacteria are present in Florida, including brown dog ticks, American dog ticks, lone star ticks, Gulf Coast ticks, and blacklegged ticks. Human ehrlichiosis and anaplasmosis have not been a severe problem in Florida with no more than 40 confirmed cases every year for each disease (FDOH 2018). However, underreporting or misdiagnosis of cases may occur due to mild symptoms and lack of laboratory testing.

In 2018, there were 4,899 reported positive canine ehrlichiosis cases identified from 273,051 tested samples and 1,410 canine anaplasmosis cases identified from 273,001 tested samples (CAPC 2020). For more information, please visit the [Companion Animal Parasite Council's website](#). Infected ticks may be brought to Florida by migratory birds or on imported reptiles, which could result in the introduction of *Ehrlichia ruminantium* into our native tick species, such as Gulf Coast ticks, which have been demonstrated to be competent vectors of *Ehrlichia ruminantium* in the laboratory (Mahan et al. 2000). A breeding population of African tortoise ticks (*Amblyomma marmoreum* Koch), reported to be a competent vector of *Ehrlichia ruminantium* within the laboratory (Peter et al. 2000), was discovered in a reptile breeding facility located in Florida (Allan et al. 1998). It was thought to be introduced with the tortoises imported from Africa. This tick population was eradicated, but this example shows the potential for introduction. Other exotic tick species, such as central African tortoise tick (*Amblyomma sparsum* Neumann), have been found on imported reptiles in Florida (Burrige et al. 2000). Thus, reptile importation is closely monitored in Florida.

## Prevention and Management

For human ehrlichiosis and anaplasmosis, there is no vaccine that can be used, and the best prevention is tick management. Ticks usually live in grassy, brushy, or wooded areas, except the brown dog tick that can survive both indoors and outdoors. Thus, many people acquire ticks from their yard or from hiking. There are multiple personal protection methods that can be used to reduce human-tick contact and avoid tick bites, such as long pants tucked into socks, acaricide-treated clothes, Environmental Protection Agency-registered insect repellents (for more information, please visit [EPA](#)), and conducting thorough body checks for ticks after visiting tick habitat. For other animals,

tick prevention can be accomplished by many methods including sprays, spot-ons, collars, and ear tags containing approved acaricides such as permethrin, fipronil, amitraz, as well as tick checks and grooming. However, all acaricide uses must follow label directions to avoid poisoning and acaricide resistance in tick populations. Consult with your veterinarian because some species or breeds are sensitive to some acaricides, and severe illness or death can result. Some products are available only by prescription.

Ticks found on humans and other animals should be removed immediately using fine-tipped forceps to reduce the risk of pathogen infections. When removing the ticks, grasp the tick as near the skin as possible and pull straight back without twisting to avoid breaking and leaving the mouthparts in the skin, which can cause bacterial infections (Figure 9). After tick removal, symptoms should be monitored closely. If illness occurs within 30 days of a tick bite, a doctor or veterinarian visit should be made. Only a doctor or a veterinarian can prescribe the appropriate treatments for ehrlichiosis and anaplasmosis.

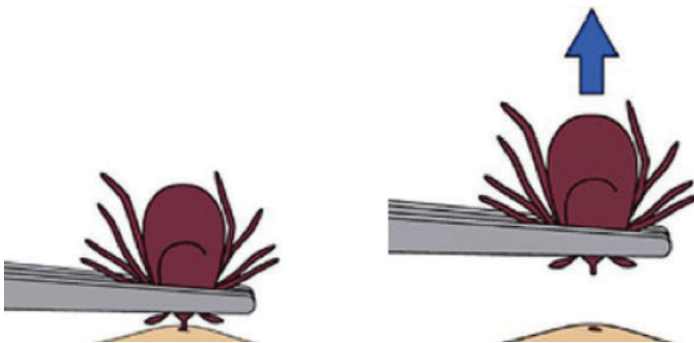


Figure 9. How to properly remove a tick using tweezers.  
Credits: Centers for Disease Control and Prevention

For more information, please visit [Ticks \(Family Ixodidae\)](#), [EDIS Publication #ENY-206](#), the [CDC's Ehrlichiosis website](#), and the [CDC's Anaplasmosis website](#).

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