



Ticks and Tick-Borne Zoonotic Diseases: A Comprehensive Review

Faraz Malek Bagali¹, Zahra Asim², Samaneh Arafeh³, Zahra Nickvar⁴¹Department of Microbiology, School of Medicine, Ardabil University of Medical Sciences, Iran^{2,3,4} Students Research Committee, Ardabil University of Medical Sciences, Iran**Submitted:** July 11, 2025**Revised:** September 24, 2025**Accepted:** November 05, 2025

Correspondence

Faraz Malek Bagali

farazmalek36@gmail.com

Abstract Ticks are among the most important arthropod vectors, responsible for transmitting a wide variety of zoonotic pathogens, including bacteria, viruses, and protozoa, which pose serious threats to both human and animal health worldwide. Changes in the environment and increased interactions between humans and wildlife have expanded the geographic range of ticks, contributing to a rise in tick-borne diseases. This review provides a comprehensive overview of tick biology, ecology, and vector competence, alongside the epidemiology, pathogenesis, and clinical features of major tick-borne zoonotic diseases such as Lyme disease, ehrlichiosis, tularemia, and Crimean-Congo hemorrhagic fever (CCHF). It also discusses current challenges in diagnosis, treatment, and prevention, emphasizing the importance of integrated surveillance and control strategies. By summarizing recent findings and highlighting knowledge gaps, this review aims to guide future research and support public health efforts to reduce the global impact of tick-borne zoonotic diseases. Ticks play a prominent role in causing new and re-emerging diseases. This review aims to provide an overview of ticks and tick-borne diseases.

Keywords: Ticks, Tick-borne pathogens, Arthropod vectors, Zoonosis.

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Introduction Ticks are blood-feeding arthropods with relatively large bodies, found worldwide (Table 1). They belong to the order *Metastigmata* within the class *Arachnida* and subclass *Acari*, and over 900 species have been identified, divided into three families: *Argasidae* (soft ticks, ~200 species), *Ixodidae* (hard ticks, ~700 species), and *Nuttalliellidae* (just one species). Soft ticks (*Argasidae*) have flexible, leathery bodies without a hard dorsal shield, which allows them to hide in narrow crevices for long periods (1). Important genera include *Argas*, *Ornithodoros*, and *Otobius*. They usually feed quickly, often at night, and can carry viruses and bacteria that infect both animals and humans. Hard ticks (*Ixodidae*) have a rigid scutum on their backs and include 692–750 species. They are split into two groups: *Prostriata* (*Ixodes*) and *Metastricata* (all other genera), with life cycles that often involve one to three hosts (2). *Nuttalliellidae* is represented by a single species, *N. namaqua*, found in South Africa. Its unique traits make it a kind of evolutionary bridge between hard and soft ticks. Ticks are obligate parasites; they must feed on blood, lymph, or tissue fluids to survive. They target a wide range of animals, from mammals and birds to reptiles and amphibians, but livestock are particularly

affected (3). Beyond being a nuisance, ticks can transmit numerous diseases to humans and animals, including Rocky Mountain spotted fever, Q fever, Lyme disease, Tularemia, Anaplasmosis, Ehrlichiosis, Crimean-Congo hemorrhagic fever, tick-borne encephalitis, babesiosis, and theileriosis. Some female ticks can even pass pathogens to their offspring through their eggs (4). Although only about 10% of ticks feed on domestic animals, infestations in livestock can cause serious problems: reduced milk production, weight loss, paralysis, anemia, and skin irritation, leading to substantial economic losses. Knowing which tick species are present in a region, and where they are most common, is crucial for controlling tick populations and preventing the spread of diseases (5). Ticks play a prominent role in causing new and re-emerging diseases. This review aims to provide an overview of ticks and tick-borne diseases.

Table 1. Tick family

Family	Key Genera / Species	Main Pathogens Transmitted	Geographic Distribution
Argasidae (Soft ticks)	<i>Argas persicus</i> , <i>Ornithodor</i>	<i>Borrelia</i> spp., African	Africa, Middle East,

	<i>os moubata</i> , <i>Otobius megnini</i>	swine fever virus, tick-borne relapsing fever, <i>Rickettsia</i> spp.	Europe, Americas
Ixodidae (Hard ticks)	<i>Ixodes scapularis</i> , <i>Rhipicephalus microplus</i> , <i>Amblyomma americanum</i> , <i>Dermacentor variabilis</i>	<i>Babesia</i> spp., <i>Anaplasma</i> spp., <i>Rickettsia rickettsii</i> , Powassan virus, tick-borne encephalitis virus	North America, Europe, Africa, Asia, Australia
Nuttalliellidae (Monotypic)	<i>Nuttalliella namaqua</i>	Unknown or experimental pathogens; potential intermediate traits	Southern Africa

Methods

This review was based on an extensive literature search carried out in PubMed, Google Scholar, Scopus, and Web of Science, covering studies published between 2000 and 2025. The search strategy used combinations of keywords such as “ticks,” “tick-borne pathogens,” “arthropod vectors,” and “zoonosis.” We included peer-reviewed articles, original research, reviews, and case reports that addressed human and animal infections, epidemiology, clinical features, diagnostics, and control measures. Studies were excluded if they were not in English, lacked primary data, or were only available as conference abstracts. Relevant publications were carefully screened, and data were extracted on pathogen taxonomy, transmission, geographic distribution, clinical presentation, diagnostic methods, treatment, and prevention. The collected information was synthesized narratively and organized into tables to ensure clarity and accessibility.

Tick-borne bacteria

Tick-borne bacteria (Table 2) are a group of pathogens transmitted to humans and animals through various tick species, causing a wide range of diseases. These bacteria can multiply within ticks and be

passed on through bites, secretions, or even vertically to their offspring. Due to the great diversity and widespread distribution of ticks, infections caused by these bacteria have been reported in many parts of the world. A key feature of these pathogens is their ability to cause both acute and chronic infections, posing significant challenges for public health and veterinary medicine in terms of diagnosis, prevention, and control. This makes the study and monitoring of tick-borne bacteria critically important (6).

Q fever

Q fever is a globally distributed zoonotic disease caused by the intracellular bacterium *Coxiella burnetii*, which infects a wide range of domestic and wild animals and can be transmitted to humans through inhalation of contaminated aerosols, contact with infected birth products, or consumption of unpasteurized dairy products (7). Although many human cases are mild or asymptomatic, some can develop chronic infections, including endocarditis, requiring prolonged treatment. The bacterium is highly resilient in the environment, capable of surviving for months in wool, meat, or milk, and can spread through aerosols, making it a significant public and veterinary health concern (8). Ticks play an important role in maintaining and spreading *C. burnetii* among animals, with more than 40 hard tick and 14 soft tick species documented as carriers. These ticks can maintain infection across life stages and transmit the bacterium vertically to offspring. Recent studies have highlighted the epidemiological importance of Q fever, particularly in Africa (9). Systematic reviews indicate that cattle seroprevalence is generally below 13%, though in Western and Central Africa it can reach 18–55%. Small ruminants show 11–33% seroprevalence. In humans, rates are typically under 8%, with higher figures in children and regions like Egypt (10–32%). Major risk factors include close contact with livestock, especially camels, and rural living. Q fever continues to be linked to livestock abortions and contributes to 2–9% of febrile hospitalizations and 1–3% of infective endocarditis cases in humans, yet precise incidence and control data remain limited. These findings underscore *C. burnetii* as an ongoing, under-recognized threat to both human and animal health (10).

Lyme disease

Borrelia burgdorferi, the bacterium that causes Lyme disease, is one of the most important tick-borne pathogens in the Northern Hemisphere, especially in North America, Europe, and parts of Asia. It spreads to humans through the bite of hard ticks, and infections can range from mild, flu-like symptoms to

chronic complications affecting joints, nerves, and skin (11). This bacterium has a unique spiral-shaped genome with a chromosome and several plasmids that help it survive in both ticks and mammals, adapt to different hosts, and evade the immune system. Small rodents and birds often carry the bacterium without showing symptoms, but humans typically develop a red rash at the bite site, fever, fatigue, and muscle aches. If left untreated, the disease can progress to long-term issues like Lyme arthritis, neurological problems, or chronic skin conditions. Interestingly, the clinical manifestations vary by region: *B. burgdorferi sensu stricto* is linked mostly to arthritis in North America, *B. garinii* to neurological disease in Europe, and *B. afzelii* to chronic skin disorders (12). Ticks are most likely to transmit the infection during their nymphal stage because these tiny ticks often go unnoticed. The bacterium relies on host nutrients for survival and expresses specific surface proteins to adapt to ticks and mammals at different stages of its life cycle. Laboratory studies in mice and primates have helped reveal how the bacterium causes disease and how the immune system responds (13). Lyme disease is steadily emerging as a significant public health concern. Recent estimates suggest about 300,000 cases per year in the United States and at least 85,000 in Europe, highlighting the ongoing need for awareness, prevention, and early diagnosis (14).

Relapsing fever

Relapsing fever was first described following an outbreak in Edinburgh, UK. Otto Obermeier identified the infectious agent in 1868, but confirmation of Koch's postulates was delayed until 1873 (15). The human body louse (*Pediculus humanus*) was later recognized as the vector for epidemic louse-borne relapsing fever (LBRF), which caused high mortality in overcrowded and impoverished settings (16). Another form of relapsing fever is transmitted by soft ticks (*Ornithodoros* spp.), first linked to disease by Livingstone in 1857 and later confirmed by Ross, Milne, Dutton, and Todd in the early 20th century. Dutton himself contracted the disease, highlighting the occupational risk of research. Many *Borrelia* species show strong adaptation to specific tick vectors, though *B. Recurrentis* is transmitted by lice. Some hard-tick-transmitted species, such as *B. miyamotoi* and *B. lonestari*, challenge traditional vector-based classification (17). Currently, 23 relapsing fever *Borrelia* species are recognized, with genetic studies revealing diverse clades and subpopulations within species like *B. hermsii* and *B. duttonii*. Relapsing fever *Borrelia* are Gram-negative, spiral-shaped

bacteria with 3–10 coils and up to 30 periplasmic flagella, enabling rapid motility (18). Their outer membranes contain conserved porins (e.g., p66, Oms38) and they express variable major proteins (*Vmps*), which are key for immune evasion, tissue tropism, and adaptation to hosts. *Vmps* are divided into small (*Vsps*) and large (*Vlps*) groups; specific *Vsp* variants are linked to clinical outcomes, such as CNS or bloodstream infections (19). These bacteria are microaerophilic and metabolically fastidious, relying on host-derived nutrients. Their limited biosynthetic pathways make culturing difficult, reflecting their high adaptation to host environments. The recurrent nature of relapsing fever is largely due to sequential expression of *Vmps*, which allows immune evasion and successful transmission to vectors. Despite genetic diversity, structural and physiological traits are conserved, offering potential targets for diagnostics and vaccine development (20).

Anaplasmosis

Anaplasma species are Gram-negative, obligate intracellular bacteria that primarily infect the blood cells of mammals. They lack a complete cell wall and lipopolysaccharides (LPS), which allows them to evade host immune responses (21). These bacteria cannot survive outside a host and rely on transmission through hard ticks, including species of *Ixodes*, *Dermacentor*, *Rhipicephalus*, *Amblyomma*, and *Haemaphysalis*. The distribution of these tick vectors varies geographically, such as *I. ricinus* in Europe, *I. persulcatus* in Northern Asia, *I. scapularis* and *I. pacificus* in North America, and *R. sanguineus* and *A. americanum* in tropical regions. Tick activity is influenced by environmental factors, including climate, season, and host availability (22). Different *Anaplasma* species affect specific hosts and tissues. *A. marginale* infects red blood cells of cattle, causing bovine anaplasmosis with symptoms such as anemia, fever, weight loss, and abortion. *A. centrale* is less pathogenic and is used as a live vaccine against bovine anaplasmosis. *A. ovis* infects sheep and goats, leading to anemia and reduced milk production, while *A. bovis* targets monocytes in cattle and small mammals, causing weakness, fever, and lymphadenopathy. In dogs, *A. platys* infects platelets and causes cyclic thrombocytopenia. *A. phagocytophilum* is the primary species pathogenic to humans, causing human granulocytic anaplasmosis (HGA), a multisystem illness characterized by fever, headache, muscle pain, and, in severe cases, neurological or hepatic complications (23, 24). The life cycle of *Anaplasma* involves intracellular replication in animal or human hosts and transmission through tick vectors. Ticks acquire the pathogen by

feeding on infected hosts and can transmit it horizontally via bites or vertically to their eggs. In animals, anaplasmosis results in significant economic losses due to reduced productivity, abortions, treatment costs, and mortality. In humans, early treatment with doxycycline is effective, while alternative antibiotics are used in cases of resistance or drug allergies (25). Environmental changes, including climate change, deforestation, expansion of livestock farming, and increases in wildlife populations, have contributed to the proliferation of ticks and the spread of *Anaplasma* infections. The movement of pathogens from endemic to non-endemic regions further complicates disease detection and control, highlighting the need for molecular tools for effective diagnosis, surveillance, and epidemiological assessment (26).

Ehrlichiosis

Ehrlichiosis is an emerging tick-borne zoonotic disease caused by *Ehrlichia chaffeensis*, an obligate intracellular Gram-negative bacterium that primarily infects monocytes and macrophages. First identified in the late 20th century in the southeastern United States, HME can range from a mild febrile illness to a severe and sometimes fatal disease. The Lone Star tick (*Amblyomma americanum*) is the primary vector responsible for transmission to humans, and it is widely distributed throughout the south-central and southeastern United States (27). The pathogenicity and persistence of *E. chaffeensis* are closely linked to its ability to survive and replicate within host mononuclear phagocytes. After entering host cells via receptor-mediated endocytosis, the bacterium exploits early endosomes to extract iron directly from the transferrin-iron complex. It also upregulates transferrin receptor expression on host cells to enhance iron availability (28). Normally, interferon-gamma (IFN- γ) restricts bacterial growth by downregulating transferrin receptors and lowering intracellular iron levels. *E. chaffeensis* rapidly neutralizes this effect by activating the host's protein kinase A (PKA) signaling pathway. The bacterium remains within membrane-bound vacuoles that avoid acidification and lysosomal fusion, protecting it from degradation. A 37-kDa bacterial protein similar to iron-binding proteins is likely involved in iron storage or acquisition (29). Studying *E. chaffeensis* has been challenging due to limited animal models. White-tailed deer (*Odocoileus virginianus*) serve as the primary natural reservoir, maintaining persistent bacteremia without clinical signs and transmitting the pathogen to feeding ticks (30). Dogs can be naturally infected, showing clinical signs similar to related *Ehrlichia* species. Experimental infection in mice

with related species, such as *Ehrlichia muris*, causes mild illness, while the *Ixodes ovatus ehrlichia* (IOE) strain induces a severe, often fatal disease resembling human HME. The IOE-mouse model remains the most effective for studying severe ehrlichiosis (31). The incubation period in humans typically lasts 1 to 2 weeks after a tick bite. Early symptoms are nonspecific, including malaise, headache, muscle aches (myalgia), nausea, and joint aches (arthralgia). Additional features may include cough, pharyngitis, lymphadenopathy, gastrointestinal symptoms, and altered mental status (32). Cutaneous rash occurs in 30–40% of patients, particularly in children and immunocompromised individuals, presenting as petechiae, macules, or maculopapules, usually around day five of illness. Laboratory findings often include leukopenia (mostly lymphopenia), thrombocytopenia, anemia, elevated liver enzymes, electrolyte disturbances such as hyponatremia, and coagulation abnormalities (33). The Lone Star tick is the principal vector in the United States, feeding on various vertebrate hosts at all life stages. Transstadial transmission is well established, while transovarial transmission remains unconfirmed (34). Adult ticks are most active in early summer, coinciding with increased human cases. *A. americanum* exhibits aggressive feeding behavior and feeds on humans, white-tailed deer, domestic dogs, and small mammals. White-tailed deer act as the main reservoir, sustaining infection without symptoms and transmitting the pathogen to ticks. Other wildlife, such as raccoons, opossums, coyotes, and rodents, may harbor *E. chaffeensis*, but their role in long-term maintenance is less clear. Humans are incidental hosts who acquire infection via tick bites but do not contribute to the natural cycle (35).

Tularemia

Francisella tularensis is a Gram-negative, non-spore-forming coccobacillus, usually aerobic or microaerophilic, classified within the order *Thiotrichales*. It is encapsulated and exhibits notable resistance to certain antibiotics due to its unique cell wall structure (36). The bacterium grows on enriched media, such as chocolate agar, but is difficult to culture on standard laboratory media. Because of these characteristics, *F. tularensis* is considered a biosafety level 3 pathogen. Genetically, several species exist within the genus *Francisella*, but only *F. tularensis* is recognized as the primary human pathogen causing tularemia (37). This species is divided into three main subspecies based on genetic, biochemical, and geographic differences: *F. tularensis* subsp. *tularensis* (Type A), predominantly found in North America and highly virulent; *F.*



tularensis subsp. holarctica (Type B), distributed across Eurasia and parts of North America, and less virulent; and *F. tularensis* subsp. Mediasiatika is limited to Central Asia, with limited knowledge about its human pathogenicity. Another species, *F. novicida*, is closely related genomically but generally affects immunocompromised individuals rather than healthy humans (38). Tularemia is endemic in the Northern Hemisphere, reported across Europe, northern and Central Asia, North America, and recently in some Southern Hemisphere regions such as Tasmania. Type A disease is mainly associated with cottontail rabbits and hard ticks (*Dermacentor variabilis* and *D. andersoni*) and causes more severe illness with higher mortality (39). Type B is more widespread, typically causing milder disease, and is often transmitted through contact with contaminated water, soil, or infected rodents. Type mediasiatica has been reported only in regions such as Kazakhstan and Turkmenistan, with very limited data on its pathogenicity. The bacterium can enter humans through skin wounds, inhalation, ingestion, or arthropod bites, including ticks, mosquitoes, and deer flies. Small mammals serve as natural reservoirs, while ticks and other blood-feeding arthropods act as vectors (40). Aerosolized bacteria pose particular risks for respiratory infection, which can lead to severe pneumonic tularemia, especially in laboratory or agricultural settings. Clinical manifestations of tularemia vary depending on the route of infection. Ulcerglandular tularemia is the most common, characterized by a painful skin ulcer and swollen lymph nodes, often following a tick bite or contact with animals (41). Glandular tularemia lacks the skin ulcer but also presents with lymphadenopathy. Oculoglandular tularemia affects the eye, causing redness, pain, discharge, and nearby lymph node swelling. Oropharyngeal tularemia occurs after ingestion of contaminated food or water, with sore throat, mouth ulcers, fever, and cervical lymphadenopathy (42). Typhoidal tularemia is a severe systemic form without local signs, leading to high fever, weakness, digestive symptoms, and potential pneumonia or sepsis. Pneumonic tularemia, resulting from inhalation of the bacteria, is the most dangerous form and can be life-threatening if untreated (43).

Rocky Mountain spotted fever (RMSF)

RMSF is a severe and potentially fatal infectious disease in the Western Hemisphere caused by *Rickettsia rickettsii*. First identified in the early 20th century in the western United States, RMSF now occurs throughout North, Central, and South America. As a tick-borne zoonotic disease, its

transmission is closely linked to the ecology and behavior of ticks. This article reviews the microbiology, epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment, and host immune response associated with RMSF (44). *R. rickettsii* is a small, obligate intracellular Gram-negative bacterium belonging to the family *Rickettsiaceae* and the Spotted Fever Group (SFG). Its reduced genome contains only essential genes for intracellular survival, making it highly dependent on host cells. The bacterium has a unique cell wall with immunogenic lipopolysaccharides, contributing to host immune recognition (45). RMSF is endemic in parts of the United States, Mexico, Central America, and Brazil. In the U.S., the primary vectors are *D. variabilis* in the east and *D. andersoni* in the west, while *A. cajennense* is important in South America. Disease incidence peaks in spring and summer due to increased tick activity and human exposure to nature (46). Hard ticks have a four-stage life cycle, including egg, larva, nymph, and adult, feeding once per stage. *R. rickettsii* enters ticks during blood feeding and localizes in organs such as the gut, salivary glands, and ovaries. Transmission to new hosts occurs via saliva during feeding and through transovarial and transstadial transmission, allowing the bacteria to persist independently of mammalian hosts. After an infected tick bite, *R. rickettsii* infects endothelial cells, replicates intracellularly, and triggers cell lysis, vascular leakage, thrombosis, and systemic inflammation (47). This leads to widespread vasculitis, tissue edema, multi-organ damage, and, in severe cases, death. The host immune response is delayed due to the intracellular lifestyle of the pathogen, which significantly influences disease severity (48). Early clinical symptoms include high fever, severe headache, myalgia, nausea, and a characteristic petechial rash that typically begins on the wrists and ankles before spreading toward the trunk. In some patients, particularly the elderly, the rash may be absent, complicating diagnosis. Severe cases can involve shock, bleeding, organ failure, and coma. Diagnosis is primarily clinical, supported by serological tests such as immunofluorescence assay (IFA) for specific IgM/IgG, PCR from blood or tissue samples, and immunohistochemical staining of skin biopsies in later stages. Due to delays in laboratory confirmation, treatment should begin based on clinical suspicion (49). Doxycycline is the drug of choice for all age groups, including pregnant women, and should be administered promptly at a standard adult dose of 100 mg orally or intravenously twice daily for at least seven days. Preventive measures focus on avoiding tick exposure, wearing protective

clothing, using DEET-containing repellents, inspecting skin after outdoor activities, and controlling tick populations in endemic regions. No effective vaccine is currently available for RMSF (50). Tick saliva contains immunomodulatory compounds that suppress host immune responses, facilitating bacterial entry and establishment. Molecules such as prostaglandin E2 inhibit dendritic cell activity and delay immune responses. Different tick species vary in their ability to transmit, replicate, and support *R. rickettsii*. For example, *A. maculatum* transmits the bacteria more efficiently due to higher bacterial loads in saliva. Variations in tick saliva composition may influence the severity of immune and clinical responses (51).

Table 2. Tick-borne bacteria

Bacterium	Disease	Main Vector(s)	Natural Host(s)	Pathogen Characteristics	Clinical Manifestations	Diagnosis	Treatment	Prevention
<i>Borrelia burgdorferi</i>	Lyme disease	<i>Ixodes spp.</i> (hard ticks)	Small mammals, birds	Gram-negative spirochete lacks classical LPS and toxins, and plasmid diversity.	Erythema migrans, fever, fatigue, later: arthritis, neuroborreliosis	PCR, Serology (ELISA, Western blot)	Doxycycline, Amoxicillin	Avoid tick bites, protective clothing, and repellents
<i>Borrelia spp.</i> (relapsing fever)	Relapsing fever	<i>Ornithodoros spp.</i> (soft ticks), <i>Pediculus humanus</i> (body louse)	Rodents, humans	Gram-negative spirochete, variable major proteins (Vmps) for immune evasion	Recurrent fever, chills, myalgia, sometimes CNS involvement	PCR, Microscopy, Serology	Doxycycline, Tetracycline	Vector control: Avoid contact with rodents and contaminated clothing
<i>Anaplasma phagocytophilum</i>	Human granulocytic anaplasmosis (HGA)	<i>Ixodes spp.</i> , <i>Dermacentor spp.</i> , <i>Rhipicephalus spp.</i> , <i>Amblyomma spp.</i>	Sheep, cattle, dogs, rodents	Obligate intracellular Gram-negative, lacks a complete cell wall and LPS, host-dependent	Fever, headache, myalgia, sometimes hepatic and hematologic abnormalities	PCR, Serology	Doxycycline	Avoid tick bites, protective clothing, and repellents

<i>Anaplasma marginale / centrale / ovis / bovis / platys</i>	Animal anaplasmosis	<i>Ixodes, Dermacentor, Rhipicephalus, Amblyomma spp.</i>	Cattle, sheep, goats, and dogs	Obligate intracellular, targets RBCs or monocytes	Anemia, fever, weight loss, reduced milk production, abortion	PCR, Blood smear	Doxycycline, supportive care	Tick control, live attenuated vaccine (A. centrale)
<i>Ehrlichia chaffeensis</i>	Human monocytic ehrlichiosis (HME)	<i>Amblyomma americanum (Lone Star tick)</i>	White-tailed deer, dogs, raccoons, rodents	Obligate intracellular, infects monocytes/macrophages, acquires iron, and avoids lysosomal degradation.	Fever, headache, myalgia, rash, sometimes severe multisystem disease	PCR, Serology	Doxycycline	Avoid tick bites, protective clothing, and repellents
<i>Francisella tularensis</i>	Tularemia	<i>Dermacentor spp., Amblyomma spp., other ticks, and flies</i>	Rabbits, small rodents	Gram-negative coccobacillus, intracellular, resistant to some antibiotics, BSL-3 pathogen	Fever, skin ulcers, lymphadenopathy, pneumonic form	PCR, culture in BSL-3, Serology	Streptomycin, Gentamicin, Doxycycline	Avoid tick bites, contact with infected animals, contaminated water, or food
<i>Rickettsia rickettsii</i>	Rocky Mountain Spotted Fever (RMSF)	<i>Dermacentor spp., Amblyomma spp.</i>	Dogs, rodents, wildlife	Gram-negative obligate intracellular, Spotted Fever Group, host-cell dependent	Fever, severe headache, myalgia, petechial rash, shock, organ failure	Serology (IFA), PCR, Immunohistochemistry	Doxycycline	Avoid tick bites, protective clothing, and repellents

Tick-borne viruses

Ticks are well-recognized as important vectors in the transmission of numerous pathogens, including a wide range of viruses (Table 3). These tick-borne viruses (TBVs) represent a highly diverse group with varying genetic characteristics, currently classified into two orders, nine families, and at least twelve genera. While some TBVs are notorious for causing severe, often fatal diseases in humans and livestock, others remain less well understood, with their potential risks to public health still uncertain. In this review, we provide an overview of current knowledge on TBVs, focusing on their history of discovery and identification, their associated tick vectors, and their pathogenic potential in both humans and animals. This includes discussion of established viral species

as well as newly discovered or unclassified ones. Expanding our understanding of the diversity and ecology of TBVs will help guide future research into their interactions with ticks and vertebrate hosts, ultimately supporting improved surveillance and control strategies (52).

Crimean-Congo Hemorrhagic Fever (CCHF)

Crimean-Congo hemorrhagic fever (CCHF) is a severe tick-borne zoonotic disease caused by the *Crimean-Congo hemorrhagic fever virus (CCHFV)*, an enveloped, negative-sense, single-stranded RNA virus belonging to the genus *Orthonairovirus* within the family *Nairoviridae*. The disease is associated with high case fatality rates ranging from 10% to 40% in most outbreaks, although in some regions, mortality can exceed 50%. Due to its wide geographic

distribution across Africa, Asia, the Middle East, and parts of Eastern and Southern Europe, CCHF is considered one of the most important viral hemorrhagic fevers affecting both human and veterinary health (53). The virus exhibits a broad cell tropism, primarily infecting mononuclear phagocytes, endothelial cells, and hepatocytes. Viral replication within these cells results in systemic viremia, endothelial dysfunction, and multi-organ involvement. High viral loads, often exceeding 10^9 RNA copies per milliliter in fatal cases, indicate the virus's ability to evade immune surveillance. Dysregulated cytokine production, immune-mediated damage, and direct viral cytotoxicity play central roles in the pathogenesis of severe disease (54). Transmission of *CCHFV* to humans occurs through several routes, most commonly via bites from infected *Hyalomma* ticks. Additional transmission pathways include direct contact with the blood or tissues of infected livestock and wildlife, accidental crushing of infected ticks, and nosocomial exposure in healthcare settings. Humans are incidental hosts, while a wide range of domestic and wild animals, including cattle, sheep, goats, and hares, act as natural reservoirs. Although these animals usually remain asymptomatic, they can sustain viremia for up to two weeks, providing sufficient time for transmission to feeding ticks (55). Ticks of the genus *Hyalomma* are the primary vectors of *CCHFV*. Among them, *H. marginatum* is the dominant vector in Europe, while *H. asiaticum* plays a similar role in Asia. Their two-host life cycle facilitates viral maintenance and dissemination. Importantly, the virus can be transmitted both horizontally, between ticks and vertebrate hosts, and vertically, through transovarial and sexual transmission, allowing persistence throughout all tick life stages. Ecological and environmental factors such as climate change, agricultural intensification, livestock movement, and migratory birds have expanded the habitat and distribution of *Hyalomma* ticks, thereby increasing the risk of human infection (56). The incubation period of CCHF ranges from one to five days after a tick bite and may extend up to nine days following exposure to infected blood or tissues. Clinical presentation typically begins abruptly with high fever, severe headache, myalgia, and gastrointestinal disturbances such as nausea, vomiting, and diarrhea. In severe cases, patients may develop hemorrhagic manifestations, disseminated intravascular coagulation, hypovolemic shock, and multi-organ failure. Mortality is strongly associated with uncontrolled viral replication, coagulation abnormalities, and severe immune dysregulation (57).

Diagnosis of CCHF relies on both serological and molecular techniques. Detection of IgM antibodies is indicative of acute infection, while IgG seropositivity suggests prior exposure. Persistently low or absent antibody levels correlate with poor prognosis, particularly in fulminant cases. Reverse transcription polymerase chain reaction (RT-PCR) remains the gold standard for early detection and monitoring of viral load, especially during the acute stage of infection (58). Epidemiological data consistently highlight *Hyalomma* ticks as the principal vectors of the disease. Populations at greatest risk include farmers, veterinarians, animal handlers, healthcare workers, butchers, and individuals engaged in animal slaughter during cultural or religious practices. Nosocomial outbreaks underscore the importance of strict infection prevention and control measures in healthcare environments to prevent secondary transmission (59). Prevention and control of CCHF require a comprehensive One Health approach that integrates human, animal, and environmental health. Key strategies include increasing public awareness, promoting the use of personal protective equipment for high-risk groups, strengthening vector control measures, and implementing effective surveillance systems for early outbreak detection (60). **Colorado Tick Fever Virus (CTFV)**

CTFV is a double-stranded RNA virus of the family Reoviridae, genus Coltivirus, primarily transmitted by *D. andersoni* ticks in the mountainous western United States. Its genome consists of 12 segmented dsRNA components, and the virus replicates in erythroid precursor cells and white blood cells. Symptoms appear 3–6 days post-exposure and include high fever, chills, retro-orbital pain, biphasic fever, leukopenia, and occasionally meningoencephalitis in children. Laboratory findings typically show leukopenia and thrombocytopenia. Diagnosis relies on RT-PCR, serologic assays (IgM/IgG ELISA), and virus isolation. Treatment is supportive (61).

Tick-Borne Encephalitis Virus (TBEV)

TBEV is a positive-sense single-stranded RNA virus of the family *Flaviviridae*, comprising three major subtypes: European (*TBEV-Eu*), Siberian (*TBEV-Sib*), and Far Eastern (*TBEV-FE*). It is transmitted by *I. ricinus* and *I. persulcatus* ticks and is widely distributed across Europe and Asia. Human infection typically follows a biphasic course, with an initial febrile phase followed by a neurological phase that may include meningitis, encephalitis, or myelitis. The Far Eastern subtype is associated with higher mortality rates, reaching up to 20%. Diagnosis relies on serology (IgM/IgG), RT-PCR during the early



phase, and cerebrospinal fluid analysis. Vaccines are available in endemic regions (62).

Powassan Virus (POWV)

POWV is a neurotropic flavivirus with two lineages: Lineage I (*I. cookei*) and Lineage II, or deer tick virus (*I. scapularis*). Endemic to the northeastern United States and southeastern Canada, POWV can cause encephalitis with high morbidity. Transmission can occur within 15 minutes of tick attachment, highlighting the importance of early tick removal. Clinical features include fever, headache, vomiting, paralysis, and, in severe cases, coma or death. Long-term neurological sequelae are common, and diagnosis is confirmed via RT-PCR or IgM detection. No specific antiviral treatment exists (63).

Omsk Hemorrhagic Fever Virus (OHFV)

OHFV is transmitted by *Dermacentor* ticks in western Siberia, with muskrats serving as the primary reservoir. Clinical manifestations include sudden fever, hemorrhagic diathesis, gingival and nasal bleeding, and mild CNS involvement. Most cases resolve within two weeks, and laboratory confirmation is via RT-PCR and serology (64).

Kyasanur Forest Disease Virus (KFDV)

KFDV, discovered in India in 1957, is transmitted by *H. spinigera* ticks, primarily affecting forest workers and local villagers. Monkeys and rodents serve as reservoirs. Symptoms include fever, headache, bleeding (gums, gastrointestinal tract), and neurological involvement, with case fatality rates ranging from 3–10%. A formalin-inactivated vaccine is used in endemic areas (65).

Heartland Virus (HRTV)

HRTV is a *phlebovirus* in the family *Phenuiviridae*, first isolated in Missouri in 2009. *A. americanum* is the likely vector. Patients present with high fever, myalgia, leukopenia, thrombocytopenia, and elevated liver enzymes, with severe cases involving liver and kidney dysfunction. There is no specific treatment; supportive care is recommended (66).

Bourbon Virus

Bourbon Virus, first identified in Kansas in 2014, is an *orthomyxovirus*-like pathogen transmitted

potentially by *A. americanum* ticks. Less than ten human cases have been reported, with symptoms including fever, rash, leukopenia, thrombocytopenia, and fatigue. One fatality has been documented, and further studies are needed to clarify its epidemiology (67).

Langat Virus (LGTV)

LGTV, a close relative of TBEV discovered in Malaysia, is transmitted by *I. granulatus*. It is not known to cause severe human disease and has been studied as a potential model for TBE vaccine research. Early recognition of tick-borne viral infections is crucial. Diagnostic approaches include RT-PCR, virus isolation, ELISA, and immunofluorescence assays, with cerebrospinal fluid analysis revealing lymphocytic pleocytosis in neuroinvasive infections. No approved antiviral therapies exist, and management is primarily supportive; corticosteroids or intensive care may be warranted in severe cases. Tick-borne viral infections pose significant public health threats, especially in endemic regions, and their emergence is influenced by climate change, altered tick ecology, and increased human mobility. Enhanced surveillance, public education, vector control, and vaccine development are essential, and the potential for transfusion-related transmission underscores the need for improved blood screening policies. While many infections are self-limiting, others can result in long-term disability or death, making understanding their epidemiology, clinical features, and prevention critical for clinicians, public health authorities, and researchers (68).

Table 3. Tick-borne viruses

Virus	Family	Main Tick Vector	Endemic Region	Natural Reservoir	Clinical Features	Treatment / Vaccine
CCHF	<i>Nairoviridae</i>	<i>Hyalomma</i> spp.	Africa, Asia, the Middle East, and Europe	Livestock (cattle, sheep, goats), hares	Fever, myalgia, hemorrhage, multi-organ failure	Supportive; no licensed vaccine is widely available
CTFV	<i>Reoviridae</i> (<i>Coltivirus</i>)	<i>Dermacentor andersoni</i>	Western US mountains	Rodents	Fever, chills, retro-orbital pain, leukopenia, thrombocytopenia	Supportive



TBEV	Flaviviridae	<i>Ixodes ricinus</i> , <i>I. persulcatus</i>	Europe, Asia	Small mammals	Biphasic: febrile then neurological (meningitis, encephalitis)	Vaccines available in endemic areas
POWV	Flaviviridae	<i>I. cookei</i> , <i>I.</i> <i>scapularis</i>	Northeastern US, Southeastern Canada	Small mammals, deer	Fever, headache, vomiting, paralysis, encephalitis	Supportive; no specific antiviral
AHFV	Flaviviridae	<i>Ornithodoros</i> spp. (likely)	Saudi Arabia, Middle East	Livestock	Fever, myalgia, bleeding, hepatic/renal dysfunction	Supportive; no licensed vaccine
OHFV	Flaviviridae	<i>Dermacentor</i> spp.	Western Siberia	Muskrats	Fever, hemorrhage, mild CNS involvement	Supportive; no vaccine
KFDV	Flaviviridae	<i>Haemaphysalis</i> <i>spinigera</i>	India	Monkeys, rodents	Fever, headache, bleeding, neurological symptoms	Supportive; formalin- inactivated vaccine available
HRTV	Phenuiviridae (Phlebovirus)	<i>Amblyomma</i> <i>americanum</i>	Missouri, USA	Unknown	Fever, myalgia, leukopenia, thrombocytopenia, liver/kidney involvement	Supportive; no specific treatment
Bourbon Virus	Orthomyxovirus- like	<i>Amblyomma</i> <i>americanum</i> (suspected)	Kansas, USA	Unknown	Fever, rash, leukopenia, thrombocytopenia, fatigue	Supportive; no specific treatment
LGTV	Flaviviridae	<i>Ixodes</i> <i>granulatus</i>	Malaysia	Small mammals	Generally asymptomatic; model for TBEV research	Supportive; no human disease reported

Tick-borne parasites

Tick-borne protozoan parasites (Table 4) represent a diverse group of pathogens with complex life cycles that depend on hard and soft ticks as vectors, playing a critical role in both human and veterinary health. Important genera include *Babesia*, *Theileria*, and *Hepatozoon*, which are transmitted mainly through tick bites, though in some cases ingestion of infected vectors can also occur. Once inside the host, these parasites typically target blood cells, particularly erythrocytes or leukocytes, leading to a wide spectrum of clinical outcomes ranging from subclinical infections to severe diseases characterized by fever, hemolytic anemia, jaundice, and multi-organ failure. Their significance lies not only in the substantial economic losses they cause in livestock production but also in their growing recognition as emerging zoonotic threats to human health. Climate change, livestock movement, and increased human exposure to tick-infested environments are major

factors contributing to the expanding distribution and impact of these infections worldwide (69).

Theileriosis

Theileria is a genus of obligate intracellular protozoan parasites belonging to the phylum *Apicomplexa*, which are transmitted primarily by hard ticks of the family *Ixodidae*. These parasites are of considerable veterinary importance because they infect both white and red blood cells of vertebrate hosts, leading to the disease known as theileriosis. Theileriosis affects livestock species such as cattle, sheep, and goats and is recognized as one of the most important tick-borne diseases in tropical and subtropical regions of the world. The economic impact of the disease is profound, as it contributes to high mortality rates, decreased productivity, and increased costs of treatment and control measures (70). Among cattle pathogens, *Theileria annulata* and *Theileria parva* are the most significant species. *T. annulata* is the causative agent of tropical theileriosis,

a disease widely distributed across Asia, the Middle East, and North Africa. In contrast, *T. parva* causes East Coast fever, which is endemic in Eastern, Central, and Southern Africa and is considered one of the most devastating parasitic diseases of cattle in the region. In small ruminants, *Theileria lestoquardi* is regarded as the most pathogenic species, often resulting in high mortality. Other species, such as *T. ovis*, *T. separata*, *T. uilenbergi*, and *T. luwenshuni*, exhibit lower pathogenicity, but they remain regionally important in various parts of Asia and Central Asia, where they contribute to productivity losses in sheep and goat populations (71). The life cycle of *Theileria* involves both sexual and asexual stages, alternating between the tick vector and the vertebrate host. Sexual reproduction occurs within the tick, while asexual multiplication takes place in the mammalian host. During tick feeding, sporozoites are transmitted to the vertebrate host through the saliva. These sporozoites invade lymphocytes and develop into schizonts, which undergo uncontrolled proliferation. This process not only leads to transformation and clonal expansion of infected leukocytes but also results in suppression of the host immune system. Subsequently, merozoites released from schizonts invade erythrocytes and appear as piroplasms, contributing to hemolysis and anemia (72). Clinically, theileriosis presents with a wide range of symptoms, depending on the host species, parasite strain, and level of infection. Common signs include high fever, anorexia, enlargement of superficial lymph nodes, and jaundice. As the disease progresses, hemolysis and destruction of erythrocytes may cause severe anemia, respiratory distress, organ dysfunction, and, in acute cases, sudden death. The severity of disease is particularly pronounced in naïve cattle populations exposed to *T. annulata* or *T. parva* (73). The treatment of theileriosis is most effective when initiated early in the course of infection. The antiprotozoal drug buparvaquone is considered the drug of choice due to its high efficacy against *T. annulata* and *T. parva*. In contrast, oxytetracycline and related antibiotics show limited effectiveness and are generally not recommended as primary therapy. Supportive treatment, including the administration of anti-inflammatory agents and blood transfusions, may be required in severe cases to reduce complications associated with anemia and systemic inflammation (74). Control of theileriosis relies on an integrated approach combining vector management, vaccination, and herd health strategies. Tick control through acaricides, rotational grazing, and pasture management remains a cornerstone of prevention, although challenges related to acaricide resistance

and environmental concerns persist. Vaccination offers a more sustainable approach; live attenuated vaccines are available for both *T. annulata* and *T. parva* in some endemic regions and have shown considerable success in reducing disease burden. Additional measures such as movement control of livestock, quarantine of new animals, and regular veterinary surveillance are essential to prevent the introduction and spread of infection (74).

Babesiosis

Babesia species are obligate intraerythrocytic protozoan parasites belonging to the phylum *Apicomplexa*. They are transmitted primarily through the bite of infected hard ticks (*Ixodidae*), and are responsible for causing babesiosis in a wide range of vertebrate hosts, including humans, livestock, companion animals, and wildlife. The disease has a global distribution and represents a significant emerging zoonotic and veterinary concern. The burden of babesiosis has increased in recent decades due to ecological changes, expansion of tick habitats, and greater human exposure to tick-infested environments (75). In humans, babesiosis is predominantly caused by *Babesia microti*, which is the most common agent in North America and has also been reported in parts of Asia. In Europe, *B. divergens* is considered the major cause of human infection, with a tendency to cause severe and often life-threatening disease, particularly in asplenic or immunocompromised individuals. Emerging human cases have also been linked to *B. duncani* in the western United States and *B. venatorum* in Europe and Asia, reflecting the expanding spectrum of *Babesia* species infecting humans. In veterinary medicine, *B. bovis* and *B. bigemina* are recognized as highly pathogenic parasites of cattle, causing bovine babesiosis, a disease that leads to substantial economic losses in tropical and subtropical regions. In small ruminants such as sheep and goats, *B. ovis*, *B. motasi*, and *B. crassa* are important species, while in dogs, infections are mainly attributed to *B. canis* and *B. gibsoni* (76). The life cycle of *Babesia* involves two hosts, with sexual reproduction occurring in ticks and asexual multiplication taking place in vertebrate hosts. During tick feeding, sporozoites are introduced into the bloodstream, where they invade erythrocytes and undergo asexual replication. This intraerythrocytic development leads to the formation of merozoites, which rupture host cells and invade new erythrocytes, perpetuating the infection. The destruction of red blood cells is a central feature of babesiosis and results in hemolytic anemia, which contributes to many of the clinical signs observed in affected hosts (77). The clinical



spectrum of babesiosis is broad and depends on the host's immune status, parasite species, and infection intensity. Many infections remain asymptomatic or cause only mild symptoms. However, symptomatic cases typically present with fever, chills, malaise, fatigue, and anemia, often accompanied by jaundice, hemoglobinuria, and splenomegaly. Severe disease can progress to respiratory distress, renal failure, hepatic dysfunction, and multi-organ failure, particularly in immunocompromised individuals, the elderly, and those who have undergone splenectomy. In livestock, babesiosis manifests with high fever, hemolytic anemia, jaundice, and reduced productivity, sometimes leading to sudden death in acute outbreaks. In human infections caused by *B. microti*, the combination of atovaquone and azithromycin is the first-line therapy and is generally effective in uncomplicated cases. Severe infections, particularly those caused by *B. divergens*, may require the use of clindamycin in combination with quinine, sometimes along with exchange transfusion in critically ill patients to rapidly reduce parasitemia. In animals, antiprotozoal drugs such as *imidocarb dipropionate* are commonly employed, although treatment outcomes depend on early intervention (78).

Hepatozoonosis

Hepatozoonosis is a tick-borne protozoan disease caused by parasites of the genus *Hepatozoon* (phylum *Apicomplexa*) that infect a wide range of mammalian hosts worldwide. Among the species described, *Hepatozoon canis* and *Hepatozoon americanum* are of primary clinical significance in dogs, while *H. felis* and *H. silvestris* are important pathogens of cats. Although the infection has a global distribution, its recognition is increasing as diagnostic methods improve and awareness of emerging vector-borne diseases expands (79). Transmission occurs mainly through the ingestion of infected ticks, distinguishing *Hepatozoon* spp. from many other tick-borne protozoa that are typically transmitted via tick bites. The brown dog tick (*R. sanguineus*) is a major vector of *H. canis*, whereas *A. maculatum* is the primary vector of *H. americanum*. In addition, infections can be acquired through the ingestion of paratenic hosts such as rodents and other small vertebrates harboring tissue cysts, and vertical transmission from dam to offspring has also been documented in certain cases (80). Geographically, *H. canis* is widely distributed, particularly in tropical and subtropical regions, with a high prevalence reported in southern regions of the United States, southern Europe, Asia, and Africa. *H. americanum*, on the other hand, is largely restricted to the southeastern and south-central United States,

where it is responsible for a severe form of the disease in dogs known as American canine hepatozoonosis. In cats, *H. felis* and *H. silvestris* have been documented in various countries, although feline hepatozoonosis is thought to be underdiagnosed due to frequent subclinical infections and nonspecific clinical presentations (81). Clinical manifestations of hepatozoonosis depend on parasite species, host, and immune status. *H. canis* usually causes mild or subclinical infections in dogs, though severe disease can occur in immunocompromised animals, while *H. americanum* leads to severe illness with fever, muscle pain, bone changes, leukocytosis, and progressive debilitation. In cats, clinical disease is less frequent but may involve fever, lethargy, and anemia. Diagnosis relies on microscopy, histopathology, serology, and molecular methods, with PCR offering the most sensitive and specific detection for species identification (82).

Recent Outbreaks of Tick-Borne Diseases

In recent years, there has been a marked increase in the incidence and geographic spread of tick-borne diseases caused by bacterial, viral, and parasitic pathogens. This surge is largely driven by climate change, expansion of tick habitats, and increased human-animal interactions. Bacterial infections such as anaplasmosis, caused by *Anaplasma phagocytophilum*, have risen sharply in the United States, with Michigan reporting a nearly fivefold increase from 17 cases in 2020 to 82 cases in 2024, leading to severe complications including multi-organ failure and anemia. Similarly, rickettsioses, including those caused by *Rickettsia parkeri*, have emerged in new geographic regions, highlighting the expansion of disease distribution. Viral pathogens have also shown concerning trends; Powassan virus transmitted by *Ixodes scapularis* has caused severe neurological symptoms with high mortality in North America, while Oropouche virus outbreaks in South America affected over 11,600 people across Brazil, Bolivia, Peru, Colombia, and Cuba between 2023 and 2024, causing febrile illness and, in some cases, death. Alongside these, parasitic infections such as babesiosis, caused by *Babesia* species, have become increasingly prevalent in regions where *Ixodes scapularis* is common, posing a significant risk to immunocompromised humans and livestock. Additionally, newly identified viruses like Alongshan virus have been detected in Europe and Asia, causing febrile illness in both humans and animal hosts. These emerging patterns underscore the urgent need for enhanced surveillance, public health awareness (83-86). Preventive strategies to mitigate the expanding

health and economic impact of tick-borne diseases globally (87).

Conclusion

Ticks and tick-borne zoonotic diseases are increasingly recognized as a major global public health challenge. Acting as vectors for a wide range of bacteria, viruses, and protozoa, ticks are responsible for significant morbidity and mortality in both humans and animals. The rapid expansion of their geographic range, influenced by climate change, globalization, and ecological disruption, has further amplified the risks of transmission and the emergence of novel tick-borne pathogens. This review underscores the biological complexity of ticks, the vast diversity of pathogens they transmit, and the ongoing difficulties in accurate diagnosis, effective treatment, and sustainable control. To mitigate the impact of these diseases, coordinated efforts are needed, including enhanced surveillance systems, improved public education, and integrated vector management strategies. Advances in molecular diagnostics and the development of novel preventive measures will be crucial in this regard. Furthermore, interdisciplinary collaboration within the One Health framework—uniting human, animal, and environmental health—is essential for understanding and addressing the growing threat of tick-borne zoonosis worldwide.

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Conflict of interest

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