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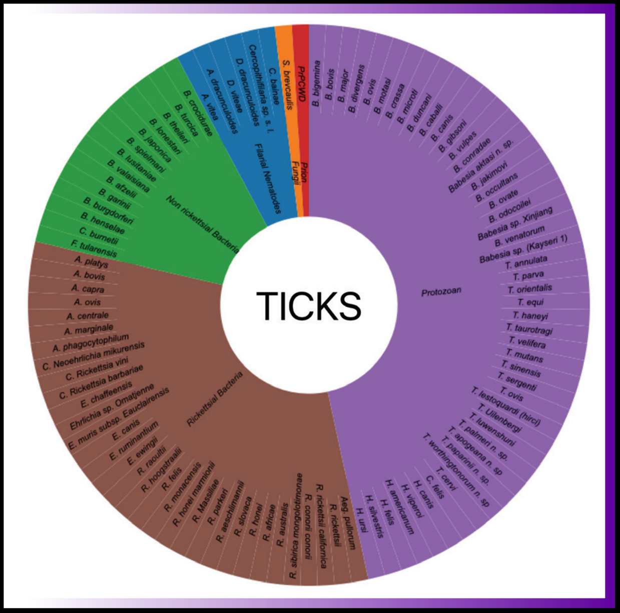
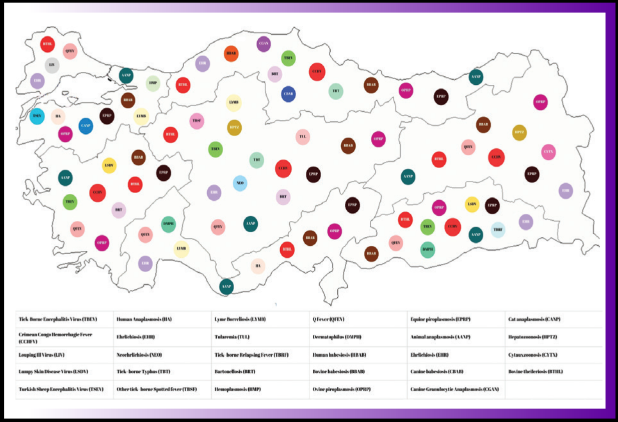


A Compendium Review of the Global Epidemiology of Ticks and Tick-Borne Diseases: Regional Insights from Türkiye

Keneler ve Kene Kaynaklı Hastalıkların Küresel Epidemiyolojisine Dair Kapsamlı Bir Derleme: Türkiye'den Bölgesel Bakış Açıları



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EDİTÖRDEN

Vektör kaynaklı hastalıklar; uzun zamandır bitkilerin, insanların, evcil hayvanların ve vahşi yaşamın sağlığını tehdit etmekte ve özellikle tropikal ve subtropikal bölgelerde yıkıcı etkiler meydana getirmektedirler. Bunlar arasında kene kaynaklı hastalıklar; kıtalar genelinde halk sağlığını ve hayvan sağlığını ciddi şekilde tehdit eden, kritik ve giderek büyüyen global bir sorun ve küresel ekonomik yük olarak ortaya çıkmaktadırlar.

Sürekli yeni türlerin teşhis edildiği kenelerin global yayılışı ve buna bağlı "*emerging*" ve "*re-emerging*" kene- kaynaklı hastalıkların artışı büyük ölçüde iklim değişikliği, arazi kullanım değişikliği, ticaretin küreselleşmesi, insan ve hayvan hareketliliğinin artması, yanlış veya yetersiz Çevresel ve Sosyal Yönetişim (*Environmental and Social Governance*) gibi insan kaynaklı multifaktörlerden kaynaklanmaktadır. Bu faktörler, kene popülasyonlarının coğrafi yayılımını hızlandırarak, kene-kaynaklı çeşitli patojenlerin (virüsler, bakteriler, protozoalar, nematodlar, mantarlar ve hatta bulaşıcı prion proteinleri) dünya çapında yayılmasını kolaylaştırmıştır. Global ölçekte hem kenelerin ve hem de kene-kaynaklı hastalıkların yol açtığı küresel kümülatif ekonomik kayıplar büyüyerek artmakta ve sonuçları yıkıcı boyutlara ulaşmaktadır.

Sonuçlar insan sağlığının çok ötesine uzanmaktadır. Kene kaynaklı enfeksiyonlar, hayvancılıkta verimliliği baltalamakta, vahşi yaşamın korunmasını tehdit etmekte, gıda sistemlerini ve gıda güvenliğini bozmakta ve özellikle düşük gelirli ve kaynak kısıtlı bölgelerde ekonomik kayıpları artırmaktadır. Bu zincirleme etkiler gıda güvensizliğini şiddetlendirmekte, yoksulluğu derinleştirmekte ve zaten kırılgan olan sağlık ve tarım sistemlerine ek yük bindirerek Sürdürülebilir Kalkınma Hedeflerini (*Sustainable Development Goals*) doğrudan tehdit etmektedir.

Sürekli büyüyen bu küresel krizle mücadele; holistik yaklaşımla bütüncül, çok disiplinli ve disiplinler arası çözümleri esas alan bir paradigma değişikliğini gerektiriyor. Bu kapsamda, insan, hayvan ve çevre sağlığı arasındaki ayrılmaz bağlantıları tanıyan Tek Sağlık yaklaşımı, kene kaynaklı hastalıkların izlenmesi, önlenmesi ve kontrolü için kritik bir çerçeve sunuyor. Bu küresel kümülatif ekonomik zorluklarla mücadele stratejileri, "Tek Sağlık" konsepti temelinde oluşturulmalıdır.

Prof. Dr. Abdullah İnci
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Türkiye'de ve bulunduğumuz coğrafyada en önemli vektör artropodlardan biri olan keneler ile ilgili bu derleme kene türleri, dağılımları, vektöryal yeterlilikleri, tıbbi ve veteriner önemleri, kene-patojen etkileşimleri, ortaya çıkan/çıkacak kene kaynaklı hastalıkların tehditleri, riskleri, entegre kene kontrol stratejileri ve bu hastalıkların ekonomik olarak maliyetlerini irdelemekte ve genel bir bakış açısı sunmaktadır.

Yaptıkları bu örneği az bulunur çalışmaya katkıda bulunan bütün hocalarımıza teşekkür eder, bilimsel çalışmalarınıza ve birikimlerinize yararlı olmasını umuyorum.

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CONTENTS /İÇİNDEKİLER

REVIEW / DERLEME

1 A Compendium Review of the Global Epidemiology of Ticks and Tick-borne Diseases: Regional Insights from Türkiye

Keneler ve Kene Kaynaklı Hastalıkların Küresel Epidemiyolojisine Dair Kapsamlı Bir Derleme: Türkiye'den Bölgesel Bakış Açıları

Abdullah İnci, Aykut Özdarendeli, Alparslan Yıldırım, Mahmodul Hasan Sohel, Sezayi Özübek, Ömer Orkun, Bayram Ali Yukarı, Ayşegül Ulu Kılıç, Zati Vatansever, Önder Düzlü, Kürşat Altay, Samba Deguene Diop, Alina Denis Kızgın, Batuhan Aşkım Arslanhan, Simge Şahin, Münir Aktaş; Kayseri, Elazığ, Ankara, Burdur, Kayseri, Kars, Sivas, Türkiye; Dakka, Bangladesh

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ABSTRACT

Vector-borne diseases have historically posed significant threats to plants, humans, domestic animals, and wildlife, with their impact being especially pronounced in tropical and subtropical regions. Among these, tick-borne diseases (TBDs) have emerged as an increasingly critical global concern. This growing threat is largely driven by the expanding geographic range of ticks and the wide array of pathogens they transmit, including viruses, bacteria, protozoa, nematodes, fungi, and infectious prion proteins. The global cumulative economic impact of the challenges caused by ticks and TBDs contributes and exacerbates the persistence of poverty and food insecurity, particularly in resource-limited and low-income regions. This multifactorial burden is further compounded by a complex network of anthropogenic factors, including climate change, habitat fragmentation and ecological degradation, rapid urbanization, changes in agroecosystem management, the resurgence of wildlife reservoirs, and increased anthropozoonotic mobility. Additionally, long-distance and intercontinental migratory birds serve as important ecological carrier hosts, naturally facilitating the widespread distribution and geographic expansion of ixodid tick populations and their associated pathogen complexes. Exacerbating these challenges are regional conflicts, weak environmental and social governance, and rising antimicrobial resistance, which complicate prevention and control efforts of TBDs. Due to the effects of numerous anthropogenic factors—primarily global warming—the risk potential of emerging and re-emerging TBDs is increasing day by day, along with the zoogeographic distribution of ticks and the global challenges they pose. From a global epidemiological perspective, the rising incidence and prevalence of TBDs hold significant implications for both medical and veterinary disciplines. This critical status necessitates an enhanced and comprehensive understanding of ticks, particularly with regard to pivotal aspects such as their vectorial capacity and pathogen transmission dynamics. According to ixodological records, approximately a total of 1,025 tick species, including fossil species, have been reported worldwide to date. Several of these species have also been documented in Türkiye. The current tick fauna reported from seven geographical regions of Türkiye comprises a total of 58 species: 8 species from 6 genera in the family Argasidae (*Argas* - 2 species, *Carios* - 1 species, *Ornithodoros* - 2 species, *Alectorobius* - 1 species, *Alveonasus* - 1 species *and Otobius* - 1 species) and 50 species from 7 genera in the family Ixodidae (*Ixodes* - 17 species, *Rhipicephalus* - 8 species, *Dermacentor* - 4 species, *Hyalomma* - 9 species, *Haemaphysalis* - 8 species, *Alloceraea* - 1 species and *Amblyomma* - 3 species).

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Notably, the genera *Hyalomma* and *Ixodes* have been reported as the most frequently associated with human infestations in Türkiye, highlighting their epidemiological significance and potential role in the transmission of tick-borne pathogens (TBPs). Many TBDs with zoonotic characteristics have been reported globally. These include approximately 100 viral diseases—about half of which are zoonotic—as well as numerous bacterial, protozoan, filarial nematode, fungal, and prion-related pathogens, the majority of which also exhibit zoonotic potential. In recent years, molecular epidemiological studies highlight the increasing importance of emerging TBDs. In particularly, closely monitoring TBPs in wildlife—such as transmissible prion proteins in deer and rickettsial pathogens identified in mountain goats and mountain sheep—and elucidating their zoonotic potential is critically important. In addition, the ecological importance of bat-associated tick species—especially those infesting cave-dwelling bats, such as *Ixodes vespertilionis*, *Ixodes simplex*, *Ixodes ariadnae*, *Ixodes kaiseri*, and *Haemaphysalis erinacei*—and their role as potential vectors for emerging and reemerging TBPs should not be overlooked. Major TBDs associated with substantial global economic losses—such as Lyme borreliosis, anaplasmosis, ehrlichiosis, babesiosis, and theileriosis—also present significant epidemiological and economic challenges in Türkiye. Notably, in the Turkish context, key TBDs including babesiosis, theileriosis, anaplasmosis, and ehrlichiosis have been documented in animals across all geographical regions, leading to considerable economic impact. Crimean-Congo hemorrhagic fever in humans has been observed predominantly in Central Anatolia and the inland areas far from the Black Sea coast, with rare cases occurring in other parts of the country. Lyme borreliosis has been reported most frequently in the Marmara Region, followed by Central Anatolia and the Mediterranean Region. The global threat of TBDs directly undermines key Sustainable Development Goals, prompting international initiatives such as the World Health Organization's "small bite, big threat" campaign and the One Health approaches and the actions, which aim to reduce zoonotic disease risks through cross-sectoral collaboration. The goal is to combat emerging and re-emerging TBDs through integrated strategies that encompass human, animal, and environmental health. Innovative strategies—including tick-derived microRNAs, *CRISPR/Cas9* gene-editing, transfection systems, extracellular vesicle research, and DNA- and miRNA-based vaccines—show promise for disrupting tick biology and pathogen transmission. These advances, combined with integrated tick control programs, early warning systems, global monitoring, and open data sharing, are essential for effective tick and TBD management. Addressing this complex challenge requires international cooperation, interdisciplinary research, and an "ecocentric education" approach that fosters environmental stewardship and scientific literacy. Ultimately, halting tick spread and reducing the global burden of TBDs depends on sustained commitment to One Health principles, robust governance, and investment in research, education, and capacity-building. This compendium provides an overview of ticks, their distribution, vector competence, medical and veterinary importance, tick–pathogen–host interactions, emerging TBD threats, integrated control strategies, and the economic impacts of ticks and TBDs.

Keywords: Epidemiology, ticks, tick-borne diseases, tick control, economic burden, Türkiye

ÖZ

Vektör kaynaklı hastalıklar, tarihsel olarak bitkiler, insanlar, evcil hayvanlar ve yaban hayatı için önemli tehditler oluşturmuş ve etkileri özellikle tropikal ve subtropikal bölgelerde belirginleşmiştir. Bunlar arasında kene kaynaklı hastalıklar (KKH'lar), giderek daha kritik bir küresel endişe kaynağı haline gelmiştir. Bu büyüyen tehdit, büyük ölçüde kenelerin genişleyen coğrafi yayılımı ve virüsler, bakteriler, protozoalar, nematodlar, mantarlar ve enfeksiyöz prion proteinleri dahil olmak üzere bulaştırdıkları çok çeşitli patojenlerden kaynaklanmaktadır. Keneler ve KKH'ların neden olduğu zorlukların küresel kümülatif ekonomik etkisi, özellikle kaynakları kısıtlı ve düşük gelirli bölgelerde yoksulluk ve gıda güvensizliğinin devam etmesine katkıda bulunmakta ve durumu daha da kötüleştirmektedir. Bu çok faktörlü yük, iklim değişikliği, habitat bozulması ve ekolojik bozulma, hızlı kentleşme, tarımsal ekosistem yönetimindeki değişiklikler, yaban hayatı rezervuarlarının yeniden canlanması ve artan antropozoonotik hareketlilik gibi karmaşık bir antropojenik faktör ağı tarafından daha da ağırlaştırılmaktadır. Ek olarak, uzun mesafeli ve kıtalararası hareket eden göçmen kuşlar, önemli ekolojik taşıyıcı konaklar olarak hizmet vererek, doğal olarak ixodid kene popülasyonlarının ve ilişkili patojen komplekslerinin yaygın dağılımını ve coğrafi yayılımını kolaylaştırmaktadırlar. Bu zorlukları daha da kötüleştiren bölgesel çatışmalar, zayıf çevresel ve sosyal yönetişim ve artan antimikrobiyal direnç, KKH'ların önlenmesi ve kontrol çabalarını zorlaştırmaktadır. Başta küresel ısınma olmak üzere çok sayıda antropojenik faktörün etkileri nedeniyle, ortaya çıkan ve yeniden ortaya çıkan KKH'ların risk potansiyeli, kenelerin zoocoğrafik dağılımı ve oluşturdukları küresel zorluklarla birlikte her geçen gün artmaktadır. Küresel epidemiyolojik bir bakış açısından, KKH'ların artan insidansı ve yaygınlığı hem medikal hem de veteriner hekimliği disiplinleri için önemli sonuçlar doğurmaktadır. Bu kritik durum, özellikle vektör kapasiteleri ve patojen bulaşma dinamikleri gibi temel hususlar açısından keneler hakkında gelişmiş ve kapsamlı bir anlayışı gerektirmektedir. İksodolojik kayıtlara göre, bugüne kadar dünya çapında fosil türler de dahil olmak üzere toplam 1,025 kene türü bildirilmiştir. Bu türlerden bazıları Türkiye'den de bildirilmiştir. Türkiye'nin yedi coğrafi bölgesinden bildirilen mevcut kene faunası toplam 58 türden oluşmaktadır: Argasidae familyasından 6 cinse ait 8 tür (*Argas* - 2 tür, *Carios* - 1 tür, *Ornithodoros* - 2 tür, *Alectorobius* - 1 tür, *Alveonasus* - 1 tür ve *Otobius* - 1 tür) ve Ixodidae familyasından 7 cinse ait 50 tür (*Ixodes* - 17 tür, *Rhipicephalus* - 8 tür, *Dermacentor* - 4 tür, *Hyalomma* - 9 tür, *Haemaphysalis* - 8 tür, *Alloceraea* - 1 tür ve *Amblyomma* - 3 tür). Özellikle *Hyalomma* ve *Ixodes* cinslerinin Türkiye'de insan enfestasyonlarıyla en sık ilişkilendirilen cinsler olarak bildirilmesi, epidemiyolojik önemlerini ve kene kaynaklı patojenlerin (KKP'ler) bulaşmasındaki potansiyel rollerini vurgulamaktadır. Dünya genelinde zoonotik özelliklere sahip birçok KKH bildirilmiştir. Bunlar arasında yaklaşık 100 viral hastalık (bunların yaklaşık yarısı zoonotiktir) ve çoğunluğu zoonotik potansiyel gösteren çok sayıda bakteriyel, protozoan, filarial nematod, fungal ve prionla ilişkili patojen bulunmaktadır. Son yıllarda moleküler epidemiyolojik çalışmalar, ortaya çıkan KKH'ların artan önemini vurgulamaktadır. Özellikle yaban hayatındaki KKP'lerin (geyiklerdeki bulaşıcı prion proteinleri ve dağ keçileri ile dağ koyunlarında tanımlanan riketsiyal patojenler gibi) yakından izlenmesi ve zoonotik potansiyellerinin açıklığa kavuşturulması kritik öneme sahiptir. Ayrıca, yarasalarla ilişkili kene türlerinin (özellikle mağaralarda yaşayan yarasaları enfeste eden *Ixodes vespertilionis*, *Ixodes simplex*, *Ixodes ariadnae*, *Ixodes kaiseri* ve *Haemaphysalis erinacei* gibi) ekolojik önemi ve ortaya çıkan ve yeniden ortaya çıkan KKP'ler için potansiyel vektörler olarak rolleri göz ardı edilmemelidir. Lyme borreliosis, anaplazmosis, ehrlichiosis, babesiosis ve theileriosis gibi küresel ekonomik kayıplara yol açan başlıca KKH'lar, Türkiye'de de önemli epidemiyolojik ve ekonomik zorluklara sebep olmaktadırlar. Özellikle Türkiye bağlamında, babesiosis, theileriosis, anaplazmosis ve ehrlichiosis gibi KKH'lar tüm coğrafi bölgelerden rapor edilmiş olup, büyük ekonomik kayıplara yol açmışlardır. İnsanlarda Kırım-Kongo hemorajik ateşi ağırlıklı olarak Orta Anadolu ve Karadeniz'in sahilden uzak iç kesimlerinde görülmüş olup, ülkenin diğer bölgelerinde de nadir olgular meydana gelmiştir. Lyme borreliosis en sık Marmara Bölgesi'nde bildirilmiş olup, bunu Orta Anadolu ve Akdeniz Bölgeleri takip etmiştir. KKH'ların küresel tehdidi, sürdürülebilir kalkınma hedeflerini doğrudan baltalamakta ve Dünya Sağlık Örgütü'nün "küçük ısırık, büyük tehdit" kampanyası ve sektörler arası iş birliği yoluyla zoonotik hastalık risklerini azaltmayı amaçlayan Tek Sağlık yaklaşımları ve eylemleri gibi uluslararası girişimleri teşvik etmektedir. Amaç, insan, hayvan ve çevre sağlığını kapsayan entegre stratejiler aracılığıyla ortaya çıkan ve yeniden ortaya çıkan KKH'larla mücadele etmektir. Kene kaynaklı mikroRNA'lar, *CRISPR/Cas9* gen düzenleme, transfeksiyon sistemleri, hücre dışı vezikül araştırmaları ve DNA ve miRNA tabanlı aşılar gibi yenilikçi stratejiler, kene biyolojisini ve patojen bulaşmasını engellemede umut vadetmektedir. Entegre kene kontrol (EKK) programları, erken uyarı sistemleri, küresel izleme ve açık veri paylaşımı ile birleştirilen bu gelişmeler, etkili kene ve KKH yönetimi için hayati önem taşımaktadır. Bu karmaşık zorluğun üstesinden gelmek, uluslararası iş birliği, disiplinlerarası araştırma ve çevre yönetimini ve bilimsel okuryazarlığı destekleyen "ekosentrik eğitim" yaklaşımını gerektirir. Nihayetinde, kenelerin yayılmasını durdurmak ve KKH'ların küresel yükünü azaltmak; Tek Sağlık ilkelerini uygulamağa, güçlü yönetişim sergilemeğe ve araştırma, eğitim ve kapasite geliştirmeye ayrılan yatırıma bağlıdır. Bu derleme, keneler ve onların dağılımları, vektör yeterlilikleri, tıbbi ve veteriner önemleri, kene-patojen-konak etkileşimleri, ortaya çıkan KKH tehditleri, EKK stratejileri ve keneler ile KKH'ların kümülatif ekonomik etkileri hakkında genel bir bakış sunmaktadır.

Anahtar Kelimeler: Epidemiyoloji, keneler, kene kaynaklı hastalıklar, kene kontrolü, ekonomik yük, Türkiye

INTRODUCTION

Pathogens, including parasites, bacteria, viruses, and fungi, cause a broad spectrum of diseases in humans, livestock, wild animals, and plants globally. These pathogens not only threaten human and animal health but also inflict substantial economic losses (1,2). A considerable proportion of these pathogens are transmitted by vector arthropods such as insects and ticks (3,4). Arthropods comprise over 80% of all identified animal species (metazoan) worldwide (5). Many of these arthropods parasitize plants (6), animals (7), and humans (8). Some feed on skin debris or host secretions, while others, such as ectoparasitic ticks, are hematophagous (9,10). Vector arthropods transmit pathogens between animals and humans through both biological and mechanical mechanisms, playing a critical role in the spread of emerging and re-emerging zoonotic diseases worldwide (11). Among blood-feeding ectoparasites, ticks rank as the second most efficient disease vectors after mosquitoes (12). As obligate ectoparasites, ticks feed on blood during their larval, nymphal, and adult stages. They are among the most important vector arthropods responsible for transmitting tick-borne pathogens (TBPs) and tick-borne diseases (TBDs) (13,14).

Ticks and TBDs, including zoonotic infections, are central to the "One Health" approach, which underscores the interconnectedness of human, animal, and environmental health (15). The epidemiological emergence of TBDs in a given region is determined by three critical components: (i) the presence of a competent tick vector species, (ii) a transmissible pathogen, and (iii) a susceptible vertebrate host (15). Tick species have been grouped into four families, both extant and extinct: Argasidae (16), Ixodidae (17,18), Nuttalliellidae (19), and Deinocrotonidae (20), although some changes have been made to the classification recently. Extant ticks are currently assigned to three families: Argasidae (soft ticks), Ixodidae (hard ticks), and Nuttalliellidae. In addition, fossil tick species attributed to extinct families have been described, namely Deinocrotonidae and Khimairidae (20,21). To date, approximately 1,025 valid tick species have been recognized globally (22,23). The family Ixodidae represents the most diverse lineage, comprising 19 genera and 790 species, whereas Argasidae includes 15 genera and 223 species (22,24-27). Until recently (i.e., through 2024), it was generally accepted that the families Khimairidae and Nuttalliellidae were each represented by a single species, and that Deinocrotonidae comprised two fossil species. However, in recent years, several additional fossil tick species have been described, including *Deinocroton bicornis*, *Deinocroton lacrimus*, *Nuttalliella gratae*, *Nuttalliella tuberculata*, *Nuttalliella placaventralis*, *Nuttalliella odyssea*, *Nuttalliella tropicasylvae*, and *Legionaris robustus*. Following subsequent taxonomic reassessments, the genera *Nuttalliella*, *Deinocroton*, and *Legionaris* were incorporated into the family Nuttalliellidae. Consequently, current tick systematics recognizes three extant families (Argasidae, Ixodidae, and Nuttalliellidae) and one extinct family (Khimairidae) (28,29).

Molecular epidemiology and phylogenetic studies of TBPs in various ixodid ticks and their vertebrate hosts have deepened our understanding of the complex ecology underlying TBDs.

The global expansion of tick populations has increased the risk of TBP transmission, exacerbating the global threat posed by emerging and re-emerging TBDs (15). In recent years, anthropogenic factors—such as climate change, legal and illegal movement of humans and animals, fragile socioeconomic conditions, ineffective governance, environmental mismanagement, misguided political decisions, and weak public health advocacy—have dramatically extended the geographical distribution of many tick species. Consequently, the global economic burden associated with ticks and TBDs has escalated, complicating progress toward the United Nations sustainable development goals (SDGs), including those targeting hunger and poverty. Current estimates suggest that ticks and TBDs cause annual global economic losses of approximately 22-30 billion United States dollar (USD) (30).

Among hematophagous vector arthropods, hard ticks (family Ixodidae) exhibit complex feeding behaviors (31). However, persistent technical challenges in maintaining laboratory colonies, sustaining tick lines, and conducting long-term studies hinder progress (32). These limitations result in substantial gaps in our understanding of tick feeding biology and vector-pathogen interactions across developmental stages (33). Bridging these gaps requires in-depth studies of the molecular mechanisms driving TBD transmission (14,34). Emerging TBPs face major challenges, including ineffective control measures, the rise of antimicrobial resistance, environmental hazards, and increasing treatment costs (35). The current control measures are ineffective, leading to reduced livestock productivity and resulting in billions of dollars in additional losses globally each year (36). Hereby, these challenges highlight the urgent need for innovative, sustainable control strategies, particularly those targeting molecular interactions between ticks and transmitted pathogens. Recent studies indicate that focusing on vector competence-related molecules may offer promising avenues, especially in the development of anti-tick vaccines (37-39).

Advanced molecular research should aim to identify and characterize antigenic targets crucial for pathogen transmission and evaluate their potential in novel control approaches. During blood feeding, ticks modulate host immune responses through their salivary secretions, which possess a variety of pharmacological properties, including anticoagulant, antiplatelet, vasodilatory, and anti-inflammatory activities (40). These salivary components are key targets for the next generation of tick control strategies. Additionally, TBPs undergo complex developmental changes in both tick vectors and vertebrate hosts. These transitions can be influenced by tick-borne factors that may suppress or enhance pathogen survival, leading to outcomes such as population reduction, attenuation, or increased virulence. Studies have shown that TBPs can actively modulate tick gene expression, affecting vector physiology and competence (41-46).

This compendium review comprehensively explores the medical and veterinary importance of ticks, their role in pathogen transmission, tick-pathogen-host molecular interactions, and the current and emerging strategies for controlling ticks and TBDs, alongside the global economic burden they impose.

Medical and Veterinary Importance of Ticks

In recent years, living in urban centers has become the norm, especially for younger generations who have limited knowledge and experience of rural life. This social situation means that they have less knowledge and experience with ecosystems, ecology, wildlife, farm animals, and their ectoparasites—especially ticks—compared to those living in rural areas. Families and their children who were born and raised in rural areas and are engaged in agriculture and animal husbandry do not pay much attention to ticks infesting humans and animals and sucking their blood. For them, this is considered a normal seasonal occurrence (47). These observational experiences help them understand the direct and indirect harms caused by ticks. In addition, these natural observations provide them with the opportunity to learn about serious medical and veterinary complications such as "tick worry" or "tick anxiety", "tick allergy and anaphylaxis", "tick toxicity", "tick paralysis", "tick anemia", and the increased risk of secondary infections and myiasis (47,48).

The first discovery, in 1893, by Smith and Kilbourne that *Babesia bigemina* (formerly *Pyrosoma bigeminum*), the pathogen of Texas fever in cattle, is transmitted by the ixodid tick *Rhipicephalus* (*Boophilus*) *microplus* and *Rhipicephalus* (*Boophilus) annulatus*, led to the recognition of the importance of ticks as vectors. This pioneering discovery was followed by Ricketts' 1907 discovery that the rickettsial agent of Rocky Mountain spotted fever (RMSF) is transmitted by the tick *Dermacentor andersoni*. These early discoveries prompted further research by demonstrating that ticks transmit a wide variety of pathogens—including viral, bacterial, protozoan, nematode, and fungal agents—to both humans and animals. Thus, ticks have become a critical focus of subsequent scientific research in both human and veterinary medicine (49). Today, approximately 10% of known tick species have been proven to be of medical and veterinary importance. The active biological substances found in the saliva of these tick species cause the tick to adhere to its host and trigger immediate reactions in the host, such as allergy, anaphylaxis, and poisoning (50).

These reactions occur as follows:

(i) Direct Damage: Various tick species cause paralysis or toxicosis in their hosts due to the toxins they inject during blood feeding (50,51). Notable examples include *Dermacentor andersoni*, which causes paralysis; *Hyalomma truncatum*, which causes sweating sickness; *Ixodes holocyclus*, which causes Australian tick paralysis (51); and *Rhipicephalus* species, which cause tick toxicosis (50,52,53). In addition, the blood loss caused by tick feeding can lead to anemia, growth retardation, and economic losses (54). Skin injuries resulting from tick bites make animals particularly susceptible to myiasis flies (54,55). An example of this is myiasis caused by *Cochliomyia hominivorax* following infestation by *Amblyomma maculatum* in cattle (56).

(ii) Allergy: Tick allergy consists of significant local reactions resulting from tick bites. These large local reactions are the minimal manifestations of tick allergies. In some sensitive hosts (humans and animals), localized allergic skin reactions—such as itching, redness, swelling, and rashes (e.g., tick bite reaction dermatitis)—may occur in response to tick bites (50).

(iii) Large Local Reactions Following Tick Bites: In mammalian hosts infested with ticks, large local reactions—like those seen in tick-specific immunoglobulin E-mediated delayed-type hypersensitivity—occur in most cases (57).

(iv) Mammalian Meat Allergy/Anaphylaxis Following Tick Bites: Tick bites can lead to mammalian meat allergy or anaphylaxis due to sensitization to α-Gal, especially in tick-endemic regions. First identified in Australia (58), this condition has since been reported globally (57,59,60), including a recent case in Türkiye (61).

(v) Anaphylaxis: Sensitized allergic individuals, such as those with severe *Amblyomma americanum* infestations, may experience anaphylaxis (62).

(vi) Tick Toxicoses: One of the most prominent direct damages of tick infestations is toxicosis (50,51). Tick-induced toxicosis in humans and animals is a complex phenomenon (56). This complex phenomenon is caused by toxic substances in tick saliva that affect various vertebrate hosts, including humans and animals. Specific toxins produced by *Rhipicephalus evertsi* (52,63) *Ixodes holocyclus* (56) *Rhipicephalus appendiculatus*, *Rhipicephalus* (*Boophilus*) *microplus*, and *Ixodes holocyclus* (52), as well as several other tick species from different genera within the Argasidae and Ixodidae families (51), cause tick paralysis in both animals and humans with severe reactions, including heart problems and paralysis. Immunity can develop in hosts, particularly with repeated tick infestations, but it is often short-lived, and toxicosis is more common in early spring when tick activity peaks. Humoral immunity plays a role in resistance, and local skin immunity is also important in preventing toxin effects. Studies show that immunity against one tick species can sometimes offer protection against others (56).

(vii) Psychological Reactions of Humans to Tick Bites: Humans tend to have a more complex psychological reaction to tick bites, driven by anxiety over potential TBDs like Lyme disease. This fear can lead to heightened concern and obsessive behaviors (64-66). This can lead to catastrophic thinking, where a simple tick bite might be feared to result in a serious illness (67). Individually, people can take comprehensive preventive measures—such as using tick repellents, avoiding tick habitats, and conducting thorough tick checks after returning from the field—to prevent tick bites and reduce concerns about the risk of TBD transmission (68-70).

(viii) Psychological Responses of Animals to Tick Bites: Although animals do not experience cognitive "anxiety" like humans, they do exhibit behavioral and emotional responses to tick bites and the associated discomfort. For example, animals may shake, scratch, or groom themselves to remove ticks, which can help relieve irritation and prevent further infestation. For instance, the dogs infested with *Rhipicephalus sanguineus* ticks may sometimes ingest the ticks. If the ingested ticks are infected with *Hepatozoon canis*, the pathogen can be transmitted to the dog through a process known as "ingested vector transmission" (71). Tick bites can cause physical symptoms such as discomfort, irritation, or restlessness. Animals previously exposed to ticks or TBDs may instinctively avoid areas where they encountered them in the past to reduce the risk of future infestation (65). Some pets, especially dogs, may show signs of distress when exposed to tick-infested environments or when treated with tick repellents. This behavior may be a "learned response" based on previous unpleasant experiences. If an animal contracts a TBD (e.g., Lyme disease in dogs), it may exhibit clinical signs such as lethargy, fever, or loss of appetite. These are biological responses to infection, not psychological anxiety. There are some basic behavioral differences between human and animal responses to tick bites. Humans often experience psychological anxiety about the possible consequences of tick bites, such as the transmission of disease. In contrast, animals react instinctively to the physical irritation caused by ticks, without the capacity to conceptualize long-term health risks. Although animals do not experience "anxiety" similar in the humans, they do exhibit behaviors that reflect discomfort and distress caused by tick bites. Pet owners often take preventive measures—such as using tick repellents and avoiding tick-infested areas—due to concerns about disease transmission (68).

Ticks

Tick Species and Their Geographical Distribution

Ticks are large chelicerate arthropods and obligate ectoparasites that rely exclusively on the blood of their hosts (72,73). These highly specialized hematophagous ectoparasites exhibit a broad host range, parasitizing a variety of terrestrial and avian vertebrates and reptiles such as lizards and snakes (48,73,74). During their feeding cycles, ticks may demonstrate both nidicolous (residing within or near host habitats) and non-nidicolous (living away from host habitats) behaviors (48). From an eco-epidemiological perspective, enzootic stability plays a critical role and is crucial for both the persistence of tick infestations and the emergence/re-emergence of TBDs (75,76). In such stable regions, the survival of most tick species is influenced by a complex interplay of physiological, structural, and ecological factors. These factors play a critical role during the extended periods that ticks spend off-host, often on the ground, for months or even longer (77). Therefore, understanding the dynamic relationship between tick-host interactions and environmental conditions is vital for comprehending the dual role of ticks as both parasites and vectors of diseases (77-79).

Ticks possess several key physiological and ecological characteristics that influence their survival and interactions within the ecosystem. These include: (i) the relationship between the tick cuticle, moisture, and water balance; (ii) sensory mechanisms involved in feeding behavior, attachment/detachment, and ingestion, including the role of mouthparts, feeding apparatus, salivary gland secretions, and host responses; (iii) immunological mechanisms involved in host resistance; (iv) processes of blood digestion; (v) regulation of ion and water balance, as well as excretion mechanisms during feeding; (vi) reproductive processes, including sperm development, cytogenetics, oogenesis, and oviposition; (vii) the structure and function of the circulatory, nervous, and neuroendocrine systems; (viii) endocrine regulation, particularly the effects of insect hormones and their analogs on development and reproduction; (ix) pheromone signaling mechanisms; (x) diapause and biological rhythms, which are essential for the physiological behavior of ticks (75,78,80).

Ticks are taxonomically classified within the phylum Arthropoda, class Arachnida, subclass Acari, order Ixodida (Metastigmata), and superfamily Ixodoidea (28). The order Ixodida comprises primarily three families: (i) Ixodidae (hard ticks), which exhibit pronounced sexual dimorphism as well as diverse mate preferences and mating behaviors (81), (ii) Argasidae (soft ticks), which also display sexual dimorphism but lack mate selection, with mating typically occurring in host-associated environments such as bird nests, or in crevices and cracks within shelters (82); and (iii) Nuttalliellidae, currently represented by 11 species (28,74,75). In addition, the extinct and monotypic family Khimairidae is represented by a single species, *Khimaira fossus* (28).

Ticks are highly efficient vectors and are considered the most significant arthropods after mosquitoes in terms of the variety and number of harmful pathogens they transmit to their hosts. While feeding on the blood of amphibians, reptiles, birds, and mammals including humans, ticks play a central role in the transmission of numerous infectious agents. Beyond their role as vectors of disease, ticks are also responsible for a range of serious health impacts on their hosts, including allergies, anaphylaxis, anemia, dermatosis, toxicosis and paralysis as mentioned above. Given these diverse health risks, it is not surprising that ticks have been extensively studied since the late 19th century, particularly with the advent of the "One Health" concept in the early 2000s (83,84). Researchers including veterinarians, physicians, and zoologists have extensively studied various aspects of tick biology and their broader implications, including their geographic distribution and the global challenges they might pose (17,18).

Ticks can infest both indoor and outdoor livestock, and approximately 80% of the global cattle population is affected by tick infestations. Consequently, ticks are considered economically significant ectoparasites of livestock production systems. The global economic losses attributed to tick infestations are substantial, with estimates ranging from approximately 14 billion USD to 18 billion USD annually (85,86). In addition, the economic burden of TBDs on ruminants, particularly in tropical and subtropical regions, is estimated to reach several billion dollars each year (1,87). In rural communities, ticks are widely recognized as problematic ectoparasites, often commonly referred to by local names such as "bloodsucker". These ectoparasites are not only a major concern but also elicit fear due to their prominent role in transmitting both human and animal diseases (47,77,88).

From an epidemiological perspective, ticks hold substantial medical and veterinary importance among arthropods. They serve as intermediate hosts for TBPs, supporting their development and reproduction, acting as efficient vectors, and are distributed across a wide range of zoogeographical regions worldwide (18,47). Indeed, ticks surpass all other arthropods in transmitting a wide range of pathogens including bacteria, viruses, protozoa, nematodes, fungi and prions that cause a variety of debilitating diseases in both humans and animals (89-94). For example, *Ixodes* species are known vectors of *Borrelia* species that cause Lyme disease (95) while *Rhipicephalus* species are vectors for *Babesia* spp., which can cause babesiosis in livestock. Beyond their role as vectors, ticks are also a significant economic burden due to the diseases they transmit, leading to decreased productivity in livestock and increased veterinary care cost (96).

Recent research has highlighted the expanding global distribution of ticks, driven by a variety of factors including climate change, deforestation, land-use alteration, urbanization and improper development, changes in animal husbandry practices, global trade, livestock and wildlife movements, human and animal migrations particularly bird migrations and changes in agricultural practices (80). This wide range of anthropogenic influences underscores the growing importance of ongoing research into tick ecology, vector competence, and pathogen transmission dynamics (10). The globalization of livestock and wildlife movement has notably intensified the challenges posed by ticks and TBDs. The complex interplay between trade, migration, and environmental changes has created a global network that facilitates the spread of ticks, sometimes introducing novel pathogens into previously unaffected areas. To address these emerging risks, a multifaceted strategy is required, one that integrates enhanced surveillance, improved biosecurity measures, increased public awareness, and climate-sensitive management approaches. Such comprehensive efforts are essential in mitigating the expanding threats posed by ticks and TBDs globally (18,80).

In enzootic stable regions, several abiotic and biotic factors play a vital role in influencing the epidemiological dynamics of TBD transmission (10). These factors are briefly discussed in the following sections.

Abiotic Factors: Temperature and relative humidity (RH) are among the most critical abiotic factors, as they directly influence tick development, survival, and feeding behavior (97-100). Temperature, in particularly, influences the ability of ticks to locate their hosts, its long-term survival, and the development and survival of pathogens within the vector (14,101-104).

Biotic Factors

(i) Host Range: Ticks with a broad host range, such as *Ixodes ricinus*, encounter a greater diversity of TBPs, in contrast to more host-specific such as *Rhipicephalus microplus*, which were exposed to fewer pathogens. This diversity in host contact directly affects the number of pathogens a tick may harbor and transmit (105). From an eco-epidemiological standpoint, reductions in biodiversity and environmental changes have been linked to the (re)emergence of infectious diseases (74,106,107). An experimental eco-epidemiological study conducted in Wales provided empirical evidence supporting the "dilution effect" hypothesis, which posits that greater biodiversity diminishes pathogen transmission by reducing the density of competent reservoir hosts (107). Specifically, the study highlighted that higher biodiversity in ecosystems mitigates the transmission of pathogens by diluting the presence of competent hosts (107). This phenomenon has been particularly evident in zoonotic, vector-borne pathogenic systems including TBPs such as *Borrelia burgdorferi* (14,107-109) and *Babesia microti* (14).

(ii) Number of Hosts: The pathogen transmission potential of ticks correlates with their host usage strategy, whether the tick is a one-host, two-host, or three-host species (110,111). For instance, ticks that utilize single or two hosts may have a more limited host contact rate compared to three-host ticks, which can interact with a broader range of hosts (10). However, this important epidemiological factor may be partially mitigated by transovarial transmission, wherein infected female ticks pass pathogens to their eggs and larvae, ensuring the transmission of pathogens to new hosts (112). In addition, Argasid ticks, which feed on blood multiple times as nymphs and adults, tend to have a higher host contact rate and are capable of acquiring and transmitting pathogens from several hosts, thus potentially increasing the transmission dynamics of TBDs (10).

(iii) Midgut Infection and Escape Barrier: To be transmitted to a vertebrate host through tick's saliva, TBPs must successfully traverse the tick's midgut and subsequently reach the salivary glands (113). In some cases, pathogens also migrate to the ovaries, facilitating transovarial transmission (112,114,115). The ability of pathogens to cross the midgut barrier is influenced by specific molecular interactions, notably those involving surface receptors such as the tick receptor for outer surface protein A (OspA). This receptor facilitates the adhesion and colonization of the midgut by *Borrelia burgdorferi* spirochetes through binding to OspA (42).

(iv) Innate Immune Response: To establish infection and be transmitted through tick saliva, pathogens must first overcome the tick's innate immune defense mechanisms (116,117). These include hemocytes, antimicrobial peptides, and RNA interference (RNAi) pathways, which collectively limit pathogen survival, replication, and dissemination within the tick vector (116). The strength and specificity of these immune responses play a critical role in determining the vector competence of a tick species (10).

(v) Salivary Gland Infection and Escape Barrier: Once within the hemocoel, pathogens must invade the salivary glands to be transmitted to a host during the next blood feeding (113). While the molecular mechanisms governing this process remain incompletely understood, successful transmission requires the pathogen to not only infect the salivary glands but also be secreted into the saliva (10). For example, *Borrelia burgdorferi* exploits specific tick salivary gland proteins to enhance its infection in mammalian host (118,119).

(vi) Pathogen Strains: Variability among pathogen strains can influence their ability to infect or be transmitted by ticks (10,120). For instance, although the African swine fever (ASF) virus strain Malawi LIL20/1 was isolated from *Ornithodoros* sp. ticks, attempts to experimentally infect ticks with this strain were unsuccessful (121). Similarly, the Florida strain of *Anaplasma marginale* was found to be non-transmissible by the tick *Dermacentor variabilis*, suggesting that in certain epidemiological contexts, controlling mechanical vectors such as blood-contaminated fomites or biting flies may be more effective than targeting ticks (122).

(vii) Tick Microbiome-pathogen Interactions: The tick microbiome plays a crucial role in shaping various physiological and immunological processes (123,124). Alterations to the microbiome—whether due to environmental changes, antimicrobial exposure, or other factors—can disrupt the peritrophic membrane, a barrier critical to pathogen containment and digestion (125). Such disruption may enhance or impair pathogen colonization and transmission dynamics (126,127).

(viii) Cross-immunity Interference: Interaction and competition between co-infecting microorganisms within the tick can significantly influence "vector competence" (10). For instance, prior infection with one *Rickettsia* species may inhibit the transovarial transmission of a second *Rickettsia* species within the same tick host (128). These competitive interactions can modulate the tick's capacity to transmit specific pathogens, thus influencing the overall epidemiology of TBDs. Understanding the intricate and multifaceted interactions among ticks, their pathogens, microbiota, and vertebrate hosts is essential for developing targeted and effective control strategies, which remain a formidable challenge due to ticks' resilience and their remarkable ability to adapt to various environmental conditions (14,129).

Tick Species

According to current ixodological records, approximately 1,025 tick species have been described worldwide, encompassing both extant and fossil taxa (28). Of these, 223 species are assigned to the family Argasidae, 790 species to the family Ixodidae, 11 species to Nuttalliellidae, and one species to the extinct family Khimairidae (28). The nidicolous Argasidae family is classified into two subfamilies, Argasinae and Ornithodorinae, based on morphological cladistic analysis (130). However, recent molecular cladistic studies, integrating both nuclear and mitochondrial data, have refined this classification. The systematics of argasid ticks remain the subject of ongoing discussion. Consequently, a revised classification has been proposed, in which the subfamily Argasinae comprises six genera: *Alveonasus*, *Argas* (including the subgenera *Argas* and *Persicargas*), *Navis*, *Ogadenus*, *Proknekalia*, and *Secretargas*. The subfamily Ornithodorinae is proposed to include nine genera: *Alectorobius*, *Antricola* (including the subgenera *Antricola* and *Parantricola*), *Carios*, *Chiropterargas*, *Nothoaspis*, *Ornithodoros* (including the subgenera *Microargas*, *Ornamentum*, *Ornithodoros*, *Pavlovskyella*, and *Theriodoros*), *Otobius* (131), *Reticulinasus*, and *Subparmatus* (22). Argasid ticks are globally distributed, with most species found in tropical and arid regions (78,132).

Among them, *Ornithodorus* is one of the most diverse genera in the family Argasidae, currently represented by approximately 60 species in the Neotropical Zoogeographic Region (22,133). However, the actual species diversity of *Ornithodorus* is likely underestimated (134). The genus *Argas* is cosmopolitan, with about 61 recognized species globally (135). Members of the Argasidae exhibit a multi-host life cycle and display diverse adaptations for host utilization (136). Unlike Ixodidae, soft ticks typically undergo multiple blood meals across two or more nymphal stages, each requiring a separate feeding for development (137). Most species take a single prolonged larval blood meal, followed by multiple brief blood-feeding events during subsequent developmental stages, often on different hosts. However, other adaptations, such as the absence of larval feeding or a lack of blood feeding in adults, have been recorded in certain species (138). Strategies facilitate the acquisition and transmission of a wide range of pathogens including viruses, bacteria, and protozoa underscoring their role as important disease vector (78).

In rural areas, Argasid ticks primarily inhabit cracks, crevices, and the ceilings of structures such as sheepfolds (particularly abandoned or infrequently used for over 15-20 years) and dwellings where humans and animals cohabit, such as mountain homes and shelters. In urban context, they can be found in the attics of unsanitary, slum-style houses, coming into contact with hosts occasionally. As a result, they have developed remarkable adaptations for prolonged fasting punctuated by rapid, opportunistic feeding bouts (139). These brief but aggressive feeding episodes by soft ticks can result in severe parasitic infestations in hosts, resulting in paralysis, toxic reactions, or even death. Moreover, during these heavy infestations, argasid ticks act as vectors for several important tick-borne zoonotic diseases. These include human relapsing fever (transmitted by *Ornithodoros* species), tick-borne relapsing fevers (TBRF) (caused by several *Borrelia* species, primarily transmitted by *Ornithodoros* and *Argas* species), and ASF (vectored by *Ornithodoros moubata*, *Ornithodoros porcinus*, *Ornithodoros erraticus*, and *Ornithodoros savignyi*), all of which cause significant economic losses (78,132). Additionally, species such as *Otobius megnini* and *Ornithodoros coriaceus* are considered of regional concern (14). *Otobius* species, particularly *Otobius megnini* and *Otobius lagophilus*, are one-host argasid ticks that infest their hosts during the larval and nymphal developmental stages. Though *Otobius megnini* has not been definitively established as a vector, it has been implicated in the transmission of several zoonotic pathogens, including *Coxiella burnetii*, *Rickettsia rickettsii*, and *Francisella tularensis* in both humans and animals. In addition, *Otobius megnini* is found to be associated with the transmission of *Anaplasma* spp., *Babesia caballi*, and *Theileria equi* in animals (140).

The family Ixodidae is characterized by a hard, chitinized dorsal exoskeleton. Females possess a partial dorsal shield or scutum, whereas males are covered entirely by a conscutum. Based on anal groove morphology, ixodid ticks are categorized into two major groups: Prostriata (e.g., *Ixodes* spp.), which have an anterior anal groove, and Metastriata (e.g., *Hyalomma excavatum* and *Rhipicephalus sanguineus*), which exhibit a small, posterior slit-like groove (17,48,141). These ticks follow three basic life cycle patterns: one-host, two-host, and three-host (47,48).

One-host ticks, such as *Rhipicephalus (Boophilus) annulatus* which transmits babesiosis, complete their entire life cycle comprising the larval, nymphal, and adult stages on a single host. On the other hand, two-host ticks, like *Hyalomma marginatum* [a major vector of Crimean-Congo hemorrhagic fever (CCHF)], use one host for larval and nymphal stages and another host for adulthood (feeding). Three-host ticks, such as *Ixodes* spp. [vectors for Lyme borreliosis (LB), babesiosis, and human granulocytic ehrlichiosis (HGE)], *Amblyomma* spp. (vectors for tularemia, ehrlichiosis, and RMSF), *Dermacentor* spp. [vectors for RMSF, Colorado tick fever virus (CTFV), tularemia, and tick paralysis], and *Rhipicephalus* spp. (vectors for RMSF and boutonneuse fever), require a different host for each developmental stage (89-93).

Besides host usage, ixodid tick distribution and behavior are influenced by environmental factors such as the latitudinal and altitudinal determinants, regional climate, vegetation, and forest dynamics (142). Seasonality also plays a role in tick activity and lifecycle patterns (47,48,143-147). However, it is important to note that these classifications are not absolute, as variations in ecological conditions may influence their host specificity or seasonal behavior. Ixodid ticks are globally distributed and exhibit a wide range of host-seeking behaviors (148). Feeding periods range from 2 to 13 days, depending on the tick species and developmental stage (32,48,149). While some, like *Rhipicephalus microplus*, are highly host-specific and monophagous (feeding exclusively on cattle), others, like *Amblyomma americanum* and *Ixodes ricinus*, display generalist feeding behavior across mammals, birds, and reptiles (48). From an epidemiological perspective, nymphal and adult stages of ticks are especially important in the transmission of tick-borne human pathogens, notably *Borrelia burgdorferi*, the causative agent of Lyme disease (91). In addition to the nymphal and adult stages, unfed larvae, especially those infected via transovarial transmission, also contribute significantly to the transmission of these pathogens. Furthermore, unfed larvae can acquire pathogens during their blood meal on a host. These larvae can molt into infectious nymphs, thereby sustaining pathogen transmission across hosts, as observed in the Lyme disease cycle (150).

Hard ticks (Ixodidae) are among the most significant arthropod vectors of various TBDs, posing considerable public health and veterinary concerns due to their widespread distribution and association with diverse pathogenic agents (47,48). Notable hard tick species that commonly parasitize humans include *Ixodes scapularis, Ixodes ricinus, Ixodes persulcatus, Ixodes holocyclus, Ixodes pacificus, Amblyomma americanum, Amblyomma hebraeum, Hyalomma anatolicum, Hyalomma marginatum, Haemaphysalis spinigera, Dermacentor variabilis,* and *Dermacentor andersoni* (14). In the context of livestock health, TBDs have profound implications, compromising the productivity, health, and welfare of economically important animals such as cattle, sheep, goats, and horses. The economic burden of TBDs is particularly pronounced in low-income regions, where these diseases contribute significantly to poverty by diminishing livestock-based livelihood (142,151,152). Loss of livestock not only results in economic hardship but also leads to decreased availability of essential food products such as meat and milk. This, in turn, exacerbates malnutrition and contributes to immune deficiencies among vulnerable populations such as children, the elderly, and individuals with compromised health, thereby creating additional public health challenges.

Common TBDs affecting livestock include anaplasmosis (146,153,154), babesiosis (155-163), theileriosis (151,152, 158-160,164-168), LB (79,108), hepatozoonosis, ehrlichiasis/neoehrlichiasis (146) and rickettsial diseases (146,169). These diseases have been extensively studied within the field of veterinary medicine with a particular emphasis on their economic impact (2,152,170,171). The devastating economic consequences of TBDs have been assessed both regionally and globally, with losses quantified across various parameters. Therefore, the importance of developing comprehensive strategies to combat both tick infestations and TBDs has been highlighted, underscoring the need for effective control measures to mitigate their public health and economic impact (2).

Ixodid ticks are distributed across all continents with diverse geographical distributions and varying levels of medical and veterinary significance (47,172). In the Americas, major genera of hard ticks infesting domestic animals include *Amblyomma*, *Dermacentor*, *Ixodes*, *Rhipicephalus*, and *Haemaphysalis* (172-175). In Australia, the primary tick genera of concern for disease transmission and economic impact are *Ixodes*, *Haemaphysalis*, and *Rhipicephalus* (176,177). Across Europe, and North Africa a total of 67 tick species have been recorded, belonging to genera such as *Amblyomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Ixodes*, and *Rhipicephalus* (178-180).

In Afrotropical regions, more than 200 hard tick species have already been reported (18). In South Africa, Pienaar et al. (181), recorded a total of 110 tick species belonging to three families: Nuttalliellidae, Argasidae, and Ixodidae. The family Nuttalliellidae was represented by a single species, *Nuttalliella namaqua*. The family Argasidae comprised 26 species distributed across two subfamilies. The subfamily Argasinae included 12 species within six genera: *Alveonasus* (1 species: *Alveonasus eboris*), *Argas* (7 species across two subgenera), *Navis* (1 species: *Navis striatus*), *Ogadenus* (1 species: *Ogadenus brumpti*), *Proknekalia* (1 species: *Proknekalia peringueyi*), and *Secretargas* (1 species: *Secretargas transgariepinus*). The subfamily Ornithodorinae comprised 14 species across six genera: *Alectorobius* (1 species: *Alectorobius capensis*), *Carios* (1 species: *Carios vespertilionis*), *Chiropterargas* (2 species: *Chiropterargas boueti* and *Chiropterargas confusus*), *Ornithodoros* (8 species across two subgenera: *Ornithodoros (Ornithodoros) compactus*, *Ornithodoros* (*Ornithodoros*) *kalahariensis*, *Ornithodoros (Ornithodoros) moubata*, *Ornithodoros (Ornithodoros) noorsveldensis*, *Ornithodoros (Ornithodoros) pavimentosus*, *Ornithodoros (Ornithodoros) phacochoerus*, *Ornithodoros* (*Ornithodoros*) *waterbergensis*, and *Ornithodoros (Pavlovskyella) zumpti*), *Otobius* (1 species: *Otobius megnini*), and *Reticulinasus* (1 species: *Reticulinasus faini*). The family Ixodidae accounted for the greatest diversity, with 83 species divided between the Prostriates and Metastriates. The Prostriates were represented solely by the genus *Ixodes*, encompassing 23 species distributed among five subgenera. *Ixodes* (23 species across 5 subgenera: *Ixodes* (*Exopalpiger*) *alluaudi, Ixodes* (*Afrixodes*) *aulacodi*, *Ixodes* (*Afrixodes*) *bakeri, Ixodes* (*Afrixodes*) *bedfordi*, *Ixodes* (*Afrixodes*) *catherinei*, *Ixodes* (*Afrixodes*) *cavipalpus*, *Ixodes* (*Afrixodes*) *corwini*, *Ixodes* (*Afrixodes*) *drakensbergensis*, *Ixodes* (*Afrixodes*) *elongatus*, *Ixodes* (*Afrixodes*) *fynbosensis, Ixodes* (*Afrixodes*) *myotomys*, *Ixodes* (*Afrixodes*) *neitzi*, *Ixodes* (*Afrixodes*) *pilosus, Ixodes* (*Afrixodes*) *procaviae*, *Ixodes* (*Afrixodes*) *rhabdomysae*, *Ixodes* (*Afrixodes*) *rubicundus, Ixodes* (*Eschatocephalus*) *simplex*, *Ixodes* (*Afrixodes*) *spinae*, *Ixodes* (*Ixodes*) *theilerae, Ixodes* (*Afrixodes*) *transvaalensis*, *Ixodes* (*Afrixodes*) *ugandanus, Ixodes* (*Ceratixodes*) *uriae*, *Ixodes* (*Eschatocephalus*) *vespertilionis*. The Metastriates comprised 60 species distributed across nine genera: *Africaniella*, *Amblyomma*, *Cosmiomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Margaropus*, *Rhipicentor*, and *Rhipicephalus*, with *Rhipicephalus* representing the most species-rich genus (30 species across four subgenera). *Africaniella* was represented by a single species (*Africaniella transversale*). *Amblyomma* included eight species across three subgenera: *Amblyomma* (*Aponomma*) *exornatum*, *Amblyomma* (*Xiphiastor*) *hebraeum*, *Amblyomma* (*Aponomma*) *latum*, *Amblyomma* (*Xiphiastor*) *marmoreum*, *Amblyomma* (*Xiphiastor*) *nuttalli*, *Amblyomma* (*Xiphiastor*) *rhinocerotis*, *Amblyomma* (*Walkeriana*) *sylvaticum*, and *Amblyomma* (*Xiphiastor*) *tholloni*. *Cosmiomma* was represented by one species (*Cosmiomma hippopotamensis*), and *Dermacentor* by one species (*Dermacentor rhinocerinus*). The genus *Haemaphysalis* comprised 13 species across four subgenera: *Haemaphysalis* (*Kaiseriana*) *aciculifer*, *Haemaphysalis* (*Rhipistoma*) *colesbergensis*, *Haemaphysalis* (*Rhipistoma*) *cooleyi*, *Haemaphysalis* (*Rhipistoma*) *elliptica*, *Haemaphysalis* (*Ornithophysalis*) *hoodi*, *Haemaphysalis* (*Rhipistoma*) *horaki*, *Haemaphysalis* (*Rhipistoma*) *hyracophila*, *Haemaphysalis* (*Rhipistoma*) *muhsamae*, *Haemaphysalis* (*Kaiseriana*) *parmata*, *Haemaphysalis* (*Rhipistoma*) *pedetes*, *Haemaphysalis* (*Haemaphysalis*) *silacea*, *Haemaphysalis* (*Rhipistoma*) *spinulosa-like*, and *Haemaphysalis* (*Rhipistoma*) *zumpti*. The genus *Hyalomma* included three species within the subgenus *Euhyalomma*: *Hyalomma* (*Euhyalomma*) *glabrum*, *Hyalomma* (*Euhyalomma*) *rufipes*, and *Hyalomma* (*Euhyalomma*) *truncatum*. *Margaropus* was represented by a single species (*Margaropus winthemi*), while *Rhipicentor* included two species (*Rhipicentor bicornis* and *Rhipicentor nuttalli*). The genus *Rhipicephalus* comprised 30 species across four subgenera: *Rhipicephalus* (*Rhipicephalus*) *afranicus*, *Rhipicephalus* (*Rhipicephalus*) *appendiculatus*, *Rhipicephalus* (*Rhipicephalus*) *arnoldi*, *Rhipicephalus* (*Rhipicephalus*) *capensis*, *Rhipicephalus* (*Boophilus*) *decoloratus*, *Rhipicephalus* (*Rhipicephalus*) *distinctus*, *Rhipicephalus* (*Digineus*) *evertsi evertsi*, *Rhipicephalus* (*Digineus*) *evertsi mimeticus*, *Rhipicephalus* (*Rhipicephalus*) *exophthalmos*, *Rhipicephalus* (*Rhipicephalus*) *follis*, *Rhipicephalus* (*Rhipicephalus*) *gertrudae*, *Rhipicephalus* (*Digineus*) *glabroscutatus*, *Rhipicephalus* (*Rhipicephalus*) *kochi*, *Rhipicephalus* (*Rhipicephalus*) *linnaei*, *Rhipicephalus* (*Rhipicephalus*) *lounsburyi*, *Rhipicephalus* (*Rhipicephalus*) *lunulatus*, *Rhipicephalus* (*Rhipicephalus*) *maculatus*, *Rhipicephalus* (*Boophilus*) *microplus*, *Rhipicephalus* (*Rhipicephalus*) *muehlensi*, *Rhipicephalus* (*Rhipicephalus*) *neumanni*, *Rhipicephalus* (*Rhipicephalus*) *nitens*, *Rhipicephalus* (*Rhipicephalus*) *oculatus*, *Rhipicephalus* (*Rhipicephalus*) *oreotragi*, *Rhipicephalus* (*Rhipicephalus*) *simpsoni*, *Rhipicephalus* (*Rhipicephalus*) *simus*, *Rhipicephalus* (*Rhipicephalus*) *sulcatus*, *Rhipicephalus* (*Hyperaspidion*) *theileri*, *Rhipicephalus* (*Rhipicephalus*) *tricuspis*, *Rhipicephalus* (*Rhipicephalus*) *warburtoni*, *Rhipicephalus* (*Rhipicephalus*) *zambeziensis*, and *Rhipicephalus* (*Rhipicephalus*) *zumpti*.

In Europe, 37 species of hard ticks are known to parasitize birds, exhibiting varying degrees of host specificity. For instance, in western and northern Europe, certain *Ixodes* species (e.g., *Ixodes rothschildi*, *Ixodes unicavatus*, and *Ixodes uriae*) are associated with seabirds, while *Hyalomma aegyptium* is found on turtles, and *Rhipicephalus* species (e.g., *Rhipicephalus turanicus* and *Rhipicephalus sanguineus*) are linked to birds of prey (182). In China, the family Ixodidae comprises 111 species distributed across seven genera:

Amblyomma, *Anomalohimalaya*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Ixodes*, and *Rhipicephalus* (183,184). In India, a total of 106 valid ixodid tick species have been reported (141,185,186). A total of 37 tick species, classified into 9 genera from the families Ixodidae and Argasidae, have been reported in Iran. Notably, a parallel trend has been observed between the rising prevalence of *Hyalomma marginatum* and *Hyalomma anatolicum* in the Sistan and Baluchistan provinces and the increasing incidence of CCHF in the region (187). Recently, Mumcuoglu et al. (28), reported the presence of 72 tick species belonging to the family Ixodidae and 29 species within the family Argasidae across Middle Eastern countries, underscoring the substantial diversity of tick vectors in the region. The family Ixodidae comprises the genera *Alloceraea*, *Amblyomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Ixodes*, and *Rhipicephalus*, whereas the family Argasidae is represented by the genera *Alectorobius, Alveonasus, Argas, Carios*, *Chiropterargas*, *Ogadenus*, *Ornithodoros*, *Otobius*, *Reticulinasus*, and *Secretargas*. Importantly, the introduction of non-native tick species has been attributed to human-mediated and animal-associated movements, including international travel and the transboundary movement of domestic livestock, wildlife, and avian hosts. This highlights potential pathways for the dissemination of TBPs and reinforces the need for strengthened regional surveillance and biosecurity measures.

A comprehensive global assessment of hard ticks of the world and documented the presence and distribution of all recognized Ixodidae species across 226 countries and territories, encompassing six zoogeographic regions—Afrotropical, Australasian, Nearctic, Neotropical, Oriental, and Palearctic—as well as remote islands (17,18). Ixodidae is the most diverse family, with 19 genera and 790 species (28). Taxonomically, Ixodidae is divided into two major groups based on the morphology of the anal groove: Prostriata and Metastriata. The Prostriata includes only the genus *Ixodes*, which is cosmopolitan in distribution and constitutes the largest genus in the family with 285 species (28) In contrast, the Metastriata group which is defined by a posteriorly positioned anal groove, includes 505 species across 18 genera: *Africaniella* (2 species), *Alloceraea* (6 species) *Amblyomma* (138 species), *Anomalohimalaya* (3 species), *Archaeocroton* (2 species), *Bothriocroton* (8 species), *Compluriscutula* (fossil, 1 species), *Cornupalpatum* (fossil, 1 species), *Cosmiomma* (1 species), *Cryptocroton* (1 species), *Dermacentor* (45 species), *Haemaphysalis* (172 species), *Hyalomma* (27 species), *Margaropus* (3 species), *Nosomma* (2 species), *Rhipicentor* (2 species), *Rhipicephalus* (90 species), and *Robertsicus* (1 species) (28).

The Status of Ticks in Türkiye

Türkiye, with its unique geographical location at the intersection of Asia, Europe, and Africa, is an ecological center for humans and animals, especially migratory birds. Additionally, due to its position on the Silk Road, it has historically been a hub for trade caravans and today serves as an important transit route. This ecological significance of Türkiye has greatly influenced tick infestations in humans and animals, as well as the epidemiology of infectious diseases, including TBDs and zoonoses. The country's subtropical climate, in combination with its rich terrestrial landscapes and wetland ecosystems across all seven geographical regions, offers essential sanctuaries for migratory bird species. Furthermore, the continuous legal and illegal movement of humans and animals across its borders amplifies the ecological and public health challenges of ticks and TBDs, emphasizing the need for comprehensive surveillance and control strategies (94,151).

Studies on ticks in Türkiye has been ongoing for over a century (188) with tick infestations being reported in humans (189-198) and animals (143,146,167,188,191,198-210) across all regions of the country. Several laboratory investigations have also focused specifically on the biology and vector competence of *Hyalomma* ticks (32,211,212). In a comparative experimental study, the vectorial capacity and competence of four *Hyalomma* tick species— *Hyalomma anatolicum*, *Hyalomma excavatum*, *Hyalomma scupence* and *Hyalomma marginatum*—were assessed. The study aimed to determine the vectorial capacity and vector competence of these *Hyalomma* species in transmitting *Theileria annulata* to cattle. Unfed nymphs of each species were infected by allowing them to feed on blood from calves experimentally infected with *Theileria annulata*. The prevalence of *Theileria annulata* sporozoites, vectorial capacity, and vector competence in the salivary glands of both male and female ticks were evaluated. While all four species showed a high prevalence of *Theileria annulata* sporozoites, no significant interspecies differences were observed. However, the mean number of infected acini per tick varied between male and female ticks, with female ticks exhibiting a higher number of infected salivary gland cells than males. This gender difference was more pronounced in *Hyalomma anatolicum* and *Hyalomma excavatum* compared to *Hyalomma scupence* and *Hyalomma marginatum*. These findings suggest that female ticks may play a more substantial role in pathogen transmission due to their higher infection rates (211). In another laboratory study, the biological features of *Hyalomma marginatum* ticks maintained as a laboratory line were analyzed under controlled conditions (32). Unfed female ticks fed on rabbits for approximately 15 days before detaching as engorged females. Oviposition commenced after an average preoviposition period of 20.5 days and continued for about 16 days. Larvae hatched after an average of 29 days and became active after approximately 8.5 days and then fed on rabbits for an average of 14.5 days before detaching from the host as engorged nymphs. The engorged nymphs then molted and reached the unfed adult stage in an average of 26 days. The process of chitinization and the transition to the active unfed adult stage was completed in an average of 10 days. Thus, the study demonstrated that *Hyalomma marginatum* ticks could progress from one unfed adult stage to the next generation of unfed adults in an average of 139.5 days under laboratory conditions. The total life cycle, from one unfed adult stage to the next generation of unfed adults, varied between 97 and 182 days, with an average duration of 139.5 days (32). Given its epidemiological importance, *Hyalomma marginatum* has also been the subject of a comprehensive mitochondrial genome (mitogenome) and phylogenetic analysis (212). The mitogenome of *Hyalomma marginatum* contains 13 protein-coding genes (PCGs), 22 transfer RNA (tRNA) genes, two ribosomal RNA (rRNA) subunits, two control regions, and three conserved motifs. The nucleotide composition of the *Hyalomma marginatum* mitogenome was found to be highly A+T-biased (79.76%), with most PCGs exhibiting negative AT and GC slopes. All PCGs initiate with ATK codons, and two truncated stop codons were identified in the *COX2* and *COX3* genes. Additionally, all tRNAs, except tRNACys and tRNASer1, exhibited the typical cloverleaf secondary structure. A total of 62 polymorphic regions and ten unique haplotypes were identified. Phylogenetic analysis, based on the 13 PCGs of 56 tick species, demonstrated that four *Hyalomma* species (*Hyalomma marginatum*, *Hyalomma asiaticum*, *Hyalomma rufipes*, and *Hyalomma truncatum*) form a monophyletic clade with strong support (212).

In various epidemiological studies conducted in Türkiye, several new records of tick species have been reported, broadening the knowledge of the country's tick fauna. In a study on tick infestation in birds, the species *Ixodes arboricola*, *Ixodes frontalis*, and *Ixodes ricinus* were identified. Notably, *Ixodes arboricola* was recorded for the first time in Türkiye's tick fauna (202). In another survey, 21,198 ticks were collected from humans infested with ticks around İstanbul between 2006 and 2011. These ticks belonged to 21 species across the genera *Ixodes*, *Hyalomma*, *Rhipicephalus*, *Haemaphysalis*, *Dermacentor*, *Argas*, *Ornithodoros*, and *Otobius*. The most common species identified were *Ixodes* and *Hyalomma* nymphs, particularly *Ixodes ricinus*. The study was the first report of *Ornithodoros lahorensis* and *Ixodes gibbosus* infesting humans in Türkiye. Additionally, *Ixodes acuminatus* was recorded as a new species for Türkiye's tick fauna (195). A report also highlighted nymphs of the *Amblyomma* genus, a tick species previously undocumented in Türkiye. These ticks infested a person who had a travel history abroad, indicating a potential introduction of the species from outside the country (192). In another field study, a red fox was found infested with nymphal and larval stages of ticks. The collected ticks were morphologically and molecularly identified as *Ixodes kaiseri*, marking the first recorded instance of *Ixodes kaiseri* in Türkiye (205). Additionally, a study focusing on ticks collected from cattle in Ordu Province in the Black Sea region reported the first occurrence of *Ixodes inopinatus* in Türkiye (208). A study on the distribution of ticks in the Çankırı Region, where geographical changes between the Black Sea and Central Anatolia are dominant, has shown the presence of different tick species (213). In another field study on tick infestations in mountain goats (*Capra aegagrus*) in the Eastern Anatolia Region, ticks were collected and identified through morphological and molecular analyses. The ticks identified included *Haemaphysalis kopetdaghica* (all active stages, n=140), *Dermacentor raskemensis* (adults, n=7), *Ixodes gibbosus* (adults, n=15), *Rhipicephalus kohlsi* (female, n=1), and *Rhipicephalus bursa* (nymphs, n=2). Notably, *Haemaphysalis kopetdaghica* and *Dermacentor raskemensis* were rediscovered species, and the phylogenetic data for these species were presented for the first time. Moreover, the *COX1* region of *Ixodes gibbosus* was characterized for the first time, and it was suggested that *Rhipicephalus kohlsi* may represent a cryptic species (214).

The morphological similarities among certain tick species can be remarkably close, often leading to potential misidentification. In this context, *Rhipicephalus secundus*, which exhibits considerable morphological resemblance to *Rhipicephalus turanicus*, was re-evaluated. A study conducted in Israel led to the reclassification of *Rhipicephalus secundus* as a valid species within the *Rhipicephalus sanguineus* group, thereby removing it from the synonymy of *Rhipicephalus turanicus*. Both male and female specimens of *Rhipicephalus secundus* were re-identified through phylogenetic analysis based on mitochondrial DNA sequencing. This re-identification study was carried out using tick samples collected from goats in Israel. Phylogenetic analyses revealed that *Rhipicephalus secundus* belongs to a clade distinct from *Rhipicephalus turanicus* sensu stricto (s.s.), *Rhipicephalus sanguineus* s.s., the *Rhipicephalus sanguineus* group, and other related taxa. Based on the results of this study, it can be concluded that *Rhipicephalus secundus* is present at least in Israel, the Palestinian Territories, Türkiye, Albania, and Southern Italy. However, additional studies are needed to determine the full geographic distribution and host range of this species (215).

Ongoing field studies on the tick fauna of Türkiye continue to provide new insights into species diversity and host associations. In this context, a comprehensive survey was conducted to investigate tick populations parasitizing bats, which are of significant veterinary and public health importance, as they serve as reservoir hosts for a wide range of emerging and re-emerging TBPs—including viruses, bacteria, and protozoa—with zoonotic potential. The study involved the collection of tick specimens from bats inhabiting 26 caves located within the borders of 18 provinces across all seven geographical regions of Türkiye. A total of 81 tick samples were collected and subjected to morphological species identification using established taxonomic keys. The identified tick specimens belonged to five species: *Ixodes vespertilionis*, *Ixodes simplex*, *Ixodes ariadnae*, *Ixodes kaiseri*, and *Haemaphysalis erinacei*. Notably, *Ixodes ariadnae* was recorded for the first time in Türkiye, representing a significant addition to the country's tick fauna. This finding expands the known distribution range of *Ixodes ariadnae* and highlights the importance of continued surveillance of ectoparasites associated with wildlife, particularly bats, which are known reservoirs for a variety of emerging zoonotic TBPs. The discovery of *Ixodes ariadnae* in Türkiye underscores the need for further taxonomic and molecular studies to clarify the ecological roles and vector potential of bat-associated tick species in the region (216).

On the other hand, urban expansion is increasing each year due to anthropogenic factors and poses a serious threat to natural habitats. This growing proximity to ecosystems dominated by wildlife has led to substantial ecological disruptions. The resulting ecological degradation heightens epidemiological risks, particularly through human–wildlife–vector interactions, thereby significantly increasing the risk of tick infestations in humans and domestic animals such as dogs. Epidemiologically, a recent field study conducted in the Thrace region on the European side of Türkiye highlighted the close interaction between human settlements and wildlife. During the survey, a total of 1,605 dogs—both owned and stray—from ten different localities were examined for tick infestation. Ticks were found on 137 dogs, resulting in a prevalence rate of 8.54%. On a monthly basis, the prevalence peaked at 34.03%, with the highest rates observed in May. A total of 1,033 ticks (1,008 adults and 25 nymphs) were collected and identified during the study. The identified species included *Rhipicephalus sanguineus* sensu lato, *Haemaphysalis parva*, *Ixodes ricinus*, *Ixodes acuminatus*, and *Ixodes kaiseri*. Epidemiologically, the study highlighted the impact of anthropogenic threats on natural habitats, which, coupled with the proximity of human settlements to wildlife, has led to an increased risk of tick infestations. Wild animals and their ticks were identified as "close sources of tick infestation" for both domestic animals and humans, especially in urban areas. The study emphasized that the transmission of ticks to urban areas, forested regions, and peri-urban gardens plays a key role in the infestation of dogs by tick species with a primarily forest cycle, such as *Ixodes acuminatus* and *Ixodes kaiseri* (217). Wild animals and migratory birds play an important role as amplifying and/or reservoir hosts in the spread of many tick species that infest livestock and humans, as well as in the epidemiology of TBDs. In a study conducted in the Hatay Region between 2014 and 2022, a total of 362 tick samples (210♀, 146♂, 6 nymphs) were collected from 18 hosts belonging to 7 wild animal species: white stork (*Ciconia ciconia*, n=1), roe deer (*Capreolus capreolus*, n=5), badger (*Meles meles*, n=2), jackal (*Canis aureus*, n=3), red fox (*Vulpes vulpes*, n=5), rabbit (*Lepus europaeus*, n=1), and wild goat (*Capra aegagrus*, n=1). The identified ticks were confirmed as *Amblyomma lepidum*, *Dermacentor marginatus*, *Haemaphysalis erinacei*, *Alloceraea inermis*, *Haemaphysalis kopetdaghica*, *Ixodes gibbosus*, *Ixodes kaiseri*, *Ixodes ricinus*, *Rhipicephalus kohlsi*, *Rhipicephalus rossicus*, and *Rhipicephalus turanicus*. The study reported, for the first time in Türkiye, the presence of adult non-native tick species *Amblyomma lepidum* specimens on storks, and the detection of *Rhipicephalus rossicus* on roe deer (210). A comprehensive molecular epidemiological investigation was conducted to elucidate the population genetic structure and demographic history of *Dermacentor marginatus*. In this study, the mitochondrial *COX1* gene and the nuclear internal transcribed spacer 2 region were sequenced and analyzed from a total of 361 adult tick specimens collected across the Central and Northeastern regions of Anatolia. The results demonstrated significant genetic differentiation and pronounced population structuring, reflecting considerable intraspecific genetic diversity within *Dermacentor marginatus* populations in the study area (218). In another study, tick samples collected from an owned dog in İstanbul in November 2024 were examined, and the presence of the Asian horned tick (*Haemaphysalis longicornis*) was detected for the first time in Türkiye. Given that this species can serve as a vector for more than 30 TBPs, including *Anaplasma*, *Babesia*, *Bartonella*, *Coxiella*, *Rickettsia*, and *Theileria,* its medical and veterinary significance was emphasized (219). In a systematic review conducted in Türkiye, it was reported that the tick species most frequently infesting humans belong to the genera *Hyalomma* (46.99%) and *Ixodes* (28.49%), followed by *Rhipicephalus* and *Haemaphysalis*. *Hyalomma* species, particularly their nymphs, were responsible for the highest bite rate (22.65%). Additionally, it was emphasized that, from an epidemiological perspective, *Hyalomma* spp. and *Ixodes* spp. are the primary vectors of significant TBDs in Türkiye. *Hyalomma marginatum* is the main vector responsible for seasonal outbreaks of CCHF in rural areas, while *Ixodes* spp. are associated with Lyme disease (220).

It has previously been reported that there are 55 confirmed tick species in Türkiye, with 47 belonging to the family Ixodidae and 8 to the family Argasidae (188). However, recent studies indicate that the number of confirmed tick species in Türkiye has increased. Currently, the tick fauna of Türkiye comprises a total of 58 species: 8 species across 6 genera in the family Argasidae (*Argas* - 2 species, *Carios* - 1 species, *Ornithodoros* - 2 species, *Alectorobius* - 1 species, *Alveonasus* - 1 species and *Otobius* - 1 species) and 50 species from 7 genera in the family Ixodidae (*Ixodes* - 17 species, *Rhipicephalus* - 8 species, *Dermacentor* - 4 species, *Hyalomma* - 9 species, *Haemaphysalis* - 8 species, *Alloceraea* - 1 species and *Amblyomma* - 3 species) (201,221,222, personal communication with Prof. Dr. Adem Keskin 2025). However, *Haemaphysalis pospelovashtromae*, reported by Özkan (223) as *Haemaphysalis (Aboimisalis) aksarensis* sp. nov. from the Erzurum and Kars provinces and shown in Table 1 for the Eastern Anatolia Region, whose presence in Türkiye was tentatively accepted by Buraslı et al. (201) and later considered by Guglielmone et al. (17), to be a synonym of *Haemaphysalis pospelovashtromae*, has not been rereported in other epidemiological field studies on ticks conducted in Türkiye to date. The geographical distribution of these reported tick species across the seven regions of Türkiye is presented in Table 1. This diverse tick fauna underscores the importance of sustained research and control efforts in Türkiye to address both veterinary and public health concerns related to TBDs.

Tick-borne Pathogens

Tick-borne Viruses (TBVs)

Viruses are obligatory intracellular parasites that require living host cells for survival and replication (224). They are transmitted through two major mechanisms: non-vectorial and vectorial transmission (90,225-227). Vector-borne viruses, commonly referred to as arthropod-borne viruses (arboviruses), are transmitted by hematophagous arthropods such as mosquitoes, ticks, and biting flies. Arboviruses constitute a major public health concern globally as they are significant drivers of epidemics and can cause substantial morbidity and mortality in both human and animal populations (228). The emergence and re-emergence of these viral infections often lead to considerable economic losses with devastating public health impacts. Arboviruses represent the largest known group of viruses associated with a profound impact on global health (229). Although arboviruses are the largest biological group of viruses, only a limited number of arthropod species serve as competent vectors (90). Current estimates indicate that approximately 300 mosquito species, 116 tick species, and 25 midge species have been identified that are serving as vectors for arboviruses. Additionally, other arthropods, including sandflies, blackflies, stink bugs, lice, mites, gadflies, and stink bugs, have also been identified as potential vectors for these viruses (230). The scientific study of arboviruses began in 1927 with the identification of yellow fever virus as the first mosquito-borne virus (231). In 1931, the Nairobi sheep disease virus (NSDV) was isolated as the first tick-borne virus (90,232), and later that year, the Louping ill Virus (LIV) was detected in ticks in Scotland (233). These early discoveries laid the foundation for subsequent research on arbovirus transmission and their epidemiology.

The discovery of tick-borne viral diseases (TBVDs) has predominantly been driven by outbreaks affecting animals or humans, rather than systematic, well-funded research initiatives (227). Early identifications were largely reactive, with viral detection often following disease emergence in affected populations. Prior to the 1950s, only a limited number of TBVD cases had been identified, characterized, and documented including ASF (1921), lumpy skin disease (LSD) (1929), LIV (1931), tick-borne encephalitis virus (TBEV) (1937), CCHF virus (CCHFV) (1944), CTF virus (CTFV) (1944) and Omsk hemorrhagic fever virus (1947) (227,234).

The second half of the 20th century witnessed an increase in TBV identification, largely due to advancements in virological techniques. Between 1953 and 1989, several new TBVs were isolated, including Quaranfil virus (1953), Bhanja virus (1954), Langat virus (1956), Kyasanur forest disease virus (1957), Powassan virus (POWV) (1958), Tribec virus (1958), Thogoto virus (1960), Turkish sheep encephalitis virus (TSEV) (1960), Dhori virus (1961), Seletar virus (1961), Kemerovo virus (KEMV) (1963), Lipovnik virus (1963), Johnston Atoll virus (1964), Farallon virus (1965), Kaisodi virus (1966), Midway virus (1966), Jos virus (1967), Hughes virus (1968), Dera Ghazi Khan virus (1970), Hazara virus (1970), Wanowire virus (1970), Issyk-Kul virus (1970), Silverwater virus (1971), Tamdy virus (1971), Royal Farm virus (1972), Sakhalin virus (1972), Taggert virus (1972), Okhotskiy virus (1973), Soldado virus (1973), Zirga virus (1973), Bahig virus (1974), Batken virus (1974), Dugbe virus (1974), Matruh virus (1974), Clo Mor virus (1976), Keterah virus (1976), Karshi virus (1976), Paramushir virus (1976), Saumarez Reef virus (1977), Razdan virus (1978), Chim virus (1979), Wad Medani virus (1980), Punta saline virus (1981), Qalyub virus (1981), Vinegar Hill virus (1983), Eyach virus (EYAV) (1984), Meaban virus (1985), Great Saltee virus (1986), Kumlinge virus (1989) (235-241).

The late 20th and early 21st centuries marked a period of continued TBV discovery, with the identification of additional species across different regions. Newly recognized TBVs included Palma virus

Table 1. Geographical distribution of reported tick species in seven regions of Türkiye

Reported ticks genus	**Central Anatolia**	**Black Sea**	**Eastern Anatolia**	**Southeast Anatolia**	**Mediterranean**	**Aegean**	**Marmara**
Ixodes (17 species)	*I. kaiseri* *I. vespertilionis* *I. gibbosus* *I. laguri* *I. simplex* *I. ariadnae* *I. frontalis*	*I. frontalis* *I. arboricola* *I. inopinatus* *I. eldaricus* *I. festai* *I. gibbosus* *I. ricinus* *I. hexagonus* *I. laguri* *I. redikorzevi* *I. trianguliceps*	*I. gibbosus* *I. vespertilionis* *I. ricinus* *I. simplex* *I. redikorzevi* *I. hexagonus* *I. trianguliceps*	*I. simplex*	*I. vespertilionis* *I. ricinus* *I. simplex* *I. kaiseri* *I. gibbosus*	*I. gibbosus* *I. vespertilionis* *I. ricinus*	*I. kaiseri* *I. redikorzevi* *I. acuminatus* *I. crenulatus* *I. hexagonus* *I. gibbosus* *I. ricinus* *I. laguri*
Rhipicephalus (8 species)	*Rh. annulatus* *Rh. bursa* *Rh. sanguineus s.l.* *Rh. turanicus* *Rh. secundus*	*Rh. annulatus* *Rh. bursa* *Rh. sanguineus s.l.* *Rh. turanicus*	*Rh. annulatus* *Rh. rossicus* *Rh. bursa* *Rh. kohlsi* *Rh. sanguineus s.l.* *Rh. turanicus*	*Rh. kohlsi* *Rh. annulatus* *Rh. bursa* *Rh. sanguines s.l.* *Rh. turanicus*	*Rh. annulatus* *Rh. bursa* *Rh. sanguines s.l.* *Rh. turanicus* *Rh. rossicus*	*Rh. annulatus* *Rh. bursa* *Rh. sanguines s.l.* *Rh. turanicus* *Rh. pumilio*	*Rh. annulatus* *Rh. bursa* *Rh. sanguines* *Rh. turanicus*
Dermacentor (4 species)	*D. marginatus* *D. reticulatus* *D. niveus*	*D. marginatus* *D. niveus* *D. reticulatus*	*D. marginatus* *D. niveus* *D. raskemensis*	*D. marginatus*	*D. marginatus* *D. niveus*	*D. marginatus*	*D. marginatus* *D. niveus*
Hyalomma (9 species)	*H. aegyptium* *H. anatolicum* *H. excavatum* *H. scupense* *H. marginatum*	*H. aegyptium* *H. rufipes* *H. anatolicum* *H. excavatum* *H. scupense* *H. dromedarii* *H. marginatum*	*H. aegyptium* *H. rufipes* *H. anatolicum* *H. excavatum* *H. scupense* *H. dromedarii* *H. marginatum* *H. asiaticum*	*H. aegyptium* *H. anatolicum* *H. excavatum* *H. scupense* *H. impeltatum* *H. marginatum* *H. asiaticum*	*H. aegyptium* *H. anatolicum* *H. excavatum* *H. scupense* *H. dromedarii* *H. marginatum*	*H. aegyptium* *H. rufipes* *H. anatolicum* *H. excavatum* *H. scupense* *H. dromedarii* *H. marginatum*	*H. aegyptium* *H. rufipes* *H. anatolicum* *H. excavatum* *H. scupense* *H. marginatum*
Alloceraea (1 species)	*A. inermis*	*A. inermis*	*A. inermis*	*A. inermis*	-	-	*A. inermis*
Haemaphysalis (8 species)	*Hae. concinna* *Hae. parva* *Hae. punctata* *Hae. sulcata* *Hae. erinacei*	*Hae. concinna* *Hae. parva* *Hae. punctata* *Hae. sulcata* *Hae. erinacei*	*Hae. parva* *Hae. punctata* *Hae. sulcata* *Hae. kopetdaghica* *Hae. pospelovashtromae*	*Hae. parva* *Hae. punctata* *Hae. sulcata*	*Hae. concinna* *Hae. parva* *Hae. punctata* *Hae. sulcata* *Hae. kopetdaghica* *H. erinacei*	*Hae. parva* *Hae. punctata* *Hae. sulcata*	*Hae. longicornis* *Hae. parva* *Hae. punctata* *Hae. sulcata* *Hae. erinacei*
Amblyomma (3 species)	*Amblyomma* sp.	-	-	-	*Am. variegatum* *Am. lepidum*	-	-
Alectorobius (1 species)	-	-	-	*A. coniceps*	-	-	-
Alveonasus (1 species)	A. lahorensis	*A. lahorensis*	*A. lahorensis*	*A. lahorensis*	*A. lahorensis*	*A. lahorensis*	*A. lahorensis*
Argas (2 species)	*A. persicus* *A. reflexus*	*A. persicus* *A. reflexus*	*A. persicus* *A. reflexus*	*A. persicus* *A. reflexus*	*A. persicus* *A. reflexus*	*A. persicus* *A. reflexus*	*A. persicus* *A. reflexus*
Carios (1 species)	-	*C. vespertilionis*	*C. vespertilionis*	-	-	-	*C. vespertilionis*
Ornithodoros (2 species)	-	-	*O. erraticus* *O. tholozani*	-	*O. erraticus*	*O. erraticus*	-
Otobius (1 species)	-	-	*O. megnini*	*O. megnini*	-	-	*O. megnini*

(1994), Alkhurma hemorrhagic fever virus (1995), Spanish sheep encephalitis virus (1995), deer tick virus (1997), Gadgets Gully virus (1997), Bovine hokovirus (2008), Greek Goat Encephalitis virus (2008), Heartland virus (HRTV) (2009), Severe fever with thrombocytopenia syndrome (2009), Ganjam virus (2009), Wellfleet Bay virus (2010), Huaiyangshan banyangvirus (2012), Bourbon virus (2014), Caspiy virus (2014), Geran virus (2014), Gissar virus (2014), Jingmen tick virus (2014), KEMV (2014), Sokoluk virus (2014), Tyuleniy virus (2014), Chobar Gorge virus (2015), Muko virus (MUV) (2015), Spanish goat encephalitis virus (2015), Avalon virus (2016), Bandia virus (2016), HRTV (2016), Tofla virus (2016), Uukuniemi virus (UUKV) (2016), Alongshan virus (2017), Chenuda virus (2017), Odaw virus (2017), Bangali virus (2018), Kabuto Mountain virus (2018), Beiji nairovirus (2019), Yezo virus (2019), Tacheng tick virus 1 (2020), Tacheng tick virus 2 (2021), Iftin tick virus (2021), Sogngling tick virus (2021), Mbalambala/Balambala tick virus (2022), Oz virus (2022), Dabieshan tick virus (2024), Guertu virus (2024), Sapphire II virus (2024) (227,234,240-247).

Since the first confirmed TBVD (the NSDV) nearly a century ago, more than 100 TBVs have been successfully isolated and characterized (227,234,245). Subsequent research efforts have expanded the known diversity of arboviruses leading to the identification of approximately 500 additional species of which 160 were classified as TBVs. Among these, around 50 are recognized as distinct viral species, with approximately 25% linked to disease (90). Notably, all known TBVs that are pathogenic to humans are zoonotic in nature (240).

Taxonomically, TBVs have been classified into a single DNA virus family: Asfarviridae and eight RNA virus families: Flaviviridae, Orthomyxoviridae, Reoviridae, Rhabdoviridae, Nyamiviridae (order Mononegavirales), and Nairoviridae, Phenuiviridae, and Peribunyaviridae (within the recently established order Bunyavirales) (240,248-250). Among these, TBVs with high pathogenicity in humans have been identified within the Flaviviridae, Nairoviridae, Phenuiviridae, Orthomyxoviridae, and Sedoreoviridae families (234).

The ZOVER database have been developed to integrate ecological, epidemiological, and virological data on zoonotic and vector-borne viruses, including TBVs (251). It currently catalogs 957 virus species from 34 virus families, associated with bats, rodents, mosquitoes, and ticks across 151 countries and regions worldwide (252). In contrast, a recent review on TBVs by Moming et al. (227) reported the presence of 870 virus species distributed across 28 orders, 55 families, and 66 genera. Currently, the United States Center for Disease Control and Prevention maintains an updated list of arboviruses comprising over 500 species, of which more than 150 cause disease in humans and/or animals (253).

It is important to note that out of more than 900 recognized tick species, approximately 10% are of significant medical or veterinary importance (10,73). The tick species known to serve as vectors for virus are predominantly distribute within the Argasidae family, particularly within the genera *Ornithodorus, Carios, Argas* and *Otobius* (132), as well as within the Ixodidae family, which includes the genera *Ixodes*, *Haemaphysalis*, *Hyalomma*, *Amblyomma*, *Dermacentor*, and *Rhipicephalus*, along with the subgenus *Rhipicephalus* (*Boophilus*) (10,73,87).

While some tick species are capable of transmitting only one or two species, a handful number can transmit multiple viruses. For instance, *Ixodes ricinus*, a widely distributed tick species in Europe and North Africa (both in cosmopolitan and forested areas), is a major vector for numerous TBVs as well as bacterial pathogens, including *Borrelia burgdorferi*, the causative agent of Lyme disease (90). Similarly, the Palearctic ixodid tick *Hyalomma marginatum* is widely distributed in parts of Southern Europe, North Africa, and Western Asia (17) serves as the primary vector for the CCHFV in humans (254,255) and also transmits *Theileria annulata*, a protozoan parasite causing tropical theileriosis in cattle (211). It is important to note that *Ixodes ricinus* is a primary vector for viruses belonging to three different families including Kadam (KEMV) and Eyach (EYAV) from the Reoviridae family, UUKV from the Bunyaviridae family, and both CCHFV and LIV from the Flaviviridae family. However, the seabird-associated tick *Ixodes uriae* transmits seven different virus species from the Reoviridae, Bunyaviridae, and Flaviviridae families (90). These observations underscore the ecological and epidemiological significance of ticks as vectors for a diverse array of viral pathogens.

Vector Specificity and Transmission Dynamics of TBVs

Despite the well-documented adaptability of arboviruses, there are several critical factors that might limit their transmission to host cells. One of the leading determinants is the vector specificity of the virus that governs the ability of a virus to be transmitted by a particular arthropod species. Traditionally, it has been suggested that arboviruses transmitted through hematophagous insects, such as mosquitoes, are not transmitted by ticks, and vice versa (90). However, exceptions to this principle exist. For instance, LSD virus (LSDV) has been reported to be transmitted by a variety of hematophagous insects, including mosquitoes (*Aedes aegypti*) (256), biting flies (*Stomoxys calcitrans*) (257-259), horse flies (*Haematopota* spp.) (257), and also ixodid ticks, such as *Amblyomma hebraeum*, *Rhipicephalus appendiculatus*, and *Rhipicephalus (Boophilus) decoloratus* (260-263), and recently non-vector-borne transmission of LSDV was also demonstrated in an experimental study using the vaccine-derived, virulent recombinant LSDV strain (Saratov/2017) in a specially created, insect-proof and vector-free field (226).

Epidemiologically, TBVs are primarily transmitted to vertebrate hosts through the bite of an infected tick. The transmission cycle involves complex ecological interactions between tick vectors and vertebrate hosts. Transmission begins when ticks acquire the virus by feeding on an infected reservoir host, typically small mammals or birds. These infected ticks subsequently transmit the virus to new hosts, including humans, during subsequent blood meals. It is important to note that vertebrate hosts including rodents, birds, and humans serve as reservoirs or amplification hosts, facilitating viral persistence within the ecosystem and ensuring its circulation in nature (73). A comprehensive summary of 94 known TBVs, their transmissions, geographical distributions is listed in Table 2, and the zoonotic status of TBVs were shown in Figure 1.

Another important factor is the competence of vectors. Most TBVs exhibit high degree of vector specificity and are typically transmitted by either Ixodidae (hard ticks) or Argasidae (soft ticks), but rarely by both. This phenomenon, known as vector competence, plays a critical role in determining the transmission dynamics of TBVs. As a result, some TBVs have a much more restricted range of competent vectors (90). The ability of a tick species to acquire, maintain, and transmit a virus is influenced

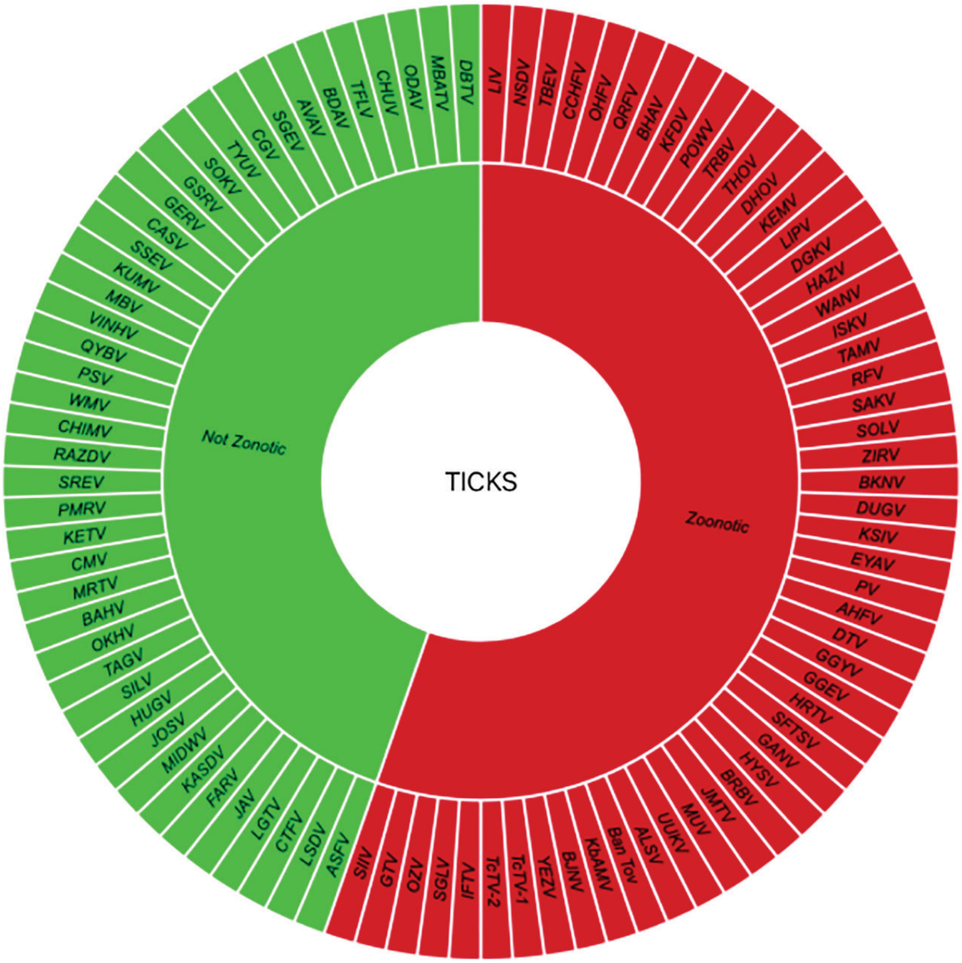


Figure 1. Zoonotic and non-zoonotic viruses transmitted by ticks

by a combination of intrinsic genetic factors, viral interactions, and host immune responses (10). Vectorial capacity, the overall efficiency of a vector in transmitting a pathogen, is modulated by host factors such as viral interference and interferon (IFN)-mediate immune responses (90,264-266). While viral interference and IFN responses are primarily host-driven immune mechanisms, they have a profound impact on viral replication, co-infections and overall transmission dynamics. The interplay between immune mechanisms and vector-virus interactions can influence the prevalence and spread of TBDs in natural settings. These determinant characteristics affect features such as virus-tick-host and susceptibility (240).

The transmission cycle of TBVs can be best conceptualized within the framework of a three-component parasitic interaction model: (i) virus-vector tick interaction, (ii) virus-vertebrate host interaction, and (iii) vector tick-vertebrate host interactions (90). Within this model, viral transmission is influenced by a series of physiological as well as molecular barriers within the tick vector. Studies of arboviral infections in insect vectors have identified four key infection barriers that are critical in the transmission of TBVs: (i) the midgut infection barrier, (ii) the midgut escape barrier, (iii) the salivary gland infection barrier, and (iv) the salivary gland escape barrier (90,266). These infection barriers dictate the virus's ability to pass through the cell membrane into the cytoplasm or, after infecting a cell, the virus may replicate but fail to exit the cell and ultimately be transmitted to a new host. At the cellular level, viral transmission requires successful entry, replication, and subsequently spread to other cells. It is important to note that both intrinsic genetic and extrinsic environmental factors greatly influence a tick's inherent ability to become infected, support viral replication, and ultimately transmit the virus (240). The outcome of the infection exclusively depends on the interactions between the viral genome and the tick's physiological environment. Although molecular mechanisms underlying tick-virus interaction are not clearly understood, recent research has highlighted that the importance of RNAi as a key antiviral defense mechanism in arthropods, including ticks (266,267). RNAi is a nucleic acid-based regulatory mechanism that modulates post-transcriptional gene expression, gene function and metabolic pathways, and antiviral immune response in arthropods. While widely used as a reverse genetics tool to manipulate gene function, RNAi has also been employed to investigate tick-pathogen interactions, identify protective antigens in ticks, and screen for potential vaccine targets.

RNAi method was originally developed through *in vitro* incubation of double-stranded RNA (dsRNA) with tick salivary glands and *in vivo* injection of dsRNA into live female ticks (268).

Table 2. Tick-Borne viruses which were listed chronologically worldwide

Virus	Family	Isolation date	Vector ticks	Geographical distributions	Zoonotic status	References
ASFV	Asfarviridae	1921	*O. moubata,* *O. porcinus*	Africa, Asia, Europe	Not zoonotic	(289)
LSDV	Poxviridae	1929	*Rh. decoloratus, Rh. appendiculatus, Am. hebraeum*	Africa, Middle East, Asia	Not zoonotic	(290)
LIV	Flaviviridae	1929	*I. ricinus*	Europe	Zoonotic	(291)
NSDV	Nairoviridae	1931	*Rh. appendiculatus*	Africa, Asia	Zoonotic	(292)
TBEV	Flaviviridae	1937	*I. ricinus, I. persulcatus*	Europe, Asia	Zoonotic	(293)
CCHFV	Nairoviridae	1944	*H. marginatum, Ixodes* spp.	Africa, Asia, Europe	Zoonotic	(294)
CTFV	Reoviridae	1944	*D. andersoni*	America	Not zoonotic	(295)
OHFV	Flaviviridae	1947	*D. reticulatus*	Asia	Zoonotic	(296)
QRFV	Orthomyxoviridae	1953	*Argas* spp.	Africa, Asia,	Zoonotic	(297)
BHAV	Phenuiviridae	1954	*Haemaphysalis* spp., *Dermacentor* spp., *Hyalomma* spp., *Rhipicephalus* spp., *Amblyomma* spp.	Asia, Europe	Zoonotic	(298)
LGTV	Flaviviridae	1956	*Hae. longicornis*	Asia	?	(299)
KFDV	Flaviviridae	1957	*Haemaphysalis* spp., *Rhipicephalus* spp.	Asia	Zoonotic	(300)
POWV	Flaviviridae	1958	*I. scapularis*	America	Zoonotic	(301)
TRBV	Reoviridae	1958	*I. ricinus*	Europe	Zoonotic	(302)
THOV	Orthomyxoviridae	1960	*Rh. decoloratus, Hae. longicornis, Am. variegatum, Rh. annulatus, H. nitidum*	Africa, Asia, Europe	Zoonotic	(303,304)
DHOV	Orthomyxoviridae	1961	*H. dromedarii*	Asia	Zoonotic	(304)
KEMV	Reoviridae	1963	*Ixodes* spp., *D. reticulatus*	Europe, Russia	Zoonotic	(305,306)
LIPV	Reoviridae	1963	*Ixodes* spp.	Europe	Zoonotic	(241)
JAV	Orthomyxoviridae	1964	*Ornithodoros capensis*	Europe	Not zoonotic	(307)
FARV	Nairoviridae	1965	*Ornithodoros* spp.	America	Not zoonotic	(308)
KASDV	Phenuiviridae	1966/1957	*Hae. turturis, Hae. wellingtoni, Hae. spinigera*	Asia	Not zoonotic	(309)
MIDWV	Nyamiviridae	1966	*Ornithodoros* spp.	Asia	Not zoonotic	(310)
JOSV	Orthomyxoviridae	1967	*Amblyomma* spp., *Rhipicephalus (Boophilus)* spp.	Africa	Not zoonotic	(311)
HUGV	Bunyaviridae	1968	*Carios (Alectorobius) denmarki*	America	Not zoonotic	(312)
DGKV	Bunyaviridae	1970	*H. dromedarii*	Asia	Zooonotic	(295)
HAZV	Bunyaviridae	1970	*Ixodes* spp.	Europe	Zoonotic	(313,314)
WANV	Bunyaviridae	1970	*Hyalomma* spp.	Asia, Africa	Zoonotic	(315)
ISKV	Nairoviridae	1970	*Argas* spp.	Asia	Zoonotic	(316)
SILV	Reoviridae	1971	*Hae. leporispalustris*	America	Not zoonotic	(317)
TAMV	Bunyaviridae	1971	*H. asiaticum*	Asia	Zoonotic	(318)
RFV	Flaviviridae	1972	*H. asiaticum*	Asia	Zoonotic	(319)
SAKV	Bunyaviridae	1972	*I. uriae*	Asia	Zoonotic	(320)
TAGV	Bunyaviridae	1972	*I. uriae*	Europe	Not Zoonotic	(321)

Table 2. Continued

Virus	**Family**	**Isolation date**	**Vector ticks**	**Geographical distributions**	**Zoonotic status**	**References**
OKHV	Nairoviridae	1973	*I. putus*	Asia	Not Zoonotic	(322)
SOLV	Nairoviridae	1973	*Am. variegatum, Rhipicephalus (Boophilus)* sp., *Hyalomma* spp.	Africa	Zoonotic	(323)
ZIRV	Nairoviridae	1973	*Ornithodoros* spp.	Asia	Zoonotic	(308)
BAHV	Bunyaviridae	1974	*H. marginatum, H. rufipes*	Europe, Africa	Not zoonotic	(324)
BKNV	Bunyaviridae	1974	*H. marginatum*	Asia	Zoonotic	(325)
DUGV	Bunyaviridae	1964	*Am. variegatum*	Africa	Zoonotic	(326)
MRTV	Bunyaviridae	1974	*H. marginatum*	America	Not zoonotic	(327)
CMV	Bunyaviridae	1976	*I. uriae*	Europa	Not zoonotic	(308)
KETV	Nairoviridae	1976	*Argas* spp.	Asia	Not zoonotic	(328)
KSIV		1976	*Ornithodoros* spp., *H. asiaticum*	Asia	Zoonotic	(319)
PMRV	Bunyaviridae	1976	*I. signatus, I. uriae, I. putus*	Asia	Not zoonotic	(329)
SREV	Flaviviridae	1978	*Ixodes* spp., *O. capensis*	Europe	Not zoonotic	(330)
RAZDV	Phenuiviridae	1978	*D. marginatus*	Europe	Not Zoonotic	(331)
CHIMV	Nairoviridae	1978	*O. tartakovskyi,* *O. papillipes, Rh. turanicus, H. asiaticum*	Asia	Not zoonotic	(332)
WMV	Reoviridae	1978	*H. asiaticum, H. anatolicum, Am. cajennense, Rh. microplus, Rh. guilhoni, Rh. evertsi*	Asia, Africa, America	Not zoonotic	(333)
PSV	Bunyaviridae	1981	*Argas arboreus, I. ricinus*	Africa, Europe	Not zoonotic	(334)
QYBV	Bunyaviridae	1981	*O. erraticus*	Africa	Not zoonotic	(335)
VINHV	Nairoviridae	1983	*Argas robertsi*	Europe	Not zoonotic	(336)
EYAV	Reoviridae	1984	*Ixodes* spp.	Europe,	Zoonotic	(337)
MBV	Flaviviridae	1985	*Carios (Alectorobius) maritimus*	Europe	Not zoonotic	(338)
KUMV	Flaviviridae	1986	*I. ricinus*	Europe	Not zoonotic	(339)
PV	Bunyaviridae	1994	*Ixodes* spp., *Hae. punctata*	Europe	Zoonotic	(340)
AHFV	Flaviviridae	1995	*O. savignyi,* *H. dromedarii*	Asia, Africa	Zoonotic	(341)
SSEV	Flaviviridae	1995	*Ixodes* spp.	Europe	Not zoonotic	(342)
DTV	Flaviviridae	1997	*I. scapularis*	America	Zoonotic	(343)
GGYV	Flaviviridae	1997	*Ixodes* spp.	Europe	Zoonotic	(330)
GGEV	Flaviviridae	2008	*I. ricinus*	Europe	Zoonotic	(344)
HRTV	Bunyaviridae	2009	*Am. americanum*	USA	Zoonotic	(345)
SFTSV	Phenuiviridae	2009	*Hae. longicornis*	Asia	Zoonotic	(346)
GANV	Bunyavirdae	2009	*Haemaphysalis* spp., *Rh. haemaphysaloides*	Asia	Zoonotic	(347)
HYSV	Phenuiviridae	2012	*Hae. longicornis, Am. testudinarium, I. nipponensis, Rh. microplus*	Asia	Zooonotic	(243)
BRBV	Orthomyxoviridae	2014	*Am. americanum*	USA	Zoonotic	(348)
CASV	Bunyaviridae	2014	*O. capensis*	Asia	Not zoonotic	(349)
GERV	Bunyaviridae	2014	*Ornithodoros* spp., *Argas* spp.	Asia	Not zoonotic	(350)
GSRV	Bunyaviridae	2014	*A. reflexus*	Asia	Not zoonotic	(244)
JMTV	Flaviviridae	2014	*Rh. microplus, Rh. sanguineus, Hae. longicornis, Hae. campanulata, Hae. flava, Ixodes granulatus, I. sinensis*	Asia, Europe, Africa	Zoonotic	(351)

Table 2. Continued

Virus	Family	Isolation date	Vector ticks	Geographical distributions	Zoonotic status	References
SOKV	Flaviviridae	2014	*Argas* spp.	Asia	Not zoonotic	(352)
TYUV	Bunyaviridae	2014	*Ixodes putus*	Asia	Not zoonotic	(353)
CGV	Reoviridae	2014	*Ornithodoros* spp.	Asia	Not zooonotic	(354)
MUV	Reoviridae	2015	*Ixodes* spp.	Asia	Zoonotic	(355)
SGEV	Flaviviridae	2015	*Ixodes* spp.	Europe	Not zoonotic	(356)
AVAV	Bunyaviridae	2016	*Ixodes* spp.	Europe	Not zoonotic	(357)
BDAV	Nairoviridae	2016	*O. erraticus*	Africa	Not zoonotic	(308)
TFLV	Bunyaviridae	2016	*Hae. flava, Hae. formosensis*	Asia	Not zoonotic	(227)
UUKV	Bunyaviridae	2016	*I. ricinus*	Europe	Zoonotic	(358)
ALSV	Flaviviridae	2017	*I. ricinus, I. persulcatus, I. ricinus, D. nuttalli, D. reticulatus, Hae. concinna*	Europe, Asia	Zoonotic	(359)
CHUV	Bunyaviridae	2017	*Argas* spp.	Asia	Not zoonotic	(360)
ODAV	Nairoviridae	2016	*Ixodes* spp.	Asia	Not zoonotic	(361)
Ban Tov	Tobaniviridae	2018	*H. truncatum, H. rufipes*	Asia	Zoonotic	(362)
KbAMV	Phenuivirida	2018	*Hae. formosensis*	Asia	Zoonotic	(363)
BJNV	Nairoviridae	2018	*I. persulcatus*	Asia	Zoonotic	(364)
YEZV	Nairoviridae	2019	*I. persulcatus, I. ovatus, Hae. megaspinosa*	Asia	Zoonotic	(365)
TcTV-1	Phenuiviridae	2020	*H. aegyptium, H. asiaticum*	Asia	Zoonotic	(366)
TcTV-2	Phenuiviridae	2021	*Rh. sanguineus, D. reticulatus, H. scupense, D. marginatus, H. asiaticum, H. anatolicum,*	Asia, Europe	Zoonotic	(367)
IFTV	Phenuiviridae	2021	*H. dromedarii*	Asia, Africa	Zoonotic	(368)
SGLV	Nairoviridae	2021	*Hae. concinna*	Asia	Zoonotic	(369)
MBATV	Phenuiviridae	2022	*Amblyomma* spp.	Africa	Not zoonotic	(361)
OZV	Orthomyxoviridae	2022	*Am. testudinarium*	Asia	Zoonotic	(370)
DBTV	Phenuiviridae	2024	*Hae. longicornis*	Asia	Not zoonotic	(371)
GTV	Phenuiviridae	2024	*Am. gemma*	Africa, Asia	Zoonotic	(372)
SIIV	Phenuiviridae	2024	*A. cooleyi*	America	Zoonotic	(227,373)

Recent advancements in genome-editing technologies such as clustered regularly interspaced short palindromic repeats and associated protein 9 system (CRISPR/Cas9) have further expanded the scope of tick research (269). The successful application of the CRISPR/Cas9 system in ticks provides a unique opportunity for precise genetic manipulation (268). The integration of RNAi-based gene silencing and CRISPR/Cas9-mediated genome editing allows researchers to systematically investigate the molecular pathways governing tick-virus interactions. These approaches have also facilitated the identification of tick-derived genes that could serve as potential targets for the development of next-generation tick vaccines and vector control strategies (270,271). Further elucidation of dsRNA-induced RNAi mechanisms is essential for optimizing this technique and leveraging its full potential in tick-virus research. A deeper understanding of these molecular pathways might provide valuable insight into tick-virus interactions, support vaccine development, and pave the way to creating new strategies for mitigating the transmission of TBVs (266).

IFN-mediated Interference and Viral Mutations

Epidemiologically, the interplay between viral interference, IFN responses, and the transmission cycle of TBVs represents a complex dynamic that encompasses multiple aspects of virus-host interactions, immune evasion, and viral dissemination. These interactions vary significantly depending on the zoonotic stability or instability of a given region, influencing the epidemiology of TBVs. Viral interference is a well-documented phenomenon in which the presence of one virus inhibits the replication or propagation of another. This interference can occur at various stages of the viral life cycle, often through mechanisms such as competition for cellular resources, modulation of host immune responses, or direct suppression of viral replication (264). One of the primary host defense mechanisms involved in this process is the IFN response. IFNs, produced upon viral infection, play a crucial role in innate immunity by establishing an antiviral state in surrounding cells, suppressing viral replication, and enhancing the host immune system's ability to detect and eliminate infected cells (272). IFN-mediated antiviral activity is largely facilitated by the induction of interferon-stimulated genes, which encode proteins with potent antiviral properties. Among these, Mx proteins and 2’-5’ oligoadenylate synthetase are well-characterized effectors that contribute to viral inhibition by blocking replication and degrading viral RNA (273-275). In the context of TBVs, IFN-mediated interference can significantly impact co-infections, wherein an IFN response triggered by one viral infection may suppress the replication of a secondary virus through cross-protective mechanisms. This process, referred to as IFN-mediated viral interference, is a key factor in shaping the co-circulation dynamics of TBVs in endemic regions (240).

Overall, IFN signaling and viral interference play critical roles in the ecological and evolutionary dynamics of TBVs. Further research is needed to elucidate the precise molecular mechanisms governing these interactions, particularly in the context of vector competence, host immune modulation, and viral adaptation.

TBVs: Immune Evasion and Resistance Mechanisms

Ticks exhibit remarkable resilience to the viruses they harbor, facilitating the long-term persistence and transmission of TBVs. The interaction between ticks and TBVs involves complex immunological mechanisms, including the production of IFNs and other antiviral factors within the tick’s innate immune system (240). However, unlike vertebrate hosts, ticks may not mount a robust IFN response against TBVs, as they have evolved mechanisms that allow them to tolerate infections without experiencing significant pathological effects. This vector-virus adaptation is critical for maintaining the enzootic cycle of TBVs and ensuring their transmission to vertebrate hosts (240). Conversely, TBVs have also developed sophisticated immune evasion strategies that allow them to circumvent host antiviral defenses, particularly IFN-mediated responses. Notably, the non-structural protein 5 protein of various tick-borne flaviviruses, such as TBEV and LIV, has been shown to suppress JAK-STAT signaling through direct interactions with tyrosine kinase 2. This inhibition effectively blocks IFN signaling, allowing the virus to evade antiviral immune responses and establish persistent infections in vertebrate hosts (276). In addition to immune evasion, flaviviruses exhibit a diverse array of resistance mechanisms, primarily driven by genetic mutations that enable them to evade the effects of antiviral drugs and vaccines (277). One major strategy involves mutations in viral targets, such as RNA-dependent RNA polymerase, which reduce the efficacy of antiviral agents by decreasing their binding affinity or altering enzymatic activity. Similarly, mutations in viral surface proteins can modify entry receptor interactions, diminishing the effectiveness of entry inhibitors and complicating infection prevention during the initial stages of viral replication.

Flaviviruses can also enhance their replication capacity by upregulating the expression or activity of key viral proteins involved in genome replication and assembly. This adaptive mechanism enables the virus to counteract the inhibitory effects of antiviral treatments, sustaining high viral loads even in the presence of therapeutic intervention.

A crucial aspect of flaviviral resistance is the virus’s ability to evade host immune detection. Over time, flaviviruses can acquire mutations (278-280) that allow them to escape recognition by the adaptive immune system, thereby reducing the effectiveness of immunomodulatory therapies and vaccine-induced immunity (281). Continuous exposure to antiviral agents and immune pressure selects for viral strains that possess enhanced resistance to neutralizing antibodies, further complicating treatment and prevention strategies. This ongoing evolutionary adaptation underscores the dynamic nature of flaviviral evolution and highlights the challenges associated with developing long-lasting therapeutic and prophylactic measures (282).

TBVDs in Türkiye

Türkiye’s location and varied climate create a wide range of habitats. These include extensive marshes and key migratory bird stations, fostering remarkable biodiversity. This ecological richness, along with a population exceeding 100 million, over 50 million tourists annually, approximately 250 million transit passengers per year, and a livestock population nearing 100 million, positions Türkiye as a critical hub for the epidemiology of emerging and re-emerging infectious diseases (283). Furthermore, Türkiye’s ecological landscape serves as a natural bridge for the spillover of emerging and re-emerging TBVDs across the European, Asian, and African continents (151,152). To date, more than 50 tick species have been identified in Türkiye. Among these tick species several are prominent vectors of viruses (94,188,200,201,208,235). So far, several TBVDs have been reported in Türkiye including TBEV, LIV, CCHFV, LSDV, and TSDV, have been identified in Türkiye (4,14,151,152,235,247,255,284).

TBEV: Several seroprevalence studies conducted across Southeastern Anatolia, Central Anatolia, Central-Northern Anatolia, Mediteranean and the Aegean regions have reported TBEV seropositivity rates ranging from 1.4% to 20.5% (235,242,285).

CCHFV: CCHFV is an endemic tick-borne virus that causes a severe, often fatal hemorrhagic fever. The first case recorded case occurred in the Black Sea region in 2002. Since then, the virus has predominantly affected rural areas of central and northern Türkiye, especially in semi-forested regions with active agriculture and animal husbandry. Epidemiologic surveys and diagnostic studies on CCHF in Türkiye have primarily focused on detecting CCHFV in ixodid ticks, particularly *Hyalomma marginatum*. It is important to note that recently this virus has also been reported in Eastern Anatolia, Southeastern Anatolia, Northwestern Anatolia, and the Aegean (14,247,255,285).

LIV: LIV is primarily transmitted to sheep and goats, and occasionally to cattle and horses, by *Ixodes ricinus*. It causes encephalomyelitis with characteristic symptoms including muscle tremors, incoordination, circling, and ataxia. LIV has been reported in the northwestern region of Türkiye (151,152,284,286).

LSDV: LSDV is an arbovirus causing cutaneous nodules in cattle and buffalo. The virus is transmitted mechanically by blood-sucking flies and vertically by certain hard ticks, including *Rhipicephalus (Boophilus) decolatus*, *Rhipicephalus appendiculatus*, and *Amblyomma hebraeum*. LSDV outbreaks in Türkiye have resulted in significant economic losses (151,152,287).

TSEV: TSEV was first isolated in Türkiye in 1960 (242,286). It is currently classified as a Western subtype of TBEV (227,247,288).

In conclusion, scientific advancements in the study of TBVs have significantly enhanced our understanding of the complex evolutionary interactions between viruses, tick vectors, and vertebrate hosts. The identification and characterization of over 160 TBVs, including highly pathogenic species such as TBEV, CCHFV, and LIV, have revealed critical insights into virus-vector-host dynamics, transmission pathways, and mechanisms of immune evasion. These discoveries have also underscored the ecological and epidemiological factors that drive the emergence and re-emergence of TBVs in different geographic regions. Within the One Health framework, a multidisciplinary approach combining virology, entomology, epidemiology, and immunology is essential for developing sustainable and effective intervention strategies. Coordinating these efforts with global surveillance initiatives, such as the Global Early Warning System, will enhance outbreak prediction capabilities and facilitate rapid responses to emerging and re-emerging TBV threats. Ultimately, these advancements will be instrumental in mitigating the impact of TBVs on both human and animal health, reinforcing the need for continued investment in TBV research and public health preparedness.

Tick-borne Bacterial Diseases

From an epidemiological perspective, tick-borne bacterial diseases in humans and animals can generally be categorized into rickettsial and non-rickettsial infections (91).

Rickettsial Infections in Humans

Anaplasma spp., *Ehrlichia* spp., and *Neorickettsia* spp. are the causative agents of emerging and/or reemerging tick-borne rickettsial infections that affect both humans and animals, particularly in enzootically stable regions (374).

Anaplasmosis: Anaplasmosis is an opportunistic, zoonotic, and widespread arthropod-borne infection affecting both humans and animals (375). In humans, the disease is also known as human granulocytic anaplasmosis (HGA) or HGE (376,377). *Anaplasma* species are obligate intracellular pathogens primarily transmitted by ticks, where they reside exclusively within parasitophorous vacuoles in the host cell cytoplasm. The genus *Anaplasma* is part of the Anaplasmataceae family, which also includes *Ehrlichia*, *Neorickettsia*, and *Wolbachia* (374). In 2001, a reclassification of the Rickettsiales order (378) led to the expansion of the *Anaplasma* genus. It previously only included ruminant-specific pathogens such as *Anaplasma marginale*, *Anaplasma centrale*, and *Anaplasma bovis*. However, after the reclassification, *Anaplasma phagocytophilum* was added, a species resulting from the merger of three *Ehrlichia* species: *Ehrlichia equi*, *Ehrlichia phagocytophila*, and the unnamed agent of HGE. Moreover, *Anaplasma* now includes *Anaplasma bovis* (formerly *Ehrlichia bovis*), *Anaplasma platys* (formerly *Ehrlichia platys*), and *Aegyptianella pullorum*. Despite their genomic relatedness, these microorganisms exhibit significant biological differences, including variations in host specificity, host cell preferences, major surface proteins (MSPs), and tick vectors (374,378). The primary reservoir host for the obligate intracellular gram-negative bacterium *Anaplasma phagocytophilum* is the white-footed mouse (*Peromyscus leucopus*). However, a diverse array of both wild and domestic mammals has also been identified as potential reservoirs (379,380). The causative agent of human anaplasmosis is the zoonotic bacterium *Anaplasma phagocytophilum*, which also causes anaplasmosis in horses (381), cattle (382,383), and dogs (381). In addition, *Anaplasma phagocytophilum*-like bacteria have been reported in small ruminants, such as sheep and goats (384,385). The infection is primarily transmitted intrastadially by vector ticks of the *Ixodes* species, particularly *Ixodes scapularis*, *Ixodes pacificus*, *Ixodes ricinus*, and *Amblyomma americanum* (386). Vector competence is strongly associated with genetic determinants that influence a vector's ability to transmit pathogens. These genetic factors affect tick-host-pathogen interactions and traits such as the vector's susceptibility to pathogen infection. Therefore, gaining a deeper understanding of the mechanisms that govern tick-pathogen interactions is essential for identifying the molecular drivers behind TBDs (10). Although data on tick-pathogen interactions remain limited, significant progress in metabolomics, transcriptomics, and proteomics (387-391) has significantly advanced our understanding of these complex systems. Notably, the recent publication of the *Ixodes scapularis* genome—a primary vector for *Borrelia burgdorferi* and *Anaplasma phagocytophilum* in North America (391)—represents a significant milestone in tick research. In particular, the development of experimental tools, such as tick-derived cell lines, along with the widespread adoption of RNAi for functional genomics (44,392), has opened up new opportunities for identifying the molecular determinants that influence tick vector competence. *Anaplasma phagocytophilum*, acquired by the vector tick during a blood meal from an infected host, initially infects the tick's midgut cells, where it begins to replicate before moving to the salivary glands. The pathogen is then transmitted to a susceptible host when the infected tick takes another blood meal. However, the infection can also be transmitted iatrogenically through needles and other equipment contaminated with infected blood (393), as well as through blood transfusion (394). In humans, the clinical symptoms typically develop 1 to 2 weeks after an infected tick bite. Many patients, however, do not recall being bitten by a tick. Individuals with anaplasmosis commonly present to healthcare providers with symptoms such as headache, chills, and muscle pain (395). Epidemiologically, anaplasmosis is a globally prevalent tick-borne rickettsial infection affecting humans (396). The disease has been reported particularly in the northeastern United States, northern Europe, and parts of southeastern Asia, including China, Mongolia, and Korea. Transmission occurs through the bite of infected nymphs or adult ticks, with the specific tick vector species varying by region. In the eastern and midwestern United States, the primary vector is *Ixodes scapularis*—a three-host and forest-dwelling tick commonly known as the black-legged or deer tick. In the western United States, the main vector is *Ixodes pacificus*. In western Europe, *Ixodes ricinus* serves as the principal vector, while in Asia, *Ixodes persulcatus* plays a similar role. Epidemiological studies have also noted that *Ixodes* ticks are frequently co-infected with other TBPs. As a result, they can concurrently transmit multiple diseases, including Lyme disease (*Borrelia burgdorferi),* babesiosis (*Babesia* spp.), ehrlichiosis (*Ehrlichia* spp.), spotted fever group (SFG) rickettsioses (*Rickettsia* spp.), and POWV (397). An obligate intracellular rickettsial bacterium, *Anaplasma phagocytophilum* evades neutrophil antimicrobial defenses and replicates within host cells. Specifically, it survives and multiplies within cytoplasmic vacuoles of polymorphonuclear cells (primarily neutrophils), which are key components of the innate immune system. After transmission through the bite of an infected tick, *Anaplasma phagocytophilum* spreads to the bone marrow and spleen, where it targets myeloid and monocyte progenitor cells. The organism is typically observed within neutrophils in peripheral blood and various tissues. The incubation period of *Anaplasma phagocytophilum* following transmission by an infected tick typically ranges from 1 to 2 weeks. Infections are often subclinical, but clinical manifestations can range from mild to severe. The most common symptoms reported by patients include fever, malaise, myalgia, and headache. In some cases, additional symptoms such as nausea, vomiting, diarrhea, cough, joint pain, neck stiffness, and even confusion may occur (398). In patients with HGA, central nervous system (CNS) involvement is rare, with meningoencephalitis occurring in approximately 1% of cases. However, peripheral nervous system involvement is more common and may manifest with symptoms such as brachial plexopathy, cranial nerve palsy, demyelinating polyneuropathy, and bilateral facial nerve palsy. It has been reported that neurological function recovery can take several months (397,399). In the microscopic examination of peripheral blood smears from patients with HGA, characteristic intracytoplasmic aggregates—known as morulae—are observed within neutrophils. This finding is present in approximately 25% to 75% of patients who have not yet begun treatment. The sensitivity of peripheral blood smears for diagnosing HGA is highest during the first week of infection, when morulae are more readily detectable. Examination of lymphoid organs plays a critical role in the evaluation of HGA patients. Microscopic analysis of organs such as the liver, spleen, bone marrow, and lymph nodes is essential for identifying changes in mononuclear phagocytes associated with infection. Additionally, lung damage and a systemic inflammatory response may occur as secondary complications, further complicating the clinical picture (397).

Immune Modulation and Pathogenesis: The presence of *Anaplasma phagocytophilum* in neutrophils triggers a proinflammatory immune response, which paradoxically results in: (i) neutrophil deactivation, (ii) neutrophil degranulation, (iii) cytokine release, particularly interleukin-10 (IL-10), IL-12, and IFN-gamma (IFN-γ). IFN-γ, primarily produced by natural killer (NK) and NKT cells, as well as CD8+ T lymphocytes, plays a central role in amplifying inflammation and contributing to sustained tissue damage. This damage, in turn, compromises neutrophil antimicrobial effectiveness. These cytokine-driven mechanisms help explain the clinical symptoms of HGA, which may include fever, pancytopenia, liver dysfunction, in severe cases, septic shock or multi-organ failure (397). Laboratory findings in patients with HGA commonly include leukopenia and thrombocytopenia in the peripheral blood. Additionally, elevated transaminase levels are observed in nearly 70% of cases (397,399). In severe cases, laboratory abnormalities may indicate organ dysfunction, including elevated levels of creatinine, lactate dehydrogenase, creatine phosphokinase, and amylase, with or without electrolyte imbalances and metabolic acidosis. Clinical complications may include significant hypotension, disseminated intravascular coagulation (DIC), hepatic and renal insufficiency, adrenal insufficiency, and myocardial dysfunction. In patients presenting with CNS symptoms, cerebrospinal fluid analysis may reveal lymphocytic pleocytosis and moderate protein elevation (397).

Diagnostic Methods: The diagnosis of HGA can be confirmed through a combination of methods: (i) Serological testing: a fourfold rise in antibody titers is considered diagnostic. (ii) Microscopic examination: Identification of characteristic morulae in neutrophils on peripheral blood smear. (iii) Polymerase chain reaction (PCR): detection of *Anaplasma phagocytophilum* DNA, offering a sensitivity of 67% to 90% and specificity of 60% to 85%, with the advantage of rapid turnaround time (396), (iv) Immunohistochemistry: detection of the organism in tissue samples. (v) Culture isolation: although definitive, it is less commonly used due to time and resource limitations (397). The differential diagnosis of anaplasmosis includes several other TBDs, such as human monocytotropic ehrlichiosis (HME), RMSF, relapsing fever, tularemia, Lyme disease, CTF, and babesiosis. In the treatment of HGA, following differential diagnosis, doxycycline is the first-line treatment for both adults and pediatric patients. Antibiotic therapy is typically recommended for a duration of 14 to 21 days, or for at least 3 days after fever resolves. For patients co-infected with Lyme disease (whether known or suspected), treatment should be extended to a minimum of 10 days**.** In enzootic regions, it is strongly recommended that individuals of all ages take precautions to prevent tick infestations and reduce the risk of *Anaplasma phagocytophilum* infection. If a tick is attached, it should be promptly removed within 4 to 24 hours using the proper technique to minimize the risk of transmission (395,397).

Ehrlichiosis: Ehrlichiosis in humans is primarily caused by the bacterial species *Ehrlichia chaffeensis* and *Ehrlichia ewingii* (73). The disease caused by *Ehrlichia chaffeensis* is known as HME, while the disease caused by *Ehrlichia ewingii* is referred to as human ewingii ehrlichiosis (HEE). Additionally, a newer species, *Ehrlichia muris* subspecies *eauclairensis*—discovered in the United States in 2009—has also been identified as a cause of ehrlichiosis in humans (400). The primary vectors for *Ehrlichia chaffeensis* and *Ehrlichia ewingii* are *Amblyomma americanum* (lone star ticks), and their main reservoir host in North America is the white-tailed deer**.** However, other tick species such as *Haemaphysalis longicornis* and *Rhipicephalus sanguineus* have also been implicated in the transmission of these bacteria in other regions (73). Epidemiologically, infections caused by *Ehrlichia chaffeensis* (HME) tend to be more severe than those caused by *Ehrlichia ewingii* (HEE) (73). Typical symptoms of ehrlichiosis include fever, chills, fatigue, muscle pain (myalgia), and nausea. It has been reported that approximately 60% of patients require hospitalization, and about 3% of cases result in death due to severe disease progression (73). *Ehrlichia ewingii* infections are more commonly observed in immunocompromised individuals (401). In the case of *Ehrlichia muris eauclairensis*, rodents—particularly white-footed mice (*Peromyscus leucopus*)—act as reservoir hosts, and blacklegged ticks (*Ixodes scapularis*) are responsible for transmitting the pathogen to humans (402). Infections with *Ehrlichia muris eauclairensis* present with symptoms such as fever, headache, myalgia, lymphopenia, and thrombocytopenia (400). As with HGA, doxycycline remains the treatment of choice for ehrlichiosis and is generally effective when administered promptly (73).

Neoehrlichiosis: Neoehrlichiosis is a tick-borne rickettsial infection that primarily affects humans, particularly those with weakened immune systems. The causative agent of the disease is *Candidatus Neoehrlichia* mikurensis, also referred to simply as *Neoehrlichia mikurensis*. This emerging bacterium was first identified in the blood of febrile patients in 2010 (403). Transmission to humans occurs through the bite of infected ticks. Infected individuals may present with symptoms such as recurrent fever, often accompanied by thromboembolic events, such as blood clots. The disease tends to be more severe in immunocompromised patients (73). From an epidemiological perspective, wild rodents are considered the primary reservoir hosts of *Neoehrlichia mikurensis*. The main tick vectors responsible for its transmission are *Ixodes* species, particularly *Ixodes ricinus* and *Ixodes persulcatus*. These vectors have been found to carry the pathogen across various regions of Asia, Russia, and Europe (404). As with other tick-borne rickettsial diseases, doxycycline has been reported to be an effective treatment for neoehrlichiosis (405).

Tick-borne Typhus: Tick-transmitted typhuses are the Queensland tick typhus (QTT) caused by *Rickettsia australis* and the Flinders Island spotted fever (FISF) group rickettsiae caused by *Rickettsia honei* (406). The etiological agent of QTT is *Rickettsia australis*, a pathogen increasingly recognized in Australia for causing acute febrile illness in humans. Factors such as changing human demographics, climate change, and improved understanding of the expanding distribution of tick vectors suggest that QTT is an emerging public health concern (406). The epidemiology of QTT is closely linked to the geographic distribution of its tick vectors. *Rickettsia australis* is transmitted to humans through the bite of certain *Ixodes* species (407,408). These tick species are primarily found along the eastern coast of Australia (407,408). *Rickettsia australis* has been isolated from both *Ixodes holocyclus*—commonly known as the Australian paralysis tick or bush tick—and *Ixodes tasmani* (408,409) *Rickettsia honei* subsp. *marmionii* is a newly recognized member of the SFG *Rickettsia* and is phylogenetically related to *Rickettsia australis* (406). It was first described in a *Haemaphysalis novaeguineae* tick collected in Cape York, Queensland (410). The first human case of SFG rickettsiosis in the region was reported in a 55-year-old male entomologist who had been infested with *Haemaphysalis novaeguineae* (411). Additionally, it has been suggested that *Haemaphysalis* species may serve as important vectors of SFG *Rickettsia* in Queensland (406).

Rocky Mountain Spotted Fever (RMSF): RMSF is a tick-borne infection in humans caused by *Rickettsia rickettsii*. The disease, named after the Rocky Mountains, is primarily transmitted by *Dermacentor* species, including the American dog tick (*Dermacentor variabilis*) and the Rocky Mountain wood tick (*Dermacentor andersoni*). Epidemiologically, RMSF is endemic across North, Central, and South America. In the Rocky Mountain region, the disease's prevalence is estimated at around 2%, with mortality rates ranging from 20% to 30%, depending on the population and region. Clinically, RMSF typically presents with symptoms such as fever, nausea, vomiting, loss of appetite, headache, and muscle pain. A hallmark of the infection is the appearance of a distinctive rash, which is usually non-itchy, small, flat, and pink. The rash typically begins on the wrists, ankles, and forearms and may blanch when pressure is applied. Treatment with the antibiotic doxycycline has proven effective in managing the infection, including in children (412).

Other Tick-borne Spotted Fever Rickettsial Infections*:* Infections caused by *Rickettsia parkeri*, *Rickettsia rickettsii* subsp. *californica*, and *Rickettsia akari* are generally categorized as other tick-borne spotted fever rickettsial infections (413). Epidemiologically, *Rickettsia parkeri*, transmitted by the Gulf Coast tick (*Amblyomma maculatum*), is primarily found in the Southeastern United States, with focal populations in the northeastern, midwestern, and southwestern regions. Pacific Coast tick fever is another tick-borne SFG rickettsial infection. It is caused by *Rickettsia rickettsii* subsp. *californica* (formerly known as *Rickettsia* sp. 364D) and is transmitted by the Pacific Coast tick (*Dermacentor occidentalis*). Pacific Coast tick fever occurs along the western coastline of California, Oregon, and Washington. Rickettsialpox is caused by *Rickettsia akari*. Unlike the other spotted fevers described here, *Rickettsia akari* is transmitted by the bite of infected mouse mites (*Liponyssoides sanguineus*) (413). While cases have been reported sporadically throughout the United States, they are most commonly seen in the northeastern United States, particularly in New York City. It was recommended that early treatment with the antibiotic doxycycline (253).

Non-rickettsial Tick-borne Bacterial Infections in Humans

LB, tularemia, TBRF, bartonellosis, hemoplasmosis, Q fever and dermatophilosis are non-rickettsial bacterial infections in humans and in animals (91,414,415).

Lyme Borreliosis (LB): LB or Lyme disease, is a spirochete tick-borne infection. It is one of the most common zoonotic tick-borne bacterial infections affecting humans and dogs, primarily in the Northern Hemisphere (415). Lyme disease is caused by spirochetes of the *Borrelia burgdorferi* sensu lato complex, which includes five main species that can cause human disease. The term *Borrelia burgdorferi* is commonly used to refer to the entire species complex. The infection is transmitted to humans and dogs by ticks of the genus *Ixodes* (91). Epidemiologically, vertebrates such as mice, including voles, and certain bird species serve as the primary reservoir hosts for *Borrelia* spp. Additionally, in enzootically stable areas where vector ticks are present, deer play a significant role in maintaining tick populations. On the other hand, it has been suggested that hosts like deer, cattle, and sheep are not suitable reservoirs for Spirochaetales; however, research on this topic remains limited (73). Clinical symptoms of Lyme disease in humans vary depending on the stage and duration of the infection, with erythema migrans (EM) being the most common. EM, a skin rash, occurs in approximately 70-80% of infected individuals. These rashes typically appear within 3 to 14 days (with an average of 7 days) after a tick bite, gradually expanding and sometimes reaching up to 30 cm in diameter. Patients with EM often present with fatigue, fever, headache, mild neck stiffness, and joint or muscle pain (416). If untreated, the infection can lead to neurological complications (such as facial paralysis, meningitis, and radiculopathy), cardiac issues (such as carditis with atrioventricular block), and arthritis (typically monoarticular or oligoarticular, affecting fewer than five joints) (417). Arthritis caused by *Borrelia burgdorferi* sensu stricto is more common in North America than in Europe, occurring in approximately 60% of untreated EM patients (73). The neurological form of the disease, known as "Lyme neuroborreliosis", has been suggested to be associated with *Borrelia garinii* (418). Additionally, it has been noted that higher spirochete loads are observed in Lyme patients infected with the recently identified *Borrelia mayonii* (419). The primary treatment for Lyme disease traditionally involves antibiotic regimens, which have generally been considered effective in eliminating the infection and improving patient well-being (73). However, a study by (420) indicated that the benefits of antibiotics can be short-lived, with a significant proportion of patients experiencing symptom recurrence after treatment, leading to the development of a persistent form known as "chronic Lyme disease" (420,421) demonstrated that disulfiram monotherapy holds potential as a treatment option for Lyme disease patients (421). Additionally, the introduction of a recombinant OspA-based vaccine against LB in the United States was initially promising (422), but it was withdrawn from the market due to safety concerns, particularly its potential association with autoimmune arthritis (423).

Shouthern Tick-associated Rash Illness (STARI): STARI is an emerging zoonotic disease characterized by a centrally clearing, ring-shaped rash, clinically resembling the EM associated with Lyme disease. The illness is transmitted through the bite of the *Amblyomma americanum* tick (91). Although its etiology remains controversial, *Borrelia lonestari*, a spirochete bacterium, is suspected to be the causative agent. Currently, there are no definitive diagnostic tests or approved treatments for STARI, making clinical recognition and supportive care essential. A rare case of STARI was reported in a 63-year-old woman, further highlighting the need for awareness and research into this under-recognized condition (424).

Tularemia: Tularemia is a non-rickettsial bacterial zoonotic infection caused by *Francisella tularensis*, which can be transmitted by tick vectors. Cases typically occur in the Northern Hemisphere, particularly in rural or semi-rural areas. The disease encompasses a range of clinical syndromes, varying from mild to severe (91).

Tick-borne Relapsing Fever (TBRF): TBRF is a disease caused by certain species of *Borrelia* bacteria, which are transmitted through the bite or coxal fluid of argasid ticks from the genus *Ornithodoros*. This disease occurs in a wide endemic region across Africa, Asia, and the Americas, with distinct Borrelia-tick vector complexes in each geographic area (91).

Bartonellosis: Bartonellosis is a blood-sucking arthropod-borne zoonotic infection caused by *Bartonella henselae*, with a wide distribution in the Northern Hemisphere (425). Domestic cats serve as the primary reservoir for the pathogen, while the cat flea is the primary vector for transmission (426). Additionally, transstadial transmission of *Bartonella henselae* by *Ixodes ricinus* ticks has been demonstrated (427). In a recent study, molecular analysis of *Bartonella, Borrelia*, and *Rickettsia* was performed on hard ticks (Ixodidae) collected from birds in the Kızılırmak Delta in Türkiye. The presence of *Bartonella henselae* was revealed in *Haemaphysalis concinna*, *Haemaphysalis punctata*, *Hyalomma marginatum*, *Ixodes frontalis*, and *Ixodes ricinus* tick samples. *Rickettsia aeschlimannii* was detected in *Hyalomma marginatum* tick samples, and *Rickettsia helvetica* in *Ixodes ricinus* and *Ixodes* sp. This study is the first report on the detection of *Bartonella* and *Rickettsia* species in ticks collected from passerines in Türkiye (428)**.**

Hemoplasmosis: Hemoplasmosis is another non-rickettsial bacterial infection in humans and animals caused by *Mycoplasma* species (429). Although the infection is primarily described as vector-borne, transmitted by blood-feeding arthropods such as ticks and fleas, it can also be transmitted through other routes, including mechanical transmission via contaminated surgical tools, blood transfusions, and vertical transmission during pregnancy (430). *Rhipicephalus appendiculatus* transmits the infection to dogs through cofeeding (431). In one case, a *Mycoplasma haemofelis*-like infection in an human immunodeficiency virus (HIV)-positive patient, co-infected with *Bartonella henselae*, was identified in a 34-year-old man in Brazil (432). In another case, a novel hemotropic *Mycoplasma* (*Hemoplasma*) was detected in a 62-year-old woman with hemolytic anemia and pyrexia, and the patient was treated with doxycycline (433).

Q Fever: Q fever is a zoonotic disease caused by the non-Rickettsiales bacterium *Coxiella burnetii* (434). This small, obligate intracellular, gram-negative bacterium—belonging to the family Coxiellaceae—is responsible for Q fever in humans and *coxillosis* in animals (435). Epidemiologically, the primary reservoir hosts of *Coxiella burnetii* are domestic farm animals such as cattle (*Bos taurus*), sheep (*Ovis aries*), and goats *(Capra hircus)* (436). However, an increasing number of other animals—including domestic and wild mammals, birds, reptiles, and even cetaceans—have been reported to shed the bacterium (437). Airborne transmission is the most common route of infection in humans, typically through the inhalation of aerosolized particles contaminated with birth products or secretions from infected animals (438). Although the role of ticks in mammalian transmission remains controversial (439), several studies support that ticks act as reservoirs and play a significant role in transmitting *Coxiella* to wild mammals (440). Numerous tick species have been found to harbor *Coxiella burnetii*, including several hard ticks (*Amblyomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma* and *Rhipicephalus*) and one soft tick (*Ornithodoros*) (441-443). Recent studies have also revealed the presence of *Coxiella*-like endosymbionts in ticks—bacteria that are genetically related to *Coxiella burnetii* but are likely tick-specific. For example, *Coxiella*-like organisms and possibly *Coxiella burnetii* itself have been detected in tick species such as *Haemaphysalis bispinosa*, *Haemaphysalis hystricis*, *Dermacentor compactus*, *Dermacentor steini*, and *Amblyomma* spp., collected from wildlife and domesticated goats across various regions in Malaysia (444).

Dermatophilosis (streptothricosis): Dermatophilosis, also known as "mud fever", is a skin disease caused by the gram-positive actinomycete *Dermatophilus congolensis*. It is often mistakenly referred to as mycotic dermatitis (445). The disease is characterized by the formation of crusted sores or scabs that contain the microorganism. Transmission typically occurs through mechanical means, primarily via biting insects such as flies and ticks (94,284,446). Dermatophilosis affects both domestic and wild animals and is of particular economic significance in regions where wool production from sheep is an important industry, due to its impact on fleece quality. Although primarily an animal disease, human infections with *Dermatophilus congolensis* are rare but have been documented, mostly in tropical regions (445,447). In one such case, a 26-year-old woman who had worked as a volunteer on a dairy farm in Costa Rica for 15 days was diagnosed with *Dermatophilus congolensis* infection after returning to Spain—marking the first reported human case of dermatophilosis in the country (448).

Gaps: Several critical gaps in the understanding and management of tick-borne bacterial diseases hinder progress in both research and clinical practice have been reported (449).

Rickettsial and Non-rickettsial Infections of Humans in Türkiye

Rickettsial Infections in Humans in Türkiye

Anaplasmosis: There is limited documentation on cases of human anaplasmosis in Türkiye (94). However, in one reported case, *Anaplasma phagocytophilum* was identified in a human patient (450). Additionally, *Anaplasma phagocytophilum* was detected in *Ixodes ricinus* ticks that had been removed from humans (451) suggesting a potential risk of zoonotic transmission. A 6-year-old boy who was hospitalized in Konya in 2019 with complaints of fever, chills, weakness, headache, loss of appetite, runny nose and cough that had been ongoing for 2 days was found to be remarkable. The medical history revealed that the child had been in contact with a dog 10 days earlier, and a tick had been removed from his body the day before hospital admission. Upon physical examination, the child exhibited fever, oropharyngeal hyperemia, and cracked, reddened lips. Laboratory results were mostly normal, with the exception of lymphopenia and hyponatremia. A peripheral blood smear showed cytoplasmic morulae in both monocytes and granulocytes, prompting the immediate initiation of doxycycline therapy. The child's fever resolved within 48 hours of treatment. Further investigation using real-time PCR analysis returned negative results for *Anaplasma* but positive for *Ehrlichia*, confirming the diagnosis. This case was recorded as the first confirmed human case of *Ehrlichia* infection in Türkiye (452). Additionally, several serological studies were conducted to detect antibodies against *Anaplasma phagocytophilum* in humans across various regions of Türkiye (453-455). The reported seroprevalence rates of *Anaplasma phagocytophilum* include 8% in the Antalya province (453), 25% in the Thrace region (454), and 4% in the same region (455).

Ehrlichiosis: As with anaplasmosis, only a single confirmed case of human ehrlichiosis has been reported in Türkiye to date (452).

Tick-borne Typhus: In a study conducted in Türkiye, several species of SFG rickettsiae, including *Rickettsia aeschlimannii*, *Rickettsia sibirica mongolitimonae*, *Rickettsia slovaca*, *Rickettsia raoultii*, *Rickettsia monacensis*, and *Rickettsia hoogstraalii*, were isolated from host-seeking *Haemaphysalis parva* adults (456).

Other Tick-borne Spotted Fever Group Rickettsial infections: A study was performed to detection of *Babesia* spp., *Borrelia burgdorferi* sensu lato, and SFG Rickettsiae in tick samples collected from humans in Ankara, Türkiye. *Babesia* spp., *Borrelia burgdorferi* sensu lato, and SFG rickettsiae were molecularly screened in tick samples belonging to the genera *Haemaphysalis, Hyalomma, Ixodes*, and *Rhipicephalus*, which had attached to humans in the region of Ankara. As a result of the study, four *Babesia* species (*Babesia crassa, Babesia major, Babesia occultans,* and *Babesia rossi*), one *Borrelia* species (*Borrelia burgdorferi* sensu stricto), and three SFG rickettsiae (*Rickettsia aeschlimannii, Rickettsia slovaca,* and *Rickettsia hoogstraalii*) were detected in ticks that had taken a blood meal from humans. This study demonstrated that *Babesia rossi* and *Babesia crassa* are epidemiologically associated with *Haemaphysalis parva, Babesia major* with *Haemaphysalis punctata*, and *Babesia occultans* with *Hyalomma marginatum*. Furthermore, two species of SFG rickettsiae pathogenic to humans— *Rickettsia aeschlimannii* and *Rickettsia slovaca*—were found at high prevalence in the examined tick samples. In addition, *Borrelia burgdorferi* sensu stricto was identified in *Hyalomma marginatum, Hyalomma excavatum, Hyalomma* spp. (nymph), and *Haemaphysalis parva* ticks, an important epidemiological finding concerning LB in Türkiye (457). Following the detection of SFG rickettsial pathogens in ticks that had fed on humans, only one confirmed human case caused by these pathogens has been documented in Türkiye. In this case, reported in Konya, the causative agent of disease in a three-year-old girl was identified as *Rickettsia slovaca* (458).

Non-Rickettsial Tick-borne Bacterial Infections in Humans in Türkiye

Lyme Borreliosis (LB): In Türkiye, studies on human cases of LB are quite limited (94,151,284). Additionally, LB is not widespread, despite the fact that *Ixodes ricinus*, the vector of this disease, is widely distributed in the northern parts of the country (14). The first documented cases of Lyme disease were reported in two separate studies in 1990 (459,460). Later, the Lyme disease agent was cultured from three cases (461). However, only a few reports on human LB cases have been documented (462-464). The seropositivity rate for Lyme disease was reported as 17% in individuals from the Central Anatolia region (465). Additionally, 20% of patients (n=50) at Erciyes University Hospital in the Kayseri province reported symptoms compatible with LB (466). In the Marmara Region, three LB cases have been confirmed serologically (461). Vector and molecular findings: epidemiologically, *Borrelia burgdorferi* was isolated from *Ixodes ricinus* ticks collected from cattle in the Black Sea region in 1998 (467), and spirochetes of *Borrelia* were detected in an unfed tick nymph (468). Furthermore, several strains of *Borrelia burgdorferi sensu lato* were characterized molecularly (469). A novel *Borrelia* species, *Borrelia turcica* sp. nov., was isolated from *Hyalomma aegyptium* ticks collected from tortoises (*Testudo graeca*) (470,471). More recently, *Borrelia burgdorferi* sensu stricto was isolated from unusual tick species such as *Hyalomma marginatum*, *Hyalomma excavatum*, *Haemaphysalis parva*, and nymphs of *Hyalomma* spp. in Türkiye (457).

Tularemia: Tularemia is a significant endemic zoonotic disease in Türkiye, first identified in 1936, with a reemergence reported in 1998. The first officially recorded outbreak occurred in 2005 (472). The disease is primarily transmitted to humans through contaminated water and infected arthropods, including mosquitoes and ticks (473). The initial outbreak-associated case was diagnosed near Kayseri, leading to the classification of the region as an endemic focus for tularemia (474). However, molecular testing of mosquito and tick pools collected from the Kayseri area showed no evidence of *Francisella tularensis* (474). Between 1988 and 2004, a total of 507 tularemia cases were reported. In 2005, tularemia was officially included in the list of nationally notifiable diseases, and from 2005 to 2011, approximately 4,824 cases were recorded. Despite the rising number of human cases, a comprehensive study using molecular techniques conducted in the Kayseri region again found no *Francisella tularensis* in tick samples (284).

Tick-borne Relapsing Fever (TBRF): TBRF is an emerging tick-borne infection, and no cases have been reported to date in Türkiye. However, the presence of relapsing fever caused by a spirochete of the *Crocidurae* group, *Borrelia crocidurae*, was identified in *Ornithodoros erraticus* ticks collected from rodent holes in the southeastern regions near the Syria border (475).

Bartonellosis: In a study, 333 blood donor samples from Aydın province were screened for antibodies against *Bartonella* species, including *Bartonella henselae*. The results revealed that 3% of the samples tested positive for *Bartonella henselae* (476). In another epidemiologically significant study conducted in Ankara, a total of 256 domestic cats were screened serologically for *Bartonella henselae*. The seropositivity rate was found to be 8.2% (477). In a cross-sectional epidemiological study conducted in Aydın province, serum samples from 333 blood donors were tested for *Bartonella henselae* and *Bartonella quintana* positivity. The study found a seroprevalence of 3.3% for both pathogens (476). This epidemiological context concerning regional *Bartonella* seropositivity in humans considered the potential for ticks feeding on the blood of seropositive individuals to become infected with *Bartonella* spp.

Hemoplasmosis: To date, no cases of hemoplasmosis in humans have been reported in Türkiye. However, a single study reported a clinical case of feline hemoplasmosis associated with *Mycoplasma haemofelis* (478).

Q fever: Documentation on the epidemiology of the disease in Türkiye is relatively limited. One study reported that *Coxiella burnetii* is an endemic TBP with zoonotic potential, and that domestic animals such as cattle, sheep, goats, and dogs serve as potential reservoir hosts. Additionally, the tick vector *Ornithodoros lahorensis* is widespread throughout the country (479). More recent studies have also provided evidence of *Coxiella burnetii* exposure in certain human populations. For instance, in the Central Black Sea region, *Coxiella burnetii* immunoglobulin G (IgG) seropositivity was detected in 15.6% of women with a history of abortion and 11.1% of women with healthy births, suggesting a possible association between infection and adverse pregnancy outcomes (480). Additionally, an epidemiological study conducted in Bolu province found a significant association between *Coxiella burnetii* seropositivity and direct contact with birth products of farm animals, highlighting occupational and environmental risk factors for infection (481).

Dermatophilosis (streptothricosis): Dermatophilosis (also known as streptothricosis) is a skin disease caused by *Dermatophilus congolensis*. In Türkiye, documentation on dermatophilosis is very limited (284). However, a few reported cases have involved both animals (482) and humans (483) indicating that the disease does occur sporadically in the region.

Tick-borne Bacterial Infections in Animals in Türkiye

Rickettsial Infections in Animals in Türkiye

Anaplasma spp., *Ehrlichia* spp., *Neoehrlichia* spp., *Neorickettsia* spp. and *Aegyptianella pullorum* cause emerging and/or remerging tick-borne rickettsial infections in both humans and animals in epidemiologically enzootic stable regions. *Anaplasma* and *Ehrlichia* species are obligate intracellular rickettsial pathogens, known to cause serious diseases in cattle, small ruminants, dogs, and humans. These pathogens are mostly transmitted through ticks, especially ticks in the genera *Ixodes*, *Amblyomma*, *Dermacentor*, and *Rhipicephalus*. Transmission though is not restricted to ticks; biting flies, other blood-feeding arthropods and iatrogenic procedures like needle reuse or blood transfusions can contribute to infection dissemination (484-486) Moreover, molecular and sero-epidemiological studies performed on various animal and vector species in Türkiye revealed an increasing knowledge of their epidemiology, genetic diversity and their diverse phylogenetic relationship. In cattle, the main *Anaplasma* species known to cause clinical and subclinical infections are *Anaplasma marginale*, *Anaplasma centrale*, *Anaplasma bovis*, *Anaplasma phagocytophilum*, and *Anaplasma capra* (486,487). Among these, *Anaplasma marginale* is the most clinically significant and widely reported species globally and in Türkiye (488). *Anaplasma centrale* generally causes mild or subclinical infections and has been used as a live vaccine strain in other countries, though it also circulates naturally in Türkiye (381,386). *Anaplasma bovis*, while less common, has been sporadically detected in Türkiye through moleculer studies and is known to cause fever, lymphadenopathy, and weight loss in ruminants (381,489). *Anaplasma phagocytophilum*, typically associated with tick-borne fever, has only recently been molecularly confirmed in cattle in Türkiye (381). Clinical data are mostly available for *Anaplasma marginale* and *Anaplasma phagocytophilum*, with *Anaplasma bovis* and *Anaplasma centrale* being identified more often in subclinical or co-infection contexts (488). In addition to *Anaplasma marginale*, whose genetic diversity has been well documented in Türkiye through *MSP1a* and *MSP4* gene analyses (490,491), genetic studies have also identified the presence of both *Anaplasma phagocytophilum*-like 1 and like 2 strains in cattle based on 16S *rRNA* gene sequences (492). Moreover, molecular investigations have reported the presence of *Ehrlichia* species, including *Ehrlichia* sp. and the *Ehrlichia* sp. Omatjenne strain (382), further highlighting the diversity of tick-borne rickettsial agents circulating in bovine populations in Türkiye (492-495).

In small ruminants, the primary *Anaplasma* species of veterinary relevance are *Anaplasma ovis* and *Anaplasma phagocytophilum*. *Anaplasma ovis* is the most frequently detected species in sheep and goats worldwide and is also widely distributed across Türkiye (488). It generally causes subclinical infections; however, in cases of immunosuppression or co-infection with other TBPs such as *Babesia ovis* or *Theileria ovis*, it may lead to acute disease characterized by hemolytic anemia, icterus, weight loss, and decreased milk yield (486). Molecular prevalence studies conducted in various regions of Türkiye have reported in sheep and goats (488). Genetic characterization of *Anaplasma ovis* strains using the *MSP1a* gene has revealed significant diversity, including multiple novel tandem repeats and distinct genotypes, which suggests a dynamic population structure (495,496). Tick infestation data from these studies frequently identified *Rhipicephalus bursa* and *Rhipicephalus turanicus* as the most common vectors associated with infection (486). On the other hand, *Anaplasma phagocytophilum*, the causative agent of tick-borne fever in ruminants, has been molecularly confirmed in small ruminants in Türkiye (488). Its detection, particularly the *Anaplasma phagocytophilum*-like 1 variant, has raised interest due to its unclear pathogenicity and genetic divergence from classical strains. Phylogenetic analyses of 16S *rRNA* and *GroEL* gene sequences indicate that *Anaplasma phagocytophilum*-like 1 forms a distinct clade, yet its clinical relevance remains to be fully elucidated (497). Recent molecular studies have also identified *Anaplasma ovis*, *Ehrlichia canis*, and *Ehrlichia chaffeensis* in *Rhipicephalus bursa* ticks collected from sheep in eastern Türkiye, specifically in Van province (498,499).

In dogs, the most clinically relevant tick-borne Rickettsiales are *Anaplasma platys*, *Anaplasma phagocytophilum*, and *Ehrlichia canis*. These pathogens are associated with well-defined disease syndromes: *Anaplasma phagocytophilum* causes canine granulocytic anaplasmosis (CGA), *Anaplasma platys* causes infectious cyclic thrombocytopenia, while *Ehrlichia canis* is the causative agent of canine monocytic ehrlichiosis (CME) (499). Serological and molecular methods have detected all three agents in canine populations in Türkiye (488). While most cases of *Anaplasma platys* infection are subclinical, the clinical forms have also been documented. A significant case includes the first corroborated evidence of *Anaplasma platys* infection in a dog in Türkiye, recorded in a Pinscher with chronic intermittent fever, inappetence, and weight loss. Diagnosis was confirmed by PCR and the dog improved with doxycycline (500). Acute CGA due to *Anaplasma phagocytophilum* is usually characterized by non-specific clinical signs such as fever, lethargy, anorexia, lymphadenopathy, and musculoskeletal pain. However, reports of *Anaplasma phagocytophilum* detection in dogs in Türkiye are scarce, and its clinical disease role is undetermined (381). *Ehrlichia canis* is so far the only one of the *Ehrlichia* species that is detected on a large scale in dogs in Türkiye (488). CME is also characterized by clinical signs like fever, pallor of the mucous membranes, lymphadenomegaly, anorexia, and splenomegaly in cases more serious, compromised to the pansitopenia (499). Molecular characterization of Turkish *Ehrlichia canis* isolates based on the *TRP36* gene has revealed three genotypes, including a novel variant phylogenetically related to a human isolate from Costa Rica (501). Although less frequently studied, water buffaloes (*Bubalus bubalis*) in Türkiye have also been shown to harbor tick-borne *Anaplasma* species. Molecular investigations have confirmed the presence of *Anaplasma phagocytophilum*-like 1 and *Anaplasma capra* in buffalo populations, indicating their potential role as reservoirs in the epidemiology of these pathogens (487,502). Similarly, studies on feline TBPs in Türkiye are limited; however, several case reports and molecular investigations have confirmed the presence of *Anaplasma* and *Ehrlichia* species in domestic cats. One of the earliest reports described a clinical case of ehrlichiosis in an 11-year-old cat from Burdur province, which presented with fever, lethargy, icterus, and anorexia. Diagnosis was based on blood smear examination and indirect fluorescent antibody test (IFAT), and the cat recovered following doxycycline treatment (503). In a more recent and comprehensive molecular study conducted in Tekirdağ province, *Anaplasma platys* and *Anaplasma phagocytophilum* were identified by species-specific PCR in symptomatic cats, providing further evidence of feline exposure to tick-borne rickettsial agents (504). HGA and human ehrlichiosis are emerging tick-borne zoonoses of growing concern (505). In Türkiye, human infections data are limited. A seroepidemiological study in Sinop and Tokat provinces indicated *Anaplasma phagocytophilum* seropositivity with significant co-seropositives with *Borrelia burgdorferi*, especially in regions suitable to *Ixodes ricinus* ticks (450). The first confirmed human case of ehrlichiosis in Türkiye was reported in a 6-year-old boy from Konya province following a tick bite, where cytoplasmic morulae were detected in leukocytes and PCR confirmed *Ehrlichia* infection, although species characterization was not performed (452), *Anaplasma capra* is globally acknowledged as a zoonotic pathogen, and some human cases were confirmed in Asia. In contrast, *Anaplasma ovis* has only one published report suggesting zoonotic potential (506). However, although both *Anaplasma capra* and *Anaplasma ovis* were detected in the domestic animals in Türkiye, such as sheep, goats, and buffalo, infections in humans in the country have not yet been reported. Equine granulocytic anaplasmosis, caused by *Anaplasma phagocytophilum*, is a TBDs affecting horses and various other mammalian species, including humans. Although *Anaplasma phagocytophilum* has been widely reported in cattle, small ruminants, dogs, and humans in Türkiye, data on its presence in equine populations are scarce. The first serological evidence of *Anaplasma phagocytophilum* in horses in Türkiye was reported in a study that detected anti- *Anaplasma phagocytophilum* IgG antibodies in 8.57% of 105 mares using IFAT (507). More recently, a molecular survey conducted in Muş province revealed a seroprevalence of 8.6% and detected *Anaplasma phagocytophilum* DNA in 6.4% of sampled horses by nested PCR targeting the 16S *rRNA* gene (508).

Rickettsia species are gram-negative, obligate intracellular bacteria that encompass several prominent TBPs, especially within the SFG. These pathogens cause a wide variety of human and animal diseases which typically present with febrile illness with non-spesific clinical signs, including fever, malaise, headache, myalgias, and depending on the disease, eschar and regional lymphadenopathy. The diversity of *Rickettsia* spp. has increasingly become apparent with the evolution of molecular diagnostic tools (509). To date, at least 12 SFG *Rickettsia* species have been detected in ticks infesting humans, domestic animals, and wildlife in Türkiye. These include *Rickettsia conorii*, *Rickettsia slovaca*, *Rickettsia raoultii*, *Rickettsia helvetica*, *Rickettsia monacensis*, *Rickettsia massiliae*, *Rickettsia aeschlimannii*, *Rickettsia felis*, *Rickettsia africae*, *Rickettsia sibirica mongolitimonae*, *Candidatus Rickettsia barbariae, Candidatus Rickettsia* vini, and *Candidatus Rickettsia goldwasserii* (146,457,504,510-514). These agents have been isolated mostly from ixodid ticks including *Rhipicephalus sanguineus*, *Rhipicephalus bursa*, *Hyalomma marginatum*, and *Ixodes ricinus* from several areas of the country. One study identified *Candidatus Rickettsia barbariae*, *Rickettsia aeschlimannii*, and *Rickettsia* sp. Chad in *Rhipicephalus turanicus* ticks collected from cattle, based on phylogenetic analysis of the 16S *rRNA*, *gltA*, and *ompA* genes. Notably, *Rickettsia* sp. Chad, previously reported in a human case of Astrakhan fever, was detected in Türkiye for the first time, suggesting a possible zoonotic risk (494). Human infections caused by SFG *Rickettsia* species have been reported in Türkiye. Mediterranean spotted fever due to *Rickettsia conorii* subsp. *conorii* is the most commonly reported clinical presentation however, individual cases of rickettsialpox due to *Rickettsia akari* and *Rickettsia sibirica mongolitimonae* have additionally been published (515,516). More recently, *Rickettsia slovaca*, a known causative agent of SENLAT syndrome (scalp eschar and neck lymphadenopathy after tick bite) was detected in a pediatric patient, being the first confirmed case of this clinical entity in Türkiye (458). Molecular studies beyond human infections have also demonstrated the detection of *Rickettsia* DNA in domestic animals. *Rickettsia aeschlimannii*, *Rickettsia slovaca*, *Candidatus Rickettsia barbariae*, and *Rickettsia raoultii* were recently identified in blood samples from domestic cats (510). Data on human infections, however, are still limited and geographically confined, despite the growing evidence of diversity of *Rickettsia* in arthropods and domestic animals. The greatest focus of investigations was in central and northern Türkiye, especially where CCHF was endemic; southern and western provinces remained underrepresented. Beyond rural and wildlife-associated environments, urban and peri-urban tick populations in Türkiye have also been shown to harbor medically important rickettsial and emerging bacterial pathogens. Notably, *Rickettsia aeschlimannii*, *Rickettsia slovaca*, and even *Rickettsia africae* have been identified in ticks collected from major metropolitan areas such as Ankara and İstanbul, particularly in *Hyalomma aegyptium* and *Dermacentor marginatus* ticks (457,511). Adding to the complexity, the emerging zoonotic agent *Candidatus Neoehrlichia mikurensis*, a bacterium associated with febrile illness and infectious vasculitis in humans, was also recently reported in *Ixodes ricinus* ticks collected from cattle and unfed questing ticks in Anatolia (146).

Non-rickettsial Infections in Animals in Türkiye

Lyme Disease or Lyme Borreliosis (LB): LB is a multisystemic tick-borne infection, predominantly due to the *Borrelia burgdorferi* sensu lato complex, and its geographical distribution is largely linked to the distribution of *Ixodes* tick species, especially *Ixodes ricinus*. *Ixodes ricinus* is widely distributed along the Black Sea coast, Thrace, and along the coastal regions of the Marmara, Aegean, and Mediterranean in Türkiye (517).

However, studies investigating the epidemiology of LB in Türkiye remain scarce, and the disease is likely underrecognized. Confirmed seropositive cases are mainly clustered in humid forested coastal provinces of the Black Sea region, where both vector density and human risk of exposure are highest. Until now six *Borrelia burgdorferi* s.l. genospecies (*Borrelia afzelii*, *Borrelia garinii*, *Borrelia burgdorferi* s.s., *Borrelia lusitaniae*, *Borrelia valaisiana*, and *Borrelia spielmanii*) were identified in Türkiye, however, in many studies on both human and animal sources species-level determination is absent. Molecular evidence of *Borrelia burgdorferi* s.l. in *Ixodes ricinus* from humans, cattle and questing populations, mainly in the Black Sea and Thrace regions suggests active enzootic transmission (517). Similarly, *Borrelia burgdorferi* s.s. has also been detected in other than *Ixodes ricinus* ticks such as *Hyalomma marginatum*, *Hyalomma excavatum*, *Haemaphysalis parva*, and *Rhipicephalus turanicus*, indicating a possible role of different ticks as vectors (457,514). To date, no study has offered genospecies-level typing in animal hosts, despite reports of seropositivity in dogs (including one clinical case), horses, and wild rodents. Given the ecological presence of competent vectors and confirmed seropositivity in both humans and animals, Türkiye can be considered a region with significant zoonotic risk for LB. However, the lack of timely and comprehensive molecular epidemiological data, particularly at the strain level, highlights the necessity for high-resolution surveillance and One Health-based approaches to both disease recognition and prevention (517).

Outstanding Questions: (i) Which tick species are competent vectors for recently identified or poorly understood pathogens such as *Anaplasma capra*, *Rickettsia* sp. Chad, and *Candidatus Neoehrlichia mikurensis* in Türkiye? (ii) Could *Anaplasma capra* and *Anaplasma ovis* be infecting humans in Türkiye but remain undiagnosed due to limited awareness and lack of routine testing? (iii) What is the clinical relevance of *Anaplasma phagocytophilum*-like 1 and like 2 variants detected in cattle and small ruminants in Türkiye? (iv) Given that *Anaplasma phagocytophilum*-like 1 and like 2 variants have been reported in regions of Türkiye where *Ixodes ricinus*, the primary vector of *Anaplasma phagocytophilum*, is absent, could these strains be transmitted by alternative tick species with distinct vector competencies? (v) How significant is the zoonotic risk posed by urban and peri-urban tick populations in Türkiye? (vi) What is the extent of co-infection with multiple Rickettsiales species in animal and tick hosts, and how does this impact disease manifestation and diagnosis? (vii) What strategies can be developed to integrate veterinary, human health, and environmental surveillance into a unified One Health framework for tick-borne rickettsial diseases in Türkiye? (viii) What is the true nationwide prevalence of *Borrelia burgdorferi* s.l. genospecies in humans and animals in Türkiye, and how does it correlate with *Ixodes ricinus* distribution? (ix) Why is genospecies-level characterization of *Borrelia* strains lacking in most confirmed animal and human cases in Türkiye (x) What is the role of wild and domestic reservoir hosts, including rodents, tortoises, and dogs, in maintaining enzootic cycles of *Borrelia burgdorferi* s.l. in Türkiye? (xi) What strategies are needed to improve early-phase diagnostics and genospecies identification in both clinical and surveillance settings?

Overall, emerging and re-emerging threats posed by tick-borne bacterial pathogens require a comprehensive and coordinated approach. Implementing strategies aligned with priorities under the One Health umbrella will not only reduce the risks posed by TBDs but also contribute to global health security and sustainability.

Tick-borne Protozoa

The transmission of TBPs is fundamentally based on the tick-host-pathogen interactions. Ticks have evolved to counteract host defense mechanisms, such as haemostasis and immune responses, through the secretion of salivary molecules with anti-haemostatic, anti-inflammatory, and immunomodulatory properties (94). At the site of attachment, ticks modulate host immune responses to facilitate blood feeding and create a favorable environment for the transmission of TBPs. The mechanisms by which ticks transmit pathogens to vertebrate hosts while simultaneously protecting themselves from these pathogens have long been a subject of scientific curiosity. Despite possessing only non-specific and primitive immunity, ticks are shielded from pathogenic microorganisms through an evolutionarily developed natural immune system. This protective system consists of several key components: (i) structural, (ii) normal flora, (iii) hemocytes, (iv) cell-mediated immunity, (v) soluble factors, (vi) innate immune systems, and (vii) regulation of innate immunity (88). Both morphological (e.g., salivary gland acini cells, coxal glands, digestive system barriers) and biological (e.g., the complex development of argasid and ixodid ticks) factors influence the transmission of pathogens by tick vectors to their hosts. Vector ticks are responsible for transmitting a broad spectrum of pathogens, including bacterial, viral, fungal, nematode, protozoan species, and prions which are associated with emerging and re-emerging diseases in humans and animals in regions exhibiting enzootic stability. These diseases not only pose significant health risks but also contribute to poverty due to the considerable and devastating economic losses they cause. In natural environments, vector-borne pathogens typically infect vertebrate hosts individually; however, in some cases, multiple pathogens can induce concurrent infections (518). Tick vectors transmit pathogens to their hosts primarily through various routes, including intrastadial, transstadial (or interstadial), transovarial, co-feeding, mechanical transmission, coxal fluid, ingestion, and venereal routes (94,518).

Tick-borne Protozoan Diseases

Tick-borne parasitic protozoan species are systematically classified within the Apicomplexa phylum and are responsible for causing significant diseases that result in considerable economic losses, primarily in animals (519). Tick-borne Apicomplexa are divided into two distinct orders: Piroplasmida, which includes the genera *Babesia* (Babes, 1888), *Theileria* (Bettencourt, França and Borges, 1907), and *Cytauxzoon* (Neitz and Thomas, 1948) (piroplasmids); and *Eucoccidiorida,* which includes the genera *Hepatozoon* (Miller, 1908) and *Hemolivia* (520) (hemogregarines). Piroplasmids are primarily transmitted through the bite of infected ticks, whereas transmission of *Hemolivia* and *Hepatozoon* typically occurs through the ingestion of infected ticks, leading to the release of the parasites into the host's digestive tract. Tick-borne Apicomplexa represent the predominant group of mammalian blood parasites (521). In livestock animals, various species cause a range of clinical signs, resulting in significant morbidity and mortality, as well as a considerable economic burden (114,522).

Molecular Clades of Piroplasms: Phylogenetic Insights and Biological Characteristics

Molecular phylogenetic studies using 18S *rRNA* gene sequences (523) have provided clear distinctions between the Theileriidae and Babesiidae piroplasms, further identifying several distinct clades within the latter. These clades include unguli-babesids (e.g., *Babesia bovis*), babesiids (e.g., *Babesia canis*), proto-theilerids (e.g., *Babesia gibsoni*), and archaeo-piroplasmids (e.g., *Babesia microti*). To date, six broad clades have been identified: (i) the "*Babesia microti*" clade comprising species from rodents; (ii) the "Western" clade from deer and dogs in the United States; (iii) the *Theileria/Cytauxzoon* clade from felids; (iv) the *Theileria* clade from equids and rhinoceroses; (v) the *Theileria* clade from bovids; and (vi) the *Babesia* clade from ruminants, carnivores, and rodents (524,525). These molecular studies suggest that the genus *Babesia* can be divided into two major lineages: *Babesia* sensu stricto and *Babesia* sensu lato, with an intermediary lineage (*Theileria/Cytauxzoon*) potentially acting as a bridge between the two. When mapping biological characteristics to these phylogenetic divisions, several key features emerge. The *Babesia* sensu stricto clade encompasses species that form two merozoites within the erythrocytes of ruminants, carnivores, and rodents. In contrast, the *Babesia* sensu lato clade includes species that form four merozoites within the erythrocytes of rodents, carnivores, and deer. Species belonging to the intermediary *Theileria/Cytauxzoon* clade also form four merozoites within the erythrocytes of ungulates and felids, but they additionally exhibit pre-erythrocytic schizogony a characteristic absent in any *Babesia* species. Piroplasms across all clades exhibit trans-stadial transmission in their tick vectors; however, only those within the *Babesia* sensu stricto clade undergo trans-ovarian transmission (526).

Babesia and *Theileria* Species in Animals and Humans

In cattle and buffalo, several species of *Babesia* and *Theileria* are of significant veterinary importance. These include *Babesia bigemina*, *Babesia bovis*, *Babesia major*, *Babesia divergens*, *Babesia jakimovi*, *Babesia occultans*, *Babesia ovate*, *Theileria annulata*, *Theileria parva*, *Theileria lawrenci*, *Theileria taurotragi* (synonym: *Cytauxzoon*), *Theileria velifera*, *Theileria mutans*, *Theileria sinensis*, *Theileria sergenti* (synonym: *Theileria orientalis*) (114), *Theileria orientalis* (527), *Theileria orientalis* genotype (528,529), *Theileria* sp. (buffalo), and *Theileria* sp. (bougasvlei) (530). Other *Babesia* species, such as *Babesia ovis*, *Babesia motasi*, *Babesia crassa*, *Babesia* sp. Xinjiang, *Theileria ovis*, *Theileria lestoquardi*, *Theileria separata*, *Theileria uilenbergi*, *Theileria luwenshuni*, *Theileria* sp. *MK*, and *Theileria* sp., are of particular relevance in small ruminants (114,496,531-534). In deer and antelope, notable species include *Theileria taurotragi*, *Theileria separata*, *Theileria uilenbergi*, *Theileria luwenshuni*, *Theileria capreoli*, *Babesia odocoilei* and *Theileria cervi*, while *Theileria bicornis* is responsible for benign theileriosis in rhinoceros. Among equids, key species include *Theileria equi*, *Theileria haneyi* (535) and *Babesia caballi* (534). In canines, the following *Babesia* species are significant: *Babesia canis canis*, *Babesia canis vogeli*, *Babesia canis rossi*, *Babesia gibsoni*, *Babesia vulpes*, *Babesia conradae, Theileria. annae*, as well as *Hepatozoon canis*. In felines, the prominent species include *Babesia felis*, *Babesia cati*, *Babesia herpailuri*, *Babesia pantherae*, *Cytauxzoon felis*, and *Hepatozoon felis*. In pigs, *Babesia trautmanni* and *Babesia perroncitoi* are relevant, while in rodents, *Theileria* sp. (sable), *Babesia microti*, and *Babesia rodhani* (synonym: *Nuttallia rhodhaini*) are significant (532,533,536). In poultry, numerous *Babesia* species, such as *Babesia moshkovskii*, *Babesia shortii*, *Babesia uriae*, *Babesia bennettii*, *Babesia poelea*, *Babesia kiwiensis*, *Babesia kazachstanica*, *Babesia ardeae*, *Babesia frugilegica*, *Babesia emberizzica*, *Babesia balearicae*, *Babesia rustica*, *Babesia mujunkumica*, *Babesia peircei*, and *Aegyptionella pullorum*, have been documented (532). Although more than 100 species of *Babesia* have been described, only a limited number of these species are associated with zoonotic babesiosis or have zoonotic potential. These include *Babesia microti*, *Babesia divergens*, *Babesia divergens*-like, *Babesia duncani*, *Babesia venatorum* (EU1), MO-1, *Babesia ovis*, KO-1, *Babesia bovis*, *Babesia motasi*, *Babesia crass*-like and XXB/HangZhou, (114,532,534,537-541).

Furthermore, the discovery of novel species of tick-borne protozoan pathogens within the genera *Babesia*, *Theileria*, and *Hepatozoon* continues to advance globally. In Australia, several novel species of *Babesia* and *Theileria* have been identified, including *Babesia lohae* nov. sp., *Babesia mackerrasorum* nov. sp., *Hepatozoon banethi* nov. sp., *Hepatozoon ewingi* nov. sp., *Theileria apogeana* nov. sp., *Theileria palmeri* nov. sp., *Theileria paparinii* nov. sp., and *Theileria worthingtonorum* nov. sp. (542). These species were detected in *Ixodes holocyclus* ticks collected from a dog. Furthermore, the *Theileria orientalis* Ikeda genotype was identified in *Haemaphysalis longicornis* ticks collected from dogs in Ikeda, New South Wales (543). Of particular note is the identification of the exotic TBP *Hepatozoon canis* in an *Ixodes holocyclus* tick collected from a dog in Queensland (542). In Japan, the prevalence of tick-borne protozoan parasites in wild sika deer in western Japan was investigated using PCR techniques. The results revealed the presence of *Theileria* sp. (sika 1), *Theileria* sp. (sika 2), another *Theileria* sp., and a *Babesia* sp. (544). Recent studies in Southern Italy have examined the prevalence of *Babesia* spp. in wild animals, particularly focusing on the epidemiological role of free-ranging canids and mustelids. PCR analysis targeting the 18S *rRNA* gene on spleen samples revealed the presence of *Babesia* spp. in 36 (43.9%) of 82 red foxes (*Vulpes vulpes*), 7 (53.8%) of 13 Eurasian badgers (*Meles meles*), and 1 (7.7%) of 13 grey wolves (*Canis lupus*). Sequence analysis confirmed the presence of two distinct sequence types of *Babesia vulpes* in red foxes and badger-associated *Babesia* spp. in Eurasian badgers. Additionally, the *Babesia* sp. detected in the grey wolf showed identical sequencing to that of the badger-associated *Babesia* sp. These findings suggest that these wildlife hosts play a significant role in the epidemiology of babesiosis, particularly in maintaining the forest cycle of *Babesia* transmission (545).

Genetic Manipulation and Transfection Studies in *Babesia* Species

The interactions of tick-transmitted protozoan parasites with their vectors and vertebrate hosts are poorly understood, especially concerning the *Babesia* genus. These parasites dynamically express different genes when they transition between an invertebrate and vertebrate host, which has made it challenging to dissect the molecular interactions that underpin infection and transmission. Among *Babesia* species, *Babesia bovis* is currently the most thoroughly studied in terms of genetic manipulation and transfection (546,547). To investigate parasite biology and develop intervention tools, transgenic strategies have been established using in vitro cultures of *Babesia bovis*-infected erythrocytes. The microaerophilic stationary phase (MASP) cultivation system has been pivotal, facilitating insights into intraerythrocytic developmental stages, surface antigens as vaccine targets, and responses to antiparasitic drugs. These in vitro conditions have also enabled the implementation of CRISPR/Cas9 and stable transfection systems (546-549). The use of the elongation factor 1 alpha (EF1α) intergenic region as an effective expression platform is one of the major innovations in *Babesia bovis* transfection. This method enables the integration of foreign genes in the *Babesia bovis* genome, for example, green fluorescent protein (GFP), *Rhipicephalus microplus* BM86, and tick glutathione-S-transferase (HlGST). Such transfected parasites remain infective in vertebrate and tick hosts and thus have facilitated studies of parasite invasion, gene function and host immune responses (550-552). A promising application has been the generation of a dual-purpose vaccine, in which *Babesia bovis* is genetically modified to express HlGST so that anti-tick immunity is raised. This transfected line of parasites also prevented *Rhipicephalus microplus* engorgement and fecundity of egg, indicating that calves were partially protected and providing new integrated strategies to control both babesiosis and ticks (553). While *Babesia bovis* remains the model species, transfection tools have been successfully extended to other *Babesia* spp. Given the remarkable conservation of the EF1α intergenic regions and strong promoter activity, similar strategies have been adapted for *Babesia bigemina*, *Babesia ovata*, *Babesia gibsoni, Babesia divergens*, *Babesia duncani*, *Babesia microti*, *Babesia ovis* and *Babesia* sp. Xinjiang. These studies, while largely limited to transient expression, have established foundational systems for promoter validation, protein localization, and potentially future vaccine or drug target discovery (547). Collectively, the continued refinement of stable and transient transfection platforms across *Babesia* species enhances our capacity to explore their biology, virulence factors, and host interactions. These tools will be indispensable for dissecting parasite gene function and for advancing next-generation vaccine and therapeutic development against babesiosis.

Bovine Theileriosis and Babesiosis: Economic Impact and Control Challenges

Bovine theileriosis, also referred to as Mediterranean coast fever or tropical theileriosis in cattle and buffalo, is caused by *Theileria annulata* and affects approximately 250 million cattle across a vast geographical range, including Southern Europe, the Mediterranean region, the Middle East, the Caucasus, Central Asia, and South Asia. Another form of theileriosis in cattle and buffalo, East Coast fever (Theileriosis), caused by *Theileria parva*, is a major tick-borne piroplasmosis disease in Africa (1,2,85,554,555). Additionally, piroplasmosis in sheep and goats, commonly referred to as "ovine theileriosis", is caused by *Theileria lestoquardi*, *Theileria uilenbergi*, *Theileria luwenshuni*, *Theileria ovis*, *Theileria annulata* and *Theileria* sp. MK (555,556) presents a significant threat to small ruminant farming. These diseases result in substantial economic losses and contribute to poverty and destitution in low-income, underdeveloped societies. Furthermore, several species of *Babesia* are responsible for babesiosis in cattle, horses, dogs, and occasionally humans. Infection with *Babesia* species leads to poor growth, decreased milk production, and high mortality in affected animals, prompting widespread efforts to control piroplasmosis. Prior to the implementation of successful vector control programs, the direct and indirect costs of piroplasmosis in the United States alone were estimated to exceed 100 million USD annually. Although these diseases have been successfully controlled in developed countries, they continue to cause significant economic losses in tropical and subtropical regions. In many tropical countries, the eradication of tick vectors is often unrealistic, thus increasing the demand for alternative strategies to effectively control piroplasmosis. Vaccines using live attenuated *Babesia bovis* and *Babesia bigemina* have been developed and are commercially available. Millions of doses of this combined vaccine have been administered in regions such as the New World and Australia (557). The development of live vaccines against bovine babesiosis was initially prompted by early observations that cows surviving natural *Babesia* infections developed long-lasting immunity. Although vaccines consisting of live *Theileria* parasites, soluble antigens from *Babesia* species (such as a vaccine for canine babesiosis marketed in parts of Europe), or subunit vaccines are under development or in clinical trials, they have yet to be tested on a large scale.

Babesiosis: Babesiosis is a globally widespread, zoonotic TBD that affects both domestic and wild animals, as well as humans. It causes significant economic losses and poverty worldwide.

Bovine babesiosis, also referred to as piroplasmosis, Texas fever, red water disease, and cattle tick fever, is primarily caused by *Babesia bigemina*, *Babesia bovis*, *Babesia major*, and *Babesia divergens*. The disease is transmitted by the ticks *Rhipicephalus microplus* and *Rhipicephalus annulatus*, with *Babesia bovis* and *Babesia bigemina* being the main etiological agents (163,532). Bovine babesiosis can lead to mortality rates exceeding 90% in susceptible cattle populations. Beyond the direct costs associated with treatment, the economic burden of additional expenses, such as tick control, exacerbates the financial impact. Annual economic losses from bovine babesiosis and anaplasmosis worldwide have been reported to range from 16.9 million USD in Australia and 21.6 million USD in South Africa to 57.2 million USD in China (163). The cumulative economic loss resulting from these factors contributes significantly to poverty and economic instability in affected regions. In enzootic areas, such as Mexico the economic losses due to vector tick control have been recently estimated at approximately 573.6 million USD annually (558). In the United States, the eradication of *Rhipicephalus microplus* (and consequently babesiosis) has saved the livestock sector an estimated 3 billion USD per year (534). The life cycles of *Babesia bovis* and *Babesia bigemina* are similar, with both species being transmitted transovarially by *Rhipicephalus microplus* and *Rhipicephalus annulatus*. *Babesia bovis* is transmitted exclusively by infected larvae. There exists an evolutionary compatibility between the short blood mealtimes of fasting larvae infected transovarially and the maturation of infective *Babesia bovis* sporozoites. In line with this evolutionary adaptation, *Babesia bovis* sporozoites are transferred to the host within 2-3 days after larvae attachment, initiating infection. In contrast, *Babesia bigemina* sporozoites require 9 days to develop, and as such, they are transmitted by the earliest nymphs or fasting adults of the vector tick (532,559). Immunization of cattle against bovine babesiosis primarily relies on the use of live vaccines. While these live vaccines offer protection, they are associated with significant limitations (560). Consequently, substantial research is being conducted to explore enhanced vaccination strategies, particularly in countries where large cattle populations are at high risk. It is anticipated that next-generation vaccines, which focus on the development of both non-live and/or live vaccines incorporating parasite antigens involved in host cell invasion, pathogen-tick interactions, and protective immunity against infection, may offer improved protection (560). In this regard, the continuous expansion of available parasite genomes is seen as a promising avenue for identifying potential vaccine candidates. In Argentina, vaccine research efforts against *Babesia bovis* are ongoing (561). One approach involves the use of transfection techniques for *Babesia* (562), while another focuses on a novel recombinant vaccine candidate utilizing a viral vector (563). Additionally, in USA, the culture attenuated strain Att-S74-T3Bo was shown to be non-tick transmissible and could safely protect calves against a virulent strain of *Babesia bovis* (564). Metabolic responses to infection can vary significantly depending on both the arthropod species and the specific pathogen involved. In the *Rhipicephalus microplus* ticks which are vectors of *Babesia bovis*, metabolic rates, specifically the volume of carbon dioxide (VCO2) were examined to assess how infection influences metabolic processes during various life stages. The hypothesis tested in the study was that the metabolic rate (as measured by VCO2) would be altered in ticks during stages infected with *Babesia bovis*. The results showed a decrease in VCO2 in infected engorged females, indicating a reduction in metabolic activity during this stage. In contrast, an increase in VCO2 was observed during the egg and larval stages, suggesting heightened metabolic activity at these earlier developmental phases. A critical observation from the study was that engorged females infected with *Babesia bovis* experienced a 25% reduction in body mass compared to uninfected controls. This suggests that infection might lead to significant energy depletion in adult female ticks. Additionally, larvae from uninfected females had a higher hatching success rate, twice as likely to hatch compared to those from infected, intact females. From an epidemiological perspective, particularly in regions endemic for babesiosis, these findings present important insights into the role of metabolic alterations in the transmission dynamics of *Babesia bovis*. The reduced metabolic rate in infected engorged females and the impaired hatching success of larvae from infected females can be viewed as key factors that might limit the persistence of the parasite within tick populations. This data highlights a potential reducing determinant of *Babesia bovis* transmission by *Rhipicephalus microplus* ticks, offering a deeper understanding of how infection impacts vector fitness and, by extension, the epidemiology of babesiosis (565). However, live and attenue vaccine have been using against bovine babesiosis caused *Babesia bigemina* and *Babesia bovis* in different countries such as Uzbekistan (566), Australia (567-570), Israel (571-573), South Africa (574) and Mexico (575,576).

Human Babesiosis: Human babesiosis is a tick-borne, zoonotic protozoan disease caused by various *Babesia* species notably *Babesia microti*, *Babesia divergens*, and *Babesia bovis* (577). Transmission can also occur, though less commonly, through blood transfusion, perinatal transmission, or organ transplantation. More than 100 species of *Babesia* infect a wide range of wild and domestic animals worldwide, but only six species have been identified as human pathogens. *Babesia microti* is the predominant species infecting humans globally, causing endemic disease in the United States and China. Additionally, *Babesia venatorum* and *Babesia crassa*-like agents cause endemic infections in China. In Europe, *Babesia divergens* is the main species responsible for human infections, with sporadic cases of severe disease reported. In recent years, the number of *Babesia microti* infections has been increasing worldwide. Although more than 2,000 cases are reported each year in the United States, the actual number is believed to be significantly higher (578). However, it has been emphasized that the claim that *Babesia bovis* and *Babesia bigemina* are the etiological agents of human babesiosis should be approached with caution due to cross-reactions between *Babesia microti* and *Babesia bovis* in human babesiosis cases caused by *Babesia microti* or *Babesia microti*-like organisms reported from South America (Bolivia and Ecuador) and Mexico, as well as the inadequacy of epidemiological studies on the vector tick species (579).

Human babesiosis presents with a spectrum of clinical symptoms, ranging from mild to severe. Common manifestations include fever, chills, fatigue, anorexia, muscle and joint pain, and hepatosplenomegaly. In immunocompetent individuals, the disease is often asymptomatic or self-limiting. However, in immunocompromised patients—such as those with HIV/acquired immunodeficiency syndrome (AIDS), malignancies, or those undergoing immunosuppressive therapy—babesiosis can lead to severe complications, including hemolytic anemia, DIC, multi-organ failure, and death (580). Both the incidence and geographic range of the disease are increasing, giving it an emerging global profile. It poses a significant health burden, especially in individuals with compromised immune systems, who can also acquire the infection through blood transfusion. The mortality rate in this high-risk group can be as high as 20%. Diagnosis is made by identifying characteristic intraerythrocytic parasites in a thin blood smear prepared from the peripheral blood of a suspected patient and is further confirmed by detecting *Babesia* DNA using PCR. Treatment typically consists of a combination of atovaquone and azithromycin, or clindamycin and quinine. In severe cases, exchange transfusion may be necessary. In epidemiologically stable enzootic regions, personal and community-level preventive and control strategies—primarily aimed at reducing tick exposure—can help lower the incidence of infection. However, it is important to recognize that these measures alone are unlikely to prevent the geographic spread of *Babesia* into non-endemic areas (581).

In a reported case of human babesiosis in Korea, the occurrence of sheep deaths due to *Babesia* spp. infection in 2005 was considered a potential zoonotic link in the epidemiology of human babesiosis. In the study that conducted the epidemiological analysis of the case, polymorphic merozoites of the *Babesia* parasite were observed through microscopic examination of peripheral blood smears from the patient. The molecular identification of the pathogen, *Babesia* spp., the causative agent of the disease, was performed using the PCR technique. The pathogen showed 98% sequence homology with the *Babesia* species responsible for the 2005 sheep fatalities. Furthermore, phylogenetic analyses of 18S rDNA, cytochrome b, and *COX3* genes revealed a close genetic relationship with *Babesia motasi*. From an epidemiological perspective, tick surveillance was conducted around the patient's former residence. Two tick species—*Haemaphysalis longicornis* and *Haemaphysalis flava*—were collected from the area. *Babesia* DNA was screened in the ticks, and three *Haemaphysalis longicornis* ticks tested positive. Of these, one sample was identified as *Babesia microti*, while the other two showed 98% sequence similarity to *Babesia motasi*. These findings implicate *Haemaphysalis longicornis* as a potential vector of both *Babesia microti* and other *Babesia* species in the epidemiology of human babesiosis (539). In the United States, human babesiosis is primarily caused by two species: *Babesia microti* and *Babesia duncani*. The enzootic cycle of *Babesia microti*, which is endemic to the Northeastern and upper Midwestern regions, has been well characterized. In contrast, the natural reservoir host and tick vector of *Babesia duncani* in the western United States remain unidentified, posing challenges for understanding and managing this zoonotic disease. More than twenty-five years after *Babesia duncani* was first identified in a human patient in Washington State, recent studies have suggested that the winter tick (*Dermacentor albipictus*) may serve as the primary enzootic vector, while the mule deer (*Odocoileus hemionus*) is likely the principal reservoir host. These two species have a broad and overlapping geographic range that extends across much of western North America. The identification of *Babesia duncani* cases in the westernmost United States supports the hypothesis of an established and stable enzootic transmission cycle in the region (537). *Babesia motasi* is recognized as the etiological agent of babesiosis in both humans and sheep in China. Diagnosis of babesiosis has traditionally relied on microscopic examination of Giemsa-stained peripheral blood smears. However, from both clinical and epidemiological perspectives, rapid and accurate identification of the pathogenic species is highly desirable. In a study conducted in China, researchers reported the development of a practical, easy-to-use alternative method for the epidemiological and point-of-care diagnosis of *Babesia motasi* infection: the cross-priming amplification (CPA)-vertical flow imaging strip. This method allows for rapid detection and identification of *Babesia motasi*. However, the study also emphasized the need for increased caution regarding false-positive results when using the CPA technique in clinical screening settings (541). Epidemiologically, in North America, the most common pathogen affecting humans is *Babesia microti*, which is transmitted by the tick *Ixodes scapularis*, primarily found in the Northeastern and Upper Midwestern regions of the United States. In contrast, in tropical Mexico, *Babesia bovis* and *Babesia bigemina*—the primary agents of bovine babesiosis—pose a significant threat to US cattle. Despite ongoing eradication efforts targeting their tick vector, *Rhipicephalus microplus*, the risk of reintroduction into the southern United States remains a persistent concern for the American cattle industry. In the United States, sporadic outbreaks of *Theileria equi* in horses and *Theileria orientalis* in cattle have led to the enforcement of quarantine measures, resulting in substantial economic losses, including decreased productivity and the euthanasia of infected animals. Moreover, the recent identification of a novel species, *Theileria haneyi*, in horses along the Mexico-United States border has raised additional concern. At least four *Babesia* species have been reported to cause anemia and both acute and subclinical disease in domestic dogs across North America. Furthermore, multiple species of *Babesia* and *Theileria* are recognized as significant pathogens affecting humans, domestic animals, and wildlife throughout Canada, the United States, and Mexico (534).

Human Babesiosis in Türkiye: Babesiosis, a TBD caused by various *Babesia* species and recognized as a significant public health concern in North America, Europe, and Asia, has been reported in all geographical regions of Türkiye. The infection is prevalent among domestic animals and poses a serious threat to the cattle industry (163,582,583). Despite its widespread presence in animals, no clinical cases have been reported in humans to date (4). Nevertheless, serological studies suggest that human exposure to the parasite does occur. Reported seropositivity rates include 6.23% for *Babesia microti*, 8% for *Babesia divergens*, and 18% for *Babesia bovis* (284). For instance, a study conducted in Sinop province using the IFAT method identified a 6.23% seroprevalence of *Babesia microti* among individuals residing in rural areas (584).

Babesiosis in Türkiye

One of the global TBDs, bovine babesiosis, is prevalent in all geographic regions of Türkiye (163). Early studies on bovine babesiosis in Türkiye date back to as early as 1890. The first case of bovine babesiosis was reported in 1890 by Nicoll and Adil Bey. Subsequently, researchers such as Samuel and Raif, İbrahim Ekrem, Lestoquard, Gören, Yetkin, and Aysoy published several reports on ovine and equine babesiosis before 1950. The history of babesiosis research in Türkiye can be divided into three periods: (i) 1950-1980: Classic parasitological examinations using microscopy. (ii) 1980-2000**:** Microscopic examinations combined with serological tests. (iii) After 2000: Molecular confirmation and the use of advanced imaging technologies. In parallel with developments in the rest of the world, numerous studies on all forms of babesiosis have been reported from all regions of Türkiye (532).

Theileriosis in Türkiye

Various tick-borne parasitic protozoa belonging to the family Theileridae are pathogenic species that invade blood cells (including lymphocytes and erythrocytes), leading to both malignant and benign theileriosis in livestock and wildlife (1). These pathogens exhibit a complex life cycle, involving both vertebrate hosts and vector ticks, with transmission primarily occurring through the transstadial route via various species of ixodid ticks. Theileriosis is a widely prevalent disease, causing significant economic losses due to high mortality rates (approaching 100%) in untreated farm animals such as cattle, water buffalo, sheep, and goats. Consequently, the disease imposes severe economic burdens, exacerbating poverty in lower socio-economic communities in developing countries (555). In Zimbabwe, small-scale farmers are reportedly facing significant challenges in cattle breeding due to theileriosis and other TBDs that cause substantial economic losses (585). The two most pathogenic *Theileria* species that infect cattle and are of substantial economic importance are *Theileria parva* and *Theileria annulata*, which cause East Coast fever and Mediterranean cost fever or tropical theileriosis, respectively. *Theileria parva*, the causative agent of East Coast fever, affects cattle in South, East, and Central Africa, with corridor disease being endemic to East and Central Africa. In contrast, tropical theileriosis caused by *Theileria annulata* can be fatal to animals in Mediterranean regions extending from Morocco to the Middle East, and from Russia and the former CIS (formerly USSR) to the Indian subcontinent. The pathogen responsible for East Coast fever, *Theileria parva*, is transmitted by the vector ticks *Rhipicephalus appendiculatus* and *Rhipicephalus zambeziensis*, and it causes severe and often fatal (malignant) theileriosis in cattle and water buffalo (*Bubalus bubalis*) (586,587). African buffalo (*Syncerus caffer*) and wild cattle serve as important reservoir hosts for this pathogen. On the other hand, *Theileria annulata*, transmitted by ticks of the genus *Hyalomma*, infects cattle, yaks, and water buffalo, leading to fatal tropical theileriosis. In contrast, the *Theileria orientalis/buffeli* complex, which includes two species (*Theileria orientalis* and

Theileria buffeli) along with *Theileria taurotragi*, *Theileria mutans*, and *Theileria velifera*, are generally non-pathogenic and cause benign theileriosis (1,555). An experimental study was conducted to evaluate the hypothesis that the annual production of 150,000 doses of *Theileria annulata* schizont vaccine (10^6 cells) in Türkiye is insufficient to meet domestic demand, and that the number of vaccine doses could be increased by reducing the number of vaccine cells per dose. The study aimed to assess the protective efficacy of doses containing varying numbers of attenuated schizont vaccine cells against tropical theileriosis. A total of 42 sterile Holstein calves, aged 2.5 to 3 months, were included in the study. In addition, eight sterile test calves were used in challenge trials to assess the pathogenicity of tropical theileriosis. Three separate experiments were designed to evaluate the effectiveness of different vaccine doses containing varying numbers of schizont cells. In the first experiment, three groups of four calves (one of which served as a control) were used; in the second experiment, five groups of three calves (including one control group) were used; and in the third experiment, one group of ten calves and one group of five calves (control) were included. In the first experimental group, calves were vaccinated with 10^6 and 10^7 vaccine cells, while in the second experiment, calves received 10^3, 10^4, 10^5, and 10^6 vaccine cells. In the third experiment, calves were vaccinated with 10^6 vaccine cells. Control group calves received no vaccination. No significant clinical reactions were observed in any of the vaccinated calves across all experimental groups. Furthermore, *Theileria annulata* schizonts were not detected in lymph node smears, nor were piroplasmic forms of the parasite observed in peripheral blood smears. Blood cell counts (packed cell volume) in vaccinated calves showed no significant differences when compared to controls. Thirty-five days post-vaccination, all animal groups, including the control groups, were subjected to a challenge with *Theileria annulata* using different tick stabilate: in the first experiment, the Sarıoba *Hyalomma scupence* tick stabilate (4 t.e.); in the second experiment, the Akdere *Hyalomma scupence* tick stabilate (4 t.e.); and in the third experiment, a mixed stabilizer prepared from 8 ticks (1 mL each of *Theileria annulata* Akdere and *Theileria annulata* Sarıoba). Following the challenge, both vaccinated and unvaccinated calves developed signs of infection, including schizonts, piroplasmic forms, and fever. Notably, compared to the vaccinated calves, unvaccinated calves exhibited significantly higher levels of parasitemia, schizont counts, body temperatures, and more severe clinical reactions. Specifically, calves in the third experimental group, which were exposed to higher levels of challenge material, displayed more severe symptoms than those in the first two experimental groups. In this group, elevated levels of schizonts and piroplasm were detected, and 4 out of 10 vaccinated calves (40%) and all control calves (100%) succumbed to tropical theileriosis. The findings of this study demonstrate that vaccine doses containing 10^3, 10^4, 10^5, 10^6, and 10^7 cells provided effective protection against infection, with no significant difference in protective efficacy observed among the different doses. However, in the group subjected to a higher number of infected *Hyalomma* ticks (8 t.e.) in the challenge, the 10^6 cell dose proved inadequate to confer sufficient protection (588). Following these findings, the cell counts in the live attenuated schizont cell culture vaccine for tropical theileriosis, produced by the private sector in Türkiye, was increased to 10^7 cells per dose (589). These results are crucial for understanding the epidemiology of tropical theileriosis, particularly highlighting the severe and often fatal consequences of extensive tick infestations in enzootically stable regions, where elevated tick exposure significantly contributes to the transmission of the disease. In a field study conducted in the eastern part of Türkiye, an area with enzootic stability for *Theileria annulata* and its tick vectors, (199) found *Theileria annulata* infection in three out of the four *Hyalomma* species collected, namely *Hyalomma anatolicum, Hyalomma excavatum, Hyalomma scupence, and Hyalomma marginatum* in cattle. These findings underscore the role of *Hyalomma* ticks in the transmission of *Theileria annulata* in enzootic regions. On the other hand, a study conducted in Egypt identified *Hyalomma anatolicum* as the most prevalent and highly potent tick vector for the transmission of *Theileria annulata* infection, further highlighting the significance of this species in the epidemiology of the disease (590). Various attenuated schizont cell culture vaccines, stored at -196 °C, are currently being employed in vaccination programs aimed at protecting European cattle breeds that are susceptible to tropical theileriosis. These vaccines have been deployed in response to producer demand in several countries, including Israel (566), Uzbekistan (591), Tunisia (592), Türkiye (168,593-595), and Egypt (596). From a holistic perspective, the use of these attenuated vaccines is a significant strategy in controlling tropical theileriosis in cattle populations, particularly in regions where the disease poses a major threat to livestock productivity. In contrast, the “infection and treatment” method, which involves the administration of live *Theileria parva* sporozoites, has been utilized as a vaccination strategy against East Coast fever in various African countries, including Kenya, Tanzania, and Malawi (597,598). This method, while similar in its goal of inducing immunity through controlled infection, presents a different approach to disease prevention. The interest in comparing the effectiveness and safety of these two vaccination strategies—attenuated schizont vaccines versus live sporozoite infection and treatment—contributes to a deeper understanding of how best to mitigate the impact of *Theileria* spp. on livestock in endemic regions. These approaches highlight the diverse strategies in veterinary parasitology aimed at controlling TBDs in cattle. In addition, the pathogen *Theileria lestoquardi*, transmitted by *Hyalomma* ticks, is of significant economic importance as it causes malignant and fatal theileriosis in small ruminants. *Theileria lestoquardi*, which infects sheep and goats, is found in Africa, Asia, and southern Europe. In sheep and goats, non-pathogenic species such as *Theileria uilenbergi*, *Theileria luwenshuni*, *Theileria ovis*, *Theileria annulata*, and *Theileria* sp. MK are also present, causing benign theileriosis (556). On the other hand, *Theileria* species have been reported in equids as well as in non-ruminant species, including woodrats and foxes (599-601). In the United States, *Theileria orientalis*, genotype *buffeli*, has been identified as a non-pathogenic species (602,603). However, in 2017, *Theileria orientalis*, genotype *ikeda*, was detected in a cattle herd in Virginia and is now considered an emerging species (604). Other *Theileria* species, such as *Theileria mutans*, *Theileria velifera*, and *Theileria cervi*, have also been reported in North America. Notably, *Theileria cervi* has been shown to cause subclinical infections in deer (605-608). *Theileria cervi*, transmitted exclusively by the *Amblyomma americanum* tick, has been documented in the south-central United States (609-611) and northern Mexico (611). There is no evidence to suggest that *Theileria* species found in ruminants are capable of infecting humans (555).

Piroplasmosis in Small Ruminants: Piroplasmosis in small ruminants, also referred to as "ovine piroplasmosis", is a TBD caused by *Babesia* and *Theileria* species, transmitted primarily by ixodid ticks. The disease manifests in both sheep and goats with peracute, acute and subacute clinical courses, often leading to significant economic losses due to high mortality rates. The impact of this disease is particularly pronounced in regions with low socio-economic status, where it exacerbates poverty and poses additional challenges to local populations. The pathogenic agents responsible for piroplasmosis in sheep and goat herds include *Babesia ovis, Babesia motasi, Babesia crassa*, *Babesia taylori, Babesia foliata*, *Babesia* sp. Xinjiang, and *Babesia aktasi* nov. sp. (114,496,531,536) Among these species, *Babesia ovis* is particularly notorious for causing severe clinical babesiosis with high mortality rates (612). Epidemiologically, in enzootically stable regions, *Babesia ovis* is primarily transmitted by the vector *Rhipicephalus bursa*, whereas *Babesia motasi* is spread by *Haemaphysalis* species. Advances in molecular studies of *Babesia* species have led to the identification of several novel isolates. In China, new *Babesia* isolates, including *Babesia motasi*-like species such as *Babesia* sp. BQ1 (Lintan), *Babesia* sp. BQ1 (Ningxian), *Babesia* sp. Tianzhu, *Babesia* sp. Madang, *Babesia* sp. Hebei, and *Babesia* sp. Liaoning, have been reported in small ruminants (613,614). Genome analysis of *Babesia* sp. Xinjiang, transmitted by *Hyalomma anatolicum* and *Haemaphysalis quinghaiensis* ticks infesting sheep in China, revealed that this isolate is genetically distinct from the *Babesia motasi*-like group (613,615,616). Furthermore, *Babesia venatorum*, a zoonotic pathogenic species that infects deer in Europe, has also been identified in sheep in the United Kingdom (540). The salivary glands in ticks play essential roles in both feeding and pathogen transmission. A study was conducted to investigate how the sialoproteome of the vector tick *Rhipicephalus bursa* is influenced by *Babesia ovis* infection and blood feeding. Using a proteomic approach, the researchers characterized the sialoproteome of *Rhipicephalus bursa* and identified two potential tick protective antigens. These antigens were further evaluated for their effects on tick biological parameters and pathogen infection. The findings revealed that blood feeding had a significant impact on the *Rhipicephalus bursa* sialoproteome, suggesting that feeding alters the tick's salivary protein composition. However, the infection with *Babesia ovis* appeared to be well tolerated by the tick cells, as there were no major disruptions in cellular function or survival. From an academic perspective, these results highlight the complex interplay between tick physiology and pathogen infection. The identification of protective antigens in the tick's sialoproteome opens new avenues for understanding the mechanisms of pathogen transmission and for developing potential strategies for controlling TBDs (617).

In Türkiye, molecular epidemiological studies on sheep piroplasmosis have demonstrated that *Theileria annulata*, the causative agent of tropical theileriosis—a fatal, TBD of cattle—can also infect sheep (556). Additionally, a novel *Babesia* species, *Babesia aktasi* nov. sp., was identified in goats (496). In epidemiologically stable enzootic regions, there is a well-established relationship between the incidence of sheep babesiosis caused by *Babesia ovis* and the seasonal activity of the tick vector *Rhipicephalus bursa*. Traditionally, it has been suggested that transovarially infected *Rhipicephalus bursa* larvae may provide mild immunity against subsequent *Babesia ovis* infection in sheep within endemic areas (618,619). This hypothesis was tested in an experimental study aimed at investigating whether infection with transovarially infected *Rhipicephalus bursa* larvae reduces the severity of subsequent challenge infection with *Babesia ovis*-infected, unfed, adult ticks. In the experiment, three sheep were infested with *Babesia ovis*-infected larvae, while three control sheep were infested with *Babesia*-free larvae. Both groups were subsequently challenged with *Babesia ovis*-infected, unfed adult *Rhipicephalus bursa* ticks. Clinical, molecular, and serological parameters were monitored daily throughout the experiment. The results showed that infestation with infected larvae did not induce any clinical signs of babesiosis or *Babesia ovis* infection. However, after exposure to infected adult ticks, all sheep developed severe clinical babesiosis. Notably, no significant differences in disease severity, parasitemia levels, or clinical outcomes were observed between the experimentally infected and control groups. This indicates that infection with *Babesia ovis*-infected larvae did not provide protection against infection from infected adult ticks, nor did it result in milder disease outcomes. These findings challenge the notion that transovarial infection of *Rhipicephalus bursa* larvae provides protective immunity against *Babesia ovis* in sheep. The results underscore the critical role of adult *Rhipicephalus bursa* ticks in the transmission of *Babesia ovis*, with larvae playing no protective role in the disease cycle. From an academic and epidemiological perspective, this study emphasizes the importance of targeting adult tick populations during peak activity periods for effective vector control strategies. Moreover, the findings contribute to a deeper understanding of the dynamics of transstadial transmission of *Babesia ovis* by *Rhipicephalus bursa* and highlight the significance of considering stage-specific transmission barriers when managing vector-borne diseases. These insights have important implications for the development of more targeted strategies for controlling babesiosis in sheep populations (620). *Theileria ovis*, *Theileria hirci* (synonym: *Theileria lestoquardi*), *Theileria separata*, *Theileria uilenbergi*, *Theileria luwenshuni*, *Theileria* sp. *MK*, and *Theileria* sp., cause small ruminant piroplasmosis. *Theileria hirci* (formerly *Theileria lestoquardi*) and *Theileria* sp. (China 1) are responsible for causing malignant theileriosis in sheep and goats, while *Theileria ovis*, *Theileria separata*, and other species are associated with non-malignant forms of the disease (621).

Equine piroplasmosis (EP): EP is an important TBD of equids caused by *Babesia caballi*, *Theileria equi*, and *Theileria haneyi* transmitted by ixodid ticks. The disease presents significant burdens to equine health, athletic proficiency and international movement, especially impacting race and breeding horses. In Türkiye, *Theileria equi* has been more frequently detected than *Babesia caballi* in various regions through microscopic, serological, and molecular methods (622-624). However, studies show significant regional variation in distribution of both pathogens. Increased frequencies of infection have been associated with some regions of the country and possibly linked to livestock movements, environmental conditions, and tick distribution. It is worth mentioning as well that thoroughbred racehorses appear to be significantly more affected than stud horses, probably because of higher stress levels and transport. In Türkiye, different genotypes of *Theileria equi* and *Babesia caballi* were defined based on the genotyping studies (599,625). Furthermore, other non-equine *Babesia* and *Theileria* species including *Theileria annulata*, *Babesia ovis* and *Babesia canis* have been sporadically detected in equine samples by molecular investigations, suggesting that incidental infections or transient parasitemia may occur (625,626).

Canine babesiosis: Canine babesiosis is a veterinary important TBD of canine that is characterized by hemolysis, anemia, thrombocytopenia, fever, and hemoglobinuria. In dogs, several genetic variants of *Babesia*, including *Babesia vogeli*, *Babesia canis*, *Babesia rossi*, and *Babesia gibsoni*, all of which belong to the *Babesia* sensu stricto group, have been identified worldwide. The emergence of less frequently reported species in canids, such as *Babesia vulpes*, *Babesia conradae*, and *Babesia negevi*, has added to the described *Babesia* spp. diversity. infecting the domesticated dog (627-629). Molecular surveys in dogs in Türkiye have identified the presence of *Babesia canis*, *Babesia gibsoni* and *Babesia vogeli* (488,491,630) as well as a clinical disease associated with both *Babesia canis* (631) and *Babesia gibsoni* (632). Moreover, *Babesia rossi*, which is usually restricted to sub-Saharan Africa, was reported in *Haemaphysalis parva* ticks obtained from humans and wild boars in Türkiye (457,633). *Babesia vulpes*, responsible for infecting domestic dogs, has also been found in wild foxes (633). Indeed, a new and still unnamed *Babesia* spp. was recently described on dogs, suggesting that diversification is still ongoing and requires molecular characterization (491). Remarkably, *Babesia ovis*, a parasite usually linked to sheep, has also been identified unexpectedly in dogs (634).

Cytauxzoonosis: *Cytauxzoon felis* is an apicomplexan protozoan transmitted by ticks that causes cytauxzoonosis, an often-fatal illness in domestic cats. The parasite is mainly transmitted by *Dermacentor variabilis* and *Amblyomma americanum*, while bobcats (*Lynx rufus*) are the principal wildlife reservoirs. After tick transmission, undergoes schizogony in mononuclear phagocytes before invading erythrocytes as piroplasms. Clinical features of acute cytauxzoonosis include high fever, lethargy or dullness, jaundice, and high case fatality rate. Recent therapeutic developments, especially using a combination of atovaquone and azithromycin, have greatly improved survival (635). In Europe, *Cytauxzoon* spp. molecularly detected in domestic cats in Spain, France, Portugal, Italy, Switzerland and Germany. Although many of these infections were originally assigned to *Cytauxzoon felis*, they most probably represent closely related but different *Cytauxzoon* species. Most European cases are mild with a mild anemia, and subclinical presentation; however, rare severe disease and mortality have been reported (636). In Türkiye, *Cytauxzoon felis* was first described microscopically in domestic Van cats (637), and later molecularly confirmed for the first time in stray cats from Tekirdağ province, with a reported prevalence of 6.6% (504).

Hepatozoonosis: Hepatozoonosis is a protozoan infection associated with members of the genus *Hepatozoon*, which affect a variety of vertebrate hosts, from mammals to reptiles, birds, and amphibians (71). Of the approximately 350 described species, *Hepatozoon canis* and *Hepatozoon americanum* are the most clinically significant in dogs, while in cats *Hepatozoon felis* is regarded as the most significant causative agent. Likewise, transmission happens not via tick bites but via consumption of infected ticks. The principal vectors for *Hepatozoon canis* and *Hepatozoon americanum* are *Rhipicephalus sanguineus* and *Amblyomma maculatum*, respectively. However, *Hepatozoon canis* oocysts have also been found in other tick species, including *Rhipicephalus turanicus*, *Rhipicephalus microplus*, *Haemaphysalis flava*, *Haemaphysalis longicornis*, and *Amblyomma ovale*. *Hepatozoon canis* has also been shown to be transmitted transplacentally (488). In Türkiye, hepatozoonosis was first reported in 1933, and subsequent molecular studies have confirmed that *Hepatozoon canis* is endemic in dog populations across various regions. Recents studies have broadened the knowledge on *Hepatozoon* diversity in cats. Besides *Hepatozoon felis*, more recently described *Hepatozoon silvestris*, have been obtained from domestic cats, thus indicating that feline hepatozoonosis may be a complex involving a broader spectrum of species than previously recognized. In Türkiye, molecular surveys have detected *Hepatozoon canis*, *Hepatozoon felis*, *Hepatozoon ursi*, and *Hepatozoon* sp. MF in multiple carnivore species, dogs, red foxes, and brown bears. Furthermore, *Hepatozoon* DNA has been identified in various tick species, including *Rhipicephalus sanguineus*, *Rhipicephalus turanicus*, *Dermacentor marginatus*, *Haemaphysalis parva*, *Haemaphysalis sulcata*, and *Ixodes ricinus*. *Hepatozoon felis* DNA has been reported in *Rhipicephalus sanguineus* collected from domestic cats and in *Haemaphysalis parva* from Eurasian lynx, while *Hepatozoon ursi* has been identified in *Hepatozoon marginatum*, *Rhipicephalus turanicus*, and *Ixodes ricinus* removed from brown bears. One of the remarkable recent advancements regarding the fauna of Türkiye is *Hepatozoon viperoi* sp. nov. in *Vipera ammodytes* (nose-horned viper) from the Thrace region (94,638-641).

Heartwater (Cowdriosis): Heartwater (cowdriosis) is an economically important TBD of ruminants, primarily caused by the obligate intracellular bacterium *Ehrlichia ruminantium*, means affecting cattle, sheep, and goats. The disease is mainly transmitted by ticks of the genus *Amblyomma*, particularly *Amblyomma variegatum* and *Amblyomma hebraeum*. It is endemic in sub-Saharan Africa and some of the Caribbean islands, running to high morbidity and mortality in susceptible livestock populations (642). To date, no confirmed cases of heartwater have been reported in Türkiye. However, with increasing animal trade and climate-driven changes in tick distribution, continued monitoring is needed, particularly for exotic or imported animals that may become potential vessels.

Tick-borne Filarial Nematods

Filarial Worms: Filarial worms typically inhabit the lymphatic or subcutaneous tissues of their hosts. Gravid female worms produce microfilariae, which circulate in the bloodstream or migrate between tissues. When a suitable blood-sucking arthropod, such as mosquitoes or flies, ingests the microfilariae, they are transferred to the skin of the next host during an insect bite. In the host's skin, the microfilariae then develop into infectious larvae. While the life cycles of all filarial worms generally follow a similar pattern, they can vary depending on the site of infection. Ticks are known to transmit a variety of pathogens, including viruses, bacteria, fungi, apicomplexan protozoa, and filarial nematodes (15,94,640,643). Recent studies have confirmed that filarial larvae can also be transmitted by both argasid (soft) (644-647) and ixodid (hard) ticks, thus broadening the potential vectors for these parasites (648-655). This expanded range of tick species capable of transmitting filarial larvae highlights the growing complexity in understanding the transmission dynamics of these parasites.

A series of experimental studies on the argasid tick *Ornithodoros tartakowskyi* investigated the transmission of filarial nematode larvae. Histological sections and dissections of infected

Ornithodoros tartakowskyi ticks revealed that, in resting ticks, third-stage larvae of *Dipetalonema viteae* were distributed in clusters throughout the hemocoel. However, in feeding ticks, the larvae migrated forward and concentrated specifically in the capitulum. Further migration of the larvae continued even in the absence of blood ingestion, suggesting that the act of biting, rather than blood feeding itself, is the critical factor driving larval migration. The larvae may reach the buccal cavity via four possible routes: (i) the junction between the pharynx and the buccal cavity, (ii) the esophagus, (iii) the salivary ducts, and (iv) the roof of the hypostome. The developing larval forms directly damage the tick's muscle fibers. It is also hypothesized that the migration of the larvae further disrupts the tick's muscle tissue and interferes with its normal activities to some extent (644). To investigate the behavior of *Dipetalonema viteae* in the tick vector *Ornithodoros tartakowskyi*, ticks were fed on jirds at intervals of 30 to 35 days after receiving a single infectious blood meal. The number of larvae transmitted by the ticks during each bite was determined using three methods: (i) extracting adult worms from jird tissues, (ii) collecting larvae from skin flaps at the feeding site immediately after the bite, and (iii) obtaining larvae from serum and tissue following artificial feeding through a skin membrane. All methods yielded similar results. Ticks harboring fewer larvae transmitted most of them (82%) during the first bite and required only two bites to transmit all the larvae. In contrast, moderately or heavily infected ticks needed three or four bites to transmit all their larvae. Several factors may explain these differences: (i) heavily infected ticks may have shorter feeding durations due to irritation and damage to their mouthparts and pharyngeal muscles caused by the larvae, (ii) the foregut's resistance to larval penetration, and (iii) the retarding effects of larval crowding on their development and migration. Aging of the tick infection did not seem to affect the rate of larval transfer. Infection impaired feeding and delayed the molting of young nymphs. However, the ability to feed was restored as the ticks' lost larvae during successive bites (645). In studies on the acquisition and transmission of *Dipetalonema viteae* infection by *Ornithodoros tartakowskyi* ticks, it was found that larvae, nymphs, and unfed medium-sized ticks fed on recently blood-fed and engorged adult ticks. As a result, the larvae and nymphs acquired microfilarial infection, which developed normally within them. After 30 days of development, these infected ticks were able to transmit the microfilariae to a jird. Ticks harboring infectious filarial larvae can transmit these larvae when attempting to feed on adult ticks that have recently had a blood meal. While it is not yet confirmed whether this transmission mechanism occurs in nature, it has been suggested that it may play a complementary role in the natural maintenance of this filarial species. Additionally, ticks were observed to eliminate microfilariae from their coccal fluid in small quantities within one hour after infectious feeding. The number of microfilariae increased over time, peaking between three and five hours. This process may serve as a mechanism to prevent ticks from becoming over infected (646). In the following years, the development of the dog filaria *Dipetalonema dracunculoides* in larvae, nymphs, and adults of the brown dog tick *Rhipicephalus sanguineus* was investigated. The study revealed that only infected nymphal ticks can support the full development of the filarial worm. In contrast, infected larval ticks and adult ticks do not serve as suitable intermediate hosts. The successful development of the filarial worm depends on specific stage-related characteristics of the tick vector. Notably, the maturation of the filarial larva to the infectious stage is triggered during the nymph-to-adult molt (648). On the other hand, the transmission of the genus *Acanthocheilonema* by ticks remains controversial. The life cycle of *Acanthocheilonema viteae* has been experimentally studied with the aim of reducing the number of animals used and increasing the number of infective larvae. The filarial larval line was maintained in jirds (*Meriones unguiculatus*) and soft ticks (*Ornithodoros moubata*). The optimal infection dose for jirds was determined to be 80 infective larvae (L3). The average number of adult worms in groups of animals ranged between 18 and 30. A stable microfilaremia developed in the jirds, with only a few animals showing pathological changes because of the infection. A simple membrane feeding apparatus was used for mass feeding of ticks, and infection of ticks with microfilariae (mf) using this method resulted in an average of 594±527.2 L3 per tick. Both L3 larvae and mf were successfully cryopreserved in liquid nitrogen using a simple technique. This approach has significantly reduced the number of experimental animals required, with the current need being only 30-40% of the number originally needed to complete the life cycle (647). In a study where *Wolbachia* endosymbionts, previously found in filarial nematodes, were detected in tick pools consisting of nymphs and adults of *Amblyomma americanum* collected in Maryland, the presence of filarial nematodes in the tick samples was investigated using PCR. The results showed that filarial nematodes were present in 70% of the *Wolbachia*-positive ticks, compared to only 9% of the *Wolbachia*-negative tick samples (649). This finding highlights a potential association between *Wolbachia* infection and the presence of filarial nematodes in ticks. In another study, dermal microfilariae *Cercopithifilaria* sp. s. l. was investigated in skin samples (n=917) and ticks (n=890) collected from dogs at various times in Italy, Central Spain, and Eastern Greece. The overall prevalence of *Cercopithifilaria* sp. in the sampled dog populations was 13.9% by microscopy of skin sediments and 10.5% by PCR analysis of skin samples. In Spain, up to 21.6% of dogs tested positive by microscopic examination, while 45.5% were positive by PCR. In Italy, cumulative incidence rates in dogs from two sites ranged from 7.7% to 13.9%. A low level of agreement was observed between the two diagnostic methods (microscopic examination and PCR) at sites where samples were processed simultaneously. The tick infestation rate, as determined by tick dissection, ranged from 5.2% to 16.7%, which was higher than the rate detected by PCR (from 0% to 3.9%). Tick infestation was significantly associated with *Cercopithifilaria* sp. infestation in dogs at two out of four sites. Morphometric analysis of developing larvae found in ticks revealed as many as 1,469 larvae in a single tick. This study highlights the variability in diagnostic techniques and the significant role of tick infestation in the transmission of *Cercopithifilaria* sp. among dogs across multiple regions (650). Following the discovery of filarial nematodes of the genus *Acanthocheilonema* in *Amblyomma americanum* ticks, further investigation was conducted to examine the presence of filarial nematodes and their potential role as intermediate hosts in *Ixodes scapularis* ticks collected from southern Connecticut. *In situ* hybridization, using filarial nematode-specific sequences, was performed on both fasted nymphs and fasted mature *Ixodes scapularis* ticks, which were collected through standard sheet dragging techniques from the field in southern Connecticut. This analysis confirmed the presence of filarial nematodes in *Ixodes* ticks. Filarial nematode-specific DNA sequences were successfully amplified and verified through direct sequencing in both nymphal and adult *Ixodes* ticks using PCR primers specific to general filarial nematodes or the Onchocercidae family. Phylogenetic analysis of the 12S *rDNA* gene sequence revealed that the filarial nematode infecting *Ixodes scapularis* ticks is most closely related to the species found in *Amblyomma americanum* ticks and belongs to the genus *Acanthocheilonema*. Furthermore, our data demonstrated that the infection rate of these filarial nematodes in *Ixodes* ticks was relatively high, with infection rates of approximately 22% in nymphs and 30% in adults. These findings confirm that the filarial nematode infection in *Ixodes* ticks is similar to that observed in *Amblyomma americanum* ticks (651). This study highlights the significant presence of filarial nematodes in *Ixodes scapularis* ticks and underscores the potential role of these ticks as intermediate hosts for *Acanthocheilonema* species. The results contribute to a deeper understanding of the ecological dynamics between ticks and filarial nematodes and their potential public health implications. Due to the morphological similarities among species in the *Rhipicephalus sanguineus* group, identification is challenging. Recently, following the morphological and molecular characterization of tick samples collected from dogs across all continents, *Rhipicephalus sanguineus* s.l., *Rhipicephalus turanicus*, and three different operational taxonomic units (i.e., *Rhipicephalus* sp. I-III) were defined. To further investigate, a comprehensive molecular epidemiological study was conducted to detect vector-borne pathogens in dogs, including *Anaplasma platys*, *Cercopithifilaria* spp., *Ehrlichia canis*, and *Hepatozoon canis*, in ticks belonging to the *Rhipicephalus sanguineus* group. A total of 204 tick samples collected from infested dogs were examined. The samples were identified as: *Rhipicephalus sanguineus* s.l. (n=81), *Rhipicephalus turanicus* (n=17), *Rhipicephalus* sp. I (n=66), *Rhipicephalus* sp. II (n=37), and *Rhipicephalus* sp. III (n=3). PCR tests were performed to detect mitochondrial and ribosomal target genes of *Cercopithifilaria* spp., *Anaplasma platys*, *Ehrlichia canis*, and *Hepatozoon canis*. Among the 204 tick samples examined, 2.5%, 7.4%, and 21.6% were found positive for *Anaplasma platys*, *Hepatozoon canis*, and *Cercopithifilaria* spp., respectively. Additionally, coinfections with two pathogens (*Cercopithifilaria bainae* and *Anaplasma platys* or *Hepatozoon canis*) were detected in four tick samples. Epidemiologically, this study suggests a relationship between ticks belonging to the *Rhipicephalus sanguineus* group and the geographical distribution of *Anaplasma platys*, *Hepatozoon canis*, and *Cercopithifilaria* spp. (652).

In a study, *Ambylomma americanum* ticks collected from the Northern District of Virginia, United States, were tested for the presence of filarial nematode genetic material. Positive samples were sequenced for further analysis. The results revealed DNA from a *Monanema*-like filarial nematode. Phylogenetic analysis showed that this DNA was closely related to a filarial nematode previously found in *Amblyomma americanum* populations in Maryland, as well as to parasites identified in *Ixodes scapularis* from southern Connecticut. This suggests a potential connection between these parasites and different tick species across regions. However, further research is needed to clarify whether these ticks act as intermediate hosts or vectors for filarial nematodes (653). In a study conducted in Brazil, the presence of *Cercopithifilaria* spp. was investigated in the tick population of *Rhipicephalus sanguineus* s.l. collected from tick-infested dogs. A total of 1,906 ticks (one larva, 294 nymphs, and 1,611 adults) were collected from 155 infested dogs. All ticks were identified as *Rhipicephalus sanguineus*. Filaroid larvae detected during tick dissection were identified to species level based on morphological and morphometric characteristics. In this study, *Cercopithifilaria bainae* larvae were found in 2.68% of the *Rhipicephalus sanguineus* s.l. ticks, and molecular methods were used to confirm their identity. This prevalence was considered epidemiologically significant (656).

A study on the molecular prevalence of tick-borne filarioids was conducted in French Guiana, South America, focusing on areas covered by tropical forests. The researchers collected 682 tick samples from 22 species across six tick genera. Of these, 21 ticks (3.1%) from the species *Amblyomma cajennense*, *Amblyomma oblongoguttatum*, *Amblyomma romitii*, *Ixodes luciae*, and *Rhipicephalus sanguineus* s. l. were found positive for filarioid infections. Molecular typing and phylogenetic analysis revealed that all of these filarioids belong to the genus *Dipetalonema*. Notably, while the filarioid detected in *Rhipicephalus sanguineus* s. l. is a previously described species, *Cercopithifilaria bainae*, the other filarioids identified are new to science. They are closely related to but distinct from known species in the genera *Cercopithifilaria*, *Cruorifilaria,* and *Dipetalonema*. From an epidemiological standpoint, the study highlights a concerning finding: a wide range of mammals in French Guiana could potentially serve as hosts for these filarioid species. Specifically, dogs, capybaras, and opossums are identified as the most likely candidate hosts for some of the filarial worms. The detection of *Dipetalonema* species in ticks that are of high medical and veterinary importance underscores the potential health risks, both for humans and animals, linked to these emerging tick-borne filarioids. This epidemiological data calls for increased attention to their role in disease transmission in the region (655). In a review of filarial nematodes focusing on the family Onchocercidae, recent scientific literatures on tick-borne genera have been evaluated. Five genera of onchocercid filarial nematodes—*Cercopithifilaria*, *Cherylia*, *Cruorifilaria*, *Monanema*, and *Yatesia*—were highlighted for their demonstrated vector-parasite relationships with ticks. In contrast, *Acanthocheilonema* was detected only through molecular methods, without confirmed vector competence (657).

Consequently, ongoing studies on tick-borne filarial nematodes focus on the epidemiological significance of their presence in ticks.

Tick-borne Filarial Nematodes in Türkiye

Although there are limited reports of canine filariasis in dogs (151) no articles have been documented cases of tick-borne filarial nematodes in Türkiye.

Tick-borne Fungal Pathogen: A Cosmopolite and opportunistic *Scopulariopsis brevicaulis*

Scopulariopsis brevicaulis Bainier, 1907, is a saprophytic fungus commonly found in soil and the environment and is also mechanically and maternally transmitted by ticks (658). Many fungi of this type are anamorphs of ascomycetes, with *Scopulariopsis brevicaulis* being one of them, known for producing abundant conidia (658). *Scopulariopsis brevicaulis*, systematically classified in the Microascaceae family (659), has been identified as a cause of dermatomycosis in both humans (94,660,661) and animals (662-665). The genus *Scopulariopsis* consists of non-dermatophytic filamentous fungi, and *Scopulariopsis* species are important pathogens, particularly in immunocompromised individuals (666). This typically saprophyte fungus, can occasionally cause infections that may persist despite extended antifungal treatments, often leading to severe outcomes, including death (667).

Possible Association of Ticks and *Scopulariopsis brevicaulis*

Emerging Concerns in Human Mycoses: A nondermatophyte filamentous fungus, *Scopulariopsis brevicaulis* has been increasingly identified as a causative agent in human infections, particularly onychomycosis, accounting for about 2% of nail fungal infections (668). Traditionally considered a saprophytic soil fungus, it has recently gained clinical attention as an opportunistic pathogen in immunocompromised individuals, including patients with AIDS, organ or stem cell transplants, leukemia, and those receiving corticosteroids (660,661,669).

Environmental Exposure and the Hypothesized Role of Ticks: Given its natural habitat in soil, decaying wood, and organic matter, *Scopulariopsis brevicaulis* can be found in the same environments that ticks inhabit. Though direct evidence linking ticks as biological vectors of *Scopulariopsis brevicaulis* is lacking, their potential role as mechanical carriers of fungal spores is plausible, especially in rural settings where tick-human contact is common. Ticks, due to their frequent contact with soil and animal hosts, could potentially transmit fungal spores into skin abrasions or bite sites. The incidence of mycoses in dogs and other domestic animals is believed to increase the risk of human exposure to mycotic infections (670). This hypothesis gains support from epidemiological data showing that *Scopulariopsis brevicaulis* infections are more prevalent in rural populations, particularly in individuals with dermatoses, circulatory insufficiency, trauma, or metabolic disorders all of which may increase susceptibility following tick bites or environmental exposure (669).

Clinical Presentations Possibly Linked to Environmental or Tick Exposure: Clinical manifestations of *Scopulariopsis brevicaulis* range from onychomycosis and cutaneous lesions to deep systemic infections. Skin infections may present as erythematous, scaly plaques or ulcerative granulomas, often mistaken for dermatophytosis (671-673). A notable granulomatous skin infection caused by *Scopulariopsis brevicaulis* was documented (674). Another notable case involved a 43-year-old male with granulomatous cheilitis, responding to itraconazole (672). Recurrent infections after treatment discontinuation suggest possible environmental re-exposure, potentially through unnoticed skin breaks or tick bites (675,676).

Systemic and Invasive Infections: In immunocompromised individuals, especially pediatric bone marrow transplant recipients and leukemia patients, *Scopulariopsis brevicaulis* has been linked to severe systemic infections, such as: sinonasal fungal masses (677), fungal keratitis following trauma, possibly from contaminated environmental sources (678,679) fatal disseminated infections post-transplantation (679,680), pulmonary infections mimicking fungal balls and pneumonitis (660). These infections could arise from inhalation or transcutaneous inoculation of fungal spores, with ticks acting as inadvertent carriers of such spores in immunologically vulnerable individuals.

Therapeutic Resistance and Management Challenges: *Scopulariopsis brevicaulis* shows significant resistance to many antifungals (681) Flucytosine and itraconazole are largely ineffective (682), Amphotericin B, voriconazole, and terbinafine show high MICs (682), clinical outcomes often remain poor despite prolonged treatment, especially in cases of disseminated disease (683-685). Refractory cases often require surgical intervention, long-term antifungal combinations, and, potentially, immunotherapy (677,686).

Increased Risk in Immunocompromised and Rural Populations: Patients with AIDS, undergoing chemotherapy, or stem cell transplantation are especially at risk (687-691). In these groups, fungal infections caused by non-*Aspergillus* species, including *Scopulariopsis brevicaulis*, are rising (692,693). Environmental exposure—including from animal reservoirs or insect vectors like ticks—may be an overlooked factor (670). A unique case also reported *Microascus cirrosus* (teleomorph of *Scopulariopsis brevicaulis*) in a leukemia patient, with presumed origin from stored grains, another tick-associated environment (666).

In conclusion, although there is no direct confirmation that ticks are biological vectors for *Scopulariopsis brevicaulis*, it is important to consider reports of their potential as mechanical vectors in environmental transmission.

The Transmission of *Scopulariopsis brevicaulis* by Ticks

Indeed, there is an endosymbiotic association between ticks and *Scopulariopsis brevicaulis*. Both ticks and higher fungi (e.g., conidial fungi) are well-known parasites of humans and livestock. Due to global warming, tick infestations have become a significant global challenge in recent years, resulting in substantial economic losses. These infestations contribute to poverty and hardship, especially in developing countries and regions with lower socioeconomic levels. Intensive efforts are being made worldwide to control these parasites, and as such, several studies have been conducted. For instance, the American dog tick *Dermacentor variabilis*, a well-known vector of RMSF (92), has been associated with the widespread fungus *Scopulariopsis brevicaulis*, which causes dermatomycosis (669). These two distinct groups of parasites, ticks and fungi, have been found to be closely related both in nature and under laboratory conditions (694,695). *Scopulariopsis brevicaulis* is generally not entomopathogenic to the tick *Dermacentor variabilis*, and its potential for biological control against this tick species is low (694). However, the association between ticks and this fungus raises significant health concerns. The presence of one parasite (the tick) may facilitate the spread of the other (the fungus). This relationship has often been interpreted as a type of endomycosymbiosis between ticks and fungi, a type of commensalism in which the tick is neither harmed nor benefited, while the fungus probably provides some nutritional benefit (696). Understanding this relationship is crucial for exploring how these organisms coexist. In epidemiologically enzootic stable regions, ixodid ticks infest their hosts for blood feeding and remain attached during the feeding process. When not feeding, ticks typically prefer organic-rich and moist environments (microhabitats such as soil, leaves, and organic debris) to protect themselves from natural enemies. However, these organic materials also serve as breeding grounds for certain entomopathogens. Among the microorganisms in these habitats, there are fungi that are entomopathogenic to ticks and act as natural regulators of tick populations in the wild (696-698). Most fungal spores (e.g., conidia) that come into contact with the tick's cuticle fail to germinate. However, in more aggressive fungal species, conidia can produce infectious hyphae that penetrate through external openings (e.g., glands, mouth, anus, or stigmas) or directly through the cuticle (696). Once the fungus enters the tick, it proliferates and releases proteolytic and chitinolytic enzymes, which break down the tick's internal tissues and allow the fungus to use the nutrient-rich contents as a substrate (699). This growing mass of fungal hyphae disrupts the tick's ability to regulate its water balance, leading to dehydration and death. This process involves not only the depletion of water and nutrients but also the uncontrolled spread of the fungus within the tick, causing erratic movements and excessive water loss (700). Conidia of various entomopathogenic fungi (e.g., *Metarhizium anisopliae*, *Beauveria bassiana*) have been utilized for biological control of ticks (697,701). This approach has proven effective in controlling adult ticks of several species (e.g., *Amblyomma*, *Ixodes*, *Rhipicephalus*), achieving nearly 100% mortality. However, it has been less effective (0-20% mortality) against *Dermacentor variabilis* (702,703). The mechanism behind the high resistance observed in *Dermacentor variabilis* remains unclear. It has been suggested that this resistance may be due to the commensal relationship between *Scopulariopsis brevicaulis* and *Dermacentor variabilis*. Actually, *Scopulariopsis brevicaulis*, like other entomopathogenic fungi (696), typically enters ticks through external orifices. However, Benoit and Yoder (704) demonstrated that this fungus is transmitted maternally (but not transovarially) from one generation to the next, contaminating eggs within the female tick's genital chamber before oviposition. Remarkably, the fungus persists in the tick until adulthood. The life cycle of *Scopulariopsis brevicaulis* in *Dermacentor variabilis* favors areas around the large wax glands (previously referred to as "sagittiform sensilla") as a germination site, producing conidia that infect adjacent glands. Notably, no fungal species other than *Scopulariopsis brevicaulis* have been recovered from *Dermacentor variabilis* ticks. In fact, only *Scopulariopsis brevicaulis* has been found, with more than 85% of eggs, larvae, nymphs, and adults testing positive for *Scopulariopsis brevicaulis* (695). Another important epidemiological concern is the mechanical vector capacity of ixodid tick species for *Scopulariopsis brevicaulis*. A study investigating the ability of ticks to transmit the fungus found that over 85% of ticks examined were infected with *Scopulariopsis brevicaulis*. However, the presence of conidia in saliva samples from larvae, nymphs, and adults was low (0-5%), and the fungus was rarely recovered from feeding sites. These findings suggest that ticks primarily act as mechanical vectors for fungal transmission, physically transferring the fungus to new hosts without actively infecting them through blood feeding (705). On the other hand, a study tested the hypothesis that *Dermacentor variabilis* ticks, which have an endosymbiotic relationship with *Scopulariopsis brevicaulis*, are protected against another entomopathogen, *Metarhizium anisopliae*. Results showed that the susceptibility of female ticks varied based on the presence or absence of *Scopulariopsis brevicaulis*, with the fungus offering protection against *Metarhizium anisopliae* (706). However, in nature, various entomopathogenic fungi serve as natural enemies of ticks (701). In some African countries, ticks and TBDs represent a significant economic burden. In Sudan, tick challenges and TBDs are widespread, causing high morbidity and mortality. They also contribute substantially to economic losses, including production losses, as well as control and treatment costs. Tick control in Sudan is primarily reliant on the use of chemical acaricides. However, due to the known disadvantages of chemical control, the use of entomopathogenic fungi as an alternative control method has been considered. In a study aimed at evaluating the use of entomopathogenic fungi, *Amblyomma lepidum* ticks were collected from animals brought to the El Damazin slaughterhouse in the Blue Nile State of Central Sudan. The ticks were collected mainly to establish laboratory colonies. During the process of colony establishment, it was observed that the ticks developed fungal growth and subsequently died. The ticks were incubated at 27 °C with 85% RH. Scrapings taken from the white mat covering the scutum of the dead ticks were inoculated onto Sabouraud and brain heart infusion agar, resulting in the isolation of pure fungal cultures. *Scopulariopsis brevicaulis* was isolated from the pure culture, and the isolate identification was confirmed by the biotechnical laboratory in Denmark. The pathogenicity of spore suspensions and culture filtrates from the isolated fungus was tested on the larvae, nymphs, and adult stages of *Hyalomma anatolicum* and *Amblyomma lepidum*. The study found a high mortality rate in the larvae, while adult ticks exhibited a reduced biotic potential. These findings suggest that the metabolites of *Scopulariopsis brevicaulis* can be used as "biological control agents" in tick management (662). In another study conducted in Sudan, the use of entomopathogenic fungi as an alternative method for tick control was evaluated. Researchers examined the effects of *Scopulariopsis brevicaulis*, isolated and cultured from *Amblyomma lepidum* ticks collected in the field using the "sheet dragging method" in an enzootic stable region. This study explored the impact of this fungus on the larval, nymphal, and adult stages of *Hyalomma anatolicum* and *Amblyomma lepidum* ticks. While high mortality rates were observed in the larvae, adult ticks were found to be resistant to the fungus. This study underscores the variable effectiveness of fungal treatments across different tick life stages, with larvae showing high susceptibility and adults exhibiting resistance, which could limit the overall efficacy of fungal-based tick control strategies (707). On the other hand, *Scopulariopsis* species can cause fatal fungal infections in various domestic animals, leading to significant economic losses. In a case study of a 2-year-old mixed-breed male dog necropsied in Oklahoma, United States, a severe mycotic infection was found in addition to a distemper infection. *S. chartarum* was isolated as the mycotic agent from the dog with multisystemic infection (663). In Japan, a 6-month-old female calf gradually weakened and died over a period of 40 days. At necropsy, hyperkeratotic nodules were found covering almost the entire body surface. *Scopulariopsis brevicaulis* was isolated from the skin of the calf, and the molecular characterization of the isolate was performed (664). In a study in Türkiye, it was reported that *Scopulariopsis brevicaulis* was isolated from a dead goat and a sick kid; the sick kid was successfully treated with Itraconazole (708). Furthermore, *Scopulariopsis brevicaulis* has been recognized as a potential pathogen that poses a threat to the health of laboratory animals in experimental animal production and research centers. In a case study conducted in Türkiye in 2019, *Scopulariopsis brevicaulis* infection was identified in samples collected from male and female wistar rats exhibiting hair loss and skin lesions at a laboratory animal breeding facility (665).

Tick-borne *Scopulariopsis brevicaulis* and Environmental Considerations: Ticks, particularly *Dermacentor variabilis* ticks, have been associated with *Scopulariopsis brevicaulis* infections, especially in rural areas (669). While *Scopulariopsis brevicaulis* is not entomopathogenic (does not kill the tick), it may act as a commensal fungus, providing nutritional benefits to ticks (694). In enzootic stable regions, ticks prefer organic-rich environments that also serve as breeding grounds for various entomopathogens. *Scopulariopsis brevicaulis*, which thrives in such environments, may infect ticks, especially in their larvae and nymph stages (695). Ticks may act as mechanical vectors, transferring fungal spores to new hosts. However, *Scopulariopsis brevicaulis* is not transmitted via blood-feeding, but rather through direct contact (705). Additionally, some studies suggest that *Scopulariopsis brevicaulis* may protect ticks from other entomopathogens, such as *Metarhizium anisopliae*, demonstrating a potential protective relationship between the fungus and ticks (706).

Ultimately, the association between ticks and *Scopulariopsis brevicaulis* emphasizes the importance of enhanced surveillance for both tick-borne and fungal diseases, especially in areas with high tick populations. *Scopulariopsis brevicaulis* is an emerging opportunistic pathogen that poses serious risks to immunocompromised individuals, such as those undergoing chemotherapy or transplants. Its growing resistance to standard antifungal treatments underscores the urgent need for alternative therapies and improved disease monitoring.

Tick-borne Infectious Prion Protein (PrPCWD)

Chronic wasting disease (CWD), a fatal neurodegenerative disease, was first observed in mule deer in Colorado in 1967 and described as a “wasting syndrome” in 1978 (709). As of 2023, CWD has been documented in both captive and free-ranging deer across 30 United States and parts of Canada (710). Transmission of CWD among deer occurs through direct contact with an infected animal (e.g., through allogrooming) or indirect contact with a contaminated environment. However, it has been speculated that blood-sucking ectoparasitic arthropods, such as ticks, may also serve as mechanical vectors (710). Live animals shed prions in their saliva, feces, and urine; these prions can bind to soil and remain infectious for extended periods (709). CWD in deer is caused by an infectious prion protein (PrPCWD). It has been speculated that the presence of PrPCWD in the bloodstream may pose a risk for mechanical transmission via hematophagous ectoparasitic arthropods, such as ticks. Intensive tick infestations are commonly observed in deer, and affected animals often engage in mutual grooming behavior (allogrooming) to remove these parasites. During this behavior, they may inadvertently ingest ticks that have taken a blood meal. If these ticks carry PrPCWD, they may become vectors for horizontal transmission, potentially infecting healthy deer. Therefore, it has been hypothesized that in endemic areas, deer may be exposed to CWD by ingesting infected ticks during allogrooming (710). To investigate the potential role of ticks in CWD transmission, an experimental tick-feeding study was conducted. This study aimed to determine whether ticks collected from free-ranging and wild white-tailed deer (*Odocoileus virginianus*) could acquire and transmit infectious prions. Researchers established a real-time quaking-induced conversion (RT-QuIC) assay and fed black-legged ticks (*Ixodes scapularis*) with PrPCWD enriched blood using artificial membranes. The experiments demonstrated that ticks not only acquired but also excreted PrPCWD, indicating the potential for mechanical transmission. Using RT-QuIC, pathogenic prion activity was detected in 6 out of 15 tick samples (40%) collected from wild CWD-infected white-tailed deer. Prion seeding activity observed in ticks was compared to 10–1000 ng of CWD-positive retropharyngeal lymph node tissue from infected deer. The estimated median infectious dose per tick ranged from 0.3 to 42.4 ng, indicating that ticks can ingest biologically significant amounts of PrPCWD and potentially transmit it. These findings support the hypothesis that ticks may serve as mechanical vectors of PrPCWD, posing a potential risk for CWD transmission among deer populations (710). Essentially, comprehensive studies on the epidemiology of deer CWD are still limited. Since CWD can be transmitted through both direct and indirect mechanisms, anthropogenic activities may play a significant role in spreading the disease. One particular concern is the handling of deer and their carcasses when the CWD status is unknown. Therefore, taxidermy procedures involving deer are especially important from an epidemiological perspective. To investigate this issue, researchers screened for infectious prions using the protein misfolding cyclic amplification technique at a taxidermy facility suspected of potential exposure to CWD prions. Infectious prion protein was detected in biological and environmental samples collected from the facility (711). These preliminary data, together with epidemiological observations, may be critical for disease monitoring and the development of control strategies, especially in endemic areas. As with bovine spongiform encephalopathy (BSE, or “mad cow disease”) in cattle, the zoonotic potential of PrPCWD should be thoroughly investigated to assess the risks it may pose to other species, particularly humans (712). Tick-borne bacteria, protozoa, filarial nematodes, fungi, and prion are presented in Table 3 and Figure 2. The geographical distribution of reported TBDs in both humans and animals in Türkiye is illustrated in Figure 3, while the major TBDs affecting animals are depicted in Figure 4.

Tick Vector Competence and Emerging Threats of TBDs

Understanding how ticks interact with pathogens, how effectively they can transmit bacteria, viruses, and protozoa, and their vector competence for these pathogens is a critically important issue (10).

Tick Vector Competence: The most critical component of vector capacity is “vector competence”, which refers to a vector’s ability—in this case, the vector tick—to transmit a pathogen. In vector ticks, this ability is determined by genetic factors. These factors influence the interactions between the tick, the pathogen, and the susceptible host. Therefore, understanding the mechanisms that affect vector competence and govern tick-pathogen interactions has become crucial for developing new molecular approaches to combat TBDs. The vector competence of ticks involves the acquisition, maintenance, and transmission of pathogens—including those of bacterial, viral, protozoan, nematode, fungal, and prion origin—to susceptible hosts such as humans, domestic animals, or wildlife, particularly in areas of epidemiological enzootic stability. The vector competence of ticks is also influenced by several factors, including the tick species, the type of TBP, the mode of pathogen acquisition, and other epidemiological and ecological determinants (10).

Tick species: Not all ticks can transmit every pathogen. The tick’s physiology, immune system response, and the duration and frequency of feeding (since some pathogens take longer to transmit) all affect the vectorial capacity and competence of ticks (77). Hard ticks attach to their hosts for extended periods, feeding on blood for up to 8 days during both the larval and nymphal stages, and for 12 days or more during the adult stage (714). During blood feeding, ticks ingest large amounts of blood from the host and inject significant quantities of saliva (715). Adult females of ixodid ticks uptake blood in two phases: a slow phase lasting 7 or more days, followed by a rapid engorgement phase that occurs within 12 to 24 hours. During the rapid phase, an engorged adult female tick can increase its weight by more than 100 times its unfed weight (715). Significant morphological changes occur in the salivary glands of ixodid ticks during attachment and feeding (716). Tick salivary glands secrete a diverse array of lipids, peptides, and large proteins during blood feeding (717). Recent salivary gland transcriptome analyses have revealed the diversity of the pharmacological repertoire and the changes in gene expression that occur throughout the course of blood feeding (56,717). They usually transmit pathogens during the blood-feeding process, which occurs in different life stages (larvae, nymphs, adults). Pathogen transmission can occur at different rates depending on the life stage of the tick, with nymphs and adults typically being more competent vectors due to their longer feeding periods. Different species of ticks have varying levels of vector competence. Some ticks are more efficient vectors of specific pathogens due to their ability to acquire, maintain, and transmit them. For example, *Ixodes scapularis* is the primary vector of *Borrelia burgdorferi* (Lyme disease) in North America, *Dermacentor variabilis* is associated with transmission of *Rickettsia rickettsii* (RMSF) (10), *Rhipicephalus sanguineus* can transmit *Babesia canis* (canine babesiosis) (718).

Types of Pathogens Transmitted by Ticks: This process is primarily associated with the pathogen's capacity to survive and replicate within the tick's body. Some TBPs, for example, bacteria [*Borrelia burgdorferi, Rickettsia rickettsii*, *Anaplasma phagocytophilum*, *Ehrlichia* spp. (10), and *Francisella tularensis* (719)] viruses [TBEV, CCHF, POWV, CTFV) (234)], protozoa (*Babesia* spp.) (114,720), and (*Theileria* spp.) (10,41), nematodes (tick-borne filarials) (657), fungi (*Scapulariopsis brevicaulis* (704) and PrPCWD (710) are transmitted by ticks.

Epidemiological and Ecological Factors Influencing Vector Competence: For example, several factors influence the ability of ticks to act as competent vectors for pathogens. These factors include the tick's biology, the nature of the pathogen and pathogen adaptation, and the environmental conditions that affect tick survival and pathogen transmission (10).

Pathogen Adaptation: For a pathogen to be successfully transmitted by a tick, it must be able to survive and replicate within the tick's body (139). Vector competence depends on the compatibility between the tick and the pathogen. Some pathogens, like *Borrelia burgdorferi*, have evolved specific adaptations that

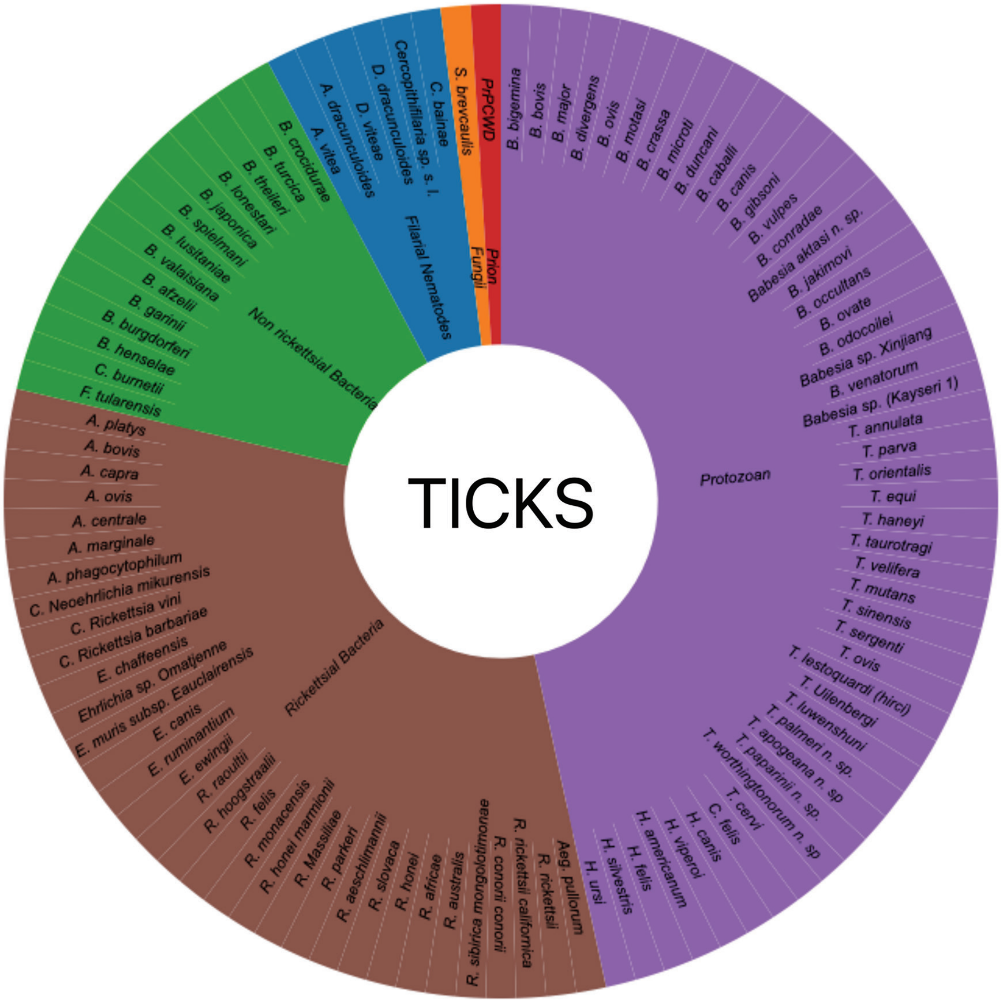


Figure 2. Tick-borne Pathogens include Bacteria, Protozoans, Filarial Nematodes, Fungi and Prion

allow them to persist in the tick's midgut and then migrate to the salivary glands, where they are injected into the host during feeding. Additionally, the pathogen must be able to infect the host and multiply. In the case of *Babesia*, the protozoan parasite can undergo stages of its life cycle within the tick's gut and salivary glands and then be transmitted to the host through tick bites (10).

Environmental and Ecological Factors of Enzootic Stable Region: The environment plays a significant role in influencing tick populations and their vector competence (303). Factors like temperature, humidity, and vegetation can affect tick survival, activity, and the likelihood of encounters between ticks and hosts. Areas with high humidity and wooded environments are often ideal habitats for ticks, which are more likely to come into contact with hosts and transmit pathogens (10).

Acquire, Maintain, and Transmit Pathogens: Ticks acquire pathogens when they feed on an infected host. Once the pathogen is ingested, it must survive and replicate within the tick (240,266,721). The process of pathogen acquisition, maintenance, and transmission generally follows these stages:

Acquisition: A tick acquires a pathogen when it feeds on an infected host. The pathogen is typically present in the host's blood, tissues, or body fluids, which the tick ingests while feeding (10).

Maintenance: Once the pathogen is acquired, it must survive and persist within the tick. For some pathogens (like *Borrelia* or *Babesia*) (722,723), this means the pathogen will undergo replication or enter a latent state within the tick's gut or other organs. In some cases, the pathogen can migrate to the tick's salivary glands, where it can be passed to the host during subsequent feedings.

Transmission: Actually, the transmission of TBPs can occur through both vertical and horizontal mechanisms. Once a pathogen is acquired and maintained within the tick, it is transmitted to a new host during subsequent blood meals. During feeding, the tick injects saliva containing the pathogen into the host's bloodstream. The duration of tick attachment plays a significant role in transmission risk, with prolonged feeding periods markedly increasing the likelihood of pathogen transfer (266).

Emerging Threats of TBDs

The combination of anthropogenic factors such as global warming, deforestation and land use changes, abandonment of agriculture and pastureland, urbanization and improper development, changes in animal husbandry have contributed to the emergence of new TBDs or the reemergence of previously controlled diseases (141). TBDs, like Lyme disease, TBE, and anaplasmosis, represent major threats to both animal and human health. The resurgence and spread of these diseases are often exacerbated by factors such as:

(i) Enzootic Stability and Instability: Some TBDs remain enzootic (localized) in certain regions, but climate changes or ecosystem disturbances can create conditions for the disease to spread into new areas (724). Similarly, changes in animal populations, host availability, and tick life cycles can lead to instability, allowing new pathogens to emerge or become more virulent (725).

Tick-Borne Encephalitis Virus (TBEV)	Human Anaplasmosis (HA)	Lyme Borreliosis (LYMB)	Q Fever (QFEV)	Equine piroplasmosis (EPRP)	Cat anaplasmosis (CANP)
Crimean Congo Hemorrhagic Fever (CCHFV)	Ehrlichiosis (EHR)	Tularemia (TUL)	Dermatophilus (DMPH)	Animal anaplasmosis (AANP)	Hepatozoonosis (HPTZ)
Louping Ill Virus (LIV)	Neoehrlichiosis (NEO)	Tick- borne Relapsing Fever (TBRF)	Human babesiosis (HBAB)	Ehrlichiosis (EHR)	Cytauxzoonosis (CYTX)
Lumpy Skin Disease Virus (LSDV)	Tick- borne Typhus (TBT)	Bartonellosis (BRT)	Bovine babesiosis (BBAB)	Canine babesiosis (CBAB)	Bovine theileriosis (BTHL)
Turkish Sheep Encephalitis Virus (TSEV)	Other tick- borne Spotted fever (TBSF)	Hemoplasmosis (HMP)	Ovine piroplasmosis (OPRP)	Canine Granulocytic Anaplasmosis (CGAN)	

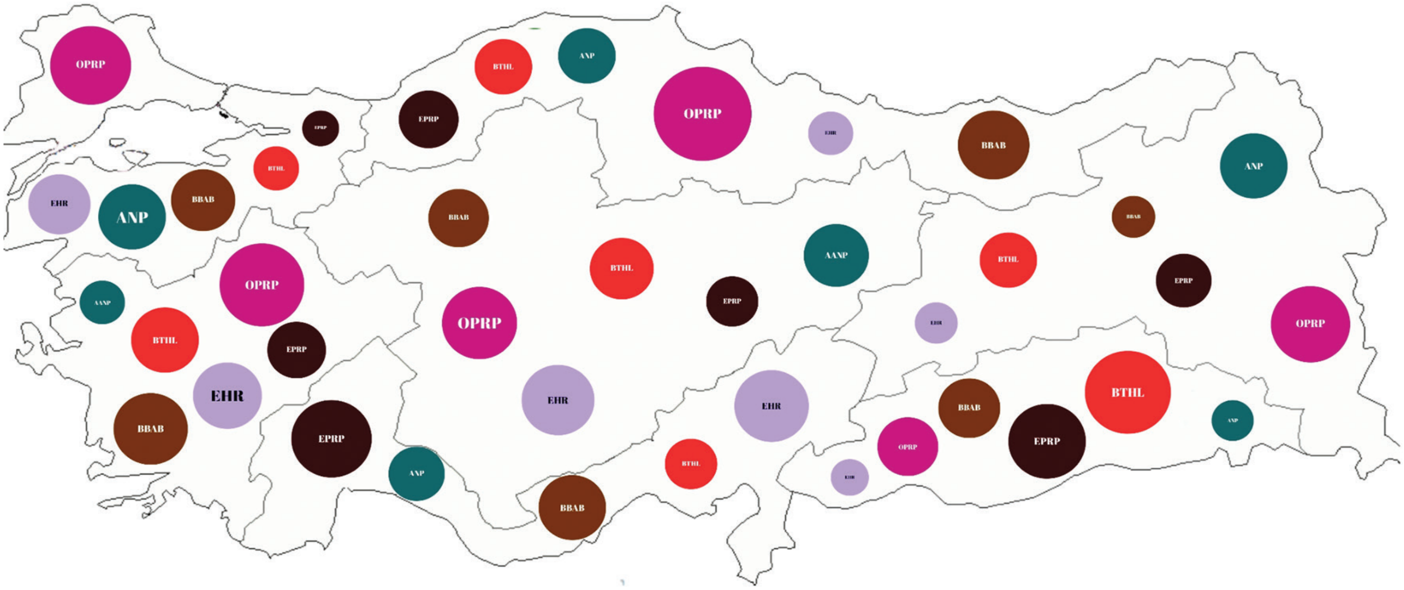
Figure 3. Geographic distribution of tick-borne diseases reported in humans and animals across seven regions of Türkiye. The presence of each infection is indicated by a circle bearing its abbreviation, as shown in the table below the map

(ii) Detection of New Pathogens: Advances in metagenomics and molecular diagnostics have dramatically improved the detection of previously unknown TBVs and pathogens (726). This has led to the identification of new or emerging diseases that were not previously recognized in endemic areas. New outbreaks, sometimes in regions that were previously free of certain diseases, pose significant public health challenges. For example, the detection of the Heartland (727) virus and POWV (728) are examples of pathogens recently identified through advances in genomic techniques.

(iii) Ecosystem and Host Dynamics: Changes in the populations of wildlife, particularly those that act as tick hosts (e.g., deer, rodents), can impact the abundance of ticks. Overabundant deer populations, for example, can act as primary hosts for ticks, leading to a rise in tick numbers in certain areas. Similarly, the dilution effect (where increased biodiversity can reduce the risk of certain diseases) may be disrupted if ecosystems are less diverse, contributing to the spread of TBPs (729-732).

(iv) Geographical Spread: Tick species that were once limited to specific regions are now being detected in areas that were historically free of ticks or TBDs. This geographical spread is often linked to global climate shifts, migration patterns, and changes in land use. For instance, ticks previously confined to southern Europe are now being found further north as warmer conditions prevail, and similarly, ticks are migrating into new regions across North America (721). Additionally, it has been suggested that population genetics plays a crucial role in the genetic diversity of tick populations and their capacity to adapt to environmental changes (141).

(v) Living Conditions: It was emphasized that TBDs pose a significant threat to public health, highlighting the need for a comprehensive understanding of risk factors (733). Among the growing risks, challenges linked to demographic structures, the vulnerability of workers in environments such as forests and fields, those handling farm animals, and inadequate ecocentric education were identified. Additionally, it was noted that owning pets and having close interactions with animals are also associated with an increased risk (734). However, some latest approaches, such as the discovery of different plasmids in various *Rickettsia* species and the use of microbial gene expression and mutational



TBDs/Region	Central Anatolia			Black Sea			Eastern Anatolia			Southeastern Anatolia			Mediterrenian			Aegean			Marmara			Turkey		
	Mic	Mol	Ser	Mic	Mol	Ser	Mic	Mol	Ser	Mic	Mol	Ser	Mic	Mol	Ser	Mic	Mol	Ser	Mic	Mol	Ser	Mic	Mol	Ser
Bovine Babesiosis (BBAB)	9,20 (n=10)	6,51 (n=28)	30,06 (n=20)	10,18 (n=4)	3,27 (n=10)	30,60 (n=13)	1,78 (n=6)	7,50 (n=2)	11,30 (n=9)	5,47 (n=2)	11,20 (n=1)	33,06 (n=3)	31,8 (n=1)	9,00 (n=3)	36,61 (n=11)	4,00 (n=1)	2,34 (n=5)	46,13 (n=3)	22,93 (n=2)	0,86 (n=2)	30,90 (n=3)	31,73 (n=13)	5,81 (n=7)	28,90 (n=13)
Bovine Theileriosis (BTHL)	30,95 (n=19)	17,63 (n=17)	31,58 (n=17)	15,75 (n=8)	-	29,13 (n=4)	21,48 (n=12)	18,99 (n=13)	30,33 (n=4)	24,50 (n=3)	-	57,97 (n=3)	5,35 (n=4)	21,13 (n=3)	10,74 (n=5)	26,4 (n=3)	43,76 (n=12)	35,50 (n=2)	20,30 (n=3)	-	19,85 (n=4)	23,63 (n=9)	19,34 (n=6)	28,67 (n=13)
Equine Piroplasmosis (EPRP)	5,43 (n=2)	5,00 (n=2)	22,60 (n=3)	6,60 (n=1)	-	25,69 (n=7)	11,35 (n=2)	-	21,51 (n=9)	-	-	43,80 (n=1)	44,10 (n=2)	-	24,78 (n=5)	-	-	26,33 (n=3)	6,22 (n=5)	3,29 (n=3)	7,15 (n=2)	19,78 (n=10)	14,49 (n=9)	26,68 (n=18)
Ovine Piroplasmosis (OPRP)	21,97 (n=28)	10,80 (n=13)	39,09 (n=12)	69,65 (n=2)	-	74,53 (n=3)	14,76 (n=8)	27,44 (n=8)	49,10 (n=9)	18,05 (n=6)	14,84 (n=2)	22,97 (n=3)	-	-	-	-	-	65,98 (n=2)	0,40 (n=1)	-	46,10 (n=1)	34,15 (n=15)	29,06 (n=16)	51,35 (n=15)
Anaplasmosis (ANP)	0,94 (n=3)	10,03 (n=9)	31,29 (n=1)	8,10 (n=2)	29,44 (n=8)	-	-	36,18 (n=8)	-	-	52,92 (n=5)	14,47 (n=3)	-	26,80 (n=2)	-	-	20,90 (n=2)	-	12,87 (n=2)	37,27 (n=5)	-	10,48 (n=4)	33,29 (n=11)	30,82 (n=5)
Ehrlichiosis (EHR)	-	44,05 (n=2)	1,00 (n=1)	-	13,50 (n=2)	-	-	14,80 (n=3)	-	-	-	7,41 (n=1)	-	-	38,25 (n=2)	-	-	40,63 (n=1)	-	-	32,18 (n=3)	-	27,91 (n=4)	30,61 (n=7)

Figure 4. Geographic distribution of major tick-borne diseases in animals across seven regions of Türkiye. Each infection is represented by its abbreviation within a circle, with circle size proportional to the highest reported prevalence determined by microscopic, serological, or molecular detection methods. A corresponding table below the map presents a detailed breakdown of prevalence data for each region, categorized by detection method

Table 3. Tick-borne pathogens include bacteria, protozoan, filarial nematodes, fungi and prion

	Genus	Species	Tick vectors	Distribution	Hosts	References
Protozoan	*Babesia*	*B. bigemina*	*Rh. microplus*, *Rh. annulatus*	Worldwide	Cattle	(114)
		B. bovis	*Rh. microplus*, *Rh. annulatus*	Worldwide	Cattle	(114)
		B. major	*Hyalomma* spp., *Ixodes* spp., and *Rhipicephalus* spp.	Worldwide	Cattle	(114)
		B. divergens	*Ixodes ricinus*	Europe	Cattle, humans	(114,532,534,537-541)
		B. ovis	*Rh. bursa*	Asia	Sheep, goats, dogs	(114,496,531-534)
		B. motasi	*Haemaphysalis* spp.	Asia	Sheep, humans	(114)
		B. crassa	*Hyalomma* spp., *Ixodes* spp., *Rhipicephalus* spp.	Asia	Small ruminants	(114,496,531,536)
		B. microti	*I. scapularis*, *Hae. longicornis*	America, Asia	Rodents, humans	(114,532,534,537-541)
		B. duncani	*D. albipictus*	America	Humans	(114)
		B. caballi	Ixodid ticks	Worldwide	Equids	(622,623)
		B. canis	*Rh. sanguineus*	Worldwide	Dogs	(625,626)
		B. gibsoni	*Rh. sanguineus*	Worldwide	Dogs	(632)
		B. vulpes	*Rh. sanguineus*	Asia	Dogs, foxes	(627-629)
		B. conradae	*Rh. sanguineus*	America	Dogs	(627-629)
		Babesia aktasi n. sp.	Ixodid ticks	Asia	Goats	(496)
		B. jakimovi	Ixodid ticks	Worldwide	Cattle	(94,114)
		B. occultans	*H. marginatum*	Worldwide	Cattle	(114)
		B. ovate	*Hae. longicornis*	Worldwide	Cattle	(114)
		B. odocoilei	Ixodid ticks	America	Deer	(114)
		Babesia sp. *Xinjiang*	*H. anatolicum*, *Hae. quinghaiensis*	Asia	Sheep	(613-615)
		B. venatorum	-	Europe, Asia	Deer, sheep	(114,532,534,537-541)
		Babesia sp. (Kayseri 1)	Ixodid ticks	Asia	Cattle	(159)
	Theileria	*T. annulata*	*Hyalomma* spp.	Asia, Africa	Cattle, sheep	(199)
		T. parva	*Rh. appendiculatus*, *Rh. zambeziensis*	Africa	Cattle, buffalo	(597,598)
		T. orientalis	*Hae. longicornis*	America, Asia	Cattle	(114)
		T. equi	Ixodid ticks	Worldwide	Equids	(599,625)
		T. haneyi	Ixodid ticks	America	Equids	(535)
		T. taurotragi	*Hyalomma* spp., *Rh. appendiculatus*, *Rh. pulchellus*.	Africa	Cattle, deer, antilope	(1,555)
		T. velifera	*Am. variegatum*	Africa	Cattle, deer	(605-608)
		T. mutans	Ixodid ticks	Africa	Cattle	(1,555)
		T. sinensis	Ixodid ticks	Asia	Cattle	(114)
		T. sergenti	*Hae. longicornis*	Asia	Cattle	(114)
		T. ovis	*Rh bursa*, *Rh. sanguineus* s.l. and *Rh. turanicus*	Africa, Asia,	Sheep, goats	(555,556)
		T. lestoquardi (hirci)	*Hyalomma* spp.	Africa, Asia, Europe	Sheep, goats	(114,713)
		T. uilenbergi	*Hae. quinghaiensis*, *Hae. longicornis*	Asia	Small ruminants	(114,496,531-534)
		T. luwenshuni	*Hae. punctata*	Asia	Small ruminants	(555,556)
		T. palmeri n. sp.	Ixodid ticks	Europe	Dogs	(542)
		T. apogeana n. sp	Ixodid ticks	Europe	Dogs	(542)
		T. paparinii n. sp.	Ixodid ticks	Europe	Dogs	(542)
		T. worthingtonorum n. sp	Ixodid ticks	Europe	Dogs	(542)
		T. cervi	*Am. americanum*	America	Deer	(605-608)

Table 3. Continued

	Genus	Species	Tick vectors	Distribution	Hosts	References
Protozoan	*Cytauxzoon*	*C. felis*	*D. variabilis, Am. americanum*	Asia, America, Europe	Cats	(636)
	Hepatozoon	*H. canis*	*Rh. sanguineus, Rhipicephalus* spp.	Asia	Dogs	(542)
		H. viperoi	-	Asia	Vipers	(94,638-641)
		H. americanum	*Am. maculatum*	America	Dogs	(639)
		H. felis	*Rh. sanguineus*	Asia	Cats	(504)
		H. silvestris	Not specified	Asia	Cats	(638)
		H. ursi	*Hae. flava*	Asia	Bears	(94,638-641)
Rickettsial bacteria	*Aegyptianella*	*Aeg. pullorum*	*A. walkerae, A. persicus, A. reflexus*	Africa, Europe, Asia	Domestic poultry	(532)
	Rickettsia	*R. rickettsii*	*D. andersoni, D. variabilis,* *Am. cajennense, Rh. sanguineus*	America	Humans, dogs	(413)
		R. rickettsii californica	*D. occidentalis*	America	Humans	(413)
		R. conorii conorii	*Rh. sanguineus*	Europe, Africa, Asia	Humans, dogs	(146,457,504,510)
		R. sibirica mongolotimonae	*H. asiaticum, H. truncatum,* *H. excavatum, Hae. parva*	Africa, Asia, Europe	Humans	(456)
		R. australis	*I. holocyclus, I. tasmani*	Europe	Humans	(407,408)
		R. africae	*Am. hebraeum, Am. variegatum*	Africa, Asia	Humans	(146,457,504,510-514)
		R. honei	*Bothriocroton hydrosauri,* *Am. cajennense*	America, Europe, Asia	Humans	(406)
		R. slovaca	*D. marginatus, D. reticulatus*	Europe, Asia	Humans	(456)
		R. aeschlimannii	*H. marginatum, H. rufipes,* *Rh. appendiculatus*	Europe, Africa	Humans	(457)
		R. parkeri	*Am. maculatum*	America	Humans	(413)
		R. massiliae	*Rh. sanguineus, Rh. turanicus, Rh. muhsamae, Rh. annulatus, Rh. sulcatus*	Europe, Asia, America	Humans	(146,457,504,510-514)
		R. honei marmionii	*Hae. novaeguineae, I. holocyclus*	Europe	Humans	(406)
		R. monacensis	*I. ricinus*	Europe	Humans	(456)
		R. felis	*Rh. sanguineus, Rh. bursa,* *H. marginatum, I. ricinus*	Worldwide	Cats	(146,457,504,510-514)
		R. hoogstraalii	*Hae. parva*	Asia	Cattle	(456)
		R. raoultii	*D. reticulatus, D. marginatus*	Worldwide	Cats	(146,457,504,510-514)
	Ehrlichia	*E. ewingii*	*Am. americanum*	America	Humans, dogs	(73)
		E. ruminantium	*Am. hebraeum, Am. gemma,* *Am. marmoreum, Am. lepidum,* *Am. variegatum, Am. americanum*	Africa	Cattle	(642)
		E. canis	*Rh. sanguineus*	America, Europe, Africa, Asia	Dogs	(499)
		E. muris subsp. *eauclairensis*	*I. scapularis*	America	Mice	(400)
		Ehrlichia sp. Omatjenne	Ixodid ticks	Asia	Cattle	(382)
		E. chaffeensis	*Am. americanum* *Rh. bursa*	America	Humans and various mammals	(498,499)

Table 3. Continued

	Genus	Species	Tick vectors	Distribution	Hosts	References
Rickettsial bacteria	*Candidatus*	*C. Rickettsia barbariae*	*Rh. sanguineus, Rh. bursa, H. marginatum, I. ricinus*	Asia, Europe	Cats	(146,457,504,510-514)
		C. Rickettsia vini	*Rh. sanguineus, Rh. bursa, H. marginatum, I. ricinus*	Asia, Europe	Cats	(146,457,504,510-514)
		C. Neoehrlichia mikurensis	*I. ricinus, I. persulcatus*	Asia	Cattle	(146)
	Anaplasma	*A. phagocytophilum*	*I. scapularis, I. pacificus, I. ricinus, I. persulcatus, Am. americanum*	America, Europe	Humans and various mammals	(379,380)
		A. marginale	Ixodid ticks	Worldwide	Cattle	(486,487)
		A. centrale	Ixodid ticks	Worldwide	Cattle	(486,487)
		A. ovis	Ixodid ticks	Worldwide	Sheep	(486,487)
		A. capra	Ixodid ticks	Asia	Sheep, goats, buffalo	(486,487)
		A. bovis	Ixodid ticks	Asia	Cattle	(374,378)
		A. platys	*Rh. sanguineus*	Asia	Dogs	(500)
Non-rickettsial bacteria	*Francisella*	*F. tularensis*	Ixodid ticks	Asia	Mammals	(284)
	Coxiella	*C. burnetii*	Ixodid ticks	Worldwide	Mammals	(480)
	Bartonella	*B. henselae*	*I. ricinus*	America, Europe, Asia and Africa	Domestic cats	(425)
	Borrelia	*B. burgdorferi*	*I. pacificus, I. persulcatus, I. ricinus, I. scapularis*	America, Europe, Asia, Africa	Humans	(457)
		B. garinii	*I. persulcatus, I. ricinus*	Europe, Asia, Africa	Humans	(457,514)
		B. afzelii	*I. persulcatus, I. ricinus*	Europe, Asia, Africa	Humans	(457,514)
		B. valaisiana	*I. ricinus*	Europe, Asia	Humans	(457,514)
		B. lusitaniae	*I. ricinus*	Europe	Humans	(457,514)
		B. spielmani	*I. ricinus*	Europe	Humans	(457,514)
		B. japonica	*I. ovatus*	Asia	Humans	(457,514)
		B. lonestari	*Am. americanum*	America	Humans	(457,514)
		B. theileri	*Rh. microplus*	Africa, America, Europe	Cattle	(457,514)
		B. turcica	*H. aegyptium*	Asia	Tortoises	(470,471)
		B. crocidurae	*Ornithodoros* spp.	Europe, Africa	Humans	(475)
Filarial nematodes	*Acanthocheilonema*	*A. vitea*	*O. tartakovskyi*	Asia, America	Rodents	(644)
		A. dracunculoides	*Rh. sanguineus*	Asia	Dogs	(648)
	Dipetalonema	*D. viteae*	*O. tartakovskyi*	America	Jirds	(644)
		D. dracunculoides	*Rh. sanguineus*	America	Dogs	(648)
	Cercopithifilaria	*Cercopithifilaria* sp. s.l.	*Rh. sanguineus* group	Europe	Dogs	(650)
		C. bainae	*Rh. sanguineus s.l.*	America	Dogs	(652)
Fungii	*Scopulariopsis*	*S. brevcaulis*	*H. anatolicum, Am. lepidum*	Africa	Cattle	(662-665)
Prion		PrPCWD	*I. scapularis*	America	White-tailed deer	(709)

analysis techniques for *Anaplasma phagocytophilum,* have been evaluated as promising in the fight against TBPs and TBDs (735). In addition, integrated pest management (IPM) approaches and emerging innovations, such as nanotechnology-enhanced acaricides and new-generation vaccines, offer promising solutions for improving tick control. To overcome the complex challenges of tick management, targeted strategies and interdisciplinary cooperation are required (736).

The Economic Burden of Ticks and TBDs

Ticks, beyond their parasitic role, are vectors of numerous emerging and re-emerging diseases, contributing to substantial economic losses worldwide (737). These burdens are particularly severe in underdeveloped and developing countries, where small-scale and economically fragile cattle and sheep farms face disproportionate impacts (163,738).

Global Economic Impact: The annual global economic burden attributed to ticks and TBDs is estimated at approximately 30 billion USD, with Africa alone incurring losses of 160 million USD and South Africa 29 million USD (1,163,554,739,740). Around 80% of the world's cattle population is affected by tick infestations, resulting in reduced productivity and increased disease transmission (163,739,741).

Main TBPs: The most economically damaging TBPs affecting cattle include *Anaplasma* spp., *Ehrlichia* spp., *Theileria* spp., and *Babesia* spp. (742). These pathogens contribute to significant economic losses due to reduced productivity, animal mortality, and treatment costs. It has been suggested that *Babesia* has become a widespread parasite, with approximately 400 million cattle worldwide exposed to bovine babesiosis. The total economic loss caused by the parasite—including death, significant reductions in meat and milk yield, and tick control expenses—is devastating (96).

Regional Case Studies: Tick infestations and the pathogens they transmit are well-known to cause significant economic challenges, especially for farmers in rural areas. However, the precise numerical magnitude of this economic burden remains unclear, both globally and on a country-by-country basis. This gap in scientific epidemiological data is critical, as it hinders a full understanding of the scale of the issue. Unfortunately, no integrated automatic recording system exists to monitor this problem globally. However, TBDs impose serious restrictions on cattle production and productivity in Asia, Africa and Australia (743). Ticks are of primary concern for both human and animal health, with reports indicating that they infest approximately 80% of the world's cattle population. These infestations contribute significantly to the economic burden by transmitting pathogens that cause deadly TBDs in cattle (739,741). Ticks also led to significant losses in cattle production by reducing both productivity and fertility (744). A few country reports on substantial economic losses caused by ticks and TBDs have been reported in some regional cases in the world. In India, annual economic losses due to tick infestations and TBDs reached 787.63 million USD, primarily from milk production losses and acaricide treatment expenses (745); in Tunisia, the economic cost of tropical theileriosis in three farms over two seasons was EUR 9,388.20 (746); in Türkiye, in the Cappadocia region, total economic losses due to tropical theileriosis was estimated as 598,133 USD with 87.26% attributed to production losses (2,163). Central to Southern Africa, East Coast fever causes annual losses of approximately 500 million USD (747). On the other hand, it was reported that effective tick control measures were shown to reduce productivity losses by up to 32%, based on productivity-adjusted life years estimates in South Africa (Eastern Cape) (748).

Drivers of Economic Losses: Multiple key factors contribute to both the direct and indirect economic impacts associated with tick-related challenges. Direct losses include product-related effects such as anemia, weight loss, mortality, and reductions in milk and meat production (2,54,744,749), as well as control costs related to acaricide applications, vaccines, and veterinary treatments (2). Indirect losses comprise insurance claims, diminished productive performance, and long-term detrimental effects on animal health (2). Additionally, other important drivers include anthropogenic and ecological factors. Anthropogenic drivers—such as climate change, biodiversity loss, and land-use changes—significantly affect tick population dynamics and the transmission of TBDs through a “butterfly effect” (724). Wildlife, including mammals (e.g., deer and rodents) (710,750), and migratory birds, particularly ornithophilic species like *Hepatozoon marginatum* (751), also contribute to the intercontinental spread of ticks and TBDs.

Public Health Implications: Ticks and TBDs also pose increasing threats to public health such as an increase in healthcare costs. For instance, Lyme disease in the United States incurs annual costs of 345-968 million USD (752), and the rise of zoonotic risks due to the global spread of TBPs increases the risk of human infection, particularly in previously unaffected areas.

Impacts on Sustainable Development and Food Security: Ticks and TBDs undermine progress toward SDGs by deepening poverty and reducing food security in rural communities, lowering animal protein intake, especially in vulnerable populations (children, pregnant women, the elderly) and weakening environmental and social governance through ecosystem disruption, public health strain, and increased economic inequality (163,724,750).

Country-Specific Economic Loss Estimates: There are a few reports for this topic. In Africa, Asia, and Australia, losses from TBDs vary significantly, with the highest in India and the lowest in the Philippines, totaling 355 million USD in 1998 (753). A bibliometric analysis in Ghana (2004-2024) highlighted increased academic interest and emphasized the importance of collaboration between academia and government to mitigate economic and health burdens (754).

Strategic Recommendations: Some important approaches to reduce the economic losses due to the infestation of ticks and caused by TBDs are urgently needed. To mitigate the substantial global economic losses caused by ticks and TBDs, the following strategies are recommended:

(i) Adopt the One Health Approach: Align human, animal, and environmental health responses to combat TBDs more effectively (724,741).

(ii) Enhance Farmer Education: Particularly in smallholder systems, lack of training is a significant barrier. Comprehensive extension programs are needed.

(iii) Implement Integrated Control Measures: Base control strategies on tick biology and seasonal life cycles**.** Promote sustainable pasture management and strengthen host immunity (36).

(iv) Establish Global Surveillance and Monitoring: Develop a standardized, integrated global tick and TBD surveillance system, which is currently lacking and urgently needed.

The Economic Impact of Ticks and TBDs in Türkiye: Although "ticks and tick-borne diseases" are seen in many regions of Türkiye, reports on economic losses are quite limited (163,170). In Türkiye, Theileriosis and Babesiosis are the most common and economically significant tick-borne hemoparasitic diseases (755). In a study conducted to generate data on the epidemiology of tropical theileriosis, statistical analyses were performed on a total of 866 cattle of different breeds, both vaccinated and unvaccinated, in the Kayseri region. The results showed that some parts of the region have enzootic stability for tropical theileriosis (165). The first study to determine the economic losses due to tropical theileriosis in Türkiye was conducted in the Kayseri region; it was found that the total economic loss during two tropical theileriosis seasons was approximately 130,000 USD (171). In another study conducted in the Cappadocia region, the total economic loss due to tropical theileriosis was calculated as approximately 598,133 USD over a 2-year period (2). Subsequently, economic losses caused by theileriosis in ruminants in Türkiye were reported to range between 130,000 and 598,000 USD (756).

Integrated Tick Control

Obligate blood-feeding external parasites, ticks are arthropods that belong to the class Arachnida along with spiders, distinguishing them from insects by various structural and biological characteristics (36,39,44,70,85,129,757-759). The ticks are arthropods that require strict control due to their parasitic nature and their role in transmitting pathogens (760). Except for the egg stage, they must feed on the blood of their hosts in all other developmental stages. To date, various strategies, including eradication, have been developed and implemented for tick control (70). However, except for a few small-scale limited areas, complete success in eradication has not been achieved. This method has demonstrated that tick eradication is currently not feasible (36). At this point, the fundamental strategy should focus on reducing the increasing tick population to acceptable levels without harming animal and human health. The key strategies for integrated tick control include acaricide use, tick vaccines and biological control.

(i) Acaricide Use: During the months when ticks are active (Spring-Autumn), domestic animals should be treated at regular intervals with easily applicable drugs that have a long-lasting effect and do not leave residues in meat or milk. Pour-on medications can be used for cattle, while sheep and goats can be treated through group dipping methods. Ixodid ticks, which are active during the spring and autumn months, spend a part of their life cycle on domestic animals. Therefore, periodic treatments carried out between these seasons, particularly during the months when tick infestations peak (April to July) can help reduce tick populations. This practice must be implemented simultaneously in all regions at risk. Formamidines, organophosphates, and synthetic pyrethroids are commonly used for the control of ixodid ticks (94). However, the use of some of these drugs in tick control is problematic due to their tendency to leave long-lasting residues in meat and milk. Flumethrin, a second-generation pyrethroid, does not pose a residue problem in meat and milk when applied as a pour-on formulation, and is therefore used in many countries (761). A 1% Flumethrin pour-on solution, when applied every 21 days, has been found to be highly effective (95-100%) in protecting domestic animals against ixodid tick infestations (762). The application of acaricides to animals has several disadvantages and drawbacks, including the development of tick populations resistant to acaricides, the necessity of frequently introducing new-generation chemicals, chemical pollution in the environment, and residue issues in animal products such as meat and milk. Moreover, developing new acaricides to counteract resistance is both time-consuming and costly. Environmental spraying should never be conducted, as it negatively impacts ecological balance. However, in order to reduce the risk of ticks attaching to humans, control of ixodid ticks can be achieved by spraying vegetation and the environment with acaricide at certain points in recreational areas (763).

(ii) Tick Vaccines: Resistance to acaricides poses a serious threat to the control of ticks and the diseases they transmit. In order to eliminate the drawbacks associated with the use of acaricides, recent years have seen an acceleration in vaccine development efforts aimed at providing immunological protection against ticks in vertebrate hosts (44,757,764). These vaccines aim to reduce the high costs associated with tick control, prevent environmental pollution, and hinder the development of resistant tick populations. To date, various vaccines have been developed against *Boophilus* and *Hyalomma* species (such as TickGARD), and partially promising results have been obtained (37,764). In ticks that feed on hosts immunized with these vaccines, effects such as a decrease in engorgement weight, feeding duration, egg mass, and egg viability have been observed. Translational biotechnological studies in this area are ongoing (758,759).

(iii) Biological Tick Control: The fundamental concept of biological control is based on eliminating or reducing a target organism by using another organism or organisms that are its natural enemies. The biological control of ticks essentially occurs naturally within the food chain of the ecosystem (70). The organisms involved in this process in nature are natural organisms and biological enemies. Ticks are among the organisms in the ecosystem with the fewest natural enemies. Various predators, parasites, and pathogens have been used against specific tick species for biological control purposes (70). However, one of the major factors limiting the success of such efforts has been the complex biological and ecological characteristics of ixodid ticks in particular. For example, although there are reports that chickens consume ticks, it has been suggested that their impact would remain localized. Studies involving *Ixodiphagus hookeri*, a natural enemy of ticks, demonstrated that the analysed indicators and characteristics of the *Ixodiphagus hookeri* wasp-tick system can be used in research on tick control (765). Various fungal species from the genera *Beauveria* and *Metarhizium* have also been used for this purpose, but the outcomes have not met expectations (703,766).

CONCLUSION

This comprehensive review, approached from a holistic and interdisciplinary perspective, synthesizes current knowledge on tick biology, diversity, distribution, and the wide array of TBDs caused by a viral, bacterial, protozoan, nematode, fungal and prion pathogens. It explores the ecological, molecular, and epidemiological dimensions of tick-pathogen-host interactions, the economic burdens associated with TBDs, and advances in integrated tick management and control strategies. Global trends reveal a concerning rise in tick populations and TBD incidence, driven primarily by anthropogenic factors such as climate change, land-use alterations, and increased global trade and mobility. These forces are facilitating the expansion of ticks into previously uncolonized, enzootically unstable regions, increasing the risk of emerging infectious diseases. The burden is especially profound in low-income countries, where TBDs not only threaten human and animal health but also exacerbate food insecurity and hinder sustainable development. This review underscores the relevance of these challenges to several SDGs, particularly those focused on health, poverty eradication, and environmental sustainability.

In light of these threats, the review advocates for globally coordinated responses grounded in the "One Health" approach, which recognizes the interconnectedness of human, animal, and environmental health. Collaborative actions by the World Health Organization, Food and Agriculture Organization, World Organisation for Animal Health, and United Nations Environment Programme are critical for developing effective surveillance, prevention, and control strategies. The evolutionary adaptations of ticks—such as their highly efficient blood-feeding mechanisms—enhance their ability to transmit pathogens (139). For instance, infection with *Babesia bovis* has been shown to increase the tick burden in cattle due to immunosuppressive effects, facilitating more efficient feeding by *Rhipicephalus* (*Boophilus*) *microplus* (767). This epidemiological pattern is often observed in enzootically stable regions and may serve as a marker of *Babesia bovis* infection.

Advances in genetic engineering have led to the development of transgenic *Babesia* strains, such as modified *Babesia bovis*, which are capable of transmission via their natural tick vectors. These genetically engineered isolates present new opportunities for vaccine development and therapeutic interventions (546). Transgenic approaches using *in vitro*-cultured erythrocyte lines and the MASP system have facilitated the study of *Babesia bovis* biology, the identification of vaccine candidates, and the testing of drug sensitivities (768-770). Notably, CRISPR/Cas9 genome editing and transfection systems have enabled the insertion of exogenous genes—such as GFP, BM86, and tick glutathione-S-transferase—into the parasite's genome, opening avenues for functional genomic studies and novel therapeutic strategies (546,549).

Additionally, recent discoveries have highlighted the immunomodulatory potential of tick saliva. Tick-derived microRNAs (miRNAs), for example, can be taken up by host cells and modulate gene expression with minimal immunogenicity, suggesting promising applications in therapeutics and immune modulation (771,772). Similarly, extracellular vesicles secreted by tick salivary glands have been found to carry bioactive molecules—such as miRNAs and proteins—that play roles in immune evasion and pathogen transmission (773). These findings are driving a growing interest in the repurposing of tick-derived molecules for use in treating human and animal diseases. Recent approaches—such as microbial gene expression studies in *Anaplasma phagocytophilum*, the discovery of diverse plasmids in *Rickettsia* species, and the application of mutational analysis techniques—have raised new hopes in the fight against TBPs and TBDs. Alongside these scientific advancements, modern IPM strategies, nanotechnology-enhanced acaricides, and next-generation recombinant anti-tick vaccines offer promising solutions for tick control. Targeted strategies and interdisciplinary collaboration remain essential to overcoming the complex challenges of effective tick management. Among the array of integrated tick control strategies, vaccine development remains a cornerstone. Innovative approaches, including DNA- and miRNA-based vaccines, have shown significant promise in eliciting robust immune responses against tick antigens in laboratory studies (73). Future breakthroughs are likely to emerge from interdisciplinary efforts combining molecular biology, immunology, ecology, and computational science, particularly in the ongoing exploration of tick saliva's molecular arsenal.

This review also incorporates a regional focus on Türkiye, where 58 tick species have been documented across diverse ecological zones. Ticks and associated TBDs pose growing threats to both public and veterinary health in the region, paralleling global trends. While Türkiye has made strides in TBDs research, the lack of a dedicated, fully operational "One Health Institute" at any national university represents a critical barrier to integrated responses at local, regional, and international levels (774). To address this gap, a paradigm shift in education is needed—one that prioritizes ecocentric curricula rooted in the One Health philosophy. Such curricula should emphasize the interconnectedness of ecological and epidemiological systems, equipping future generations with the tools to mitigate anthropogenic disruptions and combat climate change. The establishment of a standardized global curriculum, mandated by organizations such as UNESCO, could foster widespread literacy in planetary health principles. Integrating this knowledge into educational systems worldwide would empower communities to respond more effectively to the growing threat of ticks and TBDs, as well as other vector-borne diseases. In conclusion, the path forward demands coordinated global action, interdisciplinary collaboration, and a fundamental rethinking of how we approach health at the human-animal-environment interface. Strengthening the foundations of One Health through education, policy, and research will be vital in addressing the complex, evolving challenges posed by ticks and the diseases they transmit—ultimately contributing to the broader objective of achieving planetary health.

Footnotes

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