Published in final edited form as:

Lancet Infect Dis. 2015 December ; 15(12): 1467–1479. doi:10.1016/S1473-3099(15)00177-2.

Emerging tick-borne infections in mainland China: an increasing public health threat

Li-Qun Fang#, **Kun Liu**#, **Xin-Lou Li**, **Song Liang**, **Yang Yang**, **Hong-Wu Yao**, **Ruo-Xi Sun**, **Ye Sun**, **Wan-Jun Chen**, **Shu-Qing Zuo**, **Mai-Juan Ma**, **Hao Li**, **Jia-Fu Jiang**, **Wei Liu**, **X Frank Yang**, **Gregory C Gray**, **Peter J Krause**, and **Wu-Chun Cao**

State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, Beijing, China (L-Q Fang PhD, K Liu MS, X-L Li MS, H-W Yao MS, R-X Sun BS, Y Sun BS, W-J Chen BS, S-Q Zuo PhD, M-J Ma PhD, H Li PhD, J-F Jiang PhD, Prof W Liu PhD, Prof W-C Cao PhD); College of Public Health and Health Professions, and Emerging Pathogens Institute, University of Florida, Gainesville, FL, USA (S Liang PhD, Y Yang PhD); Department of Microbiology and Immunology, Indiana University School of Medicine, Barnhill, IN, USA (Prof X F Yang PhD); Duke University School of Medicine, Durham, NC, USA (Prof G C Gray MD); and Department of Epidemiology of Microbial Diseases, Yale School of Public Health, and Department of Medicine and Department of Pediatrics, Yale School of Medicine, New Haven, CT, USA (P J Krause MD)

# These authors contributed equally to this work.

Abstract

Since the beginning of the 1980s, 33 emerging tick-borne agents have been identified in mainland China, including eight species of spotted fever group rickettsiae, seven species in the family Anaplasmataceae, six genospecies in the complex *Borrelia burgdorferi* sensu lato, 11 species of *Babesia,* and the virus causing severe fever with thrombocytopenia syndrome. In this Review we have mapped the geographical distributions of human cases of infection. 15 of the 33 emerging tick-borne agents have been reported to cause human disease, and their clinical characteristics have been described. The non-specific clinical manifestations caused by tick-borne pathogens present a major diagnostic challenge and most physicians are unfamiliar with the many tick-borne diseases that present with non-specific symptoms in the early stages of the illness. Advances in and application of modern molecular techniques should help with identification of emerging tick-borne pathogens and improve laboratory diagnosis of human infections. We expect that more novel tick-borne infections in ticks and animals will be identified and additional emerging tick-borne diseases in human beings will be discovered.

Correspondence to: Prof Wu-Chun Cao, State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, Fengtai District, Beijing 100071, China **caowc@bmi.ac.cn**.

Contributors

L-QF, SL, XFY, GCG, PJK, and W-CC initiated the original ideas for the review. KL, X-LL, H-WY, RXS, YS, and W-JC contributed to the literature search and extracted data. KL, X-LL, H-WY, YY, SL, S-QZ, M-JM, HL, J-FJ, and WL assessed the data. L-QF, KL, X-LL, H-WY, R-XS, YS, W-JC, and W-CC created the figures. L-QF, GCG, and W-CC wrote the draft, and all authors contributed to the review and revision of the paper.

Declaration of interests

We declare no competing interests.

Introduction

Ticks were the first arthropods to be recognised as vectors that can transmit pathogens to human beings and are second only to mosquitoes as vectors of infectious diseases in the world.[1] Tick-borne infections are zoonoses with pathogens maintained in natural cycles involving tick vectors and animal hosts. Human beings are occasional hosts for ticks and are usually viewed as dead-end hosts that have no role in maintaining tick-borne agents in nature.[2] Different tick species favour distinct biotopes or environments, which define their geographical distribution and, consequently, the areas of risk for human tick-borne infections. In the past three decades, tick-borne pathogens have emerged worldwide and become a great threat to human health.[1,3]

China is the largest developing country in the world and has made tremendous progress in the control and prevention of infectious diseases; however, emerging infectious diseases are the new challenge now facing China.[4] Although outbreaks of severe acute respiratory syndrome and H5N1 and H7N9 avian influenza virus infections have attracted great attention, emerging tick-borne diseases have generally been neglected by primary health-care providers and clinicians. Although an increasing number of tick-borne infections have been reported in mainland China, no comprehensive review of this substantial public health problem has been undertaken. We will provide an overview of the type and distribution of emerging tick-borne infections in tick vectors, animal hosts, and human beings. We will describe the clinical characteristics of human tick-borne diseases, and discuss possible factors contributing to their emergence.

Emergence of tick-borne infections in mainland China

Since 1982, 33 emerging tick-associated agents have been identified in mainland China, including eight species of spotted fever group rickettsiae (SFGR);[5–11] three species of *Ehrlichia*,[12–14] three species of *Anaplasma*,[15–17] and *Candidatus* Neoehrlichia mikurensis[18] in the family Anaplasmataceae; six genospecies in the complex *Borrelia burgdorferi* sensu lato;[19–23] 11 species of *Babesia*;[24–33] and severe fever with thrombocytopenia syndrome virus (SFTSV).[34] The location and year in which each emerging tick-borne agent was first identified are shown in the appendix. Most (19 of 33) were initially detected in ticks; however, six were identified in domestic animals (sheep, goat, buffalo, and dog), two in wild animals (Chinese white-bellied rat and Chinese hare), and six in people. Detailed information regarding the identification of these emerging tick-borne infections is summarised in table 1.

Among the 33 newly recognised tick-associated agents, 15 have been reported to cause human infection, including: four species of SFGR;[11,35,46,48] an *Ehrlichia* species,[53] two *Anaplasma* species,[17,53] and *Candidatus* N mikurensis;[18] three genospecies of *B burgdorferi* sensu lato;[19,21,78] three species of *Babesia*;[33,104,108] and SFTSV (table 2).[34] Six of the tick-borne pathogens were first identified in febrile patients (*Candidatus* Rickettsia tarasevichiae, *Candidatus* N mikurensis, *Borrelia garinii*, *Borrelia afzelii*, *Babesia venatorum* [not yet formally described], and SFTSV) and then shown to be associated with ticks (table 1). The other nine human pathogens were initially detected in ticks or animals and subsequently shown to infect human beings (*Rickettsia heilongjiangiensis*, *Rickettsia sibirica* sp BJ-90, *Rickettsia raoultii*, *Ehrlichia chaffeensis*, *Anaplasma phagocytophilum*, *Anaplasma capra*, *Borrelia valaisiana*-related genospecies, *Babesia microti*, and *Babesia divergens*). Among these 15 emerging tick-borne diseases, severe fever with thrombocytopenia syndrome (SFTS) was first identified in mainland China[34] and subsequently reported in South Korea and Japan.[134,135] A disease similar to SFTS has been reported in the USA.[136] Human infections with *R sibirica* sp BJ-90, *Candidatus* R tarasevichiae, *A capra*, and *B valaisiana*-related genospecies have been exclusively diagnosed in mainland China.[11,17,46,78] Human infections of *Candidatus* N mikurensis, *Ba venatorum*, and *R raoultii*, which have been detected in China, were first identified in Europe.[18,33,48] Five tick-borne pathogens have been detected in ticks or reservoir hosts, or both, but have not yet been reported to cause infection in human beings in China. They include *Rickettsia monacensis*, *Rickettsia slovaca*, *Rickettsia sibirica* sp *mongolotimonae*, *B valaisiana*, and *B burgdorferi* sensu stricto.[137–141] Additionally, a *Rickettsia* species (*Candidatus* Rickettsia hebeiii), two *Ehrlichia* species (*Ehrlichia canis* and *Ehrlichia* sp Tibet), an *Anaplasma* species (*Anaplasma platys*), a genospecies of *B burgdorferi* sensu lato (*Borrelia sinica*), and eight *Babesia* species (*Babesia ovis*, *Babesia ovata*, *Babesia orientalis*, *Babesia major*, *Babesia motasi*, *Babesia caballi*, *Babesia* sp Kashi, and *Babesia* sp Xinjiang) have been identified in ticks or animals, but their pathogenicity to human beings is unknown.

Emerging SFGR infections

Eight novel species of SFGR have been recorded in mainland China since 1982 (table 1).[5–11] These species are mainly distributed in northern China (north of 36° north latitude).

Tick and animal infections

The eight emerging species and uncharacterised species of SFGR have been shown to be associated with 16 tick species (figure 1). *R heilongjiangiensis* has been proven to infect a range of tick species, three rodent species, and goats (appendix). In northeastern China, *R heilongjiangiensis* was detected in nine tick species and two rodent species from Heilongjiang Province,[36–38] and in *Haemaphysalis* spp ticks from Jilin Province.[38] In Inner Mongolia, *R heilongjiangiensis* has been reported in *Haemaphysalis verticalis*, *Detmacentor niveus*, *Hyalomma asiaticum kozlovi*, *Rhipicephalus pumilio*, and *Detmacentor nuttalli* ticks.[39] In northwestern China, *R heilongjiangiensis* has been detected in *Dermacentor silvarum* ticks from Qinghai Province.[40] In southern China, *R heilongjiangiensis* has been detected in *Haemaphysalis longicornis* ticks from Guangdong Province,[41] in goats from Yunnan Province,[42] and in chestnut white-bellied rats from Hainan Province.[43] In central and eastern China, *R heilongjiangiensis* was identified in *Haemaphysalis flava* ticks from Henan, Anhui, and Hubei provinces,[8] and in *H longicornis* from Zhejiang Province.[44] *R sibirica* sp BJ-90 was detected in *Dermacentor sinicus* ticks from a Beijing suburb.[7] *R raoultii* was detected in *Dermacentor* species ticks, including *D silvarum* and *Dermacentor marginatus*, in western China,[9,49] in *H verticalis* collected from Inner Mongolia, in *D silvarum* from Heilongjiang Province, and in *H longicornis* from Liaoning Province.[48,39,50,51] Four species, including *R sibirica* sp *mongolotimonae*, *R monacensis*, *R slovaca*, and *Candidatus* R hebeiii, have not been proven to infect human beings. Data regarding infected ticks and animal hosts are shown in figure 1 and the appendix.[7–10,47,52,54,119,142–147]

Human infections

Four species of emerging SFGR have been reported to infect human beings, including *R heilongjiangiensis*, *Candidatus* R tarasevichiae, *R sibirica* sp BJ-90, and *R raoultii* (table 2; figure 2). Of 34 people infected with *R heilongjiangiensis*, 19 were diagnosed in forested areas of northeastern China in the 1990s.[35,45] The other 15 cases of infection were reported on the island of Hainan Province in 2008.[43] In 2012, we undertook an active surveillance for human SFGR infections at the Mudanjiang Forestry Central Hospital of Heilongjiang Province in northeastern China, and eight cases of SFGR infection (including five infected by *Candidatus* R tarasevichiae, one by *R sibirica* sp BJ-90, and two by *R raoultii*) were identified by molecular detection and sequence determination. The presence of antibody against SFGR antigen in serum samples detected by immunofluorescence assay lent support to the diagnosis of SFGR.[46,48] Additionally, 37 patients were reported to have been infected with uncharacterised species of SFGR, including one in Inner Mongolia, one in Xinjiang Autonomous Region, 29 in Hainan Province, and six in Heilongjiang Province (figure 2).[119–124] The clinical manifestations of SFGR infections mainly include fever, eschar, headache, malaise, asthenia, anorexia, nausea, and lymphadenopathy. A few patients had rash and neurological manifestations such as coma, neck stiffness, and Kernig's sign.[11,35,43,45,46,48,119–124] Detailed information about the clinical and laboratory characteristics of patients infected with each of the emerging SFGR species are summarised in the appendix.

Emerging infections with agents in the family Anaplasmataceae

Seven species in the family Anaplasmataceae have been identified in mainland China, including *E chaffeensis*, *E canis*, *Ehrlichia* sp Tibet, *A phagocytophilum*, *A capra*, *A platys*, and *Candidatus* N mikurensis (table 1).

Tick and animal infections

The seven emerging agents in the family Anaplasmataceae are known to be associated with 17 tick species (figure 1). *E chaffeensis* was first detected in *Amblyomma testudinarium* ticks from Yunnan Province in 1996.[12] Several surveys report that it infects various tick species, and is widely dispersed in mainland China.[31,54–58] Furthermore, *E chaffeensis* was detected in dogs from Shandong Province, in long-tailed ground squirrels (*Citellus undulates Pallas*) and gerbils from Xinjiang Autonomous Region, in the striped field mouse (*Apodemus agrarius*) from Heilongjiang Province, and in rodents (*Rattus norvegicus*, *Rattus losea*, *Rattus flavipectus*, *Rattus niviventer*, *Mus musculus*, *Niviventer confucianus*, and *Rattus edwardsi*) and hares (*Lepus sinensis*) from Fujian and Zhejiang provinces (appendix).[36,55,59–62] *A phagocytophilum* was first detected in *Ixodes persulcatus* from Heilongjiang Province in 1997,[15] and is now the most widely encountered species in the family Anaplasmataceae over broad areas where multifarious tick species are vectors (figure 1). Additionally, *A phagocytophilum* infects domestic and wild animals, including cattle, sheep, goats, horses, dogs, hare, yaks, and 24 species of rodents (appendix).[36,51,54,55,62,64–72] *A capra* was first recognised in goats (*Capra aegagrus hircus*) and provisionally named by our group, but has since been detected in *I persulcatus* ticks in Heilongjiang Province.[17] Although *Candidatus* N mikurensis was initially identified in *I persulcatus* and *Haemaphysalis concinna* ticks,[18] it was subsequently detected in *D silvarum*, *H longicornis*, and various rodents from many areas of mainland China.[18,76,77] Three other species, including *E canis*, *Ehrlichia* sp Tibet, and *A platys*, have not been proven to infect human beings. Data regarding infected ticks and animal hosts are shown in figure 1 and the appendix.[13,14,16,57,63]

Human infections

Four species of Anaplasmataceae have been identified to cause human infections in mainland China: *E chaffeensis*, *A phagocytophilum*, *A capra*, and *Candidatus* N mikurensis. The first human case of monocytic ehrlichiosis was diagnosed in a forested area of Inner Mongolia in 1999.[53] Of the 12 human cases of monocytic ehrlichiosis reported, four were recorded in Inner Mongolia, two in Beijing, two in Tianjin, and four in Shandong Province (figure 2).[53,55] A cluster of ten cases of human granulocytic anaplasmosis caused by nosocomial transmission was identified in Anhui Province in 2006.[73] An additional 94 cases of human granulocytic anaplasmosis have been reported, including 33 in Beijing, six in Tianjin, 41 in Shandong Province, one in Anhui Province, and four to five each in Henan and Hubei provinces and Inner Mongolia (figure 2).[53,55,64,74,75] In 2015, 28 patients were reported to be infected with *A capra* in Heilongjiang Province.[17] Seven cases of *Candidatus* N mikurensis infection were identified from 622 febrile patients in the same location in 2010.[18] Patients with infections caused by species from the Anaplasmataceae family showed undifferentiated clinical manifestations, mainly including fever, malaise, myalgia, arthralgia, and gastrointestinal symptoms (diarrhoea, nausea, vomiting, and anorexia). Laboratory abnormalities included leucopenia, thrombocytopenia, and raised hepatic aminopherase, lactate dehydrogenase, and blood urea nitrogen (appendix).[17,18,53,55,64,73–75]

Emerging infections with *B burgdorferi* sensu lato

B burgdorferi sensu lato was first detected in human beings and *I persulcatus* in China (Heilongjiang Province) in 1986.[19] This isolate was later classified as *B garinii* by molecular biological methods in our laboratory. Five other genospecies were subsequently identified, including *B valaisiana*, *B sinica*, *B afzelii*, *B valaisiana*-related genospecies, and *B burgdorferi* sensu stricto (table 1).

Tick and animal infections

Over a wide geographical distribution of 25 provinces in mainland China, 26 tick species have been shown to carry *B burgdorferi* sensu lato (figure 1). *B garinii* is the most common genospecies and has been identified in many tick species (figure 1).[54,79–86] *B garinii* has been detected in rodents from many endemic areas,[23,36,79,85,87,88] in dogs from Yunnan Province, in sheep keds (*Melophagus ovinus*) from Tibet, and in hares from Gansu Province (appendix).[89] *B afzelii* is the second most common genospecies, and has been identified in the same ticks and rodents as *B garinii* with a similar distribution.[36,79,81,83–85] *B valaisiana*-related genospecies (a genetically related but distinct genospecies of *B valaisiana*) was detected in *Ixodes granulatus* and *H longicornis* from Guizhou Province, and in rodents from Guizhou and Zhejiang provinces.[22,83] Three other genospecies that have not been reported to infect human beings include *B valaisiana, B sinica,* and *B burgdorferi* sensu stricto. Data regarding infected ticks and animal hosts are shown in figure 1 and the appendix.[20,23,86,92,148–156]

Human infections

After the identification of *B burgdorferi* sensu lato in ticks and animals, human cases of *B burgdorferi* sensu lato infection have been reported frequently in almost all provinces in mainland China, except for Tibet and Shanghai metropolis (figure 2). *B garinii*, *B afzelii*, and *B valaisiana*-related genospecies have been reported to cause human infections (table 2).[19,21,23,78,90,91,125] The genospecies causing thousands of cases of Lyme disease in mainland China have not been characterised.[126–131] All the uncharacterised human cases in figure 2 were classified as *B burgdorferi* sensu lato infections irrespective of their actual genospecies. Infections with different genospecies of *B burgdorferi* sensu lato might result in slightly different clinical manifestations, including erythema migrans, arthritis or arthralgia, fever, headache, and fatigue.[19,21,23,78,90,91,125–131] Generally, clinical manifestations in mainland China are mild compared with those in USA and Europe.[78]

Emerging *Babesia* species infections

Since 1982, 11 *Babesia* species have been discovered in mainland China, including *Ba ovis*, *Ba major*, *Ba ovata*, *Ba orientalis*, *Ba motasi*, *Ba caballi*, *Babesia* sp Kashi, *Babesia* sp Xinjiang, *Ba microti*, *Ba divergens*, and *Ba venatorum* (table 1).

Tick and animal infections

The transmission of babesia is associated with 13 tick species (figure 1). *Ba microti*, *Ba divergens*, and *Ba venatorum* have been proven to infect human beings. *Ba microti* was identified in *I persulcatus* and *H concinna* ticks and in striped field mice and reed voles (*Microtus fortis*) from forested areas of Heilongjiang Province, in *H longicornis* ticks and dogs from Henan Province, and in rodents from Fujian, Zhejiang, Henan, and Heilongjiang provinces.[32,36,58,105,106] *Ba divergens* was detected in *I persulcatus*, *H concinna*, and *Haemaphysalis japonica* ticks and striped field mice in several areas of Heilongjiang Province.[32,36] *Ba venatorum* was reported in *I persulcatus* ticks from forested areas of northeastern China.[109] Other species of *Babesia* that have not been shown to infect human beings include *Ba ovis*, *Ba major*, *Ba ovata*, *Ba orientalis*, *Ba motasi*, *Ba caballi*, *Babesia* sp Kashi, and *Babesia* sp Xinjiang. Data regarding their infected ticks and animals are shown in figure 1 and the appendix.[24–31,93–103]

Human infections

Ba microti, *Ba divergens*, and *Ba venatorum* have been reported to cause human infections in mainland China (figure 2). A patient was diagnosed with *Ba microti* infection by peripheral blood and bone marrow smears and PCR assay in Zhejiang Province in 2011.[104] By use of PCR, *Ba microti* infections were identified in an additional ten patients among 449 febrile patients with malaria-like symptoms in Yunnan Province during 2012–13.[107] One patient was co-infected with *Plasmodium vivax* and another was co-infected with *Plasmodium falciparum*. Two cases of *Ba divergens* infection were detected from 377 patients with anaemia in Shandong Province in 2009.[108] A case of babesiosis caused by *Ba venatorum* was reported in a child from Xinjiang Autonomous Region.[33] Between 2011 and 2014, 48 cases of *Ba venatorum* infection were reported through our active surveillance at a sentinel hospital in forested areas of northeastern China. Among them, 32 were confirmed cases, and 16 were probable cases.[109] These infections were the first report of endemic human *Ba venatorum* disease anywhere in the world. Additionally, two cases of babesiosis caused by uncharacterised *Babesia* species were reported in Yunnan Province of southwestern China in 1982 and one in 2008 (figure 2).[132,133] Clinical manifestations for patients with *Babesia* species infections included fever, fatigue, anaemia, chills, and high levels of hepatic aminopherase and C-reactive protein.[33,108,104,109,107,132,133] Detailed information about the clinical manifestations of each of these species of *Babesia* infections is summarised in the appendix.

Emerging SFTSV infections

SFTSV is a novel member of the genus *Phlebovirus* in the Bunyaviridae family, and was first identified in China. The identification of SFTSV infections was made possible by enhanced active surveillance in selected provinces of China.[34] Since a systematic review on the epidemiology, clinical signs, pathogenesis, diagnosis, treatment, and prevention of human infection with SFTSV has been published,[157] we provide only a brief description and some new information about the infection.

Tick and animal infections

SFTSV have been reported to infect *H longicornis* and *Rhipicephalus microplus* ticks, with a higher prevalence of infection in *H longicornis* (4–9%) compared with in *R microplus* (0–6%).[34,110] Various animals, including goats, cattle, dogs, pigs, rodents, chickens, geese, and hedgehogs, might be infected by this pathogen.[110,111] Studies in Shandong, Jiangsu, and Hubei provinces showed that goats and cattle had the highest seropositive rate. Furthermore, big animals usually had higher seropositive rates than small animals.[111,112]

Human infections

As of 2013, 2543 human SFTS infections have been reported to the China Center For Disease Control And Prevention, including 154 deaths.[34,113–118] Incidence hotspots are located in Henan, Hubei, Anhui, and Shandong provinces of middle-eastern China, in addition to Liaoning Province of northeastern China (appendix). Clinical manifestations in patients with SFTS are non-specific with major symptoms including respiratory tract symptoms, sudden onset of fever up to 38–41°C, headache, fatigue, myalgia, and gastrointestinal symptoms (loss of appetite, nausea, vomiting, and diarrhoea). Multiple organ failure develops rapidly in most patients (with raised concentrations of serum alanine aminotransferase, aspartate aminotransferase, creatine kinase, and lactate dehydrogenase; and proteinuria and haematuria), and is usually accompanied by thrombocytopenia, leucocytopenia, and lymphadenopathy.[34,117]

Factors contributing to the emergence of tick-borne infections

Beyond doubt, advances in and application of molecular technologies have resulted in the discovery of novel agents and helped to identify human infections caused by agents previously detected in ticks. Thus, to some extent, the emergence of tick-borne infections has resulted from the discovery of novel pathogens through the use of more sensitive and reliable detection methods. However, various biological factors, such as tick and host population dynamics, which have caused an increase in the transmission and dissemination of tick-borne zoonotic diseases, are probably the main reasons for the emergence of these infections.[3]

Changes in land use have affected the emergence of tick-borne zoonotic diseases by altering the interactions and abundance of ticks, wild and domestic hosts, and human exposure to pathogens.[158] An example is the emergence of Lyme disease in northeastern USA. Reforestation of this region during the 20th century is thought to have increased the population of white-tailed deer, which greatly amplified the number of *Ixodes scapularis*. Consequentially, vector tick densities grew and expanded, contributing substantially to the emergence of Lyme disease in the USA.[159] Fragmentation of forests in eastern regions of Canada and the USA might have increased the relative abundance of small mammals because of a reduction in predator communities, leading to an increase in *B burgdorferi* sensu lato infection rates in *I scapularis* nymphs. Ultimately, people in these areas were confronted with a higher risk of Lyme disease.[160,161]

Since the mid-1990s, the Chinese central government has initiated the Greening Program to regain forests and grasslands from former agricultural lands.[162] Reforestation and grass replanting with high-quality vegetative cover could have increased the abundance and diversity of ticks and animal hosts, and favoured the re-establishment of pre-existing tick vector enzootic cycles in these areas. One example described in our study was in the most severely endemic region of SFTS. Our findings showed that the incidence of SFTS is significantly associated with vegetation-rich lands. A 10% increase in shrub, forest, and rain-fed cropland areas resulted in increased human SFTS incidence rates of 51%, 51%, and 90%, respectively.[163]

Additionally, urbanisation has affected the emergence and increasing incidence of tick-borne diseases. Studies in Europe suggest that encroachment into forested and uncultivated areas, and protection of existing green spaces in the process of urbanisation, have created opportunities for ticks to survive in urban and especially suburban environments. The presence of many pets and domestic animals, which can serve as tick hosts and pathogen reservoirs, might help tick transmission of various human and animal pathogens.[164,165] In the past three decades, China has gone through the most rapid urbanisation in its history. This rapid urbanisation, followed by widespread rural-to-urban migration of the human population, intensive long-distance trade, and explosive short-term travel for shopping, has led to substantial health risks including air pollution, occupational and traffic hazards, and altered diets and activity.[166] All of these changes in human activity, together with increased contact between human beings and their pets and nature, have probably contributed to the increasing abundance of tick exposure, as reported in other developed countries.[164] Further investigation is needed to show the relation between emerging tick-borne diseases and urbanisation in mainland China.

The effect of worldwide climate change on the emergence of most vector-borne zoonotic diseases (including tick-borne diseases) is thought to be less important than changes in land use, animal host communities, human living conditions, and societal factors.[3] Although the effects of climate on transmission of infectious diseases are thought to be non-linear and act in opposing directions in different climate regions, the seasonal dynamics of tick vectors are largely defined by climate conditions, which might further affect the seasonal pattern of tick-borne diseases. An increase in winter temperatures is known to cause the northward extension and increased abundance of *Ixodes ricinus*, which subsequently raises the risk of tick-borne disease dissemination.[167–169] Although this topic is still under debate, climatic change could have a role in the emergence of tick-borne diseases in China. Further studies are needed to better elucidate this issue.

Perspectives

Ticks are thought to be second only to mosquitoes as worldwide vectors of human infectious diseases.[170] Up to now, more than 120 tick species have been identified in China, including over 100 species in the Ixodidae (so-called hard tick) family and 19 species in the Argasidae (soft tick) family.[171] They transmit several pathogens when feeding on a range of animals, including human beings as accidental hosts. About 30 tick species are reported to feed on human beings.[172,173] The diverse geographical distribution and abundance of ticks are dependent on optimum environmental conditions and biotopes for each tick species, which define the risk areas for corresponding tick-borne zoonoses.[3] In addition to the emerging tick-borne infections, previously documented and well established tick-borne diseases are a continuing threat to human health, including tick-borne encephalitis in northeastern China, Crimean-Congo haemorrhagic fever in northwestern China, tularaemia and north-Asia tick-borne spotted fever in northern China, and Q fever, which is widely distributed throughout China.[174–183]

The non-specific clinical manifestations caused by tick-borne pathogens, such as SFGR, *Anaplasma* species, *B burgdorferi* sensu lato, *Babesia* species, and SFTSV, present a major diagnostic challenge. Most physicians are unfamiliar with the many tick-borne diseases that present with non-specific symptoms in the early stages of the illness. The wide distributions of the 33 emerging tick-associated agents and their tick vectors, in addition to the diversity of tick species throughout mainland China, imply that reported cases of infection might be only the tip of the iceberg in regard to the actual number of tick-borne diseases. To develop a reasonable differential diagnosis and identify a specific pathogen, laboratory diagnostic methods that are rapid, convenient, and practical are urgently needed for these emerging tick-borne diseases. Although great progress has been made in mainland China in the detection and identification of various tick-borne pathogens and diagnosis of the infections they cause, the necessary technologies are still unavailable in most general hospitals. Unfortunately, the importance of tick-borne diseases to human and animal health has not been sufficiently recognised as a result of inaccessibility to laboratory tests for aetiological diagnosis and inadequate surveillance activities.

In China, 18 tick-borne agents have been detected in ticks or animals, including four *Rickettsia* species, two *Ehrlichia* species, an *Anaplasma* species, three genospecies of *B burgdorferi* sensu lato, and eight *Babesia* species; however, the full effect of their pathogenicity to human beings is still to be established. Despite increasing knowledge about their geographical distribution, the natural cycle of these agents and the natural history of their infection in tick vectors and animal hosts have yet to be elucidated. Identifying human infections after potentially pathogenic agents are identified in ticks could take many years, in part because the microbial loads are much lower in human blood than in arthropods.[184] For example, *R sibirica* sp BJ-90 was first identified in *D sinicus* ticks in China in 1990,[7] but was not discovered to infect human beings until 22 years later.[46] Similarly, *A phagocytophilum* was initially detected in China in 1997;[15] however, nosocomial transmission of human granulocytic anaplasmosis was not recognised until 10 years later.[73] As such, the 18 tick-associated agents that have been recognised in China in either ticks or animals represent potential candidates for new tick-borne human diseases. Likewise, a search for potential new pathogens in ticks is essential for the discovery of emerging tick-borne diseases in human beings.

Conclusion

33 tick species belonging to six genuses have been reported to be naturally infected with the emerging pathogenic agents described in this Review (figure 1). Except for eight species (*Dermacentor abaensis*, *Dermacentor daghestanicus*, *Haemaphysalis bispinosa*, *H flava*, *Haemaphysalis sinensis*, *Haemaphysalis yeni*, *Ixodes myospalacis*, and *Rhipicephalus turanicus*), most species carry two or more agents. Conversely, some emerging agents such as *R heilongjiangensis*, *E chaffeensis*, *A phagocytophilum*, and *B garinii* can infect several tick species. Additionally, tick-borne pathogens that infect domestic animals might eventually cause human disease. A representative example is *B divergens*, which has long been recognised to cause cattle babesiosis in Europe, and was subsequently identified as a human pathogen.[185] In China, a wide range of emerging tick-borne agents are known to infect various domestic animals (appendix), and their potential capability to infect humans warrants great attention and further investigation. With the continued emergence of tick-borne diseases in mainland China, improving our understanding of the existence and health burden of these diseases is essential for China and for the rest of the world.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by the Natural Science Foundation of China (81290344, 81130086, and 81172728), the Special Program for Prevention and Control of Infectious Diseases in China (number 2013ZX10004218), the Basic Work on Special Program for Science & Technology Research (2013FY114600), and National Institutes of Health–National Institute of Allergy and Infectious Diseases (5R01AI083640 to XFY). The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

References

1. Dantas-Torres F, Chomel BB, Otranto D. Ticks and tick-borne diseases: a One Health perspective. Trends Parasitol. 2012; 28:437–46. [PubMed: 22902521]
2. Socolovschi C, Mediannikov O, Raoult D, Parola P. The relationship between spotted fever group Rickettsiae and ixodid ticks. Vet Res. 2009; 40:34. [PubMed: 19358804]
3. Kilpatrick AM, Randolph SE. Drivers, dynamics, and control of emerging vector-borne zoonotic diseases. Lancet. 2012; 380:1946–55. [PubMed: 23200503]
4. Wang L, Wang Y, Jin S, et al. Emergence and control of infectious diseases in China. Lancet. 2008; 372:1598–605. [PubMed: 18930534]
5. Lou D, Wu YM, Wang B. A new specie in *Rickettsia*: isolation and identification of *Rickettsia heilongjiangii*. Chin J Microbiol Immunol. 1985; 5:250. in Chinese.
6. Zhang L, Raoult D, Fournier PE. '*Rickettsia hulinii*' belongs to the *Rickettsia heilongjiangensis* species. Clin Microbiol Infect. 2009; 15(suppl 2):340–42. [PubMed: 19438613]
7. Yu X, Jin Y, Fan M, Xu G, Liu Q, Raoult D. Genotypic and antigenic identification of two new strains of spotted fever group rickettsiae isolated from China. J Clin Microbiol. 1993; 31:83–88. [PubMed: 8093253]
8. Li W, Liu L, Jiang X, et al. Molecular identification of spotted fever group Rickettsiae in ticks collected in central China. Clin Microbiol Infect. 2009; 15(suppl 2):279–80. [PubMed: 19298396]
9. Tian ZC, Liu GY, Shen H, Xie JR, Luo J, Tian MY. First report on the occurrence of *Rickettsia slovaca* and *Rickettsia raoultii* in *Dermacentor silvarum* in China. Parasit Vectors. 2012; 5:19. [PubMed: 22257726]
10. Zou Y, Wang Q, Fu Z, et al. Detection of spotted fever group *Rickettsia* in *Haemaphysalis longicornis* from Hebei Province, China. J Parasitol. 2011; 97:960–62. [PubMed: 21506802]
11. Jia N, Zheng YC, Jiang JF, Ma L, Cao WC. Human infection with *Candidatus* Rickettsia tarasevichiae. N Engl J Med. 2013; 369:1178–80. [PubMed: 24047080]
12. Cao WC, Gao YM, Zhang PH, et al. Identification of *Ehrlichia chaffeensis* by nested PCR in ticks from Southern China. J Clin Microbiol. 2000; 38:2778–80. [PubMed: 10878087]
13. Pan H, Chen XR, Ma YH, et al. *Ehrlichia canis* DNA found in ticks in the south of China. Chin J Zoonoses. 1999; 15:3–6. in Chinese.
14. Wen B, Jian R, Zhang Y, Chen R. Simultaneous detection of *Anaplasma marginale* and a new *Ehrlichia* species closely related to *Ehrlichia chaffeensis* by sequence analyses of 16S ribosomal DNA in *Boophilus microplus* ticks from Tibet. J Clin Microbiol. 2002; 40:3286–90. [PubMed: 12202567]
15. Cao WC, Zhao QM, Zhang PH, et al. Granulocytic Ehrlichiae in *Ixodes persulcatus* ticks from an area in China where Lyme disease is endemic. J Clin Microbiol. 2000; 38:4208–10. [PubMed: 11060091]
16. Hua P, Yuhai M, Shide T, Yang S, Bohai W, Xiangrui C. Canine ehrlichiosis caused simultaneously by *Ehrlichia canis* and *Ehrlichia platys*. Microbiol Immunol. 2000; 44:737–39. [PubMed: 11092236]
17. Li H, Zheng YC, Ma L, et al. Human infection with a novel tick-borne Anaplasma species in China: a surveillance study. Lancet Infect Dis. 2015; 15:663–70. [PubMed: 25833289]
18. Li H, Jiang JF, Liu W, et al. Human infection with *Candidatus* Neoehrlichia mikurensis, China. Emerg Infect Dis. 2012; 18:1636–39. [PubMed: 23017728]
19. Ai CX, Wen YX, Zhang YG, et al. Clinical manifestations and epidemiological characteristics of Lyme disease in Hailin county, Heilongjiang Province, China. Ann N Y Acad Sci. 1988; 539:302–13. [PubMed: 3190101]
20. Masuzawa T, Takada N, Kudeken M, et al. *Borrelia sinica* sp. nov., a lyme disease-related *Borrelia* species isolated in China. Int J Syst Evol Microbiol. 2001; 51:1817–24. [PubMed: 11594614]
21. Shi CX, Zhang ZF, Wan KL. Analyzing clinical samples of Lyme disease with 5s-23s rRNA gene spacer RFLP analysis. Chin J Zoonoses. 2000; 16:21–23. in Chinese.
22. Chu CY, Liu W, Jiang BG, et al. Novel genospecies of *Borrelia burgdorferi* sensu lato from rodents and ticks in southwestern China. J Clin Microbiol. 2008; 46:3130–33. [PubMed: 18614645]

23. Hao Q, Hou X, Geng Z, Wan K. Distribution of *Borrelia burgdorferi* sensu lato in China. J Clin Microbiol. 2011; 49:647–50. [PubMed: 21106783]
24. Chen DM. Investigation report on sheep babesiosis with *Piroplasma ovis* infection. Chin J Vet Sci Technol. 1982; 12:31–32. in Chinese.
25. Lv WS, Yin H, Lv WX, Yu F, Zhang QC, Dou HF. Detection of *Babesia major* and the identification of its tick vector in mainland China. Chin J Vet Sci Technol. 1988; 18:11–14. in Chinese.
26. Bai Q, Liu GY, Zhang L, Zhang JY. Discovery and isolation of *Babesia ovata* in China. Chin J Vet Sci Technol. 1990; 20:2–4. in Chinese.
27. Liu ZL, Zhao JL, Ma LH, Yao BA. *Babesia orientalis* sp. nov. parasitized in buffalo Bubalus bubalis in China (*Piroplasmida: Babesiidae*). Acta Veterinaria et Zootechnica Sinica. 1997; 28:84–89. in Chinese.
28. Yin H, Luo JX, Lv WS, et al. Isolation and configuration observation of *Babesia motasi* and *Babesia ovis* in mainland China. Chin J Vet Sci Technol. 1997; 27:7–9. in Chinese.
29. Li YZ, Lu WY, Song JG. Studies on etiology and integrated control measures of difficult equine diseases in Gansu Province, China. J Chin Agric Univ. 1998; S2:130. in Chinese.
30. Luo J, Yin H, Liu Z, et al. Molecular phylogenetic studies on an unnamed bovine *Babesia* sp. based on small subunit ribosomal RNA gene sequences. Vet Parasitol. 2005; 133:1–6. [PubMed: 15982821]
31. Liu AH, Yin H, Guan GQ, et al. At least two genetically distinct large *Babesia* species infective to sheep and goats in China. Vet Parasitol. 2007; 147:246–51. [PubMed: 17531391]
32. Yang LW, Hou Y, Li M, Wen ZQ, Yang J, Fan DH. Study of tick-borne pathogens at Heilongjiang Port. Chin Front Health Q. 2007; 30:77–82. in Chinese.
33. Sun Y, Li SG, Jiang JF, et al. *Babesia venatorum* infection in child, China. Emerg Infect Dis. 2014; 20:896–97. [PubMed: 24751126]
34. Yu XJ, Liang MF, Zhang SY, et al. Fever with thrombocytopenia associated with a novel bunyavirus in China. N Engl J Med. 2011; 364:1523–32. [PubMed: 21410387]
35. Wu YM, Wei AM, Hu LM, et al. Study on aetiology of *Rickettsia heilongianggii* tick borne spotted fever. Chin Public Health. 2001; 7:28–30. in Chinese.
36. Hu MX, Zhang J, Fan DH, Fu WM, Sun XF, Yang LW. Detection of rodent infected by new tick pathogens in Suifenhe and Dongning Ports. Chin J Vector Biol Control. 2009; 20:573–76. in Chinese.
37. Sun XF, Ding SL, Hu MX, Guo XM, Zhao G. Study on tick-borne *Rickettsia* dermacentroxenus infection at Heilongjiang Port. Chin Front Health Q. 2007; 30:154–56. in Chinese.
38. Wu YM, Liu GP, Wei AM, et al. Investigation of spotted fever group *Rickettsia* in the northeastern China. Chin J Public Health. 2003; 19:1043–44. in Chinese.
39. Hao GF, Li H, Sun Y, et al. Detection of tick and tick-borne pathogen in some ports of Inner Mongolia. Zhonghua Liu Xing Bing Xue Za Zhi. 2009; 30:365–67. in Chinese. [PubMed: 19731529]
40. Li Y, Li ZK, Chen G, Kang M, Liu DX, Zhang YM. Identification and phylogenetic analysis of spotted fever group *Rickettsia* isolated from Qinghai province. Chin J Vet Sci. 2014; 34:1956–61. in Chinese.
41. Zhang LJ, Zhang JS, Fu XP, Luan MC. First identification of a *Rickettsia* closely related to R. heilongjiangii and *R. massilliae* in South China. Infect Dis Inf. 2006; 19:65–67. in Chinese.
42. Liang CW, Zhao JB, Li J, et al. Spotted fever group *Rickettsia* in Yunnan Province, China. Vector Borne Zoonotic Dis. 2012; 12:281–86. [PubMed: 22225423]
43. Jin YM, Zhang LJ, Sun LY, et al. Epidemiological investigation of emerging spotted fever in Chengmai County, Hainan Province. Dis Surveill. 2011; 26:18–22. in Chinese.
44. Sun J, Lin J, Gong Z, et al. Detection of spotted fever group Rickettsiae in ticks from Zhejiang Province, China. Exp Appl Acarol. 2015; 65:403–11. [PubMed: 25633265]
45. Wu YM, Wei AM, Hu LM, et al. Identification of spotted fever group (SFG) H-5 strain isolated from the patient's blood samples. Chin J Zoonoses. 1998; 14:23–26. in Chinese.

46. Jia N, Jiang JF, Huo QB, Jiang BG, Cao WC. *Rickettsia sibirica* subspecies *sibirica* BJ-90 as a cause of human disease. N Engl J Med. 2013; 369:1176–78. [PubMed: 24047079]

47. Ye X, Sun Y, Ju W, Wang X, Cao W, Wu M. Vector competence of the tick *Ixodes sinensis* (*Acari: Ixodidae*) for *Rickettsia monacensis.* Parasit Vectors. 2014; 7:512–18. [PubMed: 25406413]

48. Jia N, Zheng YC, Ma L, et al. Human infections with *Rickettsia raoultii*, China. Emerg Infect Dis. 2014; 20:866–68. [PubMed: 24750663]

49. Sun X, Zhang GL, Liu R, Liu XM, Zhao Y, Zheng Z. Molecular epidemiological study of *Rickettsia raoultii* in ticks from Xinjiang, China. Zhonghua Liu Xing Bing Xue Za Zhi. 2013; 34:756–57. in Chinese. [PubMed: 24303567]

50. Zhuang L, Wang CY, Tong YG, et al. Discovery of *Rickettsia* species in *Dermacentor niveus* Neumann ticks by investigating the diversity of bacterial communities. Ticks Tick Borne Dis. 2014; 5:564–68. [PubMed: 24950854]

51. Dong X, Chen XP, Liu N, Dumler SJ, Zhang YZ. Co-circulation of multiple species of Rickettsiales bacteria in one single species of hard ticks in Shenyang, China. Ticks Tick Borne Dis. 2014; 5:727–33. [PubMed: 25131152]

52. Feng S, Wu H, Zhang LW, et al. Molecular epidemiological study of tick-borne spotted fever group *Rickettsia* in western mountain area of Hebei Province, China. Chin J Vector Biol Control. 2013; 24:308–12. in Chinese.

53. Gao D, Cao W, Zhang X. Investigations on human ehrlichia infectious people in Daxingan Mountains. Zhonghua Liu Xing Bing Xue Za Zhi. 2001; 22:137–41. in Chinese. [PubMed: 11860865]

54. Sun X, Zhang GL, Liu XM, Zhao Y, Zheng Z. Investigation of tick species and tick-borne pathogens in Hoxud County of Xinjiang Uyghur Autonomous Region, China. Chin J Vector Biol Control. 2013; 24:5–10. in Chinese.

55. Dong T, Qu Z, Zhang L. Detection of *A. phagocytophilum* and *E. chaffeensis* in patient and mouse blood and ticks by a duplex real-time PCR assay. PLoS One. 2013; 8:e74796. [PubMed: 24023963]

56. Li HM, Jiang BG, He J, et al. Detection and identification of *Ehrlichia* sp. in *Boophilus microplus* ticks from Xiamen of Fujian Province. J Pathog Biol. 2006; 1:174–76. in Chinese.

57. Meng QL, Qiao J, Sheng JL, et al. Survey on tick-borne Anaplasmataceae in the south edge of Gurbantunggut desert. Chin J Vet Sci. 2012; 32:1158–63. in Chinese.

58. Chen Z, Liu Q, Liu JQ, et al. Tick-borne pathogens and associated co-infections in ticks collected from domestic animals in central China. Parasit Vectors. 2014; 7:237. [PubMed: 24886497]

59. Zhang L, Cui F, Wang L, et al. Investigation of anaplasmosis in Yiyuan County, Shandong Province, China. Asian Pac J Trop Med. 2011; 4:568–72. [PubMed: 21803311]

60. Zhao QL, Huang L, Yang X, et al. 16s rRNA sequence analysis of *Anaplasma* and *Ehrlichia* in rodents from parts area of Xinjiang. Chin J Zoonoses. 2013; 29:743–47. in Chinese.

61. Gao YM, Zhang XT, Cao WC, et al. Detection of *Ehrlichia chaffeensis* in ticks and rodents using semi-nested PCR. Chin J Zoonoses. 2000; 16:25–28. in Chinese.

62. Xu Z, Xu XH, Zhou YL, et al. Comprehensive surveillance of tick-borne diseases in Jiande, Zhejiang province, China. Chin J Vector Biol Control. 2014; 25:350–53. in Chinese.

63. Li Y, Chen Z, Liu Z, et al. Molecular survey of *Anaplasma* and *Ehrlichia* of red deer and sika deer in Gansu, China in 2013. Transbound Emerg Dis. 2015 published online Feb 7. DOI:10.1111/tbed.12335.

64. Zhang L, Wang G, Liu Q, et al. Molecular analysis of *Anaplasma phagocytophilum* isolated from patients with febrile diseases of unknown etiology in China. PLoS One. 2013; 8:e57155. [PubMed: 23451170]

65. Zhang L, Liu H, Xu B, et al. *Anaplasma phagocytophilum* infection in domestic animals in ten provinces/cities of China. Am J Trop Med Hyg. 2012; 87:185–89. [PubMed: 22764312]

66. Li GH, Yu Q, Zhang QX, et al. Molecular epidemiology regarding Anaplasma phagocytophilum in Dermacentor silvarum in Ningwu county, Shanxi province. Zhonghua Liu Xing Bing Xue Za Zhi. 2012; 33:642–43. in Chinese. [PubMed: 22993783]

67. Jiang JF, Jiang BG, Yu JH, et al. *Anaplasma phagocytophilum* infection in ticks, China–Russia border. Emerg Infect Dis. 2011; 17:932–34. [PubMed: 21529418]

68. Li Y, Kang FY, Yang JF, Sun CQ, Liu ZJ, Yin H. Prevalence and coexistence of *Anaplasma phagocytophilum* and *Borrelia burgdorferi* sensu lato in ticks in Gansu, Hunan and Guangdong provinces, China. Chin J Zoonoses. 2013; 29:117–21. in Chinese.
69. Yang J, Liu Z, Guan G, et al. Prevalence of *Anaplasma phagocytophilum* in ruminants, rodents and ticks in Gansu, north-western China. J Med Microbiol. 2013; 62:254–58. in Chinese. [PubMed: 23105025]
70. Cao WC, Zhao QM, Zhang PH, et al. Prevalence of *Anaplasma phagocytophila* and *Borrelia burgdorferi* in *Ixodes persulcatus* ticks from northeastern China. Am J Trop Med Hyg. 2003; 68:547–50. [PubMed: 12812342]
71. Zhang HL, Sun Y, Wang JJ. Investigation on foci severe fever with thrombocytopenia syndrome and human granulocytic anaplasmosis in Lujiang County. Chin J Dis Control Prev. 2015; 19:273–76. in Chinese.
72. Zhang YZ, Wang Y, Yang WH, et al. Seroprevalence and molecular biological investigation of commonly known *Rickettsia* species in rodents in Qujing Prefecture, Yunnan Province, China. Chin J Zoonoses. 2015; 31:35–40. in Chinese.
73. Zhang L, Liu Y, Ni D, et al. Nosocomial transmission of human granulocytic anaplasmosis in China. JAMA. 2008; 300:2263–70. [PubMed: 19017912]
74. Wang S, Kou ZQ, Wang M, et al. A survey and identification of co-infection of *Anaplasma phagocytophilum* and Ehrlichia chaffeensis in Shandong. Dis Surveill. 2012; 27:642–43. in Chinese.
75. Li Z, Ding SJ, Lv H, Chen Y, Hou PQ, Wang XJ. Investigation of one case of human granulocytic anaplasmosis in Shandong Province. Infect Dis Inf. 2009; 22:165–68. in Chinese.
76. Li H, Jiang J, Tang F, et al. Wide distribution and genetic diversity of "*Candidatus* Neoehrlichia mikurensis" in rodents from China. Appl Environ Microbiol. 2013; 79:1024–27. [PubMed: 23183973]
77. Lu QY, Cheng SY, Peng WL, Zhao JL, Jiang LP, Ge JH. *Candidatus* Neoehrlichia mikurensis infection on animals and related 16S rRNA gene analysis in Zhejiang province. Zhonghua Liu Xing Bing Xue Za Zhi. 2012; 33:993–94. in Chinese. [PubMed: 23297473]
78. Ni XB, Jia N, Jiang BG, et al. Lyme borreliosis caused by diverse genospecies of *Borrelia burgdorferi* sensu lato in northeastern China. Clin Microbiol Infect. 2014; 20:808–14. [PubMed: 24438159]
79. Li M, Masuzawa T, Takada N, et al. Lyme disease *Borrelia* species in northeastern China resemble those isolated from far eastern Russia and Japan. Appl Environ Microbiol. 1998; 64:2705–09. [PubMed: 9647853]
80. Jiang B, Yao H, Tong Y, et al. Genome sequence of *Borrelia garinii* strain NMJW1, isolated from China. J Bacteriol. 2012; 194:6660–61. [PubMed: 23144406]
81. Chu CY, Jiang BG, He J, et al. Genetic diversity of *Borrelia burgdorferi* sensu lato isolates from Northeastern China. Vector Borne Zoonotic Dis. 2011; 11:877–82. [PubMed: 21870355]
82. Shi SG, Zhang F, Liu ZJ. Molecular epidemiological studies on *Borrelia burgdorferii* in ticks collected from several provinces and autonomous regions of northwestern China. Chin J Zoonoses. 2011; 27:461–63. in Chinese.
83. Chu CY, Jiang BG, Liu W, et al. Presence of pathogenic *Borrelia burgdorferi* sensu lato in ticks and rodents in Zhejiang, south-east China. J Med Microbiol. 2008; 57:980–85. in Chinese. [PubMed: 18628499]
84. Wang HW, He J, Chu CY, et al. Detection and genotyping of *Borrelia burgdorferi* sensu lato in ticks from some areas of China. J Pathog Biol. 2006; 1:81–85. in Chinese.
85. Zhang JJ, Zhang F, Li L, Liu ZJ. *Borrelia burgdorferi* infection and their genotypes in ticks and rodents collected from Maijishan region, Gansu Province, China. Chin J Zoonoses. 2015; 31:357–60. in Chinese.
86. Hou J, Ling F, Chai C, et al. Prevalence of *Borrelia burgdorferi* sensu lato in ticks from eastern China. Am J Trop Med Hyg. 2015; 92:262–66. [PubMed: 25548382]
87. Chu CY, He J, Zhao QM, et al. Molecular epidemiological studies on *Borrelia burgdorferi* in rodents collected in the forest area of several provinces and autonomous regions of China. Chin J Zoonoses. 2006; 22:817–20. in Chinese.

88. Hou XX, Geng Z, Hao Q, Zhang Y, Wan KL. Rats, the primary reservoir hosts of *Borrelia burgdorferi* in six representative provinces, China. Chin J Zoonoses. 2010; 26:1034–36. in Chinese.

89. Zhan L, Chu CY, Zuo SQ, et al. *Anaplasma phagocytophilum* and *Borrelia burgdorferi* in rabbits from southeastern China. Vet Parasitol. 2009; 162:354–56. [PubMed: 19345508]

90. Tan YH, Liu Y, Wan KL, et al. Molecular epidemiological study of *Borrelia burgdorferi* infection among population in Xinjiang, China. Chin J Vector Biol Control. 2013; 24:297–300. in Chinese.

91. Zhu X, Zhang L, Hou XB, et al. Investigation on Lyme disease of patients with arthrities or neurological disorders in Hainan province, China. Chin J Zoonoses. 2015; 31:353–56. in Chinese.

92. Zhang L, Wang Y, Chen C, et al. Isolation of *Borrelia burgdorferi* in *ixodes* from four counties, in North Xinjiang. Zhonghua Liu Xing Bing Xue Za Zhi. 2014; 35:262–65. in Chinese. [PubMed: 24831623]

93. Li W, Peng HS, Li XM. Diagnosis and treatment of a goat infected with *Babesia ovis*. Contemp Anim Hus. 2015; 1:12–13. in Chinese.

94. Luo JX, Yin H, Liu GY, et al. Collection and identification of piroplasma infected to cattle and sheep in China. Chin J Parasitol Parasit Dis. 2006; 24:S48–52. in Chinese.

95. Bai Q, Liu G, Han G, Hui Y. Isolation and complementary transmission of *Babesia ovata* in Zhangjiachuan of Gansu Province. Chin J Vet Sci Technol. 1994; 24:9–10. in Chinese.

96. He L, Feng HH, Zhang WJ, et al. Occurrence of *Theileria* and *Babesia* species in water buffalo (*Bubalus babalis*, Linnaeus, 1758) in the Hubei province, South China. Vet Parasitol. 2012; 186:490–96. [PubMed: 22154255]

97. Liu Q, Zhou YQ, Zhou DN, et al. Semi-nested PCR detection of *Babesia orientalis* in its natural hosts Rhipicephalus haemaphysaloides and buffalo. Vet Parasitol. 2007; 143:260–66. [PubMed: 17005323]

98. Niu Q, Luo J, Guan G, et al. Detection and differentiation of ovine *Theileria* and *Babesia* by reverse line blotting in China. Parasitol Res. 2009; 104:1417–23. [PubMed: 19205742]

99. Sun C, Liu Z, Gao J, et al. Investigations into the natural infection rate of *Haemaphysalis qinghaiensis* with piroplasma using a nested PCR. Exp Appl Acarol. 2008; 44:107–14. [PubMed: 18273685]

100. He SD, Che FM, Liu WQ. Investigation of *Babesia caballi* in areas around Qinghai Lake, China. Chin Anim Health Insp. 2007; 24:28. in Chinese.

101. Wang XS, Liu JY, Zhang L, Feng LG. Case report of horse *Babesia caballi* infection. Anim Breed Feed. 2014; 12:56–57. in Chinese.

102. Yi CY, Guo QY, Xue H, Peng C, Ba YCH. Detection of pathogen DNA of *Babesia caballi* from *Rhipicephalus sanguineus* and *Dermacentor nuttalli*. Heilongjiang Anim Sci Vet Med. 2014; 11:38–40. in Chinese.

103. Guan G, Ma M, Moreau E, et al. A new ovine *Babesia* species transmitted by Hyalomma anatolicum anatolicum. Exp Parasitol. 2009; 122:261–67. [PubMed: 19460377]

104. Lei YL, Wang XG, Yao LN, et al. Case report of human *Babesia* infections. Chin J Health Lab Technol. 2012; 22:651–52. in Chinese.

105. Sun Y, Liu G, Yang L, Xu R, Cao W. *Babesia microti*-like rodent parasites isolated from *Ixodes persulcatus* (*Acari: Ixodidae*) in Heilongjiang Province, China. Vet Parasitol. 2008; 156:333–39. [PubMed: 18718720]

106. Zhao XG, Li H, Sun Y, et al. Dual infection with *Anaplasma phagocytophilum* and *Babesia microti* in a *Rattus norvegicus*, China. Ticks Tick Borne Dis. 2013; 4:399–402. [PubMed: 23838022]

107. Zhou X, Li SG, Chen SB, et al. Co-infections with *Babesia microti* and *Plasmodium* parasites along the China–Myanmar border. Infect Dis Poverty. 2013; 2:24. [PubMed: 24090043]

108. Qi C, Zhou D, Liu J, et al. Detection of *Babesia divergens* using molecular methods in anemic patients in Shandong Province, China. Parasitol Res. 2011; 109:241–45. [PubMed: 21503639]

109. Jiang JF, Zheng YC, Jiang RR, et al. Epidemiological, clinical, and laboratory characteristics of 48 cases of "*Babesia venatorum*" infection in China: a descriptive study. Lancet Infect Dis. 2015; 15:196–203. [PubMed: 25539588]

110. Zhang YZ, Zhou DJ, Qin XC, et al. The ecology, genetic diversity, and phylogeny of Huaiyangshan virus in China. J Virol. 2012; 86:2864–68. [PubMed: 22190717]
111. Zhao L, Zhai S, Wen H, et al. Severe fever with thrombocytopenia syndrome virus, Shandong Province, China. Emerg Infect Dis. 2012; 18:963–65. [PubMed: 22608264]
112. Li Z, Hu J, Bao C, et al. Seroprevalence of antibodies against SFTS virus infection in farmers and animals, Jiangsu, China. J Clin Virol. 2014; 60:185–89. [PubMed: 24793967]
113. Ding F, Zhang W, Wang L, et al. Epidemiologic features of severe fever with thrombocytopenia syndrome in China, 2011–2012. Clin Infect Dis 2013. 56:1682–83.
114. Gai Z, Liang M, Zhang Y, et al. Person-to-person transmission of severe fever with thrombocytopenia syndrome bunyavirus through blood contact. Clin Infect Dis. 2012; 54:249–52. [PubMed: 22095565]
115. Yu L, Yu P, Liu DH, Hou J, Chen YF. Surveillance of syndrome of fever with thrombocytopenia in Dalian, 2012–2013. Study Trace Elem Health 2014. 31:5–6. in Chinese.
116. Bao CJ, Guo XL, Qi X, et al. A family cluster of infections by a newly recognized bunyavirus in eastern China, 2007: further evidence of person-to-person transmission. Clin Infect Dis 2011. 53:1208–14.
117. Gai ZT, Zhang Y, Liang MF, et al. Clinical progress and risk factors for death in severe fever with thrombocytopenia syndrome patients. J Infect Dis. 2012; 206:1095–102. [PubMed: 22850122]
118. Liu K, Zhou H, Sun RX, et al. A national assessment of the epidemiology of severe fever with thrombocytopenia syndrome, China. Sci Rep. 2015; 5:9679. [PubMed: 25902910]
119. Fan MY, Walker DH, Liu QH, et al. Rickettsial and serologic evidence for prevalent spotted fever rickettsiosis in inner Mongolia. Am J Trop Med Hyg. 1987; 36:615–20. [PubMed: 3578658]
120. Lin BH, Sun XJ, Zhan ZN, Lin YZ, Li WG. Serological and etiological studies on undefined rickettsiosis on Hainan Island. J Hainan Med College. 1997; 3:97–102. in Chinese.
121. Lin YZ, Sun XJ, Zhan ZN, et al. Serological and etiological studies on rickettsiosis in Hainan Island. Chin J Zoonoses. 1999; 15:90–91. in Chinese.
122. Shi H, Wang Y, Han H, et al. Analysis of 92 patients with tick-borne diseases in Mudanjiang. Chin J Vector Biol Control. 2013; 24:295–300. in Chinese.
123. Fan MY, Wang JG, Jiang YX, Zong DG, Lenz B, Walker DH. Isolation of a spotted fever group rickettsia from a patient and related ecologic investigations in Xinjiang Uygur Autonomous Region of China. J Clin Microbiol. 1987; 25:628–32. [PubMed: 3571471]
124. Wu J, Wang SL, Jin YM, et al. Detection of *groEL* gene in spotted fever group *Rickettsia* of patients with fever in Hainan province. Mod Prev Med. 2014; 41:2417–19. in Chinese.
125. Jiang BG, Zheng YC, Tong YG, et al. Genome sequence of *Borrelia afzelii* Strain HLJ01, isolated from a patient in China. J Bacteriol. 2012; 194:7014–15. [PubMed: 23209254]
126. Geng Z, Hou XX, Hao Q, Hu GL, Wan KL. Anti-*Borrelia burgdorferi* antibody response in 827 patients with suspected Lyme disease. Chin J Vector Biol Control. 2007; 18:219–21. in Chinese.
127. Zhou XY. The epidemiological and clinical analysis of Lyme disease in Mudanjiang from 1996 to 2003. Chin J Parasit Dis Control 2005. 18:159. in Chinese.
128. Peng FB, Zhang WF, Zhou GP, Zhang SY, Yuan YM, Wu YY. The detection and clinical study on Lyme disease in Beijing. Chin J Epidemiol. 1994; 15:10–13. in Chinese.
129. Huang ZY, Hou XX, Wan KL. An investigation of Lyme disease in Pingjiang County, Hunan Province, China. Chin J Vector Biol Control. 2001; 12:293–94. in Chinese.
130. Li YL, Hao JG, Zhang ZF, et al. The investigation of Lyme disease in Nanchuan County, Sichuan Province, China. Chin J Vector Biol Control. 1991; 2:54–56. in Chinese.
131. Jin SW, Hao Q, Tian Z, et al. Analysis of surveillance on Lyme disease in Xinjiang prospecting region of Henan oil prospecting bureau. Chin J Zoonoses. 2005; 21:501–02. in Chinese.
132. Li JF, Meng DB, Wang QF, Dong XR, Wang JY. The discovery of human babesiosis. Chin Vet. 1984; 6:19–20. in Chinese.
133. Wang HX. A case of human babesiosis in southwest region of China. Int J Med Parasit Dis. 2012; 39:190–92. in Chinese.
134. Kim KH, Yi J, Kim G, et al. Severe fever with thrombocytopenia syndrome. South Korea. Emerg Infect Dis 2013. 2012; 19:1892–94.

135. Takahashi T, Maeda K, Suzuki T, et al. The first identification and retrospective study of severe fever with thrombocytopenia syndrome in Japan. J Infect Dis. 2014; 209:816–27. [PubMed: 24231186]

136. McMullan LK, Folk SM, Kelly AJ, et al. A new phlebovirus associated with severe febrile illness in Missouri. N Engl J Med. 2012; 367:834–41. [PubMed: 22931317]

137. Jado I, Oteo JA, Aldámiz M, et al. *Rickettsia monacensis* and human disease, Spain. Emerg Infect Dis. 2007; 13:1405–07. [PubMed: 18252123]

138. de Sousa R, Pereira BI, Nazareth C, et al. *Rickettsia slovaca* infection in humans, Portugal. Emerg Infect Dis. 2013; 19:1627–29. [PubMed: 24050379]

139. Pretorius AM, Birtles RJ. *Rickettsia mongolotimonae* infection in South Africa. Emerg Infect Dis. 2004; 10:125–26. [PubMed: 15078607]

140. Ryffel K, Péter O, Rutti B, Suard A, Dayer E. Scored antibody reactivity determined by immunoblotting shows an association between clinical manifestations and presence of *Borrelia burgdorferi* sensu stricto, *B. garinii, B. afzelii*, and *B. Valaisiana* in humans. J Clin Microbiol. 1999; 37:4086–92. [PubMed: 10565936]

141. van Dam AP, Kuiper H, Vos K, et al. Different genospecies of *Borrelia burgdorferi* are associated with distinct clinical manifestations of Lyme borreliosis. Clin Infect Dis. 1993; 17:708–17. [PubMed: 7903558]

142. Zhang HL, Yang H, Zhang PH, et al. Spotted fever group *Rickettsia* DNA was detected in wild rodents and ticks in Dali, Yunnan Province, China. Chin J Vector Biol Control. 2004; 15:461–62. in Chinese.

143. Huang HN, Ding Z, He J, et al. Study on the coinfection status of *Borrelia burgdorferi* sensu lato and spotted fever group *Rickettsia* in ticks from Hunchun, Jilin province. Zhonghua Liu Xing Bing Xue Za Zhi. 2006; 27:379–83. in Chinese. [PubMed: 16981329]

144. Jiang LP, Mo SH, Zheng SG, et al. Spotted fever group rickettsiae DNA was first detected in ticks in Zhejiang Province. Chin J Vector Biol Control. 2006; 17:484–85. in Chinese.

145. Wang Z, Liu XG, Luo Y, et al. Investigation of tick-borne spotted fever group *Rickettsia* in northwestern Liaoning Province, China. Anim Hus Vet Med. 2015; 47:143–44. in Chinese.

146. Chai CL, Sun JM, Lu QY, et al. A cross-sectional study on tick-borne *Rickettsiae* infections among murine-like animals. Zhejiang Prev Med. 2014; 26:659–63. in Chinese.

147. Wang Z, Yu M, Yang SJ, et al. Epidemiological survey of spotted fever group *Rickettsia* in rodents in northeastern China. Chin Pre Med. 2015; 16:184–86. in Chinese.

148. Wang DM, Hao Q, Cai XH, Wan KL, Wang ZX, Chen J. Study on ribotyping of Lyme borreliosis spirochete in Guizhou province. Zhonghua Liu Xing Bing Xue Za Zhi. 2003; 24:1129–31. in Chinese. [PubMed: 14761632]

149. Yang Y, Zhang XL, Qiao S, et al. Investigation on tick-borne pathogens at Ganqimaodu Port between Sino-Mongolia border. Chin Front Health Q. 2011; 34:339–42. in Chinese.

150. Zuo SY, Tang K, Li Y, et al. DNA detection and sequence analysis of *Borrelia burgdorferi* sensu lato in rodents from Helongjiang and forest region. Zhonghua Liu Xing Bing Xue Za Zhi. 2012; 33:643–44. in Chinese. [PubMed: 22993784]

151. Yang XF, Wan KL, Lu JP, et al. Investigation of geographical epidemiology and etiological studies on Lyme disease in Inner Mongolia. Chin J Zoonoses. 1999; 15:98. in Chinese.

152. Yang XJ, Wan KL, Wang CS, et al. Etiological studies on Lyme disease in Jilin Province. Chin J Health Lab Technol. 2006; 16:1355–62. in Chinese.

153. Zhang DC, Hong Y, Zhang ZQ, et al. Isolation of *Borrelia burgdorferi* in ticks and rodents in Liaoning Province. Chin J Vector Biol Control. 1992; 3:19. in Chinese.

154. Tian WC, Moldenhauer S, Li MQ, et al. The first detection of *Borrelia burgdorferi* in H. japonica. Chin J Zoonoses. 1995; 11:22–25. in Chinese.

155. Zhang ZC, Tian WC, Guo YX, et al. Investigation of Lyme disease in Hebei Province. Chin J Public Health. 1995; 11:253–54. in Chinese.

156. Wang LJ, Chen ZL, Wan KL, et al. First isolation and identification of Lyme disease spirochete in Shandong Province. Chin J Vector Biol Control. 1997; 8:127–28. in Chinese.

157. Liu Q, He B, Huang SY, Wei F, Zhu XQ. Severe fever with thrombocytopenia syndrome, an emerging tick-borne zoonosis. Lancet Infect Dis. 2014; 14:763–72. [PubMed: 24837566]
158. Lambin EF, Tran A, Vanwambeke SO, Linard C, Soti V. Pathogenic landscapes: interactions between land, people, disease vectors, and their animal hosts. Int J Health Geogr. 2010; 9:54. [PubMed: 20979609]
159. Barbour AG, Fish D. The biological and social phenomenon of Lyme disease. Science. 1993; 260:1610–16. [PubMed: 8503006]
160. Levi T, Kilpatrick AM, Mangel M, Wilmers CC. Deer, predators, and the emergence of Lyme disease. Proc Natl Acad Sci USA. 2012; 109:10942–47. [PubMed: 22711825]
161. LoGiudice K, Duerr ST, Newhouse MJ, Schmidt KA, Killilea ME, Ostfeld RS. Impact of host community composition on Lyme disease risk. Ecology. 2008; 89:2841–49. [PubMed: 18959321]
162. Liu J, Li S, Ouyang Z, Tam C, Chen X. Ecological and socioeconomic effects of China's policies for ecosystem services. Proc Natl Acad Sci USA. 2008; 105:9477–82. [PubMed: 18621700]
163. Liu K, Cui N, Fang LQ, et al. Epidemiologic features and environmental risk factors of severe fever with thrombocytopenia syndrome, Xinyang, China. PLoS Negl Trop Dis. 2014; 8:e2820. [PubMed: 24810269]
164. Uspensky I. Tick pests and vectors (*Acari: Ixodoidea*) in European towns: introduction, persistence and management. Ticks Tick Borne Dis. 2014; 5:41–47. [PubMed: 24183576]
165. Uspensky, I. Ticks (*Acari: Ixodoidea*) as urban pests and vectors with special emphasis on ticks outside their geographical range.. In: Robinson, WH.; Bajomi, D., editors. Proceedings of the Sixth International Conference on Urban Pests. OOK-Press Kft; Hungary: 2008. p. 333-47.
166. Gong P, Liang S, Carlton EJ, et al. Urbanisation and health in China. Lancet. 2012; 379:843–52. [PubMed: 22386037]
167. Parola P. Tick-borne rickettsial diseases: emerging risks in Europe. Comp Immunol Microbiol Infect Dis. 2004; 27:297–304. [PubMed: 15225980]
168. Altizer S, Ostfeld RS, Johnson PT, Kutz S, Harvell CD. Climate change and infectious diseases: from evidence to a predictive framework. Science. 2013; 341:514–19. [PubMed: 23908230]
169. Harrus S, Baneth G. Drivers for the emergence and re-emergence of vector-borne protozoal and bacterial diseases. Int J Parasitol. 2005; 35:1309–18. [PubMed: 16126213]
170. Parola P, Raoult D. Ticks and tickborne bacterial diseases in humans: an emerging infectious threat. Clin Infect Dis. 2001; 32:897–928. [PubMed: 11247714]
171. Yang XJ, Chen Z, Liu JZ. Advances in systematics of ticks. Acta Entomologica Sinica. 2007; 50:941–49. in Chinese.
172. Meng, YC. Ticks, acari, and human diseases. 1st edn.. China Sci Tech Press; Hefei: 1995. p. 43in Chinese
173. Cao WC, Zhang XT, Xu RM. The medical significance of tick and tick-borne disease in public health. Chin J Public Health. 1999; 15:221–22. in Chinese.
174. Wu XB, Na RH, Wei SS, Zhu JS, Peng HJ. Distribution of tick-borne diseases in China. Parasit Vectors. 2013; 6:119. [PubMed: 23617899]
175. Zhao JW, Wang HY, Wang Y. Regional distribution profiles of tick borne pathogens in China. Chin J Biol Control. 2012; 18:45–48. in Chinese.
176. Zhan L, Cao WC, Jiang JF, et al. *Anaplasma phagocytophilum* from rodents and sheep, China. Emerg Infect Dis. 2010; 16:764–68. [PubMed: 20409364]
177. Wang YY, Li J, Wang S, Hu M, Lu FL. Tick-borne infectious diseases. Infect Dis Inf. 2011; 24:58–61. in Chinese.
178. Lu Z, Bröker M, Liang G. Tick-borne encephalitis in mainland China. Vector Borne Zoonotic Dis. 2008; 8:713–20. [PubMed: 18837668]
179. Xia H, Li P, Yang J, et al. Epidemiological survey of Crimean-Congo hemorrhagic fever virus in Yunnan, China, 2008. Int J Infect Dis 2011. 15:e459–63.
180. Wang Y, Peng Y, Hai R, et al. Diversity of *Francisella tularensis* subsp. *holarctica* lineages, China. Emerg Infect Dis. 2014; 20:1191–94. [PubMed: 24963721]
181. Chen M, Fan MY. A review on the research of North-Asia tick-borne spotted fever. Chin Public Health. 1997; 6:373–76. in Chinese.

182. Liu YF, Zhang Y. The study progress of Q fever and *Ehrlichiosis.* Med Recap. 2008; 6:864–67. in Chinese.

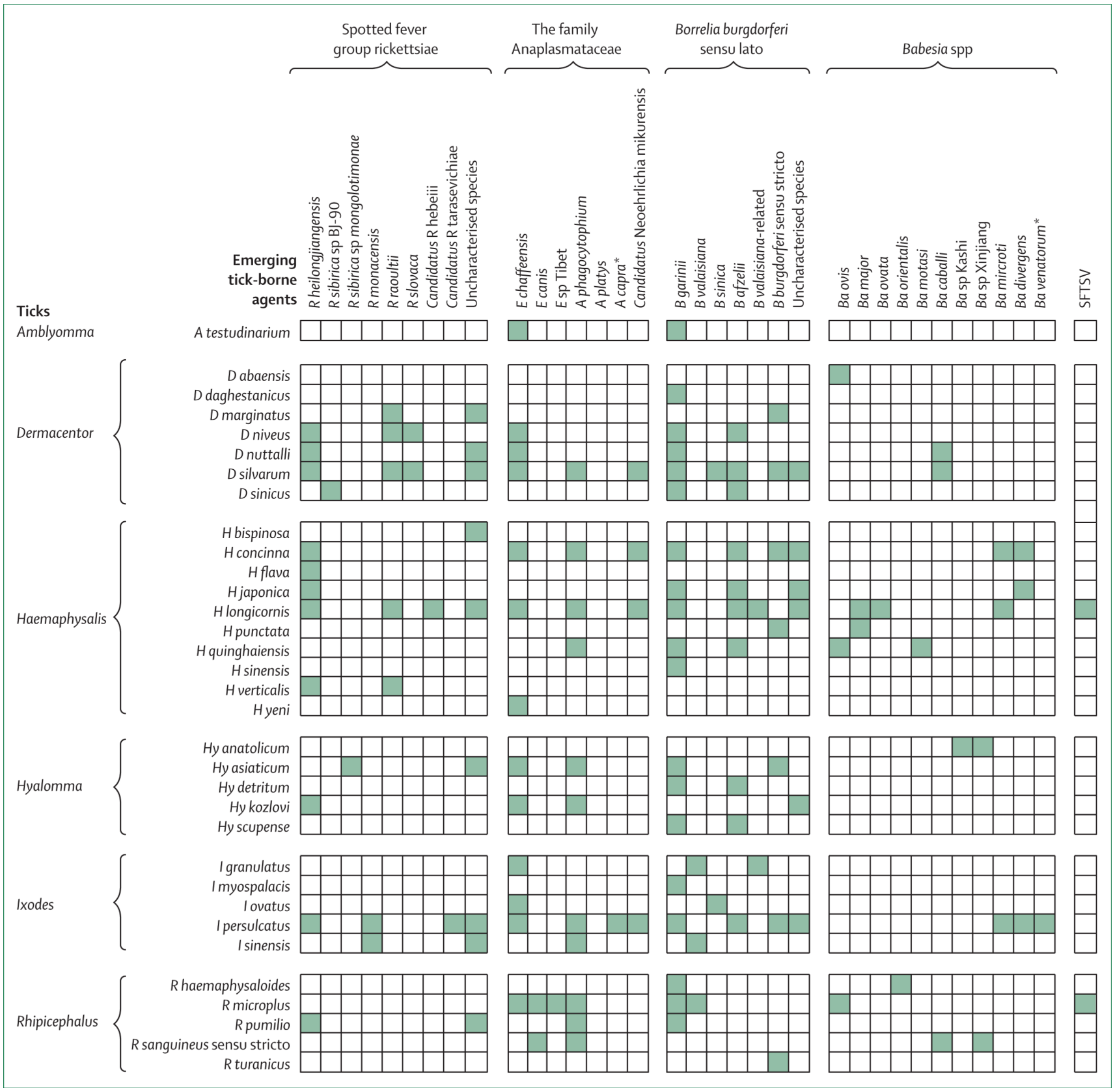
183. Süss J. Tick-borne encephalitis 2010: epidemiology, risk areas, and virus strains in Europe and Asia - an overview. Ticks Tick Borne Dis 2011. 2:2–15.

184. Parola P, Paddock CD, Socolovschi C, et al. Update on tick-borne rickettsioses around the world: a geographic approach. Clin Microbiol Rev. 2013; 26:657–702. [PubMed: 24092850]

185. Colwell DD, Dantas-Torres F, Otranto D. Vector-borne parasitic zoonoses: emerging scenarios and new perspectives. Vet Parasitol. 2011; 182:14–21. [PubMed: 21852040]

Search strategy and selection criteria

We searched PubMed and ISI Web of Science for articles published in English, and WanFang database, China National Knowledge Infrastructure, and Chinese Scientific Journal Database for articles published in Chinese between Jan 1, 1980, and May 31, 2015. We used the following search terms: “tick-borne disease”, “tick-borne zoonosis”, “tick-borne zoonotic disease”, “tick-associated agent”, “tick-associated microbe”, and “China”, in combination with each of the five genera of tick-borne agents. We did a secondary manual search of the references cited in these articles to find relevant articles. We investigated all the articles related to detection, identification, or infections of these five genera of tick-borne microbes in human beings, ticks, and animals. We contacted the corresponding authors for detailed information such as the time of discovery, location, and origin of tick-borne agents if any of this information was missing in the articles.



Ticks	Emerging tick-borne agents	Spotted fever group rickettsiae								
		R heilongjiangensis	*R sibirica* sp BJ-90	*R sibirica* sp *mongolotimonae*	*R monacensis*	*R raoultii*	*R slovaca*	*Candidatus* R hebeiii	*Candidatus* R tarasevichiae	Uncharacterised species
Amblyomma	*A testudinarium*									
Dermacentor	*D abaensis*									
	D daghestanicus									
	D marginatus					🟩				🟩
	D niveus	🟩				🟩	🟩			
	D nuttalli	🟩								🟩
	D silvarum	🟩				🟩	🟩			🟩
	D sinicus		🟩							
Haemaphysalis	*H bispinosa*									🟩
	H concinna	🟩								
	H flava	🟩								
	H japonica	🟩								
	H longicornis	🟩				🟩		🟩		🟩
	H punctata									
	H quinghaiensis									
	H sinensis									
	H verticalis	🟩				🟩				
	H yeni									
Hyalomma	*Hy anatolicum*									
	Hy asiaticum			🟩						🟩
	Hy detritum									
	Hy kozlovi	🟩								
	Hy scupense									
Ixodes	*I granulatus*									
	I myospalacis									
	I ovatus									
	I persulcatus	🟩			🟩				🟩	🟩
	I sinensis				🟩					🟩
Rhipicephalus	*R haemaphysaloides*									
	R microplus									
	R pumilio	🟩								🟩
	R sanguineus sensu stricto									
	R turanicus									

Ticks	Emerging tick-borne agents	The family Anaplasmataceae						
		E chaffeensis	*E canis*	*E* sp Tibet	*A phagocytophium*	*A platys*	*A capra**	*Candidatus* Neoehrlichia mikurensis
Amblyomma	*A testudinarium*	🟩						
Dermacentor	*D abaensis*							
	D daghestanicus							
	D marginatus							
	D niveus	🟩						
	D nuttalli	🟩						
	D silvarum	🟩			🟩			🟩
	D sinicus							
Haemaphysalis	*H bispinosa*							
	H concinna	🟩			🟩			🟩
	H flava							
	H japonica							
	H longicornis	🟩			🟩			🟩
	H punctata							
	H quinghaiensis				🟩			
	H sinensis							
	H verticalis							
	H yeni	🟩						
Hyalomma	*Hy anatolicum*							
	Hy asiaticum	🟩			🟩			
	Hy detritum							
	Hy kozlovi	🟩			🟩			
	Hy scupense							
Ixodes	*I granulatus*	🟩						
	I myospalacis							
	I ovatus	🟩						
	I persulcatus	🟩			🟩		🟩	🟩
	I sinensis				🟩			
Rhipicephalus	*R haemaphysaloides*							
	R microplus	🟩	🟩	🟩	🟩			
	R pumilio				🟩			
	R sanguineus sensu stricto		🟩		🟩			
	R turanicus							

Ticks	Emerging tick-borne agents	*Borrelia burgdorferi* sensu lato						
		B garinii	*B valaisiana*	*B sinica*	*B afzelii*	*B valaisiana*-related	*B burgdorferi* sensu stricto	Uncharacterised species
Amblyomma	*A testudinarium*	🟩						
Dermacentor	*D abaensis*							
	D daghestanicus	🟩						
	D marginatus						🟩	
	D niveus	🟩			🟩			
	D nuttalli	🟩						
	D silvarum	🟩		🟩	🟩		🟩	🟩
	D sinicus	🟩			🟩			
Haemaphysalis	*H bispinosa*							
	H concinna	🟩			🟩		🟩	🟩
	H flava							
	H japonica	🟩			🟩			🟩
	H longicornis	🟩			🟩	🟩		🟩
	H punctata						🟩	
	H quinghaiensis	🟩			🟩			
	H sinensis	🟩						
	H verticalis							
	H yeni							
Hyalomma	*Hy anatolicum*							
	Hy asiaticum	🟩					🟩	
	Hy detritum	🟩			🟩			
	Hy kozlovi							🟩
	Hy scupense	🟩			🟩			
Ixodes	*I granulatus*		🟩			🟩		
	I myospalacis	🟩						
	I ovatus			🟩				
	I persulcatus	🟩			🟩		🟩	🟩
	I sinensis		🟩					
Rhipicephalus	*R haemaphysaloides*	🟩						
	R microplus	🟩	🟩					
	R pumilio	🟩						
	R sanguineus sensu stricto							
	R turanicus						🟩	

Ticks	Emerging tick-borne agents	*Babesia* spp											
		Ba ovis	*Ba major*	*Ba ovata*	*Ba orientalis*	*Ba motasi*	*Ba caballi*	*Ba* sp Kashi	*Ba* sp Xinjiang	*Ba mircroti*	*Ba divergens*	*Ba venatorum**	SFTSV
Amblyomma	*A testudinarium*												
Dermacentor	*D abaensis*	🟩											
	D daghestanicus												
	D marginatus												
	D niveus												
	D nuttalli						🟩						
	D silvarum						🟩						
	D sinicus												
Haemaphysalis	*H bispinosa*												
	H concinna									🟩	🟩		
	H flava												
	H japonica										🟩		
	H longicornis		🟩	🟩						🟩			🟩
	H punctata		🟩										
	H quinghaiensis	🟩				🟩							
	H sinensis												
	H verticalis												
	H yeni												
Hyalomma	*Hy anatolicum*							🟩	🟩				
	Hy asiaticum												
	Hy detritum												
	Hy kozlovi												
	Hy scupense												
Ixodes	*I granulatus*												
	I myospalacis												
	I ovatus												
	I persulcatus									🟩	🟩	🟩	
	I sinensis												
Rhipicephalus	*R haemaphysaloides*				🟩								
	R microplus	🟩											🟩
	R pumilio												
	R sanguineus sensu stricto						🟩		🟩				
	R turanicus												

Figure 1. Matrix of emerging tick-associated agents and tick species in mainland China

*Not yet formally described. SFTSV=severe fever with thrombocytopenia syndrome virus.

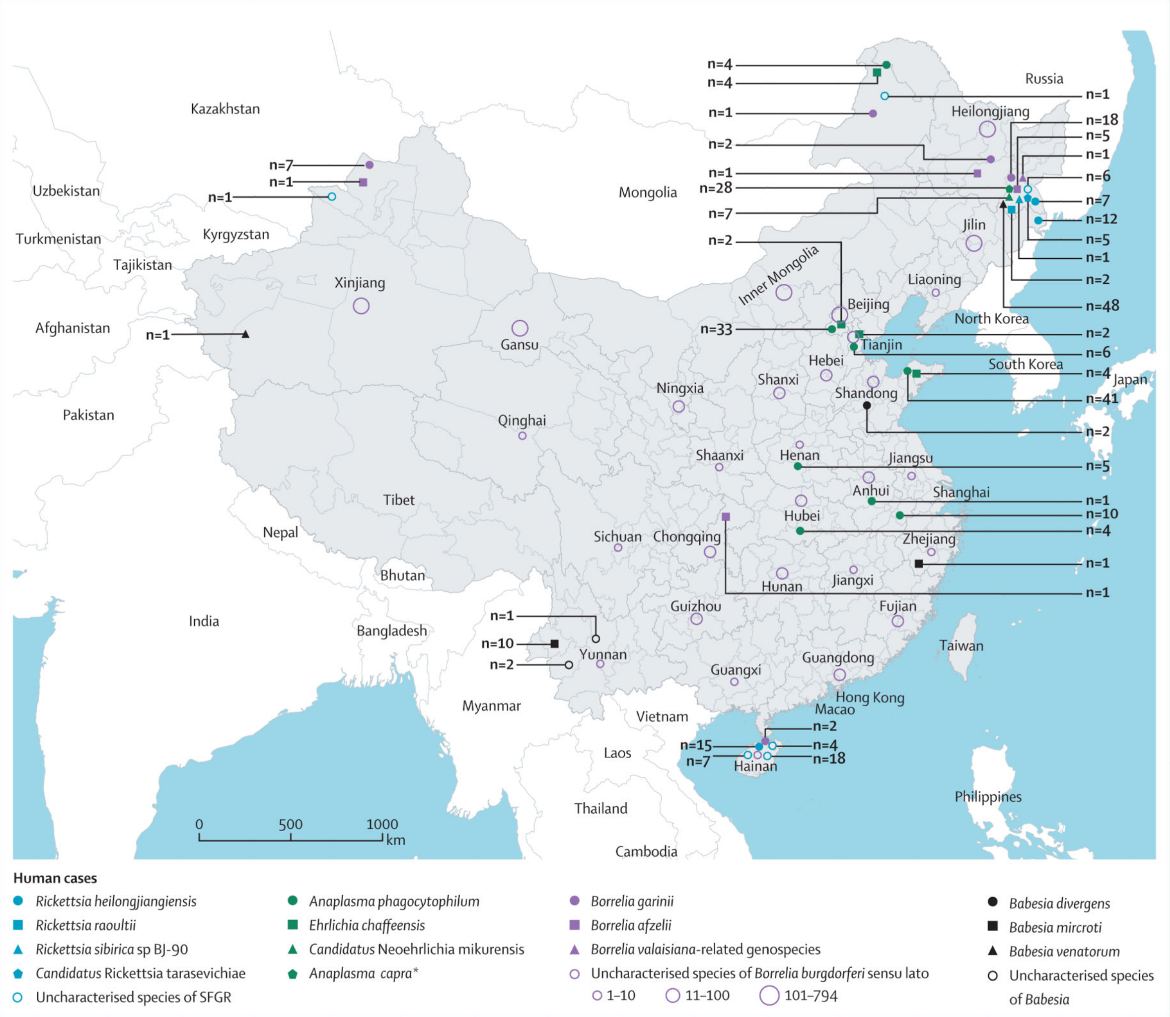


Figure 2. Geographical distribution of emerging tick-borne diseases in mainland China

Human cases of SFGR infections are shown in blue; patients infected with agents in the family Anaplasmataceae in green; patients infected with agents in the complex *Borrelia burgdorferi* sensu lato in purple; and patients infected with agents in the genus *Babesia* in black. SFGR=spotted fever group rickettsiae. *Not yet formally described.

Table 1

First identification and origin of emerging tick-borne infections in mainland China since 1982

	First identified origin[*]	**First identified province (year)**[†]	**Reference (subsequent investigations)**
Spotted fever group rickettsiae			
Rickettsia heilongjiangiensis	*Dermacentor silvarum*	Heilongjiang (1982)	5 (6,8,35-45)
Rickettsia sibirica sp BJ-90	*Dermacentor sinicus*	Beijing (1990)	7 (46)
Rickettsia sibirica sp *mongolotimonae*	*Hyalomm asiaticum kozlovi*	Inner Mongolia (1991)	7
Rickettsia monacensis	*Ixodes persulcatus*	Henan, Anhui, and Hubei provinces (2006)	8 (44,47)
Rickettsia raoultii	*D silvarum*	Xinjiang (2011)	9 (48-50)
Rickettsia slovaca	*D silvarum*	Xinjiang (2011)	9 (50,51)
Candidatus Rickettsia *hebeiii*	*Haemaphysalis longicornis*	Hebei (2011)	10 (52)
Candidatus Rickettsia *tarasevichiae*	Man (*I persulctus*)	Heilongjiang (2012)	11
Anaplasmataceae			
Ehrlichia chaffeensis	*Amblyomma testudinarium*	Yunan (1996)	12 (32,36,53-62)
Ehrlichia canis	*Rhipicephalus sanguineus* sensu stricto	Guangdong (1997)	13 (16,57,63)
Ehrlichia sp Tibet	*Rhipicephalus microplus*	Tibet (2000)	14
Anaplasma phagocytophilum	*I persulcatus*	Heilongjiang (1997)	15 (36,51,53-55,62-75)
Anaplasma platys	Dog	Guangdong (1998)	16 (63)
Anaplasma capra[‡]	Goat	Heilongjiang (2014)	17
Candidatus Neoehrlichia mikurensis	Man (*I persulctus*)	Heilongjiang (2010)	18 (76,77)
Borrelia burgdorferi sensu lato			
Borrelia garinii	Man (*I persulcatus*)	Heilongjiang (1986)	19 (21,23,36,54,78-91)
Borrelia valaisiana	*Ixodes granulatus* (*Apodemus agrarius*)	Zhejiang (1997)	20 (86,92)
Borrelia sinica	*Niviventer confucianus*	Chongqing (1997)	20
Borrelia afzelii	Man	Heilongjiang (2000)	21 (36,78,79,81,83-85,90)
Borrelia valaisiana-related genospecies	*I granulatus, H longicornis (A agrarius)*	Guizhou (2006)	22 (78,83,86,88)
Borrelia burgdorferi sensu stricto	*Caprolagus sinensis*	Hunan (2010)	23 (92)
Babesia spp			
Babesia ovis	Sheep	Sichuan (1982)	24 (93)
Babesia major	*H longicornis* (cattle)	Henan (1988)	25 (94)
Babesia ovata	Cattle	Henan (1990)	26 (95)
Babesia orientalis	Buffalo	Hubei (1997)	27 (96,97)
Babesia motasi	Sheep	Gansu (1997)	28 (98,99)
Babesia caballi	*D silvarum, Dermacentor nuttalli*	Gansu (1998)	29 (100-102)
Babesia sp Kashi	*Hyalomma anatolicum*	Xinjiang (2005)	30 (103)
Babesia sp Xinjiang	*R sanguineus* sensu stricto, *H anatolicum*	Xinjiang (2007)	31 (103)

	First identified origin[*]	**First identified province (year)**[†]	**Reference (subsequent investigations)**
Babesia microti	*I persulcatus, Haemaphysalis concinna*	Heilongjiang (2007)	32 (36,104-107)
Babesia divergens	*I persulcatus, H concinna, Haemaphysalis japonica* (*A agrarius*)	Heilongjiang (2007)	32 (36,108)
Babesia venatorum[‡]	Man	Xinjiang (2012)	33 (109)
SFTSV	Man	Henan (2009)	34 (110-118)

SFTSV=severe fever with thrombocytopenia syndrome virus.

[*] First identified origin of each emerging tick-associated agent, including man, domestic animal, rodent, and tick. The agent that was simultaneously identified from other hosts or ticks is shown in parentheses.

[†] Provinces include autonomous regions and metropolis.

[‡] Not been formally described in taxonomic papers.

Table 2

Emerging tick-borne diseases of human beings reported in mainland China as of May 31, 2015

	Pathogen	**Number of patients**	**Diagnostic methods[*] (reference)**
Rickettsiosis	*Rickettsia heilongjiangiensis*	34	A and B (35), B and C (43), A and C (45)
Rickettsiosis	*Rickettsia sibirica* sp BJ-90	1	A and B (46)
Rickettsiosis	*Rickettsia raoultii*	2	A and B (48)
Rickettsiosis	*Candidatus* Rickettsia tarasevichiae	5	B (11)
Rickettsiosis	Uncharacterised *Rickettsia* spp	37	C (119-121), B (122), A and C (123), E (124)
Human monocytic ehrlichiosis	*Ehrlichia chaffeensis*	12	B (53,55)
Human granulocytic anaplasmosis	*Anaplasma phagocytophilum*	104	B (53,55,74,75), A, B, and C (73), A and B (64), E (71)
1 Human infection with *Anaplasma capra*[†]	*A capra*[†]	28	A, B, and C (17)
Human infection with *Candidatus* Neoehrlichia mikurensis	*Candidatus* N mikurensis	7	B (18)
Lyme disease	*Borrelia garinii*	30	B (21,23,78,90,91)
Lyme disease	*Borrelia afzelii*	8	B (21,23,78,90), C (125)
Lyme disease	*Borrelia* valaisiana-related genospecies	1	B (78)
Lyme disease	Uncharacterised *Borrelia burgdorferi* sensu lato	2691	A (126-130), E (131)
Babesiosis	*Babesia divergens*	2	B (108)
Babesiosis	*Babesia microti*	11	B and D (104,107)
Babesiosis	*Babesia venatorum*[†]	49	A, B, and C (33), B, C, and D (109)
Babesiosis	Uncharacterised *Babesia* spp	3	D (132,133)
SFTS	SFTSV	2543	A, B, and C (34,117), A or B or C (113,118), A or B (114), B and C (115), B (116)

SFTS=severe fever with thrombocytopenia syndrome. SFTSV=severe fever with thrombocytopenia syndrome virus.

[*] Diagnostic methods: (A) a four-fold increase in titre of specific antibodies in blood sera collected from the acute and convalescent stages of illness, or a seroconversion of specific antibodies; (B) molecular detection and sequence determination; (C) isolation of pathogens from clinical samples; (D) light or electronic micrograph identification for thin blood smear; and (E) methods were not provided.

[†] Not been formally described in taxonomic papers.