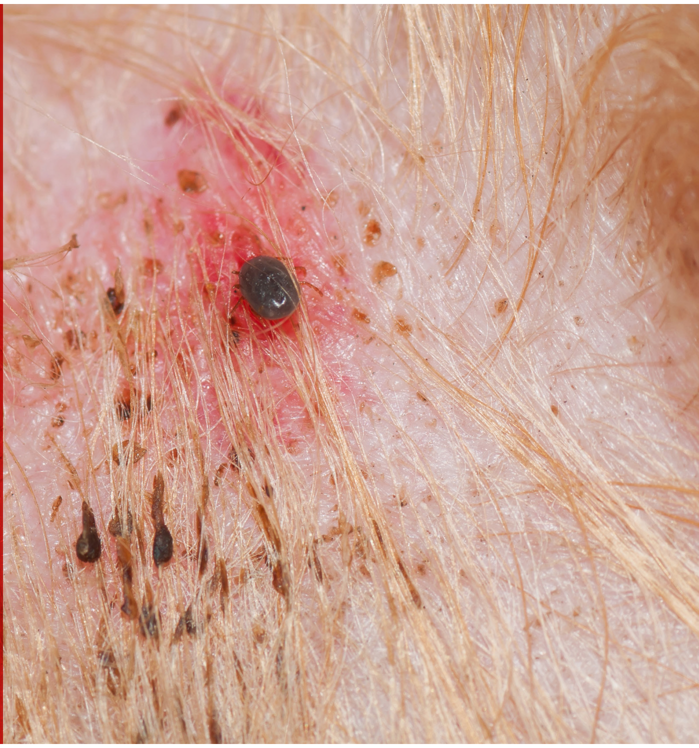
Top 5 Tick-Borne Diseases in Southeast Asia



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In many Southeast Asian (SEA) countries, there are high populations of stray dogs and cats that do not receive care. This complex problem is caused by financial constraints, lack of social interest, and cultural barriers.

These dogs and cats not only carry diseases that infect the stray animal population but also harbor many ticks (***Table 1***, next page). These serve as reservoirs and transport vehicles for tick-borne pathogens that can, through tick bite or ingestion, spread disease to other animals and humans.

Many countries in SEA have tropical climates characterized by warm, humid weather with monsoons. These environmental conditions, combined with large numbers of stray or neglected dogs and cats, provide an ideal ecosystem for tick survival. The primary tick vector for companion animals found in SEA is the brown dog tick, *Rhipicephalus sanguineus*, which is largely responsible for tick-transmitted diseases such as babesiosis, hepatozoonosis, ehrlichiosis, and mycoplasmosis.[1-3] In addition, ticks are considered potential vectors of *Bartonella* spp.[3] The lack of official findings about tick-borne diseases in this region does not reflect the reality of their existence; based on the author's experience, tick-borne diseases are more common than one might assume.

Reasons for the lack of information about cases of tick-borne diseases in companion animals may include:

- Lack of up-to-date knowledge about tick-borne diseases
- Limitations in routine diagnosis because of a modest capacity for more specific testing
- Unavailability of research; few or no published studies from financially constrained countries

TOP 5 TICK-BORNE DISEASES IN SOUTHEAST ASIA

1. Ehrlichiosis
2. Anaplasmosis
3. Hepatozoonosis
4. Babesiosis
5. Bartonellosis

SEA = Southeast Asia

As a veterinarian who practices and conducts research in Thailand and occasionally in SEA countries, the author can assert that tick-borne diseases are common.

The most prevalent tick-borne diseases in SEA among companion animals are ehrlichiosis, anaplasmosis, babesiosis, hepatozoonosis, mycoplasmosis, and bartonellosis.[9] Mycoplasmosis is endemic[1,10,11] but excluded from this discussion. Instead, this discussion focuses on bartonellosis because an increasing number of *Bartonella* spp have been discovered in this region (***Table 2***, next page).

SEA = Southeast Asia

1 Ehrlichiosis

Ehrlichiosis is caused by bacteria of the genus *Ehrlichia*. The 5 recognized species are *E canis, E chaffeensis, E ewingii, E muris,* and *E ruminantium*. Reportedly, dogs are commonly infected by *E canis*, *E chaffeensis*, and *E ewingii.*[12] Ehrlichiosis in SEA was brought to world attention by the 1965 through 1975 epizootic losses of military dogs from canine monocytic ehrlichiosis caused by *E canis* in Singapore, Thailand, Malaysia, and Vietnam. Since then, *E canis* has been considered endemic throughout SEA, where the primary tick vector, *R sanguineus*, is prevalent.[13] There are reports of ehrlichiosis from Cambodia, Lao PDR, Malaysia,[14] Myanmar, Thailand, Vietnam, the Philippines, and Indonesia. *E canis* is not considered a highly significant zoonotic pathogen because few human cases occur, although 1 subclinical case and 6 clinically ill cases of infection were reported in Venezuela in 1996 and 2006, respectively.[15,16] *E chaffeensis* causes human monocytic ehrlichiosis, and simultaneous infection in dogs and humans has been serologically reported in Thailand.[17]

2 Anaplasmosis

Anaplasmosis is caused by bacteria of the genus *Anaplasma*. Currently recognized species are *Anaplasma phagocytophilum*, *A platys, A marginale* (and *A marginale* subsp *centrale*), *A bovis,* and *A ovis.*[18] *A phagocytophilum* can cause granulocytic anaplasmosis in cats, dogs, and horses. Zoonotic infection causing human granulocytic anaplasmosis was reported in Thailand in 2001.[19] *A platys*, causative agent of cyclic thrombocytopenia in dogs, is also commonly widespread in SEA, including Malaysia, Thailand, and the Philippines.[20-22] It is strongly suspected in other SEA countries.[13] No human cases of *A platys* have been reported in SEA, but there have been 2 reports of *A platys* infection involving an American veterinarian and 2 women from Venezuela.[23,24]

3 Hepatozoonosis

Hepatozoonosis is caused by protozoans of the genus *Hepatozoon*. There are 2 described species that infect dogs: *Hepatozoon canis* and *Hepatozoon americanum.*[25,26] *H canis* has long been recognized to cause infection, mainly of hemolymphoid

TABLE 1

HARD TICKS ASSOCIATED WITH COMPANION ANIMALS IN SOUTHEAST ASIA[4-8]

Dogs	Cats
Rhipicephalus sanguineus	*R haemaphysaloides*
R haemaphysaloides	*H bispinosa*
Rhipicephalus (Boophilus) microplus	
Haemaphysalis bispinosa	
H papuana nadchatrami	
H wellingtoni	
H semermis	
H lagrangei	
H atherurus	
H spinigera	
H heinrichi	
H hystricis	
Dermacentor auratus	

TABLE 2

IDENTIFIED *BARTONELLA* SPECIES IN SOUTHEAST ASIA

SEA countries	*Bartonella* spp	Sources
Thailand[8, 27-41]	*B henselae*	Human, cat
	B clarridgeiae	Human, cat, cat flea
	B vinsonii subsp *berkhoffii*	Cat, dog
	B elizabethae	Rat flea
	B tamiae	Human, chigger mite, tick
	B coopersplainsensis	Rodent
	B phoceensis	Rodent
	B rattimassiliensis	Rat, mouse
	B tribocorum	Rodent
	B vinsonii subsp *arupensis*	Rodent
	B queenslandensis	Rodent
	B grahamii	Dog
	B quintana	Dog, human
	B taylorii	Dog
	BK1, KK1 and KK2 (novel genotypes)	Dog
	B bovis	Water buffalo
	B rochalimae	Rat flea
Indonesia[42,43]	*B henselae*	Cat
	B clarridgeiae	Cat
	B phoceensis	Rodent
	B elizabethae	Rodent
	B rattimassiliensis	Rodent
The Philippines[44]	*B henselae*	Cat flea
	B clarridgeiae	Cat flea
Myanmar[8]	*B henselae*	Cat flea
	B clarridgeiae	Cat flea
Malaysia[45,46]	*B henselae*	Cat flea
	B elizabethae	Rat
	B tribocorum	Rat
	B clarridgeiae	Rat
	B queenslandensis	Rat
Singapore[47]	*B henselae*	Cat
Lao PDR[33,48,49]	*B clarridgeiae*	Cat flea
	B henselae	Human
	B tribocorum	Rodent
	B rattimassiliensis	Rodent
	B queenslandensis	Rodent
	B coopersplainsensis	Rodent
Cambodia[33]	*B elizabethae*	Rodent
	B rattimassiliensis	Rodent
	B queenslandensis	Rodent
	B coopersplainsensis	Rodent
Vietnam[50,51]	*B elizabethae*	Rat, mouse
	B tribocorum	Rat, mouse
	B queenslandensis	Rat, mouse
	B rattimassiliensis	Rat, mouse
	B coopersplainsensis	Rat, mouse

organs. *H canis* is prevalent in Africa, Asia, southern Europe, South America, and the United States,[52-54] whereas *H americanum,* prevalent in the southeastern United States, causes myositis and severe lameness.[55] Known transmission of this tick-borne parasite differs from that of other tick-borne agents in that it is acquired by ingestion of an *H canis*–infected tick rather than tick bites.[26] In SEA, *H canis* infection has been reported in Singapore, Malaysia,[20] the Philippines, and Thailand.[56] Its prevalence strongly implies occurrence throughout SEA.[13] Canine hepatozoon infection prevalence in SEA ranges from 1.2% of the population in Malaysia and 4.54% to 36% in Thailand.[20,56] In Thailand, an *H canis* study of 308 dogs and 300 cats from 42 Bangkok metropolitan districts found 36.6% of dogs and 36.8% of cats were infected, evidenced by polymerase chain reaction (PCR). This was also the first report of *H canis* in cats in SEA.[56]

There are 2 reported genotypes of *H canis* in Thailand: Thailand 1, GenBank accession number DQ519358, and Thailand 2, GenBank accession number DQ519357.[57] *H canis* may be highly prevalent in other SEA countries where vector tick species are abundant. The lack of reports from other countries may be because of their less well-resourced research or neglected reporting to international databases. Canine hepatozoonosis is not a zoonotic disease.

In cats, hepatozoonosis has been reported from several countries, including India, South Africa, Nigeria, the United States, Brazil, Israel, Spain, France, and Thailand.[56,58-65] *Hepatozoon felis* and *H canis* have been reported to infect cats.[26,64,66]

4 Babesiosis

In dogs worldwide, babesiosis has been reported to be caused by a large piroplasm described as *Babesia canis* and a small piroplasm described as *B gibsoni*. Three *B canis* subspecies, *B canis canis*, *B canis vogeli*, and *B canis rossi*, are differentiated based on severity of clinical manifestations, antigenic properties, tick vectors, genetic characteristics, and geographic distribution.[67] Based on most prevalence studies of transmitting tick vectors and geographic distribution, the *B canis* subspecies in SEA is most likely *B canis vogeli*.[1,68]

Canine babesiosis caused by *B canis* and *B gibsoni* and is widespread throughout SEA, or its occurrence is strongly suspected.[13,69] There are reports of *B canis* and *B gibsoni* from Thailand,[70,71] Malaysia,[4] Singapore,[69] and the Philippines.[72] In Thailand, Aussawapalungchai reported the first case of canine babesiosis in Bangkok in 1971 (data reported but not published) by visualization of *Babesia* spp merozoites in blood smears consistent in size with *B canis*. In SEA, *B gibsoni* can be transmitted by *R sanguineus* and *Haemaphysallis* spp,[1] as *H bispinosa* reportedly transmits *B gibsoni* to dogs in the Philippines.[73]

Feline babesiosis is less common than canine babesisosis. To date, infection by *Babesia felis* has mostly been reported from South Africa, *B cati* from India, *B canis* from Europe, *B canis* subsp *presentii* from Israel, and *B canis vogeli* from Thailand.[55,74] In SEA, there is currently only 1 identified feline babesiosis agent, *B canis vogeli*, described in cats from Thailand.

5 Bartonellosis

Bartonellosis is caused by gram-negative bacteria in the genus *Bartonella,* which are emerging pathogens worldwide. The disease exists worldwide because of a combination of reservoir hosts (eg, rodents, ruminants, carnivores, reptiles, marine mammals, bats) and confirmed or suspected transmission vectors (eg, arthropods [such as ticks, fleas, lice, mites, and mosquitoes]). With discoveries of emerging vectors, hosts, and reservoirs, knowledge of bartonellosis is expanding.

Bvb = *Bartonella vinsonii* subsp *berkhoffii*

SEA = Southeast Asia

More than 47 described species belong to the genus *Bartonella*; 17 of these are considered human pathogens. Recent reports involving humans, cats, and dogs revealed that 5 potentially zoonotic species (*B henselae*, *B clarridgeiae*, *B koehlerae*, *B bovis,* and *B quintana*) have been isolated from cats and 7 (*B vinsonii* subsp *berkhoffii* [Bvb], *B henselae*, *B clarridgeiae*, *B washoensis*, *B elizabethae*, *B bovis,* and *B quintana)* have been isolated from dogs.

Cats are natural reservoirs (infected but rarely show clinical signs) for *B henselae* and transmit the bacteria to humans primarily via scratching with claws contaminated with *B henselae*-infected flea feces. This can cause the so-called cat-scratch disease. Some infections are transmitted via cat bites.[75] In humans, symptoms of *B henselae*, which usually develop 7 to 12 days after cat scratch, range from mild (eg, low-grade fever, malaise, aching, benign regional lymphadenopathy) in the immunocompetent to severe (eg, endocarditis, myocarditis, meningitis, encephalitis) in the immunocompromised. (Only 1 fatal case has been reported.[76]) Although the known transmission of cat bartonellosis to humans is via scratch, other emerging vectors, such as ticks and biting flies, have been reported.

In dogs, the majority of bartonellosis cases are caused by Bvb.[77] Several recent publications reported a high prevalence of *Bartonella* spp infection in ticks from various parts of the world, which strongly suggests ticks serve as potential vectors. Additional studies are needed to establish specific roles of ticks in *Bartonella* transmission. Unlike feline bartonellosis, which rarely presents with clinical signs, dogs with bartonellosis can develop endocarditis. This suggests dogs are accidental hosts rather than reservoirs. Bvb in dogs is associated with cardiac arrhythmias, endocarditis and myocarditis, granulomatous lymphadenitis, granulomatous rhinitis, and epistaxis. Unlike cats, for which clinical manifestations of natural infection are rarely documented, a wide range of clinical and pathologic abnormalities that develop in dogs (similar to those observed in humans) are well-documented.[75] Therefore, dogs serve as an excellent sentinel and important comparative model for human infections. To date, all *Bartonella* species identified in sick dogs are also pathogenic or potentially pathogenic in humans.

In SEA, the number of published *Bartonella* spp findings is increasing. Even though there are not yet published reports supporting *Bartonella* transmission by ticks, ticks are considered potential vectors of *Bartonella* spp.[3,78]

Because bartonellosis is highly zoonotic and can cause serious illness in humans, it is regarded as an important public health issue, particularly for those who regularly come into contact with its reservoirs. Those at elevated risk include veterinarians, pet owners, livestock-handlers, and those who spend time outdoors. To highlight the ever-increasing significance of *Bartonella* spp in SEA in both veterinary and public health, following are some reports of *Bartonella* spp and the illnesses they cause:

- An association between *B henselae* and endocarditis in humans was recently reported in Laos and Thailand,[79] and *B clarridgeiae* and *B quintana* have been identified in patients with infective endocarditis in Thailand.[27,79]
- Three serosurveys of veterinary professionals were conducted for antibodies against *B henselae* in Japan, Thailand, and Poland; 15%, 28%, and 45%, respectively, were seropositive for antibodies against *B henselae*.[28,80,81]

Additionally, following are examples of well-documented and reported cases from the United States that shed light on zoonotic bartonellosis in veterinarians and those in animal-related professions:

- Infection with Bvb genotype II and *B henselae* (Houston 1 strain) in a veterinarian and his daughter was reported in 2010.[77]
- Bvb infection in a veterinarian via needle-stick transmission was reported in 2010.[82]
- Fever of unknown origin and back pain caused by *B henselae* in a veterinarian after a needle puncture was reported in 2011.[83]
- Seroprevalence of antibodies to *B henselae* from 90 veterinarians and cattle breeders were investigated in 2012; 22.2% were reactive.[84]
- Coinfection of *B henselae*, *A platys,* and *Candidatus Mycoplasma haematoparvum* was found in a veterinarian in 2013.[23]
- Lantos et al (2014) molecularly detected at least 1 *Bartonella* subspecies in 32 (28%) of 114 veterinary subjects. Of 27 of the 32 infected subjects, 56%, 26%, 22%, and 4% were infected with *B henselae*, Bvb, *B koehlerae*, and a *B volans*-like organism, respectively.[85]

The prevalence of bartonellosis as an infectious disease in SEA, especially in rural areas, is unknown because up-to-date information and specific testing are not available. Veterinarians should consider bartonellosis when encountering animals with fever of unknown origin. As bartonellosis occurs more frequently than previously thought in humans, especially those in veterinary fields, physicians should consider bartonellosis as a differential diagnosis for fever of unknown origin, even when bacterial culture is negative.

Prevention

The tropical environment in SEA is ideal for the proliferation of arthropod vectors year-round. As in other countries, an ongoing effective vector-prevention and -control system is necessary to control tick-borne diseases; there are no shortcuts. Managing tick-borne diseases involving companion animals requires that control measures be in place both indoors and outdoors, as well as on pets and in the environment.

Indoor control measures available in SEA include:

- Monthly topical products containing pyrethrin, imidacloprid, or fipronil
- Sprays, powders, dips, and shampoos containing pyrethrin
- Collars containing amitraz.

Products containing amitraz, permethrin, or organophosphates are not used on cats. In SEA, extralabel ivermectin SC has long been practiced for tick control. For outdoor control, pets should be discouraged from contact with stray dogs and cats, be confined to areas where ticks are not likely to be present, and wear flea- or tick-control collars.

Diagnosis

These 5 illnesses are difficult to diagnose, especially during the early clinical course, when most signs are nonspecific. In SEA countries, the gold standard for diagnosing ehrlichiosis, anaplasmosis, babesiosis, and hepatozoonosis is visualization of the organisms under microscope. Because of the nature of *Ehrlichia* spp and *Anaplasma* spp infections, however, their presence is rare in blood circulation. In clinical settings in Thailand and in some other SEA countries, a commercial antibody test kit for *Ehrlichia canis*, *Anaplasma platys*, *A phagocytophila*, *Borrelia* spp, and *Dirofilaria immitis* is available and is commonly used in parallel with the associated clinical signs and blood profiles. Because the kit only detects pathogen-specific antibodies, it is able to detect previous exposure but not current infection. PCR techniques are used in some SEA countries where ehrlichiosis, anaplasmosis, babesiosis, hepatozoonosis, and bar-

Bvb = *Bartonella vinsonii* subsp *berkhoffii*

PCR = polymerase chain reaction

SEA = Southeast Asia

tonellosis occur, but usually only at academic institutions.

Treatment

Severe illness and death can be prevented by early empiric antibiotic therapy, but, as described above, diagnosing these diseases early in the clinical course is problematic. In SEA, doxycycline and imidocarb dipropionate are the treatments of choice for ehrlichiosis and anaplasmosis; imidocarb dipropionate and/or diminazene aceturate for babesiosis; and imidocarb dipropionate and/or sulfonamides for hepatozoonosis. At this time, there are no reported treatments for bartonellosis because it is not commonly diagnosed in SEA clinical settings.

Conclusion

Causative agents of tick-borne disease rely on a combination of the suitable climate for vectors to survive and thrive, and the presence of hosts (both accidental and natural) or reservoirs. SEA countries meet these requirements with hot and humid weather all year and numerous stray animals for ticks and other vectors to feed on. The actual incidence of these 5 tick-borne diseases in SEA is possibly underestimated because the advanced diagnostic tools necessary to diagnose them are not practical in most SEA veterinary clinical settings, especially in low-income countries. Advances in molecular biology testing mean better detection, but the information obtained generates further questions. Nevertheless, better detection provides crucial information for veterinarians in SEA to better protect the animals they care for, as well as themselves, owners, and the general public.

The tasks related to controlling tick-borne diseases are monumental. Initial important steps need to be taken, such as characterizing genetics of pathogen strains and vector ticks (as well as studies on their vectorial capacities), and prioritizing pathogens and their associated vectors, preferably in various SEA locations. Further, efforts by the ASEAN Economic Community to encourage better economic and political cooperation in SEA will have a positive impact on lifestyle and environment. With respect to tick-borne disease, however, these efforts will likely increase disease transmission because of easier movement of animals and humans; however, they will also provide opportunities to cooperate, collaborate, and develop strategies critical to developing and maintaining effective early warnings of disease and early response systems.

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