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Review Article

Tick-borne pathogens and their zoonotic potential for human infection In Thailand

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Abstract Ticks are one of the important vectors for transmitting various types of pathogens in humans and animals, causing a wide range of diseases. There has been a rise in the emergence of tick-borne diseases in new regions and increased incidence in many endemic areas where they are considered to be a serious public health problem. Recently, evidence of tick-borne pathogens in Thailand has been reported. This review focuses on the types of tick-borne pathogens found in ticks, animals, and humans in Thailand, with emphasis on the zoonotic potential of tick-borne diseases, i.e. their transmission from animals to humans. Further studies and future research approaches on tick-borne pathogens in Thailand are also discussed.

Keywords: ticks, tick-borne pathogens, tick-borne diseases, zoonosis

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บทความปริทัศน์

เชื้อก่อโรคที่นำโดยเห็บและโอกาสในการติดต่อสู่คนในประเทศไทย

ชาทะนันท์ เอี่ยมอุดมกาล

ภาควิชาปรสิตวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น จังหวัดขอนแก่น 40002

บทคัดย่อ เห็บจัดเป็นพาหะที่สำคัญชนิดหนึ่งในการแพร่กระจายของเชื้อโรคและยังนำเชื้อก่อโรคได้หลากหลายชนิดทั้งในคนและในสัตว์ ซึ่งในปัจจุบันมีอุบัติการณ์ของการเกิดโรคที่นำโดยเห็บเพิ่มมากขึ้นในพื้นที่ใหม่และในพื้นที่ที่เคยมีการระบาดอยู่ก่อนเดิมก็พบว่ามีการติดเชื้อเพิ่มมากขึ้นซึ่งจัดเป็นปัญหาที่สำคัญทางสาธารณสุขทั่วโลก สำหรับในประเทศไทยนั้นก็พบว่ามีรายงานเชื้อก่อโรคที่นำโดยเห็บ ซึ่งในบทความปริทัศน์นี้จะมุ่งเน้นไปที่ชนิดของเชื้อก่อโรคที่นำโดยเห็บที่พบในเห็บ สัตว์ และคนในประเทศไทย และเน้นในประเด็นของโรคที่นำโดยเห็บจากสัตว์สู่คน รวมถึงการศึกษาและงานวิจัยที่ต้องการเพิ่มเติมสำหรับอนาคตเกี่ยวกับเชื้อก่อโรคที่นำโดยเห็บในประเทศไทย

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Introduction

Ticks are one of the blood-feeding vectors which can transmit various types of pathogens in humans and animals; they are second to mosquitoes as a vector for human diseases (Brites-Neto et al., 2015; de la Fuente et al., 2008; Parola and Raoult, 2001) and are the major vectors of animal diseases (Chomel, 2011; Irwin and Jefferies, 2004). Tick-borne pathogens include a wide range of viruses, protozoa, bacteria, and rickettsia. Each year, more than 100,000 cases of human symptoms worldwide are caused by tick-borne pathogens (de la Fuente et al., 2008). One tick can often transmit more than one pathogen, including tick-borne diseases (TBDs) which are illnesses transmitted to humans and animals by ticks. Most TBDs are zoonotic and are considered an important public health problem. The importance of vector-borne diseases has been emphasized by the World Health Organization (WHO), which launched a global campaign in 2014 against vector-borne diseases with the quote “small bite: big threat.” In recent years, TBDs and emerging vector-borne diseases have been of increasing concern in many regions of the world, e.g. the USA, Europe, and China. In Thailand, however, TBDs have often been misdiagnosed, and their prevalence underestimated because of inadequate surveillance networks and lack of up-to-date information.

We reviewed the available literature on the various types of tick-borne pathogens found in animals especially in dogs and humans in Thailand. Moreover, this review considered the zoonotic potential of TBDs and their transmission from animals to humans in Thailand.

Tick species in Thailand

Ticks are found worldwide but major in countries with warm and humid climates with the number more than 850 species (Munderloh, 2011). The record from fossil shows that ticks are originated 65–146 million years ago (Munderloh, 2011). Tick belongs to the Phylum *Arthropoda* and the Class *Arachnida* Subclass *Acari* with consist of three families: *Ixodidae*, *Argasidae*, and *Nutalliellidae* (Schwan, 2011). Hard ticks, *Ixodidae*, including 702 described species covering most of the medical and veterinary importance, containing ticks of the genus *Ixodes*, *Amblyomma*, *Rhipicephalus*, *Dermacentor*, *Haemaphysalis*, *Cosmiomma*, *Aponomma*, *Margaropus*, *Rhipicentor* and *Hyalomma* (Brites-Neto et al., 2015). Soft ticks, *Argasidae*, including 193 described species from the genus *Argas*, *Ornithodoros*, *Otobius*, *Antricola*, *Nothoaspis* and *Carios* (Brites-Neto et al., 2015). The family *Nutalliellidae* has only one species, *Nuttalliella namaqua* that found only in South Africa and Tanzania (Brites-Neto et al., 2015). The biology of soft ticks and hard ticks are the difference in biology. The hard ticks or ixodids has three stages: larva, nymphal, and adult while soft ticks, argasids, has multiple stages: larval, multiple nymphal stages, and mature adult (Schwan, 2011). Moreover, an adult of hard tick feeds only once while soft tick adult can feed multiple times

(Schwan, 2011). The first known record of ticks in Thailand was performed at the end of the 19th century by Neuman then during the 20th century; there were 53 species of ticks were identified in Thailand by collecting ticks on domestic and wild animals in different areas of Thailand (Cornet et al., 2009). Based on the study of Nithikathkul (2002), there were only 2 species of ixodid ticks, *Rhipicephalus* (*Boophilus*) *microplus* and *Rhipicephalus sanguineus*, were found in 50 domestic animals (dogs, cattle and buffalo) in Samut prakan Province and the main species of tick was *R. sanguineus*. This result is in concordance with a study of Poolkhetkit (2015) that collected ticks in the buffer zone of Sai Yok National Park, Thailand, found that total of 85 ticks from cattle was identified as *R. microplus*. *R. microplus* is the only one species that found in cattle in Southeast Asia, including Thailand (Cornet et al., 2009; Poolkhetkit et al., 2015). Moreover, *R. microplus* was also found in humans in Thailand and represents as a potential vector for zoonosis of Seletar and Wad Medani viruses (Cornet et al., 2009). Recently, the study of wild animals and tick species in Thailand performed by Sumrandee and coworkers (Sumrandee et al., 2016), found that ticks belonging to 4 genera and 8 species from a total of 79 ticks that collected from wild boar, sambar deer and barking deer. The 4 tick genera consists of the genus *Haemaphysalis*, *Dermacentor*, *Rhipicephalus* and *Amblyomma*.

Infected with large numbers of ticks in domestic animals and wild animals causes health problems. However, the main problems caused by ticks are due to the capability of transmission of tick-borne pathogens, which are of great public health problem globally.

Tick-borne pathogens in small companion animals

Small companion animals are very close to humans. Therefore, the transmission of TBDs from companion animals to humans is of great concern. The most common TBDs of companion animals found in Southeast Asia are babesiosis, ehrlichiosis, hepatozoonosis and bartonellosis (Baneth et al., 2007; de la Fuente et al., 2008; Irwin and Jefferies, 2004). Many species of dog ticks have been identified; among these, the brown dog tick, *Rhipicephalus sanguineus*, is the most abundant and the main cause of TBDs in Southeast Asia (Irwin and Jefferies, 2004). In Thailand, these diseases also found as the most common TBDs. However different regions of Thailand have different survey data of diseases.

Canine babesiosis is caused by *Babesia canis*, which is endemic in dogs in Thailand. In a study of 303 domestic dogs in Khon Kaen province using PCR technique, 19.5% were found to be infected with *B. canis*, compared with single infection with *Ehrlichia canis* (3.0%) and co-infection with *Hepatozoon canis* and *E. canis* (0.3%) (Laummaunwai et al., 2014). Another study also found that babesiosis was the most common TBD in dogs in Khon Kaen Province (Juasook et al., 2016). Moreover, that study showed that in 280 leftover blood samples from domestic dogs that were negative for parasites by microscopic examination, 80 (28.57%) were positive for tick-borne pathogen DNA (Juasook et al., 2016). This result indicates that PCR-based technique has high sensitivity and specificity for the diagnosis of TBDs.

Babesiosis is not only important in dogs, but also in humans. Human babesiosis has been reported in other Asian countries, for example Taiwan, Japan, China, and Korea (Kim et al., 2007; Shih et al., 1997; Wang and Huang, 2014; Wei et al., 2001; Zhou et al., 2014). Even though human babesiosis has never been reported in Thailand, there is strong evidence that cases have somehow been initially diagnosed as malaria because of the similarity between the two pathogens (Zhou et al., 2013). Therefore, cases of human babesiosis in malaria-endemic countries like Thailand might have overlooked or been misdiagnosed as malaria. This emphasizes that more surveillance of TBDs is needed in Thailand. Moreover, the finding of rodent babesia in Chiang Mai province which resembled *Babesia microti*, the most common strain associated with human babesiosis, indicates that careful monitoring is needed (Dantrakool et al., 2004).

Another TBDs in humans that is well known in many parts of the world is Lyme disease, which is caused by the spirochete *Borrelia burgdorferi*. This disease is endemic in North America and Europe, and is also found in some parts of Asia, e.g. China, Taiwan and Japan (D'Arco et al., 2017; Liu et al., 2000; Shih et al., 1998; Steere et al., 2016). The skin lesion erythema migrans is commonly found in early infection. If left untreated, the infection can affect joints, the heart and the nervous system (D'Arco et al., 2017; Steere et al., 2016). Nevertheless, Lyme disease has never been reported in Thai populations. Interestingly, a recent study of blood samples and ticks from Chiang Mai and Phuket provinces found that one dog (0.3%) from Chiang Mai was positive for *B. burgdorferi* (Sthitmatee et al., 2016). This strain has 97% to 100% genetic identity when compared to strains from the USA. This finding confirms that TBDs in Thailand should be carefully monitored and that more data surveys of emerging zoonotic diseases are needed.

As mentioned above, humans can become infected by many tick-borne pathogens of dogs, and therefore TBDs in dogs are of great concern as the dog is the most common household companion animal. Furthermore, dogs have often been considered for use as effective indicator animals to assess the risk of human infection (Andersson et al., 2017; Pérez Vera et al., 2014). As there is a large population of stray dogs throughout Thailand, a much higher rate of TBDs is expected because of their greater exposure to ticks. But to date there is little data on the surveillance of TBDs in dogs, and the prevalence in humans is underestimated. Therefore, further studies could provide better knowledge for the prevention of zoonotic infections.

Spotted fever group rickettsial species in animals associated with human diseases

Tick-borne pathogens are thought to be accountable for more than 100,000 cases of infection in humans worldwide and are the most important causes of diseases in domestic and wild animals (de la Fuente et al., 2008). Febrile illness in patients throughout the world is often linked to rickettsial infections, also called typhus (Ahantarig et al., 2008; Rathi and Rathi, 2010). The types of typhus fever are louse-borne, flea-borne, mite-borne scrub typhus, and tick-borne spotted fever. To date, about 20 spotted fever group rickettsial species (SFG), which are transmitted by ticks, have been identified throughout the world, and many of them are emerging human pathogens (Wood and Artsob, 2012). The Thai tick typhus isolate of SFG, TT-118, was first obtained from a mixed pool of *Ixodes* sp. and *Rhipicephalus* sp. larval ticks collected from *Rattus rattus* in Chiang Mai province in 1962 (Ahantarig et al., 2008; Jiang et al., 2005; Robertson and Wisseman, 1973). Later, the isolate TT-118 was determined to be a strain of *Rickettsia honei*, which is the agent of Flinders Island spotted fever in Australia (Stenos et al., 1998). The first three clinical cases of SFG rickettsiosis in Thailand were reported in 1994 in Chiang Mai province (Sirisanthana et al., 1994). These cases were confirmed by serological methods, but the causative agent of the disease was not isolated and could not be specified. Subsequently, several SFG rickettsiosis cases have been reported in Thailand: 8 cases in Kanchanaburi province, 3 in Chiang Mai province, 1 in Bangkok and 9 in the north and northeastern regions (Bhengsri et al., 2016; Fournier et al., 2004; Jiang et al., 2005; Parola et al., 2003b; Sangkasuwan et al., 2007). The first molecular detection and confirmation of *R. honei* TT-118 in a clinical sample from a Thai patient was performed by polymerase chain reaction (PCR) in 2005 (Jiang et al., 2005).

Not only humans in Thailand have been infected with SFG, but also animals. The first study of SFG rickettsiosis in Thai animals was conducted in 1996 (Okabayashi et al., 1996). They studied the seroepidemiology of SFG infection in many species of wild rats captured in Kanchanaburi and Chanthaburi provinces in 1976 and 1977. The results found that 62.2% were positive for SFG by antibody detection. The species of rat which had the highest positive rate was *Bandicota indica*, indicating that it is an important reservoir of SFG in Thailand. Moreover, the results of this study indicated that wild rats were infected throughout Thailand in the 1970s, before the first report of human cases in the country in 1994. There is much available evidence on the molecular detection of *Rickettsia* spp. in ticks in Thailand. As mentioned above, the first discovery of Thai tick typhus was from a pool of *Ixodes* sp. and *Rhipicephalus* sp. larva. Subsequently, among ticks collected at Sangkhlaburi, near the Thai–Myanmar border, *Rickettsia* sp. strains RDa420 and RDla440 were detected in *Dermacentor auratus* collected from a bear and *Dermacentor* sp. collected from a wild pig nest, respectively (Parola et al., 2003a). More molecular evidence for *Rickettsia* spp. was found in ticks collected from plants in Khao Yai National Park, Nakhon Nayok province, and Khao Ang Rue Nai Wildlife Sanctuary, Chachoengsao province (Hirunkanokpun et al., 2003). The study of four hard tick species (*Haemaphysalis lagrangei*, *H. bispinosa*, *Amblyomma testudinarium* and *A. integrum*) along tourist nature trails at ten locations in Thailand found that they harbored *Rickettsia* spp. Phylogenetic analysis showed that rickettsia genotypes were closely related to the species which caused diseases in human (Malaisri et al., 2015). Recently, four species of *Rickettsia* were found in ticks collected from sambar deer (Sumrandee et al., 2016). Remarkably, most species of ticks in that study were found on humans in Thailand.

The above literature review shows that all tick species harboring *Rickettsia* spp. are potential vectors for transmitting diseases to humans. Nevertheless, a knowledge gap exists in that updated surveys of reservoirs of SFG and an estimation of the degree of zoonotic potential are not available.

Conclusions

Tick-borne diseases are considered to be of medical and veterinary importance throughout the world. This review presents an updated history of tick-borne pathogens that have been identified, both in ticks and hosts, in Thailand. It shows that tick-borne pathogens are common in animals and the environment in Thailand. Furthermore, there is much evidence showing that tick-borne pathogens can cause severe infection in humans and animals. In the past two decades, there has been a rise in the emergence of vector-borne diseases in new regions, and many endemic areas have seen increased incidence (Kilpatrick and Randolph, 2012). Several factors account for the increased number of emerging diseases, including TBDs. People are participating in more outdoor activities, which results in more contact with ticks and tick-borne pathogens (Parola and Raoult, 2001). The movement of pathogens may arise from trade and travel worldwide (Kilpatrick and Randolph, 2012). Importing of animals from TBDs endemic areas has increased. Therefore, proper quarantine of imported animals and animal products will prevent the spread of tick-borne pathogens. An awareness of tick-borne pathogens in animals and humans and their distribution will allow for the development of better plans for the prevention and control of zoonotic TBDs. However, the significance of these pathogens and the zoonotic potential remain mostly unknown in Thailand. Therefore, the vectors and animal reservoirs should be studied to provide essential information about zoonosis. Moreover, there are still many knowledge gaps on TBDs in Southeast Asia, including Thailand. Insufficient information on the epidemiology of TBDs is of great concern. The laboratory is of critical importance in the diagnosis of TBDs to provide data to facilitate control strategies.

In conclusion, TBDs should be of more concern in Thailand as there is evidence showing that tick-borne pathogens affect both humans and animals. Moreover, further studies are needed on the pathogens in tick populations and their role in diseases of humans and animals, their geographical distribution, the relationships between hosts and vectors, the reservoir hosts and the degree of zoonotic potential in humans.

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