Canine and feline vector-borne diseases of zoonotic concern in Southeast Asia

Viet-Linh Nguyen a, Filipe Dantas-Torres a,b, Domenico Otranto a,c,*

a Department of Veterinary Medicine, University of Bari, Bari, Italy
b Department of Immunology, Aggeu Magalhães Institute, Recife, Brazil
c Faculty of Veterinary Sciences, Bu-Ali Sina University, Hamedan, Iran

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ABSTRACT

Dogs and cats are important hosts and reservoirs of many viral, bacterial, protozoal, and helminthic pathogens transmitted by arthropods, including some of zoonotic concern. By sharing the same environment, these companion animals play an important role in the transmission of zoonotic pathogens to humans in various regions and socioeconomic contexts. While canine and feline vector-borne diseases (VBD) are of major concern in wealthy regions (e.g., Europe and North America), less attention has been received in developing countries such as those in Southeast Asia (SEA). This review provides summarized and updated information on canine and feline VBD with emphasis on those of zoonotic concern in SEA. Of these, zoonotic bacteria (i.e. Bartonella henselae, Bartonella clarridgeiae, and Rickettsia felis) and filarial nematodes (i.e. Brugia malayi, Dirofilaria repens, and Dirofilaria immitis) stand out as the most important in veterinary and human medicine. Additionally, the recent finding of Leishmania infantum in dogs in SEA raised more concerns about the spreading of this zoonotic agent in this region. Further epidemiological surveys, especially in countries with extremely scant information such as Cambodia, Laos, Myanmar, and Timor-Leste are advocated. Additionally, effective control measures of canine and feline VBD as well as their arthropod vectors should be simultaneously performed for the management of zoonotic infections.

1. Introduction

Southeast Asia (SEA) comprises 11 countries (Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, Timor-Leste, and Vietnam) (Fig. 1), and is home to more than 650 million people with approximately 49% of the population living in rural areas (by 2018) (The World Bank, 2019). In recent decades, SEA countries have been experiencing the fastest-ever economic transformation, which also leads to living standard and health improvements (Fukugawa, 2018). However, this region is still marked by significant social disparities, and remains as a hotspot of many infectious diseases such as dengue fever, malaria, and rabies, which are life-threatening to millions of people (Shepard et al., 2013; Hotez et al., 2017). Furthermore, although SEA is considered as outside the geographical distribution area of Leishmania infantum, the presence of this zoonotic pathogen has been reported in dogs in this region (Colella et al., 2020). The awareness regarding the importance of canine and feline VBD is continuously increasing in wealthy regions (e.g. Europe and North America). In addition to the above-mentioned diseases, many zoonotic vector-borne diseases (VBD) have been reported in SEA (Colella et al., 2020; Irwin & Jefferies, 2004; Low et al., 2020), and for some of these dogs and cats play a significant reservoir role. For instance, zoonotic vector-borne pathogens (VBP) such as Rickettsia felis and Bartonella henselae have been reported in patients having previous contact with dogs, cats and/or ticks and fleas (Edouard et al., 2014; Noopetch et al., 2018). Dirofilaria immitis, the causative agent of canine and feline heartworm disease and human pulmonary dirofilariosis (Dantas-Torres & Otranto, 2020), is widely distributed in SEA being reported in dogs from Malaysia, Singapore, and southern Thailand (Colella et al., 2020; Kamyingkird et al., 2017; Lau et al., 2017). Furthermore, although SEA is considered as outside the geographical distribution area of Leishmania infantum, the presence of this zoonotic pathogen has been reported in dogs in this region (Colella et al., 2020).

The awareness regarding the importance of canine and feline VBD is continuously increasing in wealthy regions (e.g. Europe and North America).
America), but less attention has been received in developing regions like SEA. In such regions, there is limited or no access of dogs and cats living in poor suburban or rural areas (Fig. 2A) to veterinary services and preventive measures, thus increasing their risk of acquiring VBP (Dantas-Torres et al., 2020; Otranto et al., 2017). Additionally, the limited availability of financial resources and laboratory facilities in some countries in SEA have historically impaired the scientific knowledge about canine and feline VBD in this region, which certainly has a negative impact on the establishment of appropriate strategies to mitigate zoonotic VBD. Nonetheless, recent multicenter collaborative research has positively impacted on our knowledge on several VBD in SEA, filling some research gaps and uncovering others (Colella et al., 2020). In this perspective, the present article is aimed to provide an update review on VBP and their vectors affecting dogs and cats in SEA, with the main focus on those of zoonotic concern.

2. Arthropod vectors of VBP affecting dogs and cats in SEA: what do we know

Ticks, fleas, and mosquitoes represent the most common arthropod vectors transmitting pathogens to dogs and cats in SEA (Irwin & Jefferies, 2004; Colella et al., 2020). Numerous VBP have been detected in dogs and cats as well as in their associated arthropods in this region (Table 1). The brown dog ticks, Rhipicephalus sanguineus (sensu lato) (Fig. 2B) are the most prevalent ticks found on dogs and, to a lesser extent, cats in SEA (Petney et al., 2019). These ticks act as vectors of many pathogens (e.g. Anaplasma platys, Ehrlichia canis, Babesia vogeli, and Hepatozoon canis) affecting dogs, cats, and humans in tropical and subtropical regions (Dantas-Torres & Otranto, 2015). There have been many investigations indicating the presence of two divergent lineages of this tick species (i.e. the tropical and the temperate lineage) in different parts of the world (Dantas-Torres et al., 2013; Nava et al., 2018), and the pathogens transmitted by ticks of these two lineages may also differ (Moraes-Filho et al., 2015). A recent study showed that R. sanguineus (s.l.) ticks circulating in SEA belong to the tropical lineage (Nguyen et al., 2020b). Additionally, other tick species infesting dogs such as Rhipicephalus haemaphysaloides, Haemaphysalis hystricis, Haemaphysalis wellingtoni, and Haemaphysalis papuana have been reported also sporadically (Durden et al., 2008; Kolonin, 1995; Tanskul et al., 1983). However, the role of these ticks as vectors of pathogens in the transmission to dogs in SEA remains unknown.

The cosmopolitan cat flea Ctenocephalides felis is commonly found on dogs and cats around the world, including SEA (Lawrence et al., 2019). This flea species is involved in the transmission of many zoonotic bacterial pathogens (e.g. B. henselae, Bartonella clarridgeiae, and R. felis) (Bitam et al., 2010), and also acts as the intermediate host of the tapeworm Dipylidium caninum (Guzman, 1984). Whilst the dog flea Ctenocephalides canis is climatically restricted to the temperate regions, Ctenocephalides orientis (Fig. 2C) is mainly distributed in tropical Asia (i.e. India and SEA) (Colella et al., 2020; Hii et al., 2015; Kernif et al., 2012). Indeed, recently acquired knowledge (Calvani et al., 2020; Colella et al., 2020; Lawrence et al., 2019) indicates that previous reports of C. canis parasitizing domestic dogs in SEA probably refer to C. orientis, due to their strong morphological similarity. The vector competence of C. orientis in transmitting pathogens remains unclear although this flea species has been found to carry some rickettsiae such as Rickettsia asembonensis and Rickettsia sp. genotype RF2125 (Nguyen et al., 2020; Phoosangwalthong et al., 2018).

Mosquitoes play an important role in the transmission of various pathogens to dogs, cats, and humans worldwide, including SEA. The occurrence of Dirofilaria spp. and Brugia spp. has been widely reported in this region, and mosquitoes of the genera Aedes, Armigeres, and Mansonia...
are responsible for the transmission of these filarial pathogens (Denham & McGreevy, 1977; Irwin & Jefferies, 2004).

3. Vector-borne pathogens of zoonotic concern

*Rickettsia felis* is an emerging bacterial pathogen, which can be found in mammalian hosts and arthropods worldwide, with *C. felis* acting as the main vector and reservoir for this pathogen (Legendre & Macaluso, 2017; Parola, 2011). More recently, dogs have been demonstrated as competent reservoir hosts of *R. felis* with the infection resulting mostly subclinical symptoms (Ng-Nguyen et al., 2020). Since the first human case of flea-borne spotted fever attributed to *R. felis* in Thai-Myanmar border (Parola et al., 2003a), several cases of *R. felis* infection in patients with non-specific febrile illness have been documented in SEA, including Thailand (Edouard et al., 2014), Laos (Dittrich et al., 2014), Vietnam (Le-Viet et al., 2019), and Indonesia (Mawuntu et al., 2020). This pathogen has been detected in *C. felis* from dogs and cats from Indonesia, Laos, Malaysia, the Philippines, Thailand, and Vietnam (Kernif et al., 2012; Nguyen et al., 2020b). Meanwhile, a study reported that 10.9% of 101 free-roaming owned dogs from Cambodia were molecularly positive for *R. felis* (Inpankaew et al., 2016).

Cats are the main reservoirs for *B. henselae*, *B. clarridgeiae*, and *Bartonella koehlerae*, which cause cat scratch disease and endocarditis in humans (Chomel et al., 2006). Of these, *B. henselae* and *B. clarridgeiae* were reported in cats and their fleas from Indonesia, Malaysia, the Philippines, Singapore, and Thailand with prevalences of up to 60% (Chomel et al., 1999; Marston et al., 1999; Maruyama et al., 2001; Mokhtar & Tay, 2011; Nasirudeen & Thong, 1999), whereas *B. koehlerae* was detected for the first time in SEA in cats and *C. felis* from Thailand (Assarasakorn et al., 2012). Human infection by *B. henselae* has been reported to cause endocarditis in Laos and Thailand (Noopetch et al., 2018; Rattanavong et al., 2014; Watt et al., 2014), and ocular neuroretinitis in Malaysia (Tan et al., 2017). Additionally, *Bartonella vinsonii* subsp. *berkhoffii*, another important agent of human endocarditis, was detected in cats and dogs from Thailand (Srisanyong et al., 2016; Suk-sawat et al., 2001). Several other zoonotic species and subspecies of *Bartonella* have been identified in dogs from Thailand including *B. clarridgeiae*, *Bartonella elizabethae*, *Bartonella quintana*, and *B. vinsonii* subsp. *arupensis* (Bai et al., 2016; Billeter et al., 2012), with the latter being also found in Thai patients (Bai et al., 2012). Recently, *B. henselae* was also found to infect dogs in the Philippines (Singer et al., 2020).

Lyme borreliosis by *Borrelia burgdorferi* (s.l.) is mostly prevalent in the temperate northern hemisphere (Lantos et al., 2014). These bacteria are transmitted to dogs and humans by tick species of the genus *Ixodes*, particularly *Ixodes ricinus* and *Ixodes persulcatus* in Europe and northern Asia, and *Ixodes scapularis* in North America (Dantas-Torres et al., 2012a; Jongejan & Uilenberg, 2004). The presence of *B. burgdorferi* (s.l.) has also been serologically and molecularly confirmed in dogs in Thailand (Sthitmatee et al., 2016). Recently, *B. burgdorferi* (s.l.) has been serologically diagnosed in dogs from Indonesia and the Philippines (Colella et al., 2020). Some unexplained seropositive results have also been reported in other non-endemic areas worldwide, which could also suggest the occurrence of rare, but possible cross-reaction (Azzag et al., 2015; Maggi & Kramer, 2019).

*Leishmania infantum*, the causative agent of canine leishmaniasis, is among the most important zoonotic VBP of dogs, which has been found in all continents, except Oceania (Dantas-Torres et al., 2012b). In the Old World, this parasite is transmitted by various species of phlebotomine sand flies within the genus *Phlebotomus* (Killick-Kendrick, 1990), and causes visceral and/or cutaneous leishmaniasis in dogs and humans (Dantas-Torres et al., 2012b). Canine leishmaniasis is endemic in many regions of the world, such as South America and the Mediterranean basin (Otranto & Dantas-Torres, 2013). In SEA, *L. infantum* has been serologically diagnosed in dogs in the Philippines and Vietnam (Colella et al., 2020), and the presence of *L. infantum* has also been molecularly confirmed in one patient in Thailand (Maharom et al., 2008). Even though SEA is not considered as a *L. infantum*-endemic area, a study showed a high seroprevalence (55.3%) in immigrant workers in
| Pathogen                          | Zoonotic relevance | Isolation source | Country         | Reference                                      |
|----------------------------------|--------------------|------------------|-----------------|-----------------------------------------------|
| **Bacteria**                     |                    |                  |                 |                                               |
| Anaplasma platys                 | Low                | Dog              | Indonesia       | Faizal et al. (2019)                           |
|                                  |                    |                  | Malaysia        | Mokhtar et al. (2013)                          |
|                                  |                    |                  | Philippines     | Yhaxie et al. (2016)                          |
|                                  |                    |                  | Singapore       | Colella et al. (2020)                         |
|                                  |                    |                  | Thailand        | Pinyoowong et al. (2008)                      |
|                                  |                    |                  | Vietnam         | Chien et al. (2019)                           |
| Cat                              |                    |                  | Thailand        | Salakijiet al. (2012)                         |
| Cerocaphilades felis (from dog)  |                    |                  | Laos            | Calvaniet al. (2020)                          |
| Rhipicephalus sanguineus (s.l.)  |                    | (from dogs)      | Laos            | Nguyen et al. (2020a)                         |
|                                  |                    |                  | Malaysia        | Low et al. (2018)                             |
|                                  |                    |                  | Philippines     | Yhaxie et al. (2012)                          |
| R. sanguineus (s.l.) (from dogs) |                    |                  | Thailand        | Foongladdet al. (2011)                        |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2019)                          |
|                                  |                    |                  | C. felis (from dogs) | Nguyen et al. (2020b)                       |
|                                  |                    |                  | Laos            | Kernfet al. (2012)                            |
|                                  |                    |                  | Malaysia        | Kernfet al. (2012)                            |
|                                  |                    |                  | Philippines     | Wolf and Reeves (2012)                        |
|                                  |                    |                  | Thailand        | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2020b)                         |
|                                  |                    |                  | C. orientis (from dogs) | Nguyen et al. (2020b)                       |
|                                  |                    |                  | Laos            | Kernfet al. (2012)                            |
|                                  |                    |                  | Malaysia        | Kernfet al. (2012)                            |
|                                  |                    |                  | Philippines     | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2020b)                         |
| Rickettsia felis                 | High               | Dog              | Indonesia       | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Laos            | Kernfet al. (2012)                            |
|                                  |                    |                  | Malaysia        | Kernfet al. (2012)                            |
|                                  |                    |                  | Philippines     | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Thailand        | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2020b)                         |
|                                  |                    |                  | C. felis (from cats) | Nguyen et al. (2020a)                      |
|                                  |                    |                  | Laos            | Varagnol et al. (2009)                        |
|                                  |                    |                  | Indonesia       | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Philippines     | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2020b)                         |
|                                  |                    |                  | C. orientis (from dogs) | Nguyen et al. (2020b)                       |
|                                  |                    |                  | Laos            | Kernfet al. (2012)                            |
|                                  |                    |                  | Malaysia        | Kernfet al. (2012)                            |
|                                  |                    |                  | Philippines     | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Thailand        | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2020b)                         |
| Rickettsia asembonensis          | Nil                | C. felis (from dogs) | Laos            | Nguyen et al. (2020a)                         |
|                                  |                    |                  | Indonesia       | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Philippines     | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Malaysia        | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Thailand        | Nguyen et al. (2020b)                         |
|                                  |                    |                  | Vietnam         | Nguyen et al. (2020b)                         |
| “Candidatus Rickettsia senegalensis” | Nil             | C. orientis (from dogs) | Thailand        | Nguyen et al. (2020b)                         |
| Rickettsia sp. genotype RF2125   | Nil                | Cat              | Thailand        | Phoosangwalihong et al. (2018)                |
|                                  |                    |                  | Laos            | Calvancet al. (2020)                          |
| Bartonella henselae             | High               | Dog              | Philippines     | Siger et al. (2020)                           |
|                                  |                    |                  | Indonesia       | Marston et al. (1999)                         |
|                                  |                    |                  | Malaysia        | Hassancet al. (2017)                          |
|                                  |                    |                  | Philippines     | Chomelcet al. (1999)                          |
|                                  |                    |                  | Singapore       | Nasirudeencet al. (1999)                      |
|                                  |                    |                  | Thailand        | Narumyaum et al. (2001)                       |
|                                  |                    |                  | Thailand        | Marston et al. (1999)                         |
|                                  |                    |                  | Malaysia        | Mokhtar and Tay (2011)                        |
|                                  |                    |                  | Thailand        | Parolac et al. (2003b)                        |
|                                  |                    |                  | Laos            | Calvaniet al. (2020)                          |
|                                  |                    |                  | C. felis (from dogs/cats) | Parolac et al. (2003b)                      |
|                                  |                    |                  | Malaysia        | Parolac et al. (2003b)                        |
|                                  |                    |                  | Thailand        | Faongladdat et al. (2011)                     |
| Bartonella clarridgeae          | High               | Dog              | Indonesia       | Marston et al. (1999)                         |
|                                  |                    |                  | Philippines     | Chomelcet al. (1999)                          |
|                                  |                    |                  | Thailand        | Maruyamaum et al. (2001)                      |
|                                  |                    |                  | Laos            | Varagnol et al. (2009)                        |
|                                  |                    |                  | Thailand        | Parolac et al. (2012)                         |
|                                  |                    |                  | Malaysia        | Mokhtar and Tay (2011)                        |
|                                  |                    |                  | Laos            | Calvaniet al. (2020)                          |
|                                  |                    |                  | C. orientis (from dogs) | Parolac et al. (2003b)                      |
|                                  |                    |                  | Laos            | Kernfet al. (2012)                            |
|                                  |                    |                  | Thailand        | Parolac et al. (2012)                         |
| Pathogen                        | Zoonotic relevance | Isolation source | Country       | Reference                                      |
|--------------------------------|--------------------|------------------|---------------|-----------------------------------------------|
| Bartonella koehlerae           | High               | Cat              | Thailand      | Assarasakorn et al. (2012)                    |
| Bartonella elizabethae         | High               | C. felis (from cats) | Thailand      | Bai et al. (2010)                            |
| Bartonella quintana            | High               | Dog              | Thailand      | Bai et al. (2010)                            |
| Bartonella rochalmeae          | High               | P. irritans (from dogs) | Laos         | Calvani et al. (2020)                        |
| Bartonella vinsonii subsp. argenensis | High            | R. sanguineus (s.l.) (from dogs) | Thailand | Billetter et al. (2012)                       |
| Bartonella vinsonii subsp. berkholffi | High            | Dog              | Thailand      | Bai et al. (2010)                            |
| Bartonella vinsonii subsp. vinsonii | Nil              | C. felis (from dogs) | Thailand      | Billetter et al. (2012)                       |
| Mycoplasma haemofelis          | Nil                | Cat              | Thailand      | Assarasakorn et al. (2012)                    |
| “Candidatus Mycoplasma haemominutum” | Nil              | Dog              | Thailand      | Liu et al. (2016)                            |
| “Candidatus Mycoplasma turicensis”’ | Nil              | Dog              | Thailand      | Do et al. (2020)                             |
| Mycoplasma haemocanis          | Nil                | Dog              | Cambodia      | Inpankaew et al. (2016)                       |
| Coxiella burnetii              | High               | R. sanguineus (s.l.) (from dogs) | Malaysia | Watanabe et al. (2015)                        |
| Borrelia burgdorferi (s.l.)    | High               | Dog              | Indonesia     | Colella et al. (2020)                        |
| Protozoa                        |                    |                  |               |                                               |
| Babesia vogeli                 | Nil                | Dog              | Cambodia      | Inpankaew et al. (2016)                       |
|                                |                    |                  | Malaysia      | Prakash et al. (2018b)                       |
|                                |                    |                  | Philippines   | Galay et al. (2018)                          |
| Babesia gibsoni                | Nil                | Dog              | Malaysia      | Mohitnar et al. (2013)                       |
|                                |                    |                  | Singapore     | Colella et al. (2020)                        |
| Hepatocystis canis             | Nil                | R. sanguineus (s.l.) (from dogs) | Malaysia | Prakash et al. (2018b)                       |
|                                |                    |                  | Philippines   | Prakash et al. (2018a)                       |
|                                |                    |                  | Galay et al. (2018) |
|                                |                    |                  | Malaysia      | Piratae et al. (2015)                        |
|                                |                    |                  | Vietnam       | Nguyen et al. (2019)                         |
|                                |                    |                  | Singapore     | Colella et al. (2020)                        |
|                                |                    |                  | Philippines   | Prakash et al. (2018b)                       |
|                                |                    |                  | Galay et al. (2018) |
|                                |                    |                  | Thailand      | Piratae et al. (2015)                        |
|                                |                    |                  | Vietnam       | Colella et al. (2020)                        |
| Trypanosoma evansi             | Low                | Dog              | Malaysia      | Rajamanickam et al. (1985)                   |
|                                |                    |                  | Philippines   | Ramaeechaisithamun et al. (2009)              |
|                                |                    |                  | Thailand      | Bui et al. (2020)                            |
| Leishmania infantum            | High               | Dog              | Philippines   | Colella et al. (2020)                        |
|                                |                    |                  | Vietnam       | Colella et al. (2020)                        |
| Helminths                      |                    |                  |               |                                               |
| Brugia pahangi                 | Low                | Dog              | Thailand      | Satjawongvanit et al. (2019)                 |
|                                |                    |                  | Indonesia     | Palmieri et al. (1985)                       |
|                                |                    |                  | Malaysia      | Tan et al. (2011)                            |
| Brugia malayi                  | High               | Dog              | Thailand      | Satjawongvanit et al. (2019)                 |
|                                |                    |                  | Vietnam       | Colella et al. (2020)                        |
|                                |                    |                  | Indonesia     | Palmieri et al. (1985)                       |
|                                |                    |                  | Malaysia      | Al-Abd et al. (2015)                         |
|                                |                    |                  | Thailand      | Chansri et al. (2002)                        |
|                                |                    |                  | Philippines   | Theis et al. (2008)                          |
|                                |                    |                  | Singapore     | Colella et al. (2020)                        |
|                                |                    |                  | Thailand      | Kamyingkird et al. (2017)                    |
|                                |                    |                  | Vietnam       | Colella et al. (2020)                        |
|                                |                    |                  | Indonesia     | Colella et al. (2020)                        |
|                                |                    |                  | Malaysia      | Malik et al. (1980)                          |
|                                |                    |                  | Thailand      | Kamyingkird et al. (2017)                    |
Malaysia; however, none of the tested phlebotomine sand flies from the same survey was found positive for *Leishmania* spp. by PCR (Noor Azian et al., 2016), which raises some doubts about the origin of these infections.

*Trypanosoma evansi* is a protozoan transmitted by hematophagous flies of the genera *Stomoxys* and *Tabanus*, which has been found in various mammalian hosts including bovines, rodents, canines, and humans in tropical and subtropical regions (Aregawi et al., 2019). This parasite is of great veterinary concern due to its ability to cause severe illness in animals such as dogs and horses (Desquesnes et al., 2013). Many cases of canine trypanosomiasis have been reported in South America, Africa, Europe, and Asia (Defontis et al., 2012; Howes et al., 2011; Panigrahi et al., 2015; Rashid et al., 2014; Rjebli et al., 2015). In SEA, some cases of canine trypanosomiasis have been reported in Malaysia and Thailand (Barameechaithanan et al., 2009; Rajamaniickam et al., 1985). The presence of *T. evansi* has also been molecularly detected in a dog in Vietnam (Bui et al., 2020). Other than dogs, *T. evansi* is highly prevalent in cattle and water buffaloes in SEA (Desquesnes et al., 2009; Verloo et al., 2000). Notably, some cases of human infections with *T. evansi* have been reported, including one from Vietnam (Joshi et al., 2006; Powar et al., 2006; Van Vinh Chau et al., 2016), raising concerns about its zoonotic potential in endemic regions.

Lymphatic filariasis (LF), commonly known as elephantiasis, is one of the neglected tropical diseases, and it has been considered for a long time as endemic in SEA (Noordin et al., 2013). An estimated 15 million people in SEA are affected by LF (Sudomo et al., 2010). The disease is mainly due to the infection with *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*, which are transmitted by mosquitoes (World Health Organization, 2010). In particular, *W. bancrofti* is responsible for 90% LF cases, and the remaining are mostly due to *B. malayi* (World Health Organization, 2010). Domestic cats are recognized as reservoirs of the zoonotic nocturnal subperiodic form of *B. malayi*. The infection has been reported in cats with a prevalence ranging from 8.2% in Malaysia (Al-Abd et al., 2015) up to 28.3% in southern Thailand (Chansiri et al., 2002). The prevalence of canine infections varies from 8.2% in Malaysia (Al-Abd et al., 2015) up to 28.3% in southern Thailand (Chansiri et al., 2002). The infection has been reported in dogs ranging from 16% in Cambodia to 24% in Thailand (Inpankaew et al., 2016; Kamyingkird et al., 2017). Studies also reported the presence of *D. immitis* in cats in Indonesia, Malaysia, and Thailand with the higher infection prevalence (36%) recorded in southern Thailand (Kamyingkird et al., 2017). On the other hand, *D. repens* was also found in cats from those aforementioned countries with the highest prevalence of 12% in Malaysia (Al-Abd et al., 2015). This filarial nematode is endemic in dogs from Europe, where many cases of human subcutaneous/ocular infection have been diagnosed (Capelli et al., 2018; Otranto et al., 2017). Additionally, a rare case of subcutaneous infection with *D. repens* on the posterior thoracic region was also reported in Vietnam (Le et al., 2015).

The main targets of the Global Programme for the Elimination of Lymphatic Filariasis (GPELF), which aimed to eradicate this disease as a public health problem by 2020 through mass drug administration (MDA). Some countries such as Cambodia, Thailand, and Vietnam have already achieved the eradication of LF and others are still accomplishing this goal (World Health Organization, 2020). Mosquitoes of the genus *Manson* (e.g. *Manson* sp. & *Manson* sp. dives) have a wide distribution in SEA, are recognized as the main vectors of this filarial nematode (Zielke et al., 1993). *Brugia pahangi*, a species closely related to *B. malayi*, was found in dogs and cats from Indonesia, Malaysia, and Thailand. Although this filarial nematode was not considered as infecting humans under natural conditions, the first cases of human filariasis caused by *B. pahangi* have been reported in Malaysia (Tan et al., 2011). Thereafter, *B. pahangi* was found causing ocular infection in a Malaysian patient, and the microfilariae of this filarial nematode were also found in her cat and in *Arimgena subalbatus* mosquitoes from surrounding areas (Muslim et al., 2013a). This mosquito species has been proven as vector of *B. pahangi* (Muslim et al., 2013b) along with *Manson* sp. & *Manson* dives (Laing et al., 1960).

Other mosquito-borne filarial nematodes of zoonotic concern in SEA are *D. immitis* and *Dirofilaria repens*. These parasites are widely distributed, and can be found in many animal species, including humans (Dantas-Torres & Otranto, 2020; Otranto et al., 2013; Simón et al., 2012). Approximately, 70 mosquito species mainly from the genera *Culex*, *Aedes*, and *Anopheles* are considered as competent vectors of *D. immitis* and *D. repens*, causing animal and human heartworm and subcutaneous diseases, respectively (Eldridge & Edman, 2000). Among the mosquito vectors, *Aedes aegypti*, *Aedes albopictus*, and *Culex quinquefasciatus*, which are commonly found in rural and urban areas of SEA, may be responsible for the transmission of these two *Dirofilaria* spp. (Tiawsirisup & Kaewthamason, 2007; Tiawsirisup & Nithiuthai, 2006). *Dirofilaria immitis* was reported in a human patient in Thailand with a pulmonary nodule at the right lower lobe (Sukpanichnant et al., 1998). Canine heartworm infection caused by *D. immitis* is endemic in SEA, where the prevalence reported in dogs ranges from 16% in Cambodia to 24% in Thailand (Inpankaew et al., 2016; Kamyingkird et al., 2017). Studies also reported the presence of *D. immitis* in cats in Indonesia, Malaysia, and Thailand with the higher infection prevalence (36%) recorded in southern Thailand (Kamyingkird et al., 2017). On the other hand, *D. repens* was also found in cats from those aforementioned countries with the highest prevalence of 12% in Malaysia (Al-Abd et al., 2015). This filarial nematode is endemic in dogs from Europe, where many cases of human subcutaneous/ocular infection have been diagnosed (Capelli et al., 2018; Otranto & Eberhard, 2011). In SEA, many cases of ocular infections with *D. repens* have been reported, including two cases in Thailand (Jariya & Suchart, 1983; Pradatsundarasar, 1985), four in Malaysia (Rohela et al., 2009), and 11 in Vietnam (Dang et al., 2016; Van De et al., 2012). Additionally, a rare case of subcutaneous infection with *D. repens* on the posterior thoracic region was also reported in Vietnam (Le et al., 2015).

Recently, a case of a Thai patient with subconjunctival dirofilariosis caused by *Dirofilaria* sp., closely related to the *Dirofilaria* sp. found in humans in Hongkong and India (To et al., 2012), has been documented (Sukudom et al., 2018). Moreover, two species/genotypes of

### Table 1 (continued)

| Pathogen          | Zoonotic relevance | Isolation source | Country       | Reference                      |
|-------------------|--------------------|------------------|---------------|--------------------------------|
| *Dirofilaria repens* | High               | Cat              | Indonesia     | Palmieri et al. (1985)          |
| *Thelasia callipoda* | Moderate           | Dog              | Malaysia      | AI-Abd et al. (2015)            |
| *Acanthochelomorpha reconditum* | Nil               | Cat              | Thailand      | Wongsamchani et al. (2014)      |
| *Cercopithifilaria hainae* | Nil               | *C. felis* (from cats) | Thailand      | V.-L. Nguyen (unpublished data)  |
| *Dipylidium caninum* | Low                | Dog              | Malaysia      | Ngui et al. (2014)              |
|                   |                    |                  | Philippines   | Colella et al. (2020)           |
|                   |                    |                  | Thailand      | Rojekttihuan et al. (2014)      |
|                   |                    |                  | Vietnam       | Nguyen et al. (2015)            |
|                   |                    |                  | Laos          | Scholz et al. (2003)            |
|                   |                    |                  | Malaysia      | Mohd Zain et al. (2013)         |
|                   |                    |                  | Thailand      | Jittapalapong et al. (2007)     |
|                   |                    |                  |              |                                |
| *Dirofilaria bancrofti* |                |                  |              |                                |
|                   |                    |                  |              |                                |
| *Filicola subrostratus* |               |                  |              |                                |

A “?” indicates uncertain data on species identification of *C. canis*. 
D. repens-like filarial nematodes (referred to as *Dirofilaria* sp. “Thailand II” and *Dirofilaria* sp. “Thailand III”) were reported in cats from Thailand (Yilmaz et al., 2016, 2019), which indicates that the genetic diversity of filarial nematodes in SEA may be currently underestimated.

*Thelazia callipaeda*, also known as the “oriental eye-worm” was initially described in the former Soviet Union and in many countries in the Far East (Otranto et al., 2020). Zoophilic fruit flies of the genus *Phorctica* act as intermediate hosts of this parasite in Europe (i.e. *Phorctica variegata*) and in SEA (i.e. *Phorctica okadai*) (Otranto et al., 2004). This nematode causes ocular infection in carnivores (e.g. dogs, cats, and foxes) and humans (Otranto et al., 2004). Human ocular infections have been reported in Indonesia, Thailand, and Vietnam (Bhaiubulaya et al., 1970; Kosin et al., 1989; Van De et al., 2012; Viriyavejakul et al., 2012; Yospaiboon et al., 1989). The infection was also reported in dogs from Thailand (Bhaiubulaya et al., 1970). However, none of the dogs and cats tested in a recent survey from SEA countries was found positive for *T. callipaeda* (Colella et al., 2020).

*Dipylidium caninum* is a tapeworm infecting dogs and cats worldwide, with their fleas (e.g. *C. felis*, *C. canis*, and *C. orientis*) and lice (e.g. *Trichodectes canis*) serving as intermediate hosts (Labuschagne et al., 2018). The infection in dogs and cats occurs by accidental ingestion of infected intermediate hosts (Guzman, 1984). Similarly, the infection in humans may occur through this route (Garcia-Agudo et al., 2014; Sapp & Bradbury, 2020), and it has been recorded in at least 24 countries (Jiang et al., 2017). In SEA, since a human case was documented in an old study from the Philippines (Mendoza-Guzon & Abad, 1916), no other case has been reported, although some infections have been detected in neighboring countries such as India (Narasimham et al., 2013) and China (Jiang et al., 2017). The true incidence of *D. caninum* in humans seems to be underestimated considering the asymptomatic infection, and that examination for the presence of proglottids in faeces is seldom performed (Sapp & Bradbury, 2020). Conversely, the infection is commonly found in dogs and cats, especially in stray populations or those from rural areas. Some studies in Malaysia using fecal examination revealed a prevalence of *D. caninum* infection in rural dogs and stray cats reaching up 3.7% and 11.6%, respectively (Mohd Zain et al., 2013; Ngui et al., 2014). Interestingly, a recent molecular characterization of *D. caninum* confirmed the existence of two distinct genotypes (i.e. canine and feline genotypes), which are apparently host specific (Beugnet et al., 2018; Labuschagne et al., 2018). Additionally, *C. felis* and *Felicola subrostrata* collected from cats in Malaysia were also found to harbour DNA of the feline genotype of *D. caninum* (Labuschagne et al., 2018; Low et al., 2017).

4. Other VBP affecting dogs and cats

Other VBP of veterinary concern, which affect animal health and welfare, have also been reported in SEA. Some of them may also cause mortality in dogs as it is the case of *E. canis*, the causative agent of canine monocytic ehrlichiosis. This bacterium is widespread and considered as highly virulent to dogs in SEA (Noordin et al., 2013). Although the presence of microfilariae can be microscopically identified in the bloodstream of infected animals (Panarese et al., 2020), their identification based on morphology and measurements may be troublesome. For example, microfilariae of *B. malayi* are around 220 μm in length and 5 μm in diameter, and those of *B. pahangi* are around 280 × 5 μm (Schacher, 1962; Taylor, 1966). *Dirofilaria immitis* microfilariae are 290–330 μm in length and 5–7 μm in diameter, whereas those of *D. repens* are slightly longer and wider (350–385 × 7–8 μm) (Simón et al., 2012). Moreover, false negative results may occur in cases of adult single-sex infection or low microfilarialia. Many studies have been conducted based on serological surveys by using point-of-care (POC) commercial kits to detect antigen of *D. immitis* females in serum or blood samples (Chelliah & Slapeta, 2019; Colella et al., 2020; Sukhumavasi et al., 2012; Theis et al., 2008). However, no similar serological tests are available for the diagnosis of other filarial infections. Serological tests such as immunofluorescence antibody, western immunoblot, POC tests (e.g. SNAP 4DX Plus and SNAP Leishmania) have also been applied to detect the presence of antibodies to several pathogens (i.e. *Anaplasma spp.*, *Ehrlichia spp.*, *Bartonella spp.*, *B. burgdorferi*, and *Leishmania spp.*) (Chomel et al., 1999; Colella et al., 2020; Sukswat et al., 2001). Additionally, the misinterpretation of cytology may also lead to the misdiagnosis of some microorganisms, e.g. reports of “*Babesia canis*” in dogs in SEA probably refer to *B. vogeli* (Petney et al., 2019). Therefore, the use of molecular assays for pathogen detection is recommended, as they are faster and more accurate. A study in Thailand revealed a significantly higher prevalence of *D. immitis* infection in dogs and cats by using conventional PCR (cPCR) compared to microscopic examination (Kamyingkird et al., 2017). A real-time fluorescence resonance energy transfer PCR assay has also been used to diagnose the infection with *B. malayi* and *B. pahangi* (Thanchomnang et al., 2010). More recently, a real-time PCR followed by high resolution melting analysis has been developed for the detection of multiple filarial...
with the MDA, which has been given to people living in LF endemic simulations reduced after one year of intervention (Vu et al., 2005). Along Ae. aegypti accomplishment with approximately 90% of with high incidence of dengue in Vietnam have achieved a great application of microinfection in cats has given a good eradication effect to both B. malayi of doxycycline alone or in combination with ivermectin for treatment of populations (i.e. domestic dogs and cats) should be considered as one of essential oil of many studies in Thailand revealed the high repellency (up to 8 h) of repellent properties across SEA (Tisgratog et al., 2016). For instance, more than 2,300 plant species were found to have potential mosquito repellent properties against some mosquito species, such as Ae. aegypti, Ae. albopictus, and Cx. quinquefasciatus (Champakaew et al., 2015; Tawatsin et al., 2006). The essential oil of Cymbopogon citratus (lemon grass) has been widely used in many countries in SEA as a cheap and effective mosquito repellent (Shah et al., 2011). Additionally, some biological control agents (i.e. Mosycyclops and Wolbachia) against Aedes spp. have also been applied. The application of Mosycyclops for eradication of Ae. aegypti in some provinces with high incidence of dengue in Vietnam have achieved a great accomplishment with approximately 90% of Ae. aegypti larval populations reduced after one year of intervention (Vu et al., 2005). Along with the MDA, which has been given to people living in LF endemic areas, the control programme of filarial nematodes among reservoir host populations (i.e. domestic dogs and cats) should be considered as one of the comprehensive strategies to achieve the target of the GPELF. The use of doxycycline alone or in combination with ivermectin for treatment of B. malayi infection in cats has given a good eradication effect to both microfilariae and adult worms (Khawwisetsut et al., 2017). Recently, guidelines for the diagnosis, prevention and treatments of parasitic diseases in companion dogs and cats in the tropics have been prepared by the Tropical Council of Companion Animal Parasites (Dantas-Torres et al., 2020). The guidelines are freely released in multiple languages including English, Bahasa Malaysia, Thai, and Vietnamese (http://www.troccap.com), which are very useful for local veterinarians and pet owners to improve the awareness, prevention and control of VBD.

6. Conclusions and research needs

The updated data discussed in this review illustrate a general picture of VBD affecting dogs and cats in SEA, which represent an important issue to animal and public health. Overall, zoonotic VBP, such as R. felis, B. henselae, and D. repens, are of concern to human health in this region. Despite the recently acquired scientific knowledge, many scientific gaps still persist about the eco-epidemiology of the zoonotic VBP, which limit our current understanding and our capability to control them. For instance, although many human cases of dirofilariasis by D. repens have been reported (Rohela et al., 2009; Van De et al., 2012), the source of infection as well as the species of mosquito vectors of this nematode in SEA remains unclear. Therefore, the zoonotic transmission cycle of D. repens in SEA deserves further investigations. In spite of the acquired data for some countries such as Malaysia and Thailand (Colella et al., 2020; Huggins et al., 2019; Koh et al., 2016; Low et al., 2018; Wongkamchai et al., 2014), data regarding the distribution of the zoonotic VBP in other countries (e.g. Cambodia, Laos, Myanmar, and Timor-Leste) is limited or virtually nonexistent. On the other hand, the rapidly changing of environment (e.g. climate change, land use change, and urbanization) in SEA may also alter the distribution and abundance of vectors and VBD (Dantas-Torres, 2015; Lim & Vythilingam, 2013). Therefore, further epidemiological surveillance as well as studies on the impact of those environmental factors to the distribution of the zoonotic VBP in SEA are encouraged. Finally, a stronger collaboration between governments, commercial companies, scientists, and medical and veterinary communities should be implemented for a better management of VBD in SEA. The effective control measures of canine and feline VBD as well as their arthropod vectors should be performed simultaneously for a better prevention of zoonotic infections.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors’ contributions

DO conceived the study. VLN conducted the literature screening, analyzed the data, and wrote the first draft of the manuscript. FDT and DO critically revised the manuscript. All authors read and approved the final manuscript.

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