Bartonella Infections in Rodents and Bats in Tropics

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1. Introduction

Bacteria of genus *Bartonella* are mainly hemotropic, intracellular gram-negative bacteria associated with erythrocytes and endothelial cells of mammals and other vertebrates (Anderson & Neuman, 1997; Schülein et al., 2001). Members within the genus have been expanded during last three decades with over 30 species or subspecies having been described. In addition to the well-known human pathogens *B. bacilliformis* (agent of Carrión's disease), *B. quintana* (agent of trench fever), and *B. henselae* (agent of cat-scratch disease), a growing number of *Bartonella* species, such as *B. alsatica*, *B. elizabethae*, *B. grahamii*, *B. koehlerae*, *B. claridgeiae*, *B. wassoni*, *B. vinsonii* subsp. *berkhoffii*, *B. vinsonii* subsp. *arupensis*, *B. tamiae*, and *B. rochalimae*, have been identified as human pathogens (Kordick et al., 1997; Margileth & Baehren, 1998; Kerkhoff et al., 1999; Welch et al., 1999; Roux et al., 2000; Sander et al., 2000; Kosoy et al., 2003 & 2008; Raoult et al., 2006; Eremeeva et al., 2007). Infections caused by these microorganisms have been encountered in vertebrates of virtually all species surveyed, which to date have extended to members of at least eight different orders of mammals, including Artiodactyla, Cetacea, Carnivora, Chiroptera, Insectivora, Lagomorpha, Primates, and Rodentia (Boulouis et al., 2005; Concannon et al., 2005; Maggi et al., 2005). Results have demonstrated that the prevalence of bacteremia can range from 0 to almost 100% in vertebrate populations. Persistent infections in domestic and wild animals result in a substantial reservoir of bartonellae in nature. Several mammalian species, such as rodents, cats, and dogs are reservoir hosts of some of these pathogenic *Bartonella* species. However, animal reservoirs remain unknown for some newly identified human *Bartonella* species, such as *B. tamiae* and *B. rochalimae*. Knowledge of the transmission of *Bartonella* bacteria between mammalian hosts is incomplete. However, hematophagous arthropods, such as fleas, flies, lice, mites, and ticks, have been found naturally infected and are frequently implicated in transmitting *Bartonella* species (Baker, 1946; Garcia-Caceres & Garcia, 1991; Chomel et al., 1995& 1996; Higgins et al., 1996; Pappalardo et al., 1997; Roux & Raoult, 1999; Welch et al., 1999).

Bartonella infections can cause a wide spectrum of emerging and reemerging diseases, ranging from a short-term fever that resolves quickly on its own to potentially fatal diseases with cardiovascular, nervous system, or hepatosplenic involvement (Anderson & Neuman, 1997; Koehler, 1996). These findings have shown the emerging medical importance of bartonellae. In fact, bartonella infections have become a big world-wide issue. This review
presents the current findings of Bartonella infections in rodents and bats from tropics. We are proposing the urgent need to expand studies of Bartonella infections in tropics for better understanding the ecology, reservoir potential, vector transmission, pathogenesis of bartonellosis, and their roles in tropical medicine.

2. Bartonella infections in rodents in tropics

The order Rodentia contains over 2,000 species and makes up the largest group of mammals. Rodents can carry many different zoonotic pathogens, such as Leptospira, Yersinia pestis, Toxoplasma gondii, Campylobacter, and Bartonella species. With their broad distribution and close contact with humans, rodents play an important role in serving as natural reservoir hosts of these zoonotic pathogens. The first Bartonella species found in rodents was isolated from the blood of the vole Microtus pennsylvanicus. Originally described as a rickettsial agent (Baker, 1946), this bacterium was later reclassified as Bartonella vinsonii (Weiss & Dasch, 1982). During the last three decades, numerous surveys have been conducted in a variety of rodent communities at many locations. These surveys demonstrated that Bartonella are widely distributed in rodents of numerous species in all continents (Birtles et al., 1994; Kosoy et al., 1997; Heller et al., 1998; Hofmeister et al., 1998; Laakkonen et al., 1998; Bermond et al., 2000; Fichet-Calvet et al., 2000; Bajer et al., 2001; Bown et al., 2002; Holmberg et al., 2003; Engbaek & Lawson, 2004; Gundi et al., 2004; Pawelczyk et al., 2004; Pretorius et al., 2004; Tea et al., 2004; Jardine et al., 2005; Kim et al., 2005; Telfer et al., 2005; Markov et al., 2006; Knap et al., 2007).

The very first investigation of Bartonella infection in rodents from tropic areas was conducted in Yunnan, a province located in southwestern China (Ying et al., 2002). This study revealed the important finding that Rattus rats are the reservoir hosts of B. elizabethae, a Bartonella strain associating with human diseases. With this discovery, more investigations of Bartonella infections in rodents were later carried out in several other tropical countries, including Bangladesh, Thailand, Vietnam, Indonesia, Kenya, and others (Castle et al., 2004; Winoto et al., 2005; Bai et al., 2007b & 2009b; Kosoy et al., 2009 & unpublished data). In this section, we compare the composition of rodent community, Bartonella prevalence, and genetic diversity of the Bartonella strains, mainly based on three most complete studies that were conducted in southwestern China, Bangladesh, and Thailand (Ying et al., 2002; Bai et al., 2007b & 2009b). We discuss the epidemiological significance of these findings.

2.1 Rodent community

As an environment with a moderate climate, ample food, and plenty of water, the tropics harbor highly diverse rodent communities. The rodents tested for Bartonella infections from different regions of tropics represented over 20 species of 10 genera, including Apodemus chevrieri, A. draco, A. peninsulae, Bandicota bengalensis, B. indica, B. savilei, Berylmys berdmorei, Eothenomys miletus, Lemniscomys striatus, Mastomys natalensis, Mus caroli, M. cervicolor, M. minutoides, M. musculus, Rattus argentiventer, R. exulans, R. losea, R. nitidus, R. norvegicus, R. rattus, R. remotes, R. surifer, and R. tanezumi subsp. flavipes. Among these, rats of the genus Rattus were the most widely distributed and prevalent, being found in all study areas. For example, in the survey of Bartonella infections in rodents from 17 provinces of Thailand, the total number of Rattus rats accounted for more than 80% of the tested rodents (Bai et al., 2009b); in studies in southwestern China and Bangladesh, more than 50% rodents also were
Rattus rats (Ying et al., 2002; Bai et al., 2007b). Nevertheless, the most common Rattus species varied among the study sites. In Thailand, the R. rattus, R. norvegicus, and R. exulans were the most common species; in southwestern China, R. norvegicus and R. tanezumi subsp. flaviceps were the most common species; and R. rattus were the most common species in Bangladesh (Table 1). In addition to Rattus rats, rats of the genus Bandicota also were commonly distributed in Bangladesh and Thailand. Bandicota bengalensis, for example, accounted for 41% in the local rodent community in Dhaka, Bangladesh, and were actually the most common species; Bandicota indica and Bandicota savilei accounted for 16% of all rodents in Thailand (Table 1). In fact, Bandicota indica alone accounted for 78% of tested rodents in another study conducted in Chiang Rai, a northern province of Thailand (Castle et al., 2004), indicating that Bandicota rats could be more common than Rattus rats in some areas in Thailand. Mice of the genus Apodemus were found more popular in rural areas in southwestern China, and accounted for 35% of local rodents. Rodents of some other genera, including Mus, Berylmys, and Eothenomys were also found in different areas but in smaller numbers.

2.2 Bartonella prevalence in rodents

Ecologic and bacteriologic observations of rodents in different regions of the world have shown the wide spread of bartonella infection in rats and mice of various species. Nevertheless, large variations in prevalence of infection have been observed among different studies and rodents of different genera, or even species, ranging from 0 to >80% (Birtles et al., 1994; Kosoy et al., 1997; Bai et al., 2009a & 2011). A possible explanation for such variation is the different composition of rodent communities in which the biodiversity can affect the prevalence in a local community (Bai et al., 2009a).

Similar observations were reported from studies of bartonella infection in rodents conducted in tropical areas. A relatively low prevalence of bartonella infection in rodents was reported from Kenya (15%) (Kosoy et al., 2009), while high prevalence was demonstrated in studies conducted in several countries of Southeast Asia. More interestingly, the overall prevalence of bartonella infection in rodents reported from these countries was very similar, with 42.8%, 44.5%, and 41.5% in Bangladesh, southwestern China, and Thailand, respectively (Ying et al., 2002; Bai et al., 2007b & 2009b), although composition of the rodent communities differed among the study sites. Nevertheless, the bartonella prevalence varied by rodent species. Generally, rats of the genus Rattus are highly infected with Bartonella species. In Thailand, bartonella prevalence in Rattus rats was 43% with a range of 0-86% among eight investigated species. R. norvegicus and R. rattus, as the most common species present, exhibited very high prevalence of bartonella infection with 86% and 65% in each, respectively, while only 3% of another common tropical species, R. exulans, were infected with Bartonella species. In one southwestern China study, Rattus tanezumi subsp. flaviceps was the predominant species among the local rodents and also highly infected by Bartonella species with 41% prevalence. In addition to the variation in prevalence between rodent species, the same rat species can exhibit different degrees of susceptibility to infection with Bartonella species at different locations. For example, the infection rate in R. rattus was 32% in Bangladesh, but 65% in Thailand; the infection rate in R. norvegicus was 43% in southwestern China, but 86% in Thailand (Table 1).

Rats of the genus Bandicota were also frequently infected with Bartonella species. In Bangladesh, 63% of B. bengalensis were infected; in Thailand, 33% and 57% of B. indica and B. savilei were infected with Bartonella species, respectively.
Mice of genus Apodemus were also highly susceptible to bartonella infection, with 33-71% prevalence in different species in southwestern China; in Kenya, 63% of Mastomys natalensis had bartonella infection; rodents of the genus Mus and several other genera seem to exhibit lower susceptibility to bartonella infection. In Bangladesh, none of the 12 tested Mus musculus had bartonella infection; but in Thailand, three of seven Mus cervicolor were infected with Bartonella species.

2.3 Diversity of Bartonella species in rodents

Studies from different regions of the world have demonstrated that rodents harbor extremely diverse Bartonella strains. Although many strains remain uncharacterized or were only partially characterized, quite a few novel rodent-associated Bartonella species and subspecies have been described, including B. birtlesii, B. coopersplainensis, B. elizabethae, B. doshiae, B. grahamii, B. phoceensis, B. queenslandensis, B. rattimassiliensis, B. taylorii, B. tribocorum, B. vinsonii subsp. arupensis, and B. wahooensis (Daly et al., 1993; Birtles et al., 1995; Heller et al., 1998; Kosoy et al., 2003; Gundi et al., 2004 & 2009; Bai et al., 2011). Among these, B. coopersplainensis, B. elizabethae, B. phoceensis, B. queenslandensis, B. rattimassiliensis, and B. tribocorum were all associated with rats of the genus Rattus, and they are genetically closer to each other than to other Bartonella species that are associated with Apodemus spp., Peromyscus spp., Spermophilus spp., Myodes spp., and other rodent genera.

Comparative analyses of bartonella cultures obtained from the rodents in the tropics also revealed diverse assemblages of Bartonella strains, many of which appear to represent a variety of distinct species. These bartonella isolates clustered into different lineages that mostly had a close association with their host genus or species. In southwestern China, Bartonella isolates obtained from Rattus norvegicus and R. tanazumi. subsp. flaviceps were closely related to B. elizabethae or to the closely related B. tribocorum. In fact, isolates obtained from the R. norvegicus in Vietnam were identical to the type strain of B. elizabethae (Kosoy et al., unpublished). Subsequent studies from Bangladesh, Thailand, and Kenya showed that B. elizabethae-like bacteria are highly prevalent in a large portion of the local populations of Rattus rats. In addition to B. elizabethae, several more Bartonella species were identified, including B. tribocorum, B. coopersplainensis, B. phoceensis, B. queenslandensis, and B. rattimassiliensis, all of which were previously described from Rattus rats captured in France and Australia (Heller et al., 1998; Gundi et al., 2004 and 2009), as well as the tropics (Castle et al., 2004; Bai et al., 2007b & 2009b; Kosoy et al., 2009). These results suggested that these Bartonella species probably co-speciated with rats of the genus Rattus.

The spectrum of Bartonella species found in rats of the genus Bandicota from Bangladesh and Thailand were very similar to those of the genus Rattus (Bai et al., 2007b; Castle et al., 2004), demonstrating sharing of Bartonella strains among rodents of these species. In fact, Bandicota rats share the same habitat with Rattus rats and these rats are phylogenetically related as well. Rattus rats and Bandicota rats may play equally important roles in serving as reservoir hosts of these Bartonella strains.

Interestingly, in Kenya, all bartonella isolates obtained from rodents of Mastomys natalensis and Lemniscomys striatus were relatively closely related but not identical to Bartonella tribocorum and B. elizabethae. It is questionable whether these mice can also serve as reservoirs of these highly rat-associated Bartonella species.

Bartonella isolates obtained from rodents of other species, such as Apodemus mice, Eothenomys voles, and others, were distant from strains obtained from Rattus rats and Bandicota rats, and were classified into different phylogenetic groups of Bartonella. Further characterization is needed for fully description of these strains.
Table 1. Bartonella in rodents from Bangladesh, China, and Thailand

<table>
<thead>
<tr>
<th>Rodent species</th>
<th>Bangladesh</th>
<th>China</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. tested</td>
<td>No.</td>
<td>No. tested</td>
</tr>
<tr>
<td>Apodemus chevrieri</td>
<td>32</td>
<td>62.5</td>
<td></td>
</tr>
<tr>
<td>Apodemus draco</td>
<td>6</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>Apodemus peninsulae</td>
<td>7</td>
<td>71.4</td>
<td></td>
</tr>
<tr>
<td>Bandicota bengalensis</td>
<td>76</td>
<td>63.2</td>
<td></td>
</tr>
<tr>
<td>Bandicota indica</td>
<td>46</td>
<td>32.6</td>
<td></td>
</tr>
<tr>
<td>Bandicota savilei</td>
<td>7</td>
<td>57.1</td>
<td></td>
</tr>
<tr>
<td>Berylmys berdmorei</td>
<td>1</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Eothenomys miletus</td>
<td>16</td>
<td>18.8</td>
<td></td>
</tr>
<tr>
<td>Mus caroli</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mus cervicolor</td>
<td>7</td>
<td>42.9</td>
<td></td>
</tr>
<tr>
<td>Mus musculus</td>
<td>12</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Rattus argentiventor</td>
<td>3</td>
<td>66.7</td>
<td></td>
</tr>
<tr>
<td>Rattus exulans</td>
<td>95</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>Rattus losea</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Rattus nitidus</td>
<td>3</td>
<td>33.3</td>
<td>22</td>
</tr>
<tr>
<td>Rattus norvegicus</td>
<td>7</td>
<td>42.9</td>
<td>22</td>
</tr>
<tr>
<td>Rattus rattus</td>
<td>99</td>
<td>32.3</td>
<td>135</td>
</tr>
<tr>
<td>Rattus remotus</td>
<td>2</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Rattus surifer</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Rattus tanezumi subsp.</td>
<td>58</td>
<td>41.4</td>
<td></td>
</tr>
<tr>
<td>flavipectus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>187</td>
<td>42.8</td>
<td>127</td>
</tr>
</tbody>
</table>

2.4 Host-specificity relationships between Bartonella spp. and rodents

Studies from different regions of the world have shown controversial relationships between Bartonella species and their natural rodent hosts. A study of bartonella infection in rodents from the United Kingdoms by Birtles and his colleagues (1994), questioned host-specificity of Bartonella species by finding that three Bartonella species (B. grahamii, B. taylorii, and B. doshiae) were circulating among woodland mammals of all dominant rodent species (Apodemus sylvaticus, A. flavicollis, Myomys glareolus, Microtus agrestis and Neomys fodiens). Subsequent investigations of bartonella infections in rodent communities in central Sweden reported similar results, demonstrating that Bartonella grahamii frequently infected Microtus voles (M. glareolus), Apodemus mice (A. flavicollis, A. sylvaticus) and house mice (Mus musculus) (Holmberg et al., 2003). By contrast, investigations from North America suggested a completely different picture of Bartonella species - rodent relationships from those found in Europe. In these North American studies, Bartonella species specific to a particular rodent species have been reported, such as those found in mice of the genus Peromyscus, rats of the genus Neotoma, chipmunks of the genus Tamias, ground squirrels of the genus Spermophilus, prairie dogs of the genus Cynomys, and other rodents (Kosoy et al., 1997 & 2003; Stevenson et al., 2003; Jardine et al., 2006; Bai et al., 2008), indicating definite host-specific relationships exist between these Bartonella strains and their rodent hosts.
Observations of the studies of rodent-borne bartonella infections in the tropics showed some different views in regards to a relationship between *Bartonella* species and rodents. In southwestern China and Vietnam, *Barotnella* isolates obtained from *Rattus* rats were all classified as *B. elizabethae* and/or genetically very closely related to *B. tribocorum*, showing a very specific relationship (Ying et al., 2002; Kossy et al., unpublished data); in Bangladesh and Thailand, all isolates obtained from the *Rattus* rats also fell within the cluster of *Rattus* rats-associated *Bartonella* species, including *B. elizabethae*, *B. tribocorum*, *B. cooperisplainensis*, *B. phoceensis*, *B. queenslandensis*, and *B. rattimassilonisi*. However, all of these strains were also frequently harbored by *Bandicota* rats in these same regions. Sharing of the same *Bartonella* strains by rats of two genera might suggest a lower level of host-specificity in these areas or reflect a phylogenetic relatedness between rats belonging to both genera. In Kenya, *B. elizabethae*-like bartonellae were even more widely spread, being found not only in *Rattus* rats, but also in *Mastomys natalensis* and *Lemniscomys striatus*, both which are taxonomically much further from *Rattus* rats than *Bandicota* rats are from *Rattus* rats. Such results implied that *B. elizabethae* and related *Bartonella* species, as the dominant species, may have extended the range of their animal reservoir hosts because long periods of coexistence have provided numerous opportunities to infect local rodent.

### 2.5 Rattus rats as reservoir hosts of zoonotic bartonellae

*Bartonella* species usually do not cause diseases or pathologic changes to their natural animal hosts. However, some *Bartonella* species can become opportunistic pathogens following a host switch, such as could occur when a strain of rodent bartonella infects humans. During recent years, more and more evidence has accumulated showing that bartonella infections are indeed associated with human illnesses and can be considered as emerging infections. This has raised public health concern and drawn the attention of scientists studying zoonotic diseases. Some rodents often live with or near humans. Close contact between rodents and humans throughout the world makes the study of rodent-borne *Bartonella* essential in order to determine the extent to which rodents may serve as sources of human infections. The epidemiological importance of rodent-borne bartonellae as causes of disease in animals and humans is emerging. Rodents of some species have been found to be reservoir hosts of some *Bartonella* species that are human pathogens, such as *B. elizabethae*, *B. grahamii*, *B. vinsonii* subsp. *arupensis*, and *B. washoensis* (Daly et al., 1993; Birtles et al., 1995; Ellis et al., 1999; Kerkhoff et al., 1999; Welch et al., 1999; Kossy et al., 2003; Iralu et al., 2006). It is likely that new rodent-borne bartonellae will be identified in the near future, and some of these possibly can be proven to be as zoonotic pathogens.

The most intriguing result of studying bartonella infection in rodents in tropics was the finding of a large number of *Bartonella* strains that are genetically related to the recognized human pathogen *B. elizabethae*. These strains widely infect rats of genera *Rattus* and *Bandicota* in Bangladesh, southwestern China, Thailand, Kenya, and other areas (Ying et al., 2002; Castle et al., 2004; Bai et al., 2007b & 2009b; Kossy et al., 2009). *B. elizabethae* was originally isolated from the blood of a patient with endocarditis in Massachusetts, USA (Daly et al., 1993). Subsequent studies have implicated *B. elizabethae* as a cause of additional cases of endocarditis, as well as a case of Leber’s neuroretinitis, and some have shown the presence of *B. elizabethae*-reactive antibodies in a high proportion of intravenous drug users (O’Halloran et al., 1998; Comer et al., 1996).

In Thailand, researchers have reported that febrile illnesses in human patients were associated with infections of several *Bartonella* species, including *B. elizabethae*, *B.
rattimassiliensis, B. tribocorum, B. vinsonii subsp. arupensis, B. tamiæ, and others (Kosoy et al., 2010). Homologous sequences comparison indicated that the Bartonella genotypes identified as B. elizabethae, B. rattimassiliensis, and B. tribocorum in the patients were completely identical or very close to Bartonella strains that were derived from black rats, bandicoot rats, Norway rats, and other rodents from Bangladesh, China, Thailand, and other Asian countries. These results suggested that the rodents are the potential source of the infection. Very recently, a serological survey studying source of undiagnosed febrile illness conducted in Nepal also reported antibodies specific to B. elizabethae, B. tamiæ, B. vinsonii supsp. arupensis, and other Bartonella species (Myint et al., 2011).

A natural reservoir for B. elizabethae was not implicated until 1996 when Birtles & Raoult identified a strain of Bartonella obtained in Peru from a R. norvegicus that had gltA and 16SrRNA gene sequences that matched the sequences for the respective genes of B. elizabethae (Birtles & Raoult, 1996). Numerous isolates were later obtained from R. norvegicus in United States and from R. rattus in Portugal. Genetic analyses demonstrated that these isolates formed a phylogenetic group along with the genotypes of B. elizabethae and the Bartonella strains found in rats from Peru (Ellis et al., 1999). Rattus rats occupy many different ecologic niches in the sites in Southeast Asia where these animals initially evolved (Eisenberg, 1981). These rats were introduced into other continents through the aid of humans and have become common and widespread in urban and rural environments in Europe, North America, and South America. The findings of B. elizabethae in Rattus rats from Peru, United States, Portugal, France, and other areas have led to the hypothesis of an Old World origin of B. elizabethae and related Bartonella bacteria (Childs, et al., 1999; Ellis et al., 1999). These bacteria could have spread from the Old World to other parts of the world through infected rats traveling by ship. Investigations conducted in southwestern China, Bangladesh, Thailand, and Kenya provided evidence in support of the Old World origin hypothesis. The finding of B. elizabethae-like agents in a high proportion of the rats raised potential public health concerns of humans acquiring the bartonella infection and the need to study whether these agents are responsible for cases of non-culturable bacterial endocarditis and febrile illnesses of unknown etiology in tropics.

B. vinsonii supsp. arupensis was first isolated from a bacteremic cattle rancher in USA (Welch et al., 1999). This bacterium is highly prevalent among deer mice (Peromyscus maniculatus), a strict North American rodent species, and has never been detected in any rodents from elsewhere, including tropics. However, the strain was found in stray dogs in Thailand (Bai et al., 2010). It is logical to suggest that this bacterium was acquired by dogs from wild rodents in North America and then, relocated to other continents through the translocation of infected dogs. Regardless, further investigations are needed to define the role of domestic animals as potential sources for human bartonellosis in Thailand and other tropical areas.

3. Bartonella infections in bats in tropics

Like rodents, bats (Order: Chiroptera) are another group of very abundant, diverse, and geographically dispersed vertebrates on the earth (Simmons, 2005; Calisher et al., 2006). Multiple studies have highlighted that bats may play an important role in serving as natural reservoirs to a variety of pathogens (Schneider et al., 2009). Transmission of pathogenic bat-borne viruses capable of causing disease with high human mortality has been demonstrated for a number of viruses, including rabies virus and related lyssaviruses, Nipah and Hendra
viruses, Marburg virus, Ebola viruses, and the very recently emerged inferred for SARS-CoV-like virus and other coronaviruses and others (Halpin et al., 2000; Li et al., 2005; Williams, 2005; Tang et al., 2006). The high mobility, broad distribution, social behavior (communal roosting, fission-fusion social structure) and longevity of bats make them ideal reservoir hosts and sources of infection for various etiologic agents.

There is very limited information regarding Bartonella infections in bats. In England, detection of Bartonella DNA in bats was reported recently (Concannon et al., 2005). A few studies from Egypt and United States reported presence of Bartonella species in ectoparasites collected from bats (Loftis et al., 2005; Reeves et al., 2005, 2006, & 2007). From tropic areas, two studies of bartonella infections in bats were conducted in Kenya and Guatemala very recently (Kosoy et al., 2010; Bai et al., 2011). These studies brought large information regarding distribution of bartonellae in bats. Here we present the findings from these two studies. We compare the composition of bat communities, prevalence of bartonella infections in bat populations, genetic diversity of Bartonella strains circulating among the bat populations. We also discuss the epidemiological significance of these findings.

3.1 Bat community

Belonging to 28 species, bats collected from these two studies showed large diversity. Species composition was completely different in the two studies. Bats collected from Kenya represented 13 species of 9 genera (Table 2), including Chaerephon sp., Coleura afra, Eidolon helvum, Epomophorus spp., Hipposideros commersoni, Miniopterus spp., Rhinolophus spp., Rousettus aegyptiacus, and Triaenops persicus. Accounted for 32% of all bats, Rousettus aegyptiacus was the most prevalent species in Kenya. The other common species included Eidolon helvum (27%) and Miniopterus spp. (26). Other species only accounted for a very small portion (Table 2).

<table>
<thead>
<tr>
<th>Bat species</th>
<th>No. tested</th>
<th>No. pos</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaerephon sp.</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Coleura afra</td>
<td>9</td>
<td>4</td>
<td>44.4</td>
</tr>
<tr>
<td>Eidolon helvum</td>
<td>88</td>
<td>23</td>
<td>26.1</td>
</tr>
<tr>
<td>Epomophorus spp.</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hipposideros commersoni</td>
<td>4</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Miniopterus spp.</td>
<td>87</td>
<td>49</td>
<td>56.3</td>
</tr>
<tr>
<td>Rhinolophus spp.</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rousettus aegyptiacus</td>
<td>105</td>
<td>22</td>
<td>20.9</td>
</tr>
<tr>
<td>Triaenops persicus</td>
<td>8</td>
<td>7</td>
<td>87.5</td>
</tr>
<tr>
<td>Total</td>
<td>331</td>
<td>106</td>
<td>32</td>
</tr>
</tbody>
</table>

Table 2. Bartonella in bats, Kenya

Bats collected from Guatemala represented 15 species of 10 genera (Table 3), including Artibeus jamaicensis, Artibeus lituratus, Artibeus toltecus, Carollia castanea, Carollia perspicillata, Desmodus rotundus, Glossophaga soricina, Micronycteris microtis, Myotis elegans, Myotis nigricans, Phyllostomus discolor, Platyrhinus helleri, Pteronotus davyi, Sturnira lilium, and Sturnira ludovici. Desmodus rotundus comprised 26% of all bats and was the most prevalent species. Glossophaga soricina, Carollia perspicillata, Artibeus jamaicensis, and Sturnira lilium comprised 13%, 12%, 11%, and 10%, respectively, also were frequently found. The other six species comprised a smaller portion (Table 3).
3.2 Bartonella prevalence in bats

Although composition of bat species was completely different in the Kenya and Guatemala, interestingly, the overall prevalence of bartonella infection in bats was quite similar: 32% in Kenya and 33% in Guatemala. Such high prevalence may suggest persistent infection of long-lived bats with Bartonella species, similar to their infection with some viruses (Sulkin & Allen, 1974). Nevertheless, large variations of bartonella prevalence were observed among the bat species. Bartonella species exhibit high, low, or no infectivity depending on the bat species. In Kenya, the bartonella prevalence was 88%, 56%, 44%, 26%, 25%, and 21% for Triaenops persicus bats, Miniopterus spp. bats, Coleura afra bats, Eidolon helvum bats, Hipposideros commersoni bats, and Rousettus aegyptiacus bats, respectively. In Guatemala, Phyllostomus discolor bats, Pteronotus davyi bats, and Desmodus rotundus bats were highly infected with Bartonella species, with prevalence of 89%, 70%, and 48% in each, respectively. Bartonella prevalence was relatively low in Sturnira lilium bats (8%) and Glossophaga soricina bats (13%), and no bartonellae were discovered in some bat species, such as Epomophorus spp., Rhinolophus spp., and Artibeus jamaicensis (Table 2 & Table 3).

3.3 Bartonella genetic heterogeneity and relationships with bat species

Genetic analyses of a portion of citrate synthase gene (gltA) demonstrated that the Bartonella strains obtained from bats in both Kenya and Guatemala represent a variety of distinct phylogroups, including 11 from Kenya and 13 from Guatemala. Further characterization is necessary to verify whether the Bartonella strains represent novel Bartonella species.

In Kenya, a definite host-specificity was observed for Bartonella strains in bat species. All Bartonella isolates obtained from Rousettus aegyptiacus bats are similar to each other (>96%) and clustered in a monophyletic genogroup that is distant from all other Bartonella species; similarly, Bartonella cultures obtained from Coleura afra bats, Triaenops persicus bats also clearly belonged to the specific Bartonella species group found exclusively in the particular bat species. By contrast, Bartonella cultures obtained from Eidolon helvum bats and Miniopterus bats showed great variation, clustering into three or four clades, each representing a distinct Bartonella phylogroup. Nevertheless, all strains of Bartonella species recovered from Eidolon helvum bats were typical for this species of bats only. Similarly, the gltA sequences from all strains obtained from Miniopterus spp. bats have not been found in bats of other bat genera.

Unlike the discovery in bats in Kenya, host specificity of Bartonella species was not found in bats in Guatemala. In some instances, bats of two or more species may share the same Bartonella strains. For example, one Bartonella strain recovered in Desmodus rotundus bats was also found in Carollia perspicillata bats. Similarly, same Bartonella strain was found in both Glossophaga soricina bats and Pteronotus davyi bats, or both Carollia perspicillata bats and Phyllostomus discolor bats. On the other hand, co-infection with multiple Bartonella strains in the same bat species was observed. For example, Desmodus rotundus bats and Carollia perspicillata bats each were infected with two Bartonella strains; while Pteronotus davyi bats and Phyllostomus discolor bats were infected with four Bartonella strains, respectively. The tendency of some bat species to share roosts, reach large population densities, and roost crowded together creates the potential for dynamic intraspecies and interspecies transmission of infections (Streicker et al., 2010). The observations in the Guatemala study suggested active interspecies transmission of Bartonella species likely occurs among bats in Guatemala, which may have contributed to the lack of host-specificity. Arthropod vectors that parasitize bats may also be partly associated with none host-specificity.
Bat species No. cultured No. positive Prevalence (%)

<table>
<thead>
<tr>
<th>Bat species</th>
<th>No. cultured</th>
<th>No. positive</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Artibeus jamaicensis</em></td>
<td>13</td>
<td>0</td>
<td>0</td>
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<tr>
<td><em>Artibeus lituratus</em></td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
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<td><em>Artibeus toltecus</em></td>
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<td>1</td>
<td>100</td>
</tr>
<tr>
<td><em>Carollia castanea</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Carollia perspicillata</em></td>
<td>14</td>
<td>4</td>
<td>28.6</td>
</tr>
<tr>
<td><em>Desmodus rotundus</em></td>
<td>31</td>
<td>15</td>
<td>48.4</td>
</tr>
<tr>
<td><em>Glossophaga soricina</em></td>
<td>15</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td><em>Micronycteris microtis</em></td>
<td>3</td>
<td>1</td>
<td>33.3</td>
</tr>
<tr>
<td><em>Myotis elegans</em></td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Myotis nigricans</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Phyllostomus discolor</em></td>
<td>9</td>
<td>8</td>
<td>88.9</td>
</tr>
<tr>
<td><em>Phyllorhinus helleri</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Pteronotus davyi</em></td>
<td>10</td>
<td>7</td>
<td>70</td>
</tr>
<tr>
<td><em>Sturnira lilium</em></td>
<td>12</td>
<td>1</td>
<td>8.3</td>
</tr>
<tr>
<td><em>Sturnira ludovici</em></td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>118</td>
<td>39</td>
<td>33.1</td>
</tr>
</tbody>
</table>

Table 3. Bartonella in bats, Guatemala

3.4 Epidemiology significance

Bartonellae were virtually unrecognized as pathogens of humans until 1990s. Identifications of bartonellae as agents of cat-scratch disease, bacillary angiomatosis, urban trench fever, and recent outbreaks of Carrión's disease have left no doubt about the emerging medical importance of these bacteria. Within the last two decades, new bacteria of the genus of *Bartonella* were isolated from large number of several mammalian reservoirs, including rodents, cats, dogs, and rabbits, and recognized as emerging zoonotic agents. At least 13 *Bartonella* species or subspecies have been recognized as emerging human pathogens or zoonotic agents, causing a wide range of syndromes, from a self-limiting to life-threatening endocarditis, myocarditis, and meningoencephalitis. All of these emphasize the concept that inadvertent transmission of known or currently uncharacterized *Bartonella* spp. from both wild animals and domestic animals occurs in nature.

Although evidence of overt disease in bats caused by *Bartonella* species has not been demonstrated to date, high incidence of bartonella infection in bats from the studies carried out in Guatemala, Kenya, and other regions suggested that bats may be natural reservoirs in maintaining circulation of *Bartonella* species in nature. Bats have very long life spans compared to other mammals of similar body size, such as rodents. This may make them serve as reservoirs contributing to the maintenance and transmission of *Bartonella* to other animals and/or humans. Some bat species have been known to directly transmit infections to humans. For example, the common vampire bat (*Desmodus rotundus*) has been long recognized to transmit rabies virus to humans by biting throughout Latin America (Schneider et al., 2009). These bats typically feed on the blood of mammals, including domestic animals, such as cattle, horses, pigs, dogs, but also feed on the blood of humans (Turner & Bateson, 1975). Predation of vampire bats on humans is a major problem in Latin America (Schneider et al., 2009). If *Bartonella* species can be transmitted to humans through the bite of bats, the need for further studies with vampire bats is imperative. Findings of bartonella in bats highlight the need to study whether the bat-originated *Bartonella* species...
are responsible for the etiology of local undiagnosed illnesses in humans and domestic animals in tropics. In addition to the large number of documented reservoir hosts, an increasing number of arthropod vectors, including biting flies, fleas, keds, lice, sandflies, and ticks have been confirmed or suspected to be associated with the transmission of Bartonella spp. among animal populations (Billeter et al., 2008). Bartonella species-specific DNA has been detected in ectoparasites collected from bats (Loftis et al., 2005; Reeves et al., 2005 & 2007). Presumably, if Bartonella species are transmitted through a bat ectoparasite vector, some, if not all, bat-associated Bartonella species could be transmitted to humans because bats are frequent hosts to a wide variety of ectoparasites, including bat flies, fleas, soft ticks, and mites. Very recently, two novel Bartonella species, B. tamiiae, isolated from febrile Thai patients (Kosoy et al., in press), and B. rochalimae, isolated from an American patient who traveled in Peru and developed fever and splenomegaly after return (Eremeeva et al., 2007). However, the reservoir remains unknown as do the mode of transmission, pathogenesis, and many other characteristics of these organisms. There is the need to identify the animal reservoirs of these novel Bartonella species and to understand their disease ecology. These studies of Bartonella species in bats have enlarged the scope of this zoonotic potential as we search for the reservoirs that harbor novel and known Bartonella species.

4. References


Sander, A., Zagrosek, A., Bredt, W., Schiltz, E., Piemont, Y., Lanz, C., et al. (2000). Characterization of *Bartonella clarridgeiae* flagellin (FlaA) and detection of


Tropical Medicine has emerged and remained as an important discipline for the study of diseases endemic in the tropic, particularly those of infectious etiology. Emergence and reemergence of many tropical pathologies have recently aroused the interest of many fields of the study of tropical medicine, even including new infectious agents. Then evidence-based information in the field and regular updates are necessary. Current Topics in Tropical Medicine presents an updated information on multiple diseases and conditions of interest in the field. It includes pathologies caused by bacteria, viruses and parasites, protozoans and helminths, as well as tropical non-infectious conditions. Many of them are considering not only epidemiological aspects, but also diagnostic, therapeutical, preventive, social, genetic, bioinformatic and molecular ones. With participation of authors from various countries, many from proper endemic areas, this book has a wide geographical perspective. Finally, all of these characteristics, make an excellent update on many aspects of tropical medicine in the world.

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