

# A review of the genus *Rickettsia* in Central America

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**Abstract:** In this paper, we present a historical review of rickettsiosis in Central America and also the most recent findings of *Rickettsia* in ectoparasites. All countries of Central America have records of rickettsiosis. Regarding the typhus group rickettsioses, there is clinical or serological evidence of *Rickettsia prowazekii* in Guatemala, *Rickettsia typhi* in Panama, Guatemala, and Costa Rica and unidentified species of the typhus group in El Salvador. Concerning spotted fever group rickettsiosis, there is serological evidence of infection by *Rickettsia akari* in Costa Rica and confirmed cases involving *Rickettsia rickettsii* in Panama and Costa Rica. There are also reports of spotted fever group rickettsiosis in acute patients from Guatemala, Honduras, and Nicaragua. Serological studies in Central America show reactivity of *Rickettsia amblyommatis*, *Rickettsia bellii*, *Rickettsia felis*, *Rickettsia rhipicephali*, and *R. rickettsii* in domestic and wild mammals. Eight species of *Rickettsia* have been detected in ectoparasites from Central America: *R. africae* (or very similar), *R. amblyommatis*, *R. asembonensis*, *R. bellii*, *R. felis*, *R. parkeri*, *R. rhipicephali*, and *R. rickettsii*, in addition to undescribed strains such as Atlantic Rainforest, Colombianensi, IbR/CRC, Barva, Aragoi, and *Candidatus* “*Rickettsia nicoyana*,” the latter being the only one associated with Argasidae (*Ornithodoros knoxjonesi*). *R. amblyommatis* is the most common species in Central America, seeing as it has been reported in 10 species of ticks and one of fleas in five of the seven countries of the region. In this study, we demonstrate that the genus *Rickettsia* is widely distributed in Central America and that rickettsiosis could be an underestimated problem in the absence of greater diagnostic efforts in undetermined febrile cases.

**Keywords:** rickettsiosis, *Rickettsia*, Rocky Mountain spotted fever, vector, Central America

## Introduction

*Rickettsia* is a genus composed of 27 species of obligate intracellular bacteria, and ~17 of them are considered pathogens of animals and humans.<sup>1</sup> Pathogenic species are divided into the typhus group (TG), transmitted by insects, and the spotted fever group (SFG), which is mainly transmitted by mites and hard ticks.<sup>1,2</sup> Regarding the differences between the two groups, TG rickettsiae lack the capacity to polymerize actin and produce infections only in the cytoplasm of host cells, whereas SFG rickettsiae can polymerize actin and infect nuclei; in addition, there are differences in optimal growth temperatures (35°C for TG and 32°C for SFG), G-C content (29% in TG and 32%–33% in SFG), and outer membrane proteins (type B in TG and types A and B in SFG).<sup>3</sup>

The TG includes two pathogens: *Rickettsia prowazekii* causes epidemic typhus and is transmitted mainly by contact with infected feces of the human body louse; *Rickettsia typhi* is responsible for endemic or murine typhus, and its transmission is

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associated with fleas.<sup>4,5</sup> Both the rickettsiae seem to be cosmopolitan because of the wide geographical distribution of their vectors.<sup>1</sup> General symptoms of infection with TG rickettsiae are non-specific: headache, fever (higher in epidemic typhus), muscle and joint pain; patients also present nausea and vomiting, cough, rash (moderate in murine typhus, but severe in epidemic typhus), chills, decrease in blood pressure, stupor, photosensitivity, delirium, and death in untreated cases of epidemic typhus.<sup>6</sup> In fact, mortality in untreated cases of epidemic typhus is usually high (10%–60%), but decreases significantly if the adequate antibiotic treatment is administered within the first days of infection.<sup>6</sup> In addition to these species, other pathogenic bacteria are recognized as etiological agents of “typhus,” although they belong to the SFG (eg, Queensland ticks typhus, *Rickettsia australis*) or to another genus (eg, scrub typhus by *Orientia tsutsugamushi*).

More than 25 species belong to the SFG, and they present geographical distributions in accordance with the range of their principal tick vectors, with the exception of the cosmopolitan *Rickettsia felis*, associated mainly with fleas.<sup>7</sup> Of these, currently 15 pathogenic species are reported worldwide, in addition to several other species that are considered potential human pathogens, but for which clinical evidence has not been conclusive.<sup>1</sup> The severity of SFG rickettsial infections vary greatly between species, and similar to TG rickettsial infections, there are usually no specific symptoms that can be used to clearly differentiate SFG rickettsioses from several other fevers caused by viruses (eg, dengue) or bacteria (eg, *Leptospira* sp.). In general, and depending on the *Rickettsia* species involved, patients may present mild or high fever, an eschar at the site of bacterial entry, inflammation of regional or satellite lymph nodes, and exanthema or erythematous maculopapular rash; also, damage to different organs may be involved due to vasculitis and, in extremes cases, death may occur.<sup>8</sup> *Rickettsia rickettsii* is the most lethal agent within the genus and the most important tick-borne disease in America, as it presents high fatality rates in untreated cases.<sup>9,10</sup> Infection by *R. rickettsii* causes the disease known as Rocky Mountain spotted fever (RMSF) in the USA, but it also has regional names like “fiebre maculosa Brasileira” (Brazil) or “fiebre de Tobia” (Colombia).<sup>10</sup>

In the last three decades, rickettsial diseases have awakened the interest of specialists in public health due to the increase of reported cases and the possibility that they will continue rising due to anthropogenic modifications and global climate change, in addition to the threat that these bacteria represent as a potential bioterrorism weapon.<sup>4</sup> Therefore, efforts to improve the diagnosis of rickettsioses and the

methods for detection of rickettsiae in arthropods have generated a large number of scientific literature around the world.<sup>11</sup>

In Central America, although rickettsial diseases are known, the low number of cases per year and the higher prevalence of other infectious diseases have prevented greater attention from professionals and institutions working in human health. In the present study, we present a historical review and the most recent findings pertaining species of *Rickettsia* and rickettsioses in Central America. For this, we searched for scientific publications in English and Spanish in databases and search engines such as PubMed, Scielo, LILACS, and Google Scholar, and by using keywords (*Rickettsia*, rickettsiosis, country names). An initial selection was made when the title and abstract suggested reports of rickettsiae or rickettsiosis in any country of Central America, and complete documents were read when in doubt about the content. Local libraries and retired rickettsiologists in Panama and Costa Rica were contacted to locate and obtain publications that were not readily available. All resulting articles were read in detail, as well as any additional publications that were cited in them but had not been identified previously.

## Rickettsioses in Central America TG rickettsioses

Both epidemic and endemic (murine) typhus have been documented in Central America (Table 1). Epidemic typhus is one of the most ancient human diseases known, and outbreaks have occurred along the history of humanity, with numerous deaths.<sup>4</sup> Although epidemics of this disease decreased

**Table 1** Rickettsial infections in humans reported in Central America

Country	<i>Rickettsia</i> spp.	Humans		References
		Clinical	No clinical	
Belize	SFGR	No	Yes	43
Costa Rica	<i>Rickettsia akari</i>	No	Yes	18
	<i>Rickettsia rickettsii</i>	Yes	No	18,34–37,39
El Salvador	SFGR	Yes	Yes	36,38
	TGR	No	Yes	18,19
Guatemala	SFGR	Yes	Yes	18,40
	<i>Rickettsia typhi</i>	No	Yes	18
	<i>Rickettsia prowazekii</i>	Yes	Yes	13
Honduras	SFGR	Yes	Yes	18,41
	TGR	No	Yes	18
Nicaragua	SFGR	Yes	Yes	18,42
Panamá	SFGR	Yes	Yes	20
	<i>R. rickettsii</i>	Yes	No	20,24,26–32
	<i>R. typhi</i>	Yes	Yes	17,18,20

**Abbreviations:** SFGR, spotted fever group rickettsiosis; TGR, typhus group rickettsiosis.

considerably after the control of lice populations and the use of antibiotic treatment, cases still occur in poor villages in cold regions of North America, Eastern Europe, Asia, and mountainous towns in Central and Eastern Africa, as well as South and Central America.<sup>6</sup> According to Hume, epidemic typhus may have entered Central America during the European conquest.<sup>12</sup> Since then, this disease has remained as isolated outbreaks in mountainous areas of Central America, in particular in villages and town of Guatemala with elevations between 2,500 and 3,500 m above sea level.<sup>13</sup> A high mortality was reported in Guatemala during outbreaks in 1932–1934, with ~180 fatal cases per year.<sup>13</sup>

Regarding murine typhus, it is present worldwide but predominantly in areas of tropical and subtropical regions that have poor sanitation, where humans inhabit close to rodents.<sup>14,15</sup> Currently, murine typhus is present in the Mediterranean basin, some countries of Africa, Asia, and America.<sup>16</sup> In Central America, the first mention of murine typhus was in the descriptions of clinical symptoms of cases diagnosed in Panama.<sup>17</sup> In this country, more than 50 cases were confirmed during 1932–1947, with the last outbreak (13 patients) in the City of Panama that affected mostly people working or visiting a storeroom where dead rats had been reported.<sup>17</sup>

A serological survey in Central America showed antibody titers against TG *Rickettsia* in humans in Guatemala, Honduras, El Salvador, Nicaragua, and Panama, with a high positivity to endemic typhus in the highlands of Guatemala.<sup>18</sup> Later, in a global surveillance study developed by WHO in 1993, eight volunteers (n=40) from El Salvador had a positive reaction to TG rickettsiae, using an end titer of 64 as cutoff for reactivity in immunofluorescence assays (IFAs).<sup>19</sup> More recently, IgG antibodies against TG rickettsiae have been found in humans from a rural town of Panama.<sup>20</sup> To the authors' knowledge, no more recent references of TG rickettsioses in Central America are available in the scientific literature.

## SFG rickettsioses

Currently, RMSF or other SFG rickettsioses have been confirmed in the seven countries of Central America (Table 1).

Spotted fever rickettsiosis, and specifically RMSF, was originally described in the early 20th century as “piroplasmosis hominis” from cases in Bitterroot Valley Montana (USA); *Dermacentor* ticks were associated with transmission.<sup>21</sup> Later, cases were diagnosed in México (1918), Brazil (1929), and Colombia (1938).<sup>10,22,23</sup> In Central America, the first records of RMSF were registered in Panama in the early

1950s.<sup>24</sup> During the investigation of these cases, *R. rickettsii* was isolated from the tick *Amblyomma mixtum* (cited as *Amblyomma cajennense*), and *Rhipicephalus sanguineus* s.l. was implicated as a potential vector in an urban case.<sup>25,26</sup> After these cases, no more spotted fevers were reported in Panama for several decades; however, a serosurvey showed a relatively high prevalence (5.4%–15.2%) of antibodies to SFG rickettsiae in 1,400 volunteers, but without determining the possible *Rickettsia* species.<sup>27</sup>

Indeed, almost 60 years passed until new cases of RMSF were confirmed in Panama: one case in 2004, three in 2007, one in 2008, one in 2012, one in 2015, and three in 2017 (only two of them were reported in the scientific literature).<sup>28–32</sup> Nine of the patients died, with a 90% fatality. Recently, *R. rickettsii* was detected in intradomiciliary *R. sanguineus* s.l. as part of an investigation of an urban case in the City of Panama. This may represent a new scenario as to the ecology of RMSF transmission, where dogs and their ticks may play an important role in urban areas.<sup>32</sup> In addition to these confirmed cases, a serological study revealed a relatively high seroprevalence of SFG infections (29%–31%) in people from rural areas.<sup>20,33</sup>

In Costa Rica, SFG infections were reported for the first time in 1952 from serological studies.<sup>34,35</sup> Regardless, no febrile cases were documented until 1974, when patients presented symptoms compatible with SFG rickettsiosis.<sup>36</sup> In 1975, the first confirmations of RMSF cases in Costa Rica were given, including a fatal case.<sup>37</sup> Additional serological studies in humans and animals followed.<sup>38</sup> In contrast to Panama, several cases of RMSF have been confirmed in Costa Rica since these reports in the late 1970s, and children seemed to be the most affected.<sup>34,35,39</sup>

A serological survey carried out in the late 1960s showed antibodies to SFG *Rickettsia* in sera from Costa Rica (13 positives of 507 samples), Honduras (3/348), Nicaragua (1/312), and Panama (4/336).<sup>18</sup> In that study, antibodies against *Rickettsia akari* were detected in Costa Rica. With the exception of this report, no other information is available about *R. akari* in the region.

At the beginning of the 21st century and in accordance with the re-emergence of fatal cases of RMSF in Panama, new evidence of rickettsial diseases in other countries of Central America was confirmed. In 2007, an investigation of febrile illness in a rural area of Guatemala caused at least 17 cases of SFG rickettsiosis, including two fatalities.<sup>40</sup> During the epidemiological investigation, DNA closely related to *Rickettsia africae* and *Rickettsia sibirica* was detected in *A. cajennense* s.l. Subsequently, in 2009, a case of SFG

rickettsiosis was reported from a US traveler who returned from Honduras.<sup>41</sup> In Nicaragua, the first evidence of SFG rickettsiosis was reported in 2016 from patients in the acute phase of infection, which also included diagnosis of Q fever.<sup>42</sup> In this study, the sample included 825 patients and about 1% was considered positive for SFG rickettsiosis, but specifically RMSF was not confirmed. In Belize, there is only one report that supports SFG rickettsial infection in humans; the study found a seroprevalence of 54% (IFA using *R. rickettsii* antigen) in a group of healthy pregnant women.<sup>43</sup>

It is important to note that *R. rickettsii* has been isolated and molecularly identified from symptomatic human cases only in Panama and Costa Rica, but not in the cases from Guatemala, Honduras, and Nicaragua (Table 1). In addition, only Panama and Costa Rica have serological studies in domestic and wild mammals (Table 2).

## Rickettsia species in ectoparasites in Central America

For many decades, *R. rickettsii*, *R. akari*, *R. typhi* (= *Rickettsia mooseri*), and *R. prowazekii* were the only known species of *Rickettsia* in the region, and they were mainly characterized from patients with acute phase infections or isolated from ticks in eco-epidemiological studies.<sup>23</sup> After several decades, and with the use of molecular tools, the detection of rickettsiae was extended to ecological studies, especially in more species of ticks. In recent years, research in the region has involved many species of ticks and fleas, which has resulted in the detection of pathogenic rickettsiae including

**Table 2** Serological evidence of rickettsial infection in domestic and wild mammals of Central America

Country	<i>Rickettsia</i> spp.	Mammals	References
Costa Rica	<i>Rickettsia amblyommatis</i> <sup>a</sup>	Dog	54
	<i>Rickettsia felis</i>	Dog	54
		Cat	53
	<i>Rickettsia rhipicephali</i>	Dog	54
	<i>Rickettsia rickettsii</i>	Dog	54
	SFGR	Dog	38,54
Panamá	SFGR	Wild rabbit ( <i>Sylvilagus</i> sp.)	38
		Coyote <sup>b</sup>	55
	<i>R. amblyommatis</i> <sup>a</sup>	<i>Didelphis marsupialis</i>	55
		Dog	52
	<i>Rickettsia bellii</i>	Horse	52
		<i>D. marsupialis</i>	55
		Horse	52
<i>R. rickettsii</i>	Horse	52	

**Notes:** <sup>a</sup>Cited as *Rickettsia amblyommi* or *Candidatus "Rickettsia amblyommi"*. <sup>b</sup>This coyote showed symptoms similar to those described for *R. rickettsii* infections in dogs.

**Abbreviation:** SFGR, spotted fever group rickettsiosis.

*R. rickettsii*, *R. felis*, *Rickettsia parkeri*, and *R. africae* (or very similar), as well as strains of undescribed or *Candidatus* species (Table 3).

*R. rickettsii* has been detected in *R. sanguineus* s.l. and *Dermacentor nitens* from Panama,<sup>32,44</sup> *A. mixtum* from Panama and Costa Rica,<sup>24,31,45</sup> and *Amblyomma varium* and *Haemaphysalis leporispalustris* from Costa Rica.<sup>45,46</sup> Contrary to *A. mixtum* and *R. sanguineus* s.l., the findings of *R. rickettsii* in *D. nitens*, *H. leporispalustris*, and *A. varium* were not associated with febrile cases, but may have implications in public health because these are ticks that present different behavior. For example, *D. nitens* is a one-host tick that mainly parasitizes horses in paddocks and stubble, and parasitism in humans is rare.<sup>47</sup> *D. nitens* commonly shares environments and hosts (equines) with *A. mixtum*, although this last species is considered an eclectic parasite, and the reports parasitizing humans are frequent.<sup>47</sup> In contrast, adults of *A. varium* parasite almost exclusively sloths and immature have been found parasitizing birds, but very few studies mention humans as hosts.<sup>45,48,49</sup> Similarly, *H. leporispalustris* is an almost exclusive parasite of wild rabbits (*Sylvilagus*), and parasitism of humans is rare.<sup>47</sup> Thus, it is possible that the relevance of these ticks in RMSF transmission is associated with enzootic cycles.

*A. mixtum* and *R. sanguineus* s.l. have been previously implicated as vectors of *R. rickettsii*; in fact, several species of the *A. cajennense* and *R. sanguineus* species complexes are among its main vectors in many countries.<sup>50</sup> Both are common in or around anthropogenic environments, but differ in preferences: *A. mixtum* is an eclectic parasite that inhabits paddocks, stubble, and riparian vegetation, while *R. sanguineus* s.l. feeds mainly from dogs and is a nidicolous species that may thrive inside houses, including highly urbanized areas.<sup>31,51</sup> Therefore, their presence could be considered as a first caveat in the transmission of RMSF.<sup>31</sup> Even so, many aspects of the ecology of RMSF transmission remain unknown in Central America, especially the role of domestic and wild vertebrates as reservoirs, because few studies in the region have focused on them. Research has resulted in serologic evidence of SFG exposure in dogs and horses from Panama,<sup>51</sup> domestic dogs and cats from Costa Rica,<sup>53,54</sup> and wild opossums (*Didelphis marsupialis*) and coyotes from Panama.<sup>55</sup> These results are a first clue of rickettsial infection in vertebrates that deserves further investigation.

Another closely related pathogenic species, *R. parkeri*, was recently reported in Central America, infesting *Amblyomma maculatum* and *Amblyomma ovale* (specifically the strain Atlantic rainforest) from Belize.<sup>56,57</sup> Although

**Table 3** Checklist of *Rickettsia* species detected in arthropods from Central America

Country	<i>Rickettsia</i> spp.	Arthropod species	References <sup>a</sup>		
Belize	<i>Rickettsia amblyommatis</i> <sup>b</sup>	<i>Amblyomma pacae</i>	56		
		<i>Amblyomma cajennense</i> s.l. <sup>c</sup>	57		
		<i>Amblyomma</i> nr. <i>maculatum</i>	57		
	<i>Rickettsia parkeri</i>	<i>A. maculatum</i>	57		
	<i>Rickettsia</i> st. Atlantic Rainforest	<i>Amblyomma ovale</i>	56		
	<i>Rickettsia</i> sp.	<i>Ixodes affinis</i>	56		
		<i>Rhipicephalus sanguineus</i> s.l.	56		
		<i>A. ovale</i>	56		
		Costa Rica	<i>R. amblyommatis</i> <sup>b</sup>	<i>Amblyomma longirostre</i>	96
				<i>Amblyomma mixtum</i> <sup>d</sup>	73
<i>A. ovale</i>				45	
			<i>Dermacentor nitens</i>	45	
	<i>R. sanguineus</i> s.l.		45		
	<i>Amblyomma geayi</i>		85		
	<i>Amblyomma sabanerae</i>		96		
	<i>Ctenocephalides felis</i>		73		
	<i>A. mixtum</i>		45		
	<i>Amblyomma varium</i>		45		
	<i>Haemaphysalis leporispalustris</i>	46			
	<i>Rickettsia</i> sp. st. IbR/CRC	<i>Ixodes boliviensis</i>	95		
	<i>Rickettsia</i> sp.	<i>Ixodes</i> nr. <i>minor</i>	96		
	<i>Rickettsia asebonensis</i> <sup>e</sup>	<i>C. felis</i>	74		
		<i>Pulex simulans</i>	45		
		<i>A. ovale</i>	45		
		<i>Rhipicephalus microplus</i>	45		
	<i>Rickettsia rhipicephali</i>	<i>Dermacentor latus</i>	85		
	Ca. “ <i>Rickettsia nicoyana</i> ”	<i>Ornithodoros knoxjonesi</i>	92		
	<i>Rickettsia</i> sp. st. Colombianensi	<i>Amblyomma dissimile</i>	85		
El Salvador	<i>R. bellii</i>	<i>A. sabanerae</i>	86		
Guatemala	<i>R. felis</i>	<i>C. felis</i>	74		
		<i>Rickettsia</i> sp.	<i>A. cajennense</i> s.l. <sup>c</sup>	40	
Honduras	<i>R. amblyommatis</i> <sup>b</sup>	<i>A. longirostre</i>	93		
		<i>A. mixtum</i>	93		
		<i>A. dissimile</i>	93		
Nicaragua	<i>Rickettsia</i> st. Colombianensi	<i>Amblyomma sculptum</i> <sup>f</sup>	98		
		<i>A. ovale</i>	98		
	<i>R. amblyommatis</i> <sup>b</sup>	<i>Amblyomma triste</i> <sup>g</sup>	98		
	<i>Rickettsia africae</i>	<i>A. maculatum</i>	97		
	<i>Rickettsia</i> st. Aragoi	<i>Dermacentor dissimilis</i>	97		
	<i>Rickettsia</i> spp.	<i>R. sanguineus</i> s.l.	97		
Panamá	<i>R. amblyommatis</i> <sup>b</sup>	<i>A. mixtum</i>	44		
		<i>A. ovale</i>	44		
		<i>D. nitens</i>	44		
		<i>Haemaphysalis juxtakochi</i>	99		
		<i>R. sanguineus</i> s.l.	44		
		<i>C. felis</i>	52		
		<i>A. sabanerae</i>	Unpublished		
	<i>R. bellii</i>	<i>A. sabanerae</i>	Unpublished		
	<i>R. felis</i>	<i>C. felis</i>	52		
		<i>A. mixtum</i>	52		
		<b>A. mixtum</b> <sup>d</sup>	<b>25</b>		
		<b>R. sanguineus</b> s.l.	<b>32</b>		
	<i>D. nitens</i>	44			

**Notes:** Ticks associated with human cases of RMSF are represented in bold format. <sup>a</sup>Only the first mention in the scientific literature is presented. <sup>b</sup>Cited as *Rickettsia amblyommii* or *Candidatus* “*Rickettsia amblyommii*.” <sup>c</sup>*A. cajennense* s.l. probably corresponds to *A. mixtum*. <sup>d</sup>Cited as *A. cajennense*. <sup>e</sup>Cited also as *R. felis* genotype RF2125. <sup>f</sup>*A. sculptum* probably corresponds to *A. mixtum*. <sup>g</sup>*A. triste* probably corresponds to *A. maculatum*.

**Abbreviation:** RMSF, Rocky Mountain spotted fever.

*A. maculatum* and *A. ovale* frequently parasitize humans,<sup>47,58</sup> until now there are no reports of human infection by these species in the region. Although *R. parkeri* was isolated in 1939, its involvement as a pathogen for humans was not confirmed until 2004.<sup>59,60</sup> Clinical evidence shows that *R. parkeri* infections are usually not lethal and have been confirmed in several states of the USA, Argentina, and Uruguay.<sup>61–63</sup> Vectors of *R. parkeri* include *A. maculatum* in the USA, as well as *Amblyomma triste* and *Amblyomma tigrinum* in South America.<sup>60,63</sup>

The strain Atlantic rainforest was first detected in Brazil as *Rickettsia* sp., but recent studies suggest that it belongs to the species *R. parkeri*.<sup>64–66</sup> This strain has been associated with human cases of spotted fever in Brazil, and *A. ovale* seems to be the main vector.<sup>65</sup> In addition to Brazil and Belize, *R. parkeri* strain Atlantic rainforest has been detected in Argentina (in *Amblyomma dubitatum*) and Colombia (in *A. ovale*).<sup>67,68</sup>

Of the species recognized as human pathogens in Central America, *R. felis* is the only one that has been detected in fleas, although no human cases have been confirmed in the region. This *Rickettsia* was first observed in *Ctenocephalides felis* in 1990; it was officially described in 1996 and the descriptions were emended in 2002.<sup>69,70</sup> It is distributed worldwide, as is its main invertebrate host, *C. felis*. Disease in humans, known as flea-borne spotted fever, was first reported in the USA, Mexico, and Brazil, although it has now been reported from countries around the world; when they occur, symptoms are usually mild and unspecific, but severe cases have been described.<sup>71,72</sup> The first findings of *R. felis* in Central America were documented in Panama and Costa Rica in 2011, from *C. felis*.<sup>52,73</sup> The report from Costa Rica recorded the first isolation of this *Rickettsia* in a cell line (C6/36) in the region. *R. felis* has also been detected in *C. felis* in Guatemala and in dogs from Nicaragua, which suggests that it is also present in fleas in that country.<sup>74,75</sup> The absence of reports from the other countries of Central America is probably due to a lack of investigation of rickettsiae in fleas.

It is possible that *Rickettsia amblyommatis* (referred to as *Rickettsia amblyommii* and “*Candidatus Rickettsia amblyommii*”) is the most common *Rickettsia* detected in Central America. It has been reported in 10 species of ticks and one of fleas in five of the seven countries of Central America (Tables 2 and 3). This *Rickettsia* was isolated from *Amblyomma americanum* from the USA and has since been reported along the continent.<sup>23,76</sup> The effects of *R. amblyommatis* infection on vertebrates is not clearly defined. Some authors have pointed out that repeated exposure can induce

very high serological titers in dogs.<sup>77</sup> In Central America, there is serological evidence of exposure in dogs, horses, and opossums (*D. marsupialis*) from Panama and dogs from Costa Rica.<sup>52,54,55</sup> In this country, the strain 9-CC-3-1 of *R. amblyommatis* was able to generate pathology and an immune response in guinea pigs, and it was protective against a subsequent infection with a lethal *R. rickettsii* strain. Therefore, the presence of *R. amblyommatis* in the region may modulate the epidemiology and severity of RMSF in areas where both the species circulate.<sup>78</sup> In humans, despite its frequent presence in several species of ticks, there are no confirmed cases of human rickettsiosis caused by *R. amblyommatis*, although some authors suggest that humans develop an immune response and that it may cause clinical manifestations.<sup>79–82</sup>

*Rickettsia rhipicephali* is a species that has been reported only once in ticks from Central America. It was first isolated and described in 1975 from *R. sanguineus* in the USA, but it is known to be present also in South America.<sup>83,84</sup> This species was detected by PCR in *Dermacentor latus* from Costa Rica, although currently very few information is available about this finding.<sup>85</sup> Moreover, there is also serologic evidence of possible exposure of dogs to this or a very similar *Rickettsia* sp. from that same country, which supports its possible presence in the region.<sup>54</sup> The pathogenic potential of *R. rhipicephali* in humans is unknown, although the disease has been confirmed in meadow voles after experimental infections.<sup>83</sup>

In Central America, *Rickettsia bellii* has been detected in *Amblyomma sabanerae* from El Salvador, Costa Rica, and Panama (S Bermúdez, unpublished data).<sup>85,86</sup> This tick is a parasite of reptiles, in particular turtles and tortoises.<sup>47,51</sup> This *Rickettsia* belongs to ancestral group different from the TG and SFG.<sup>3</sup> Although no studies demonstrate its pathogenicity in humans, there is experimental evidence showing rickettsial ability to elicit an immune responses in capybaras.<sup>87</sup> In Central America, there is serologic evidence of *R. bellii* exposure in horses from Panama.<sup>52</sup> Thus, the role of *R. bellii* as a potential human pathogen deserves further investigation.

*Rickettsia asemonensis*, which is closely related to *R. felis*, is also present in Central America. This is a recently described species, which was isolated from *C. felis* from Kenya,<sup>88</sup> although it seems to be the same *Rickettsia* sp. genotype RF2125 that had been reported much earlier in the same flea species in the Thailand–Myanmar border.<sup>89–91</sup> *R. asemonensis* was first documented in *C. felis* from the Caribbean slope of Costa Rica as the genotype RF2125.<sup>74</sup> It was later reported from *C. felis* in the metropolitan area of that same country (Cartago province), as well as from other species of ectoparasites including *Pulex simulans*, *Rhipicephalus*

*microplus*, and *A. ovale*.<sup>45,54</sup> It is unknown if this species is able to infect humans or generates disease.

In addition to the described species of rickettsiae, several rickettsiae that have not been formally described have been reported in Central America. “*Candidatus R. nicoyana*” was first isolated from *Ornithodoros knoxjonesi* ticks collected from bats in Costa Rica.<sup>92</sup> Two isolates of this *Rickettsia* were obtained in Vero E6 cell lines, and a partial molecular characterization placed it in the SFG, close to “*Candidatus Rickettsia wissemanni*” and *Rickettsia peacockii*. In addition, *Rickettsia* sp. strain Colombiensi has been detected in *Amblyomma dissimile* from both Honduras and Costa Rica.<sup>85,93</sup> This strain was first reported in *A. dissimile* and *R. sanguineus* from Colombia, and it groups phylogenetically with *Rickettsia tamurae* and *R. monacensis* within the SFG.<sup>94</sup> In Guatemala, a *Rickettsia* sp. genetically similar to *R. africae* and *Rickettsia sibirica* was detected in *A. cajennense* s.l. (probably *A. mixtum*).<sup>40</sup>

Recently, *Rickettsia* spp. were reported in *Dermacentor dissimilis*, *A. maculatum* and *R. sanguineus* s.l. from Nicaragua, as part of a microbiome study.<sup>97</sup> These data require further investigation in order to identify the species present and determine whether they represent a health threat for humans or animals. In addition, another study in Nicaragua reported *R. africae* in *A. ovale* and a *Rickettsia* sp. (matching strain Aragoi) in an *A. triste*.<sup>98</sup> Considering that rickettsiae related to *R. africae* have been detected in ticks from both Guatemala and Nicaragua,<sup>40,98</sup> further studies will be needed to determine their taxonomic status and related ecology.

Lastly, several *Rickettsia* strains have been detected in the species of *Ixodes* from Central America, including *I. boliviensis* (*Rickettsia* sp. strain IbR/CRC) and *I. minor* (*Rickettsia* sp. strain Barva) from Costa Rica, and *Ixodes affinis* from Belize.<sup>56,95,96</sup> These rickettsiae seem to be closely related to each other and group closely related to *R. monacensis*, as well as endosymbionts of *Ixodes* from North America. For all of these “unofficial” species, the potential pathogenicity for humans is yet to be determined.

## Conclusion

In Central America, the development of research related to the ecology of ectoparasites and their role as vectors of *Rickettsia* has generated a considerable amount of information in the last 10 years, both in anthropogenic environments and in wild areas.<sup>99</sup> However, there is still a need to improve the awareness and diagnosis of cases, as well as to expand on eco-epidemiological studies especially in countries where information is still lacking. The data available from ticks

and fleas suggest that these bacteria are widely distributed in the region; thus, rickettsioses could be an underestimated problem in the absence of greater diagnostic efforts in undetermined febrile cases.

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## Disclosure

The authors report no conflicts of interest in this work.

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