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Update on Tick-Borne Rickettsioses around the World: a Geographic Approach

Philippe Parola,[a] Christopher D. Paddock,[b] Cristina Socolovschi,[a] Marcelo B. Labruna,[c] Oleg Mediannikov,[a] Tahar Kernif,[d] Mohammad Yazid Abdad,[e]* John Stenos,[e] Idir Bitam,[f] Pierre-Edouard Fournier,[a] Didier Raoult[a]

Aix Marseille Université, Unité de Recherche en Maladies Infectieuses et Tropicales Emergentes (URMITE), UM63, CNRS 7278, IRD 198, Inserm 1095, WHO Collaborative Center for Rickettsioses and Other Arthropod-Borne Bacterial Diseases, Faculté de Médecine, Marseille, France[a]; Centers for Disease Control and Prevention, Atlanta, Georgia, USA[b]; Departamento de Medicina Veterinária Preventiva e Saúde Animal, Faculdade de Medicina Veterinária e Zootecnia Universidade de São Paulo, Cidade Universitária, São Paulo, SP, Brazil[c]; Service d'Ecologie des Systèmes Vectoriels, Institut Pasteur d'Algérie, Algiers, Algeria[d]; Division of Veterinary and Biomedical Science, Murdoch University, Australian Rickettsial Reference Laboratory, Barwon Health, Geelong, Victoria, Australia[e]; University of Boumerdes, Boumerdes, Algeria[f]

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Address correspondence to Philippe Parola, philippe.parola@univ-amu.fr.
* Present address: Mohammad Yazid Abdad, Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea.

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SUMMARY

Tick-borne rickettsioses are caused by obligate intracellular bacteria belonging to the spotted fever group of the genus *Rickettsia*. These zoonoses are among the oldest known vector-borne diseases. However, in the past 25 years, the scope and importance of the recognized tick-associated rickettsial pathogens have increased dramatically, making this complex of diseases an ideal paradigm for the understanding of emerging and reemerging in-

fections. Several species of tick-borne rickettsiae that were considered nonpathogenic for decades are now associated with human infections, and novel *Rickettsia* species of undetermined pathogenicity continue to be detected in or isolated from ticks around the world. This remarkable expansion of information has been driven largely by the use of molecular techniques that have facilitated the identification of novel and previously recognized rickettsiae in ticks. New approaches, such as swabbing of eschars to obtain material to be tested by PCR, have emerged in recent years and have played a role in describing emerging tick-borne rickettsioses. Here, we present the current knowledge on tick-borne rickettsiae and rickettsioses using a geographic approach toward the epidemiology of these diseases.

INTRODUCTION

Members of the genus *Rickettsia* (family *Rickettsiaceae*; order *Rickettsiales*) may be classified into spotted fever group (SFG) rickettsiae, typhus group rickettsiae, the *Rickettsia bellii* group, and the *Rickettsia canadensis* group (1). Tick-borne rickettsioses are caused by obligate intracellular bacteria belonging to the SFG of the genus *Rickettsia* (2). These zoonoses are among the oldest-known vector-borne diseases (2). However, the scope and importance of the recognized tick-associated rickettsial pathogens have increased dramatically in the past 25 years, making this complex of diseases an ideal paradigm to help understand emerging and reemerging infections. The last major review of tick-borne rickettsioses was published in 2005 (2). Since then, rickettsiology has undergone a significant transformation. Several species of tick-borne rickettsiae that were considered nonpathogenic for decades are now associated with human infections (Table 1), and novel *Rickettsia* species of undetermined pathogenicity (Table 2) continue to be detected in or isolated from ticks around the world.

This remarkable expansion of information has been driven largely by the use of molecular techniques that have facilitated the identification of novel and previously recognized rickettsiae in ticks. Until relatively recently, the diagnosis of tick-borne SFG rickettsioses was confirmed almost exclusively by serologic methods. Even when using a microimmunofluorescence (MIF) assay, the current reference method, a positive serologic reaction does not necessarily imply that the patient's illness was caused by the rickettsial species used as the antigen in the assay due to antigenic cross-reactivity among SFG rickettsiae (2). The recognition of multiple distinct tick-borne SFG rickettsioses during recent years has been greatly facilitated by the broad use of cell culture systems and molecular methods for identifying rickettsiae from human samples, including the use of quantitative PCR (qPCR) (2). New approaches, such as the use of swabs to obtain material from eschars to be tested by PCR, have recently emerged (2). Finally, many well-characterized SFG *Rickettsia* species and recently or incompletely described rickettsiae that were previously considered to be restricted to a specific tick host or geographical location have recently been detected on different continents and in various tick hosts.

In recent years, rickettsiologists, including clinicians, scientists, veterinarians, field investigators, and laboratory professionals, have contributed to the accumulation of knowledge in this rapidly progressing field. The 4th, 5th, and 6th International Meetings on Rickettsiae and Rickettsial Diseases, organized in Spain (2005), France (2008), and Greece (2011), gathered approximately 300 experts who traveled from 5 continents to present the results of their multifaceted work. Many original articles were published after these meetings.

The time has come to summarize current knowledge on tick-borne rickettsioses in a comprehensive review, using a geographic approach and the 2005 review as a background for historical, epidemiological, and diagnostic information. Data for the present review were obtained from publications identified by PubMed searches from 2005 to 2012. Search terms were combinations of the words "ticks," "rickettsia," "rickettsioses," "spotted fever," and "typhus." A secondary manual search of the references cited in these articles was also performed to find relevant articles that had been reviewed. Additionally, the same terms were searched in the GenBank database to identify additional rickettsiae or rickettsial DNA samples that have been detected in ticks.

TAXONOMIC AND GENOMIC BACTERIOLOGY: THE REVOLUTION

Currently, 26 *Rickettsia* species with validated and published names have been reported (http://www.bacterio.cict.fr/qr/rickettsia.html), including *Rickettsia asiatica* (3), *Rickettsia heilongjiangensis* (4), *Rickettsia hoogstraalii* (5), *Rickettsia raoultii* (6), and *Rickettsia tamurae* (7), which were reported since 2005 (2). In addition to these 26 species, subspecies have been proposed within the *Rickettsia conorii* (8) and *Rickettsia sibirica* (9) species. The taxonomic criteria used to describe new *Rickettsia* species have not changed over the past 10 years (10). However, the sizes of the *Rickettsia* genomes are small, and their sequences are available for most validated species. After proposals to include genomic data among taxonomic criteria (11), it could be suggested that genome sequences should be mandatory for the description of new *Rickettsia* species. Currently, genomes from 23 of the 26 validated *Rickettsia* species are available, and for 11 of these species, the genomes from 2 to 8 isolates are available (Table 3). Compared to the genomes of free-living bacteria, rickettsial genomes exhibit several unusual properties. These genomes are small, ranging from 1.11 Mb for *Rickettsia typhi*, the agent of the flea-borne murine typhus, to 2.1 Mb for the "*Rickettsia* endosymbiont of *Ixodes scapularis*." Their G+C content is low, ranging from 29% (*R. typhi*) to 33% (*Rickettsia* endosymbiont of *Ixodes scapularis*). By studying the genome size and gene content of bacteria in relation to their lifestyle, Merhej et al. demonstrated that genome degradation, especially gene loss, has been a driving force in the adaptation of rickettsiae and other intracellular bacteria to live within eukaryotic cells (12). By comparing the genome of *Rickettsia africae*, a mildly pathogenic organism in humans, to those of the more pathogenic species *R. conorii*, *Rickettsia rickettsii*, and *Rickettsia prowazekii*, Fournier et al. hypothesized that genome degradation in rickettsiae was associated with increasing virulence (13). This reductive evolution is marked by a notably large proportion of noncoding sequences resulting in degraded genes with functions in biosynthetic pathways. However, rickettsial genomes also contain a variety of duplicated or repeated genes or DNA fragments. In addition, some noncoding sequences are highly conserved, suggesting a potential function for these sequences (1). Among duplicated or repeated genomic elements, rickettsial genomes contain palindromic repeats, modules encoding type IV secretion systems, tetratricopeptide and ankyrin repeat motifs that possibly play a role in pathogenicity by mediating interactions with eukaryotic cells, toxin-antitoxin (TA) modules, and paralogous gene families (*sca*, *spoT*, *tlc*, *proP*, and *ampG*) (1). In addition, several

TABLE 1 Tick-borne spotted fever group rickettsial agents of human diseases

Rickettsia species or strain	Recognized or potential tick vector(s)	Comment(s) (including related disease[s])	Geographical distribution[a]
Rickettsia aeschlimannii	*Amblyomma variegatum*, *Rhipicephalus annulatus*, *Rhipicephalus evertsi evertsi*, *Rhipicephalus appendiculatus*, *Hyalomma marginatum rufipes*, *Hyalomma truncatum*	Spotted fever	Sub-Saharan Africa
	Hyalomma marginatum marginatum, *Hyalomma anatolicum excavatum*, *Ixodes ricinus*, *Rhipicephalus sanguineus*, *Rhipicephalus turanicus*, *Rhipicephalus bursa*	Spotted fever	Europe
	Haemaphysalis punctata, *Hyalomma marginatum*, *Hyalomma detritum*	No human cases; identified in ticks in Kazakhstan and Israel	Asia
	Hyalomma detritum detritum, *Hyalomma marginatum marginatum*, *Hyalomma aegyptium*, *Hyalomma marginatum rufipes*, *Hyalomma dromedari*, *Hyalomma truncatum*	Detected in humans in Tunisia and Algeria and in ticks in Algeria, Morocco, Tunisia, and Egypt	North Africa
Rickettsia africae	*Amblyomma variegatum*, *Amblyomma hebraeum*, *Amblyomma compressum*, *A. lepidum*, *Rhipicephalus annulatus*, *Rhipicephalus evertsi*, *Rhipicephalus decoloratus*, *Rhipicephalus sanguineus*, *Rhipicephalus geigyi*, *Hyalomma impeltatum*	African tick bite fever	Sub-Saharan Africa
	Amblyomma variegatum	Imported from Africa to the West Indies during the early 1800s; currently established in Guadeloupe, St. Kitts, Nevis, Dominica, U.S. Virgin Islands, Montserrat, St. Lucia, Martinique, and Antigua; causes eschar-associated illness, with clinical cases reported from Guadeloupe	North and Central America
	Amblyomma loculosum	African tick bite fever	Pacific Islands
	Hyalomma aegyptium	No human cases reported from Asia; identified in ticks in Turkey	Asia
	Hyalomma dromedarii	No human cases; detected in dromedary ticks in sub-Saharan Algeria and Egypt	North Africa
Rickettsia australis	*Ixodes holocyclus*, *Ixodes tasmani*, *Ixodes cornuatus*	Queensland tick typhus	Australia
Rickettsia sp. strain Atlantic rainforest or Bahia	*Amblyomma ovale*, *Amblyomma aureolatum*, *Rhipicephalus sanguineus*	Genetically related to *R. parkeri*, *R. africae*, and *R. sibirica*; 2 nonfatal cases reported in Brazil; symptoms include rash, eschar, and lymphadenopathy	South America
Rickettsia conorii subsp. *caspia*	*Rhipicephalus pumilio*, *Rhipicephalus sanguineus*	Astrakhan fever	Europe
	Rhipicephalus sanguineus, *Rhipicephalus pumilio*	Astrakhan fever	Sub-Saharan Africa
Rickettsia conorii subsp. *conorii*	*Rhipicephalus sanguineus*	Mediterranean spotted fever	Europe
	Rhipicephalus sanguineus	Mediterranean spotted fever human cases reported and detected in brown ticks in all North Africa areas	North Africa
	Rhipicephalus sanguineus, *Rhipicephalus evertsi evertsi*, *Rhipicephalus simus*, *Rhipicephalus mushamae*, *Haemaphysalis punctaleachi*, *Haemaphysalis leachi*	Mediterranean spotted fever	Sub-Saharan Africa
	Rhipicephalus sanguineus, *Rhipicephalus bursa*	Asiatic part of Turkey	Asia
Rickettsia conorii subsp. *indica*	*Rhipicephalus sanguineus*	Indian tick typhus	Europe, Asia
R. conorii subsp. *israelensis*	*Rhipicephalus sanguineus*	Israeli tick typhus	Europe, Asia
	Rhipicephalus sanguineus	Israeli tick bite fever; 2 cases of ISF from Sfax confirmed by detection of rickettsia in skin biopsy specimens	North Africa

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TABLE 1 (Continued)

Rickettsia species or strain	Recognized or potential tick vector(s)	Comment(s) (including related disease[s])	Geographical distribution[a]
Rickettsia heilongjiangensis	*Haemaphysalis concinna*, *Haemaphysalis japonica douglasi*, *Haemaphysalis flava*, *Dermacentor silvarum*	Far-Eastern spotted fever in Russia, China, South Korea, Japan	Asia
Rickettsia helvetica	*Ixodes persulcatus*	Serologically confirmed cases only in Laos and Thailand; in *Ixodes* ticks in Japan and Turkey	Asia
	Ixodes ricinus		Europe
	Ixodes ricinus	No human cases; detected in *Ixodes* spp. in Algeria and Morocco	North Africa
Rickettsia honei	*Bothriocroton hydrosauri*	Flinders Island spotted fever	Asia, Australia, and Pacific
	Ixodes sp.	Spotted fever identical to Flinders Island spotted fever in Australia	Asia
Rickettsia honei strain marmionii	*Haemaphysalis novaeguineae*	Australian spotted fever	Australia
Rickettsia japonica	*Haemaphysalis flava*, *Haemaphysalis hystricis*, *Haemaphysalis longicornis*, *Haemaphysalis cornigera*, *Haemaphysalis formosensis*, *I. ovatus*, *D. taiwanensis*	Japanese spotted fever in Japan and South Korea	Asia
"*Candidatus* Rickettsia kellyi"	Unknown	A single case reported from India; several amplicons from patients are referenced in GenBank	Asia
Rickettsia massiliae	*Rhipicephalus sanguineus*	Recognized pathogen in other countries and detected in brown dog ticks in Arizona and California; no confirmed human cases in the U.S.	North and Central America
	Rhipicephalus sanguineus	1 case reported in a patient in Spain, recently arrived from Argentina; also reported to infect *R. sanguineus* in Argentina	South America
	Rhipicephalus turanicus, *Rhipicephalus sanguineus*, *Rhipicephalus bursa*, *Rhipicephalus pusillus*, *Ixodes ricinus*	Spotted fever	Europe
	Rhipicephalus evertsi, *Haemaphysalis paraleachi*, *Rhipicephalus senegalensis*, *Rhipicephalus guilhoni*, *Rhipicephalus lunulatus*, *Rhipicephalus sulcatus*, *Rhipicephalus muhsamae*	Spotted fever	Sub-Saharan Africa
	Rhipicephalus turanicus, *Rhipicephalus sanguineus*	Identified in ticks in Israel	Asia
	Rhipicephalus sanguineus, *Rhipicephalus turanicus*	No human cases; detected in *Rhipicephalus* spp. in Morocco, Algeria, and Tunisia	North Africa
R. monacensis	*Ixodes ricinus*	Spotted fever (first clinical description 2007)	Europe
	Ixodes persulcatus	Found only in ticks in Turkey	
	Ixodes ricinus	No human cases; identified in *Ixodes* spp. in Tunisia, Algeria, and Morocco	North Africa
Rickettsia parkeri	*Amblyomma maculatum*, *Amblyomma americanum*, *Dermacentor variabilis*	Southeastern U.S.; causes mild, eschar-associated rickettsiosis; despite the occurrence of *A. maculatum* in Central America, no confirmed cases have been reported from that region	North and Central America

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TABLE 1 (Continued)

Rickettsia species or strain	Recognized or potential tick vector(s)	Comment(s) (including related disease[s])	Geographical distribution[a]
	Amblyomma triste, *Amblyomma tigrinum*	Causes spotted fever in Uruguay and Argentina; symptoms include rash, eschar, and lymphadenopathy; no fatal cases reported; also reported to infect ticks in Brazil and Bolivia	South America
Rickettsia philipii (364D)	*Dermacentor occidentalis*	California; causes a relatively mild, eschar-associated illness; only a few recognized cases	North and Central America
Rickettsia raoultii	*Dermacentor marginatus*, *Dermacentor reticulatus*, *Ixodes ricinus*	SENLAT (old TIBOLA/DEBONEL)	Europe
	Dermacentor silvarum, *Dermacentor reticulatus*, *Dermacentor marginatus*, *Dermacentor nuttalli*, *Dermacentor niveus*, *Haemaphysalis ornithophila*, *Haemaphysalis shimoga*, *Haemaphysalis lagrangei*, *Amblyomma testudinarium*	No human cases; identified in *Dermacentor* species ticks in North Asia and in *Haemaphysalis* and *Amblyomma* ticks in South Asia	Asia
	Dermacentor marginatus	No human cases; identified in *Dermacentor* spp. in Morocco	North Africa
Rickettsia rickettsii	*Dermacentor andersoni*, *Dermacentor variabilis*, *Dermacentor occidentalis*, *Dermacentor nitens*, *Rhipicephalus sanguineus*, *Amblyomma cajennense*, *Amblyomma americanum* *Amblyomma imitator*, *Haemaphysalis leporispalustris*	Causes Rocky Mountain spotted fever, the most severe rickettsiosis in the world; occurs sporadically and infrequently in ticks throughout Canada, the U.S., Mexico, Costa Rica, and Panama	North and Central America
	Amblyomma cajennense, *Amblyomma aureolatum*, *Rhipicephalus sanguineus*	Causes the most severe spotted fever, namely, Rocky Mountain spotted fever or Brazilian spotted fever; reported in Argentina, Brazil, and Colombia; current case fatality rate of 20–40%	South America
Rickettsia sibirica subsp. *mongolitimonae*	*Hyalomma anatolicum excavatum*, *Rhipicephalus pusillus*	LAR	Europe
	Hyalomma truncatum	LAR	Sub-Saharan Africa
	Hyalomma asiaticum	Type strain isolated in China; no cases from Asia have been reported; identified in Israel	Asia
	Hyalomma sp.	1 human case	North Africa
Rickettsia sibirica subsp. *sibirica*	*Dermacentor nuttalli*, *Dermacentor marginatus*, *Dermacentor reticulatus*, *Dermacentor silvarum*, *Dermacentor sinicus*, *Haemaphysalis yeni*, *Haemaphysalis concinna*, *Ixodes persulcatus*	Siberian tick typhus in Russia, China, and Mongolia	Asia
Rickettsia slovaca	*Dermacentor marginatus*, *Dermacentor reticulatus*	SENLAT (TIBOLA/DEBONEL)	Europe
	Dermacentor ticks	No human cases in Asia; identified in Russia and China	Asia
	Dermacentor marginatus	SENELAT (TIBOLA DEBONEL); no human cases; detected in *Dermacentor* ticks from Algeria and Morocco	North Africa
Rickettsia tamurae	*Amblyomma testudinarium*	Case was reported from Japan and Laos	Asia

[a] See figures.

mobile genetic elements have been identified. These elements include plasmids in at least 10 species, although it was previously thought that rickettsiae lacked plasmids. One notable aspect of *Rickettsia* plasmids is that there are multiple plasmids in several species (14). In addition, plasmids in rickettsiae can be polymorphic, as observed for *Rickettsia felis*, where a plasmid exists in both a 62-kb and a 39-kb form (15). The discovery of plasmids and evidence for conjugation in these organisms suggest that lateral

TABLE 2 Tick-borne spotted fever group rickettsiae of unknown pathogenicity and nonvalidated, incompletely described, or uncultivated species isolated or detected in ticks

Rickettsia species or strain	Associated tick(s)	Comment(s)	Geographical distribution[a]
Rickettsia aeschlimannii-like	*Amblyomma tigrinum*	Reported in Bolivia; very similar to Old Word *R. aeschlimannii*	South America
Strain AL	*Amblyomma longirostre*	Reported in bird ticks in Brazil; could be *R. amblyommii*	South America
"*Candidatus* Rickettsia amblyommii"	*Amblyomma americanum*, *Amblyomma cajennense*, *Amblyomma oblongoguttatum*, *Amblyomma ovale*, *Rhipicephalus microplus*, *Rhipicephalus sanguineus*, *Dermacentor nitens*, *Amblyomma maculatum*	U.S., Costa Rica, and Panama; very common and widely distributed in *A. americanum* ticks in the U.S., with avg infection frequencies of40-70%; pathogenic potential unknown	North and Central America
	Amblyomma cajennense, *Amblyomma coelebs*, *Amblyomma neumanni*, *Amblyomma longirostre*, *Amblyomma geayi*, *Amblyomma auricularium*	Possibly associated with animal infection in Brazil; also reported in Argentina and French Guyana	South America
"*Candidatus* Rickettsia andeanae"	*Amblyomma maculatum*	Occurs in *A. maculatum* ticks in the southeastern U.S.; recently isolated in cell culture, but pathogenic potential is unknown	North and Central America
	Amblyomma maculatum, *Amblyomma parvum*, *Amblyomma pseudoconcolor*, *Amblyomma triste*, *Ixodes boliviensis*	Reported in ticks from Peru and Chile; in Argentinean ticks, reported as *Rickettsia* sp. strain Argentina	South America
Strain ApPR	*Amblyomma parkeri*	Reported in bird ticks in Brazil; genetically related to *R. parkeri*, *R. africae*, and *R. sibirica*	South America
Rickettsia antechini	*Ixodes antechini*	Australia	Australia
Strain Aranha	*Amblyomma longirostre*	Reported in bird ticks in Brazil; could be *R. amblyommii*	South America
Rickettsia argasii	*Argas dewae*	Australia	Australia
Rickettsia asiatica	*Ixodes ovatus*, *Ixodes pomerantzevi*	Found in the blood of sika deer in Japan	Asia
Rickettsia sp. AvBat	*Argas vespertilionis*		Europe
"*Candidatus* Rickettsia barbariae"	*Rhipicephalus turanicus*		Europe
Rickettsia bellii	*Amblyomma sabanerae*, *Dermacentor occidentalis*, *Dermacentor variabilis*, *Dermacentor parumapertus*, *Dermacentor albipictus*, *H. leporispalustris*, *Argas cooleyi*, *Ornithodoros concanensis*	Sporadically distributed throughout the U.S. and described recently in El Salvador; rabbits and guinea pigs develop eschars following subcutaneous inoculation; no known cases of illness in humans	North and Central America
	Various species of *Amblyomma*, *Haemaphysalis juxtakochi*, *Ixodes loricatus*	Represents a distinct basal group within the rickettsiae; it is the rickettsia with the greatest variety of tick hosts in South America; reported in Argentina, Brazil, and Peru	South America
Rickettsia canadensis	*Haemaphysalis leporispalustris*	Canada and U.S.; elicits a febrile response in guinea pigs and rickettsemias of several-days' duration in meadow mice and baby chicks; suspected to cause illness in humans, but there have been no confirmed cases	North and Central America
Strain Colombianensi	*Amblyomma dissimile*, *Rhipicephalus microplus*	Reported in Colombia; genetically related to *R. tamurae* and *R. monacensis*	South America

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TABLE 2 (Continued)

Rickettsia species or strain	Associated tick(s)	Comment(s)	Geographical distribution[a]
"*Candidatus* Rickettsia cooleyi"	*I. scapularis*	Occurs at very high frequencies and broadly distributed in *I. scapularis* ticks across the eastern, upper Midwestern, and southern U.S.; may represent an endosymbiont	North and Central America
Strain COOPERI	*Amblyomma dubitatum* (reported as *Amblyomma cooperi*)	Reported in capybara ticks in Brazil; genetically related to *R. parkeri*, *R. africae*, and *R. sibirica*	South America
Rickettsia sp. strain Davousti	*Ixodes ricinus, Ixodes lividus*	Ticks from migratory birds	Europe
Rickettsia sp. strain Davousti	*Amblyomma tholloni*	Closely related to *R. heilongjiangensis*	Sub-Saharan Africa
Rickettsia derrickii	*Bothriocroton hydrosauri*		Australia
Rickettsia sp. strain DmS1	*Dermacentor*		Europe
Rickettsia gravesii sp. nov.	*Amblyomma triguttatum*		Australia
Rickettsia sp. strains G021 and G022	*Ixodes pacificus*	Northern California; possibly identical to Grants Pass or Tillamook strain isolated in Oregon and California in the late 1970s and early 1980s; pathogenic potential is unknown	North and Central America
"*Candidatus* Rickettsia goldwasserii"	*Haemaphysalis adleri*, *Haemaphysalis parva*	Israel	Asia
Rickettsia guntherii	*Haemaphysalis humerosa*	Australia	Australia
Rickettsia hoogstraalii	*Carios capensis* *Haemaphysalis punctata*, *Haemaphysalis sulcata* *Argas persicus*, *Ornithodoros moubata*	Japan	Asia Europe Sub-Saharan Africa
Rickettsia sp. strain IG-1	*Ixodes granulatus*	Taiwan, Japan	Asia
Rickettsia sp. strain IXLI1	*Ixodes lividus*	Closely related to *R. japonica*	Europe
Koala rickettsia	*Bothriocroton concolor*	Australia	Australia
"*Candidatus* Rickettsia kotlanii"	Ixodid ticks		Europe
"*Candidatus* Rickettsia kulagini"	*Rhipicephalus sanguineus*		Europe
Rickettsia sp. clone KVH-02-3H7	*Ixodes ricinus*		Europe
"*Candidatus* Rickettsia liberiensis"	*Ixodes muniensis*	Closely related to *R. raoultii*	Sub-Saharan Africa
Rickettsia montanensis	*Dermacentor andersoni* *Dermacentor variabilis* *Amblyomma americanum*	U.S. and Canada; no known cases of illness in humans	North and Central America
Rickettsia monteiroi	*Amblyomma incisum*	Recently described in Brazil; joined to *R. bellii* and *R. canadensis* in the most basal group of tick-associated rickettsiae	South America
"*Candidatus* Rickettsia moreli"	*Ixodes ricinus*		Europe
Strain NOD	*Amblyomma nodosum*, *Amblyomma calcaratum*, *Amblyomma longirostre*	Reported in bird ticks in Brazil; genetically related to *R. parkeri*, *R. africae*, and *R. sibirica*	South America

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TABLE 2 (Continued)

Rickettsia species or strain	Associated tick(s)	Comment(s)	Geographical distribution[a]
Strain Pampulha	*Amblyomma dubitatum*	Reported in Brazil; genetically related to *R. tamurae* and *R. monacensis*	South America
Rickettsia sp. strain Parumapertus	*Dermacentor parumapertus*	Western U.S.; causes mild to moderately severe disease in guinea pigs	North and Central America
Rickettsia peacockii	*Dermacentor andersoni*	Western U.S. and Canada; closely related to *R. rickettsii* but considered a nonpathogenic endosymbiont	North and Central America
"*Candidatus* Rickettsia principis"	*Haemaphysalis japonica douglasi*, *Haemaphysalis danieli*	Russian Far East, northeastern China	Asia
Rickettsia sp. RDla440	*Dermacentor auratus*	Thailand	Asia
Rickettsia sp. RDla420	*Dermacentor* spp.	Thailand	Asia
Rickettsia rhipicephali	*Rhipicephalus haemaphysaloides* *Rhipicephalus sanguineus*	Taiwan	Asia
	Rhipicephalus lunulatus, *Rhipicephalus composites* group		Sub-Saharan Africa
	Rhipicephalus sanguineus, *Dermacentor occidentalis*, *Dermacentor variabilis*, *Dermacentor andersoni*	U.S.; causes moderately severe illness when inoculated into meadow voles; no known cases of illness in humans	North and Central America
	Haemaphysalis juxtakochi	Infects ticks from the Brazilian Amazon and Atlantic rainforests	South America
"*Candidatus* Rickettsia rioja"	*Dermacentor marginatus*		Europe
Rickettsia sauri	*Amblyomma hydrosauri*	Australia	Australia
"*Candidatus* Rickettsia siciliensis"	*Rhipicephalus turanicus*		Europe
"*Candidatus* Rickettsia tarasevichiae"	*Ixodes persulcatus*	Russia and Japan	Asia
Rickettsia tasmanensis	*Ixodes tasmani*	Australia	Australia and Pacific
Rickettsia sp. strain Uilenbergi	*Amblyomma tholloni*	Closely related to the *R. massiliae* group	Sub-Saharan Africa
"*Candidatus* Rickettsia vini"	*Ixodes arboricola, Ixodes ricinus*		Europe
Rickettsia sp.	*Rhipicephalus* (*Boophilus*) spp.	Laos	Asia
Rickettsia sp.	*Ixodes persulcatus*	Northern China	Asia
Rickettsia sp.	*Rhipicephalus turanicus*	Closely related to but distinct from the *R. rhipicephali-R. massiliae* lineage	Europe
Rickettsia sp.	*Ixodes ricinus*	Sister taxon of *R. bellii*	Europe
Rickettsia sp.	*Ixodes ricinus*	High homology with *R. limoniae*	Europe
Rickettsia sp.	*Ixodes ricinus*	Sister taxon of *R. bellii*	Europe
Rickettsia sp.	*Rhipicephalus evertsi*	Closely related to the *R. rickettsii* group	Sub-Saharan Africa
Rickettsia sp.	*Rhipicephalus sanguineus*, *Haemaphysalis erinacei*		North Africa
Rickettsia sp. from *A. tuberculatum* (148)	*Amblyomma tuberculatum*	Southern U.S.; genetically similar to *R. parkeri*, *R. africae*, and *R. sibirica*; pathogenic potential unknown	North and Central America

[a] See figures.

TABLE 3 Main characteristics of currently available tick-borne *Rickettsia* genomes[a]

Species	Strain	Rickettsiosis	Chromosome size (kb)	No. of ORFs	G+C content (%)	Noncoding DNA (%)	No. of plasmids (size [kb])	GenBank accession no.
R. africae	ESF-5	African tick bite fever	1,278,540	1,260	32.4	28	1 (12.4)	CP001612
R. australis	Phillips	Queensland tick typhus	1,297,390	1,110	31.7	26	2 (26.6 and 30.1)	AKVZ00000000
	Cutlack	Queensland tick typhus	1,296,670	1,297	32.3	NA	1 (26.6)	CP003338
R. bellii	OSU 85-389	Unknown pathogenesis	1,528,980	1,470	32	20	0	CP000849
	RML369-C		1,522,076	1,429	31.7	14.8	0	CP000087
R. canadensis	McKiel	Unknown pathogenesis	1,159,722	1,129	31.1	26	0	CP000409
	CA410	Unknown pathogenesis	1,150,228	1,052	31	NA	0	CP003304
R. conorii subsp. *conorii*	Malish Seven	Mediterranean spotted fever	1,268,755	1,374	32.4	19	0	AE006914
R. conorii subsp. *indica*	ITTR	Indian tick typhus	1,249,482	1,157	32.5	19.1	0	AJHC00000000
R. conorii subsp. *caspia*	A-167	Astrakhan fever	1,260,331	1,210	33	18.8	0	AJUR00000000
R. conorii subsp. *israelensis*	ISTTCDC1	Israeli spotted fever	1,252,815	1,164	32	20.0	0	AJVP00000000
R. heilongjiangensis	054	Far-Eastern tick-borne rickettsiosis	1,278,471	1,297	32.3	17	0	CP002912
R. helvetica	C9P9	Unnamed rickettsiosis	1,369,827	1,135	32.2	15.9	1 (47.1)	CM001467
R. honei	RB	Flinders Island spotted fever	1,268,758	1,284	32.4	19	0	AJTT00000000
R. japonica	YH	Oriental spotted fever	1,331,743	1,239	32.7	28	1 (19.8)	AMRT00000000
	YH	Oriental spotted fever	1,283,087	1,010	32.4	NA	0	AP011533
R. massiliae	Mtu5	Unnamed rickettsiosis	1,360,898	1,436	32.5	31	1 (15.2)	CP000683
	AZT80	Unknown pathogenesis	1,263,719	1,243	32.6	NA	1 (15.0)	CP003319
R. montanensis	OSU 85-930	Unknown pathogenesis	1,279,798	1,254	32.6	NA	0	CP003340
R. parkeri	Portsmouth	*R. parkeri* rickettsiosis	1,300,386	1,354	32.4	NA	0	CP003341
R. peacockii	Rustic	Unknown pathogenesis	1,288,492	984	33	NA	1 (26.4)	CP001227
R. philipii	364D	Unnamed rickettsiosis	1,287,740	1,380	32.5	NA	0	CP003308
R. raoultii	RpA4	SENLAT	1,275,089	1,355	32.5	15.4	3 (20.8, 34.5, and 83.2)	CP002428
R. rhipicephali	3-7-female6-CWPP	Unknown pathogenesis	1,290,368	1,302	32.4	NA	1 (15.0)	CP003342
R. rickettsii	Sheila Smith	Rocky Mountain spotted fever	1,257,710	1,382	32.4	24	0	NC_009882
	Iowa	Avirulent	1,268,175	1,421	32.4	NA	0	NC_010263
	Arizona	Rocky Mountain spotted fever	1,267,197	1,380	32.4	NA	0	CP003307
	Brazil	Rocky Mountain spotted fever	1,255,681	1,369	32.5	NA	0	CP003305
	Colombia	Rocky Mountain spotted fever	1,270,083	1,387	32.5	NA	0	CP003306
	Hlp#2	Unknown pathogenicity	1,270,751	1,345	32.5	NA	0	CP003311
R. sibirica subsp. *sibirica*	BJ-90	Siberian tick typhus	1,254,013	1,182	32.5	17.5	0	AHIZ00000000
	246		1,250,021	1,151	32.5	17.3	0	AABW00000000
R. sibirica subsp. *mongolitimonae*	HA-91	Lymphangitis-associated rickettsiosis	1,252,337	1,138	32.4	18.5	0	AHZB00000000
R. slovaca	13-B	Tick-borne lymphadenitis	1,275,089	1,323	32.5	18.7	0	CP002428
	D-CWPP	Tick-borne lymphadenitis	1,275,720	1,386	32.5	NA	0	CP003375
Rickettsia endosymbiont of *Ixodes scapularis*		Unknown pathogenesis	1,821,709	2,059	31	22	4 (33.9, 49.8, 55.1, and 66.8)	NZ_ACLC00000000

[a] ORFs, open reading frames; NA, not applicable.

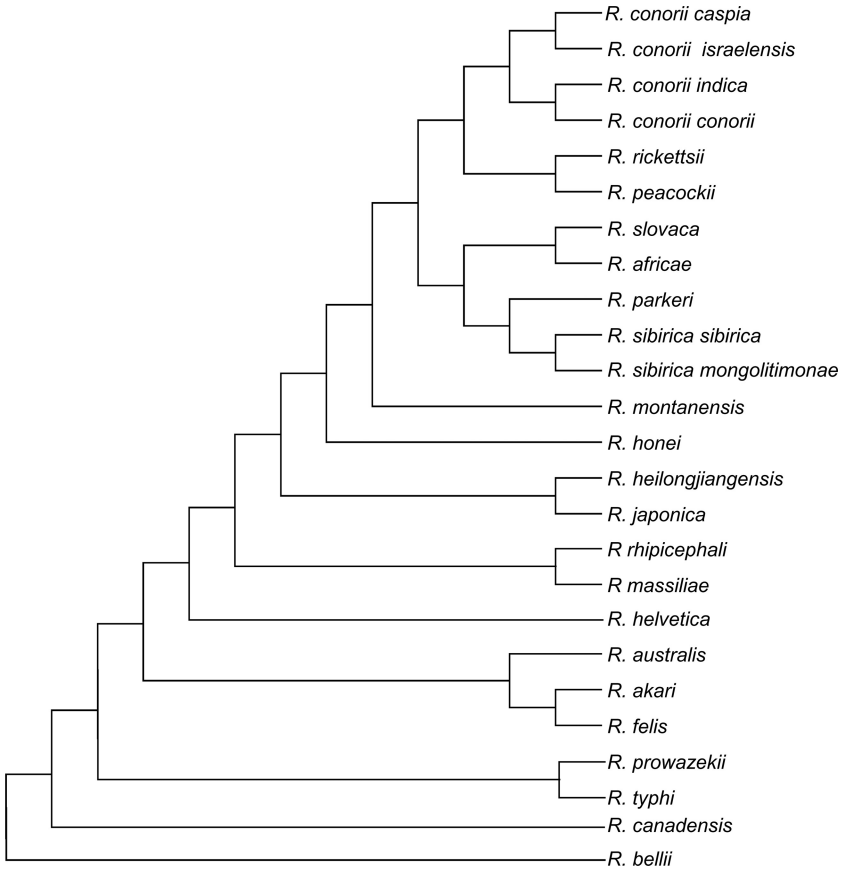

FIG 1 Genome sequence-based phylogenetic tree of *Rickettsia* species. This tree was constructed by aligning the 597 orthologous genes of all studied genomes. Phylogenetic relationships were inferred by using the parsimony method.

gene transfer (LGT) could occur among rickettsiae (16, 17). In fact, several LGT candidates were identified among *Rickettsia* genomes, including *tra* and *pat2*, genes encoding type IV secretion system proteins and ATP/ADP translocases, respectively (1). Recently, Merhej et al. identified 165 rickettsial genes that may have been acquired by *R. felis* from *R. bellii*; *R. typhi*; other bacteria, including *Legionella* sp. and *Francisella* sp.; or even eukaryotes (18) (Fig. 1). Some of these genes appear to have been transferred in blocks containing several genes. Finally, investigators have identified 13 chimeric genes in *R. felis* that were the result of recombinations with *R. typhi* genes (18), thus offering a considerably more diversified genetic picture of rickettsiae than previously expected.

RELATIONSHIP BETWEEN SPOTTED FEVER GROUP RICKETTSIAE, IXODID TICKS, AND VERTEBRATE HOSTS

Ixodid ticks are the main vectors of SFG rickettsiae (Fig. 2). The tick-rickettsia relationship has been a point of interest for many researchers, and most studies concentrate on the role of ticks as vectors. Unfortunately, less attention has been directed toward the relationship among rickettsia and tick cells, tissues, and organs. Rickettsiae have developed many strategies to adapt to different environmental conditions, including those within their arthropod vectors and vertebrate hosts (19). Many species of the genus *Rickettsia* are considered to be vertically transmitted symbionts of invertebrates, suggesting that the arthropod vectors act as reservoirs or amplifiers of rickettsiae in nature. In the last decade, the relationship between *Rickettsia conorii* subsp. *conorii* and its tick host was called into question based on the lethal effect of this species of *Rickettsia* on *Rhipicephalus sanguineus*, the brown dog tick, in experimental models of infection (20, 21). The reasons for this reduction in fitness were shown to be unrelated to the geographical origin of the ticks (22) and to the inoculation methods (20, 23). However, when naturally infected *Rhipicephalus sanguineus* individuals were used (24), larvae, nymphs, and adults were maintained under laboratory conditions over several generations with a transovarial transmission (TOT) rate (the percentage of infected females that pass microorganisms to their progeny) that reached 100% and a filial infection rate (FIR) (the percentage of infected progeny derived from an infected female) of nearly 99% (25). Similarly, two studies in Brazil obtained a <50% FIR of *R. rickettsii* in *Rhipicephalus sanguineus* and *Amblyomma cajennense* tick colonies experimentally infected with an *in vitro*-cultured strain of *R. rickettsii* (26, 27), while another Brazilian study reported a 100% FIR of *R. rickettsii* in naturally infected *Rhipicephalus sanguineus* ticks (28). Interestingly, 100% TOT and 100% FIR of *R. rickettsii* were described for experimentally infected *Amblyomma aureolatum* ticks through 4 laboratory generations (29). However, lower reproductive performance and survival of infected female ticks were attributed to *R. rickettsii* infection. The authors hypothesized that these results may explain the low infection rates (<1%) usually reported among field populations of *A. aureolatum* ticks in

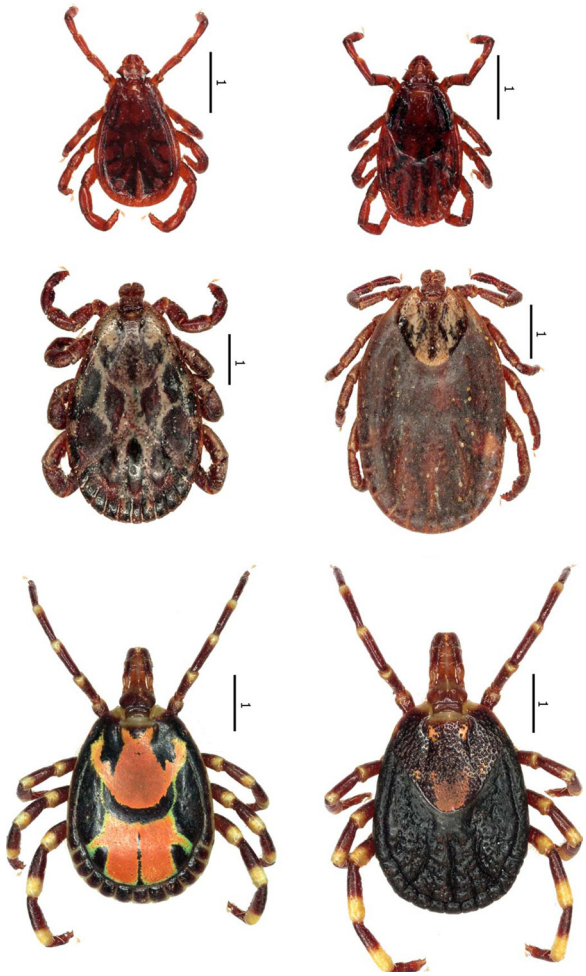

FIG 2 Three tick vectors of spotted fever group rickettsioses. From top to bottom are *Rhipicephalus sanguineus*, the primary vector of *R. conorii* subsp. *conorii*, the agent of Mediterranean spotted fever; *Dermacentor marginatus*, vector of *R. slovaca* and *R. raoultii*; and *Amblyomma variegatum*, vector of *R. africae*, the agent of ATBF. Males are on the left side, and females are on the right. Bar scale, 1 mm.

areas of Brazil where Rocky Mountain spotted fever (RMSF) is endemic. The same hypothesis was previously discussed to account for the prevalence of infected *R. conorii* subsp. *conorii* ticks in the Mediterranean (20); later, these same authors demonstrated that temperature variation could directly affect infected tick vectors and that infected, quiescent ticks may not survive the winter (25).

Regarding other *Rickettsia* species, it is interesting to note that studies using naturally infected, engorged females demonstrated 100% TOT and 98.5% FIR of *Rickettsia massiliae* in *Rhipicephalus turanicus* ticks (22), 100% TOT and 93.4% FIR of *Rickettsia africae* in *Amblyomma variegatum* ticks (30), 100% TOT and FIR of *Rickettsia bellii* in *Ixodes loricatus* (31), and 100% TOT and FIR of "*Candidatus* Rickettsia amblyommii" in *Amblyomma auricularium* ticks (32). Interestingly, there is some evidence to indicate that some typhus group rickettsiae, particularly *Rickettsia prowazekii*, the louse-borne agent of epidemic typhus, may, under certain circumstances, be associated with ticks (33). Additionally, *R. felis*, the agent of the so-called flea-borne spotted fever, has also been detected in a various nonhematophagous and hematophagous arthropod species, including soft and hard ticks (34). The role of ticks in the life cycle of these two *Rickettsia* species remains to be examined.

Recently, an analysis of all of the sequences in the toxin-antitoxin (TA) database of 33 published *Rickettsiales* genomes showed a significant link between vertical transmission and the presence of genomic copies of TA genes and modules (35). This significant statistical relationship suggests that TAs play a role in the maintenance of *Rickettsia* in their arthropod hosts via a mechanism that is currently unknown. The persistence of mobile TA genes in the genomes of some *Rickettsia* might reflect an obligate connection of the bacteria and their host cell (35).

Vertical transmission of rickettsiae in arthropods helps to maintain the infection in nature, but for some rickettsial agents, a life cycle including infected arthropods and one or more rickettsial host animals is required to guarantee survival of the bacteria in nature (36). To date, very few data are available regarding the animal reservoirs of these bacterial species, with the exception of *R. rickettsii* and *Rickettsia sibirica* subsp. *sibirica*, which were isolated from various wild mammals (2, 36). In 2012, it was shown that dogs are capable of acquiring *R. conorii* subsp. *israelensis* from infected *Rhipicephalus sanguineus* ticks and transmitting bacterial infection to cohorts of uninfected ticks, thus confirming for the first time that dogs can act as competent reservoirs for these bacteria (37). However, dogs with different genetic backgrounds appear to differ in their susceptibility to *Rickettsia conorii* subsp. *israelensis* infection (38). Recent studies of experimental infections of capybaras (*Hydrochoerus hydrochaeris*), opossums (*Didelphis aurita*), and domestic dogs with a highly virulent strain of *R. rickettsii* showed that these animals developed rickettsemia of sufficient magnitude to infect *A. cajennense* or *Rhipicephalus sanguineus* ticks during feeding (26, 28, 39, 40). These authors suggested that these vertebrate hosts could play an important role as amplifier hosts of *R. rickettsii* for ticks in nature. With regard to other *Rickettsia* species, molecular and serological studies have suggested some potential animal reservoirs; however, further studies need to be performed to confirm these hypothesized reservoirs, such as cattle for *R. africae* (41), wild boars and domestic ruminants for *Rickettsia slovaca* (42, 43), and sika deer for *Rickettsia helvetica* (44).

Humans are only occasional hosts for ticks and should be viewed as a "dead-end" host, which plays no role in maintaining these bacteria in nature (19). In humans, the site of bacterial entry sometimes develops into a localized inflammatory and necrotic skin lesion with a black crust, termed an inoculation eschar ("tache noire"). It represents the first site of challenge between the human host and the bacterium. The presence of a tache noire is associated with *Rickettsia* species that contain a large number of TA genes in their genomes. The toxic effect of TAs may increase the local reaction, thus inhibiting the spread of rickettsia organisms, which is associated with a fatal outcome of this infection. The presence of TAs is significantly inversely correlated with human host mortality (35). Also, it has been speculated that skin eschar is the reflection of a local control avoiding extreme virulence (45).

TICK-BORNE RICKETTSIAE IN THE AMERICAS

North and Central America

Species identified as pathogens. (i) *Rickettsia rickettsii*. *R. rickettsii*, the etiologic agent of Rocky Mountain spotted fever (RMSF), is distributed broadly, albeit at a low frequency, in hard ticks throughout the Western Hemisphere (2). In North and Central America, confirmed cases of RMSF have been documented in Canada, the United States, Mexico, Panama, and Costa Rica (46–51) (Fig. 3 and 4). Fatal human infections caused by a SFG *Rick-*

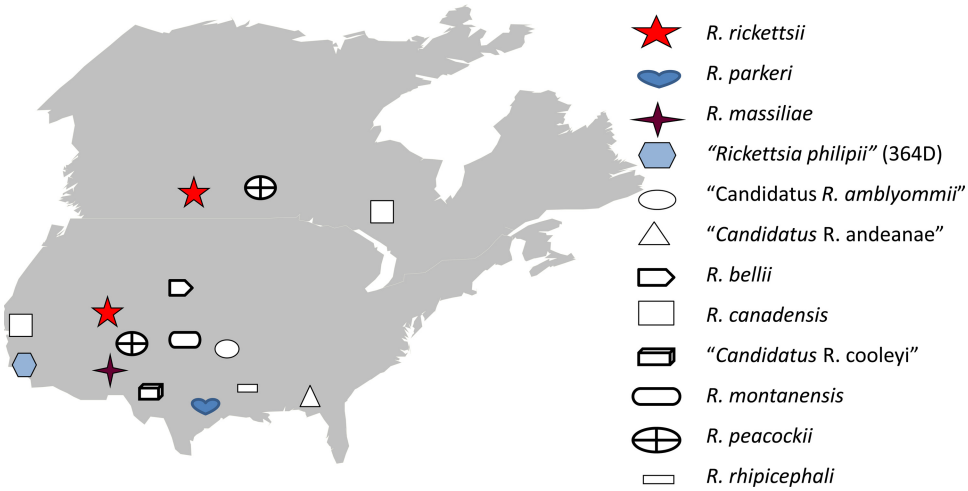

FIG 3 Tick-borne rickettsiae in North America (except Mexico). Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

ettsia species, presumably *R. rickettsii*, have also recently been described in Guatemala (52). Surprisingly, no confirmed cases of RMSF have been reported from the Caribbean, despite the presence of recognized tick vectors in this region. In the United States, RMSF still occurs predominantly in the Midwestern and southeastern states, including Oklahoma, Missouri, Arkansas, Tennessee, and North Carolina. Approximately two-thirds of the 11,531 cases of RMSF reported during 2000 to 2007 originated from these five states (53).

In Mexico, RMSF has been reported in the states of Baja California, Sonora, Sinaloa, Durango, Coahuila, and Yucatán. Hyperendemic foci have been described repeatedly in communities in the American Southwest and northern Mexico, linked directly to large numbers of *R. rickettsii*-infected *Rhipicephalus sanguineus* ticks that result from unchecked populations of stray and free-ranging dogs (54–61). During 1999 to 2007, the overall U.S. incidence of RMSF and the case-fatality rate were approximately 4 times higher among American Indians than among members of other racial groups (62, 63), related at least in part to the ecological dynamics created by large numbers of *Rhipicephalus sanguineus* and free-roaming dogs in peridomestic environments (64).

The annual incidence of RMSF has undergone 3 dominant shifts in the United States since national surveillance of this disease was initiated in 1920 (53). The reasons for these shifts are largely speculative; however, the emergence and flux of RMSF and other tick-borne diseases described below can most often be traced to specific human activities and behaviors that disrupt ecosystems and place greater numbers of susceptible hosts into the environment (65). Because some cases reported as RMSF might actually be diseases caused by other SFG rickettsiae, the surveillance case definition for RMSF in the United States was modified in 2010 to encompass the broader category of spotted fever rickettsiosis. The number of reported cases of spotted fever rickettsiosis in the United States, including cases of RMSF, rose 9% during 2009 to 2010, from 1,815 to 1,985 (66–70).

Epidemiologically important vectors of *R. rickettsii* in North

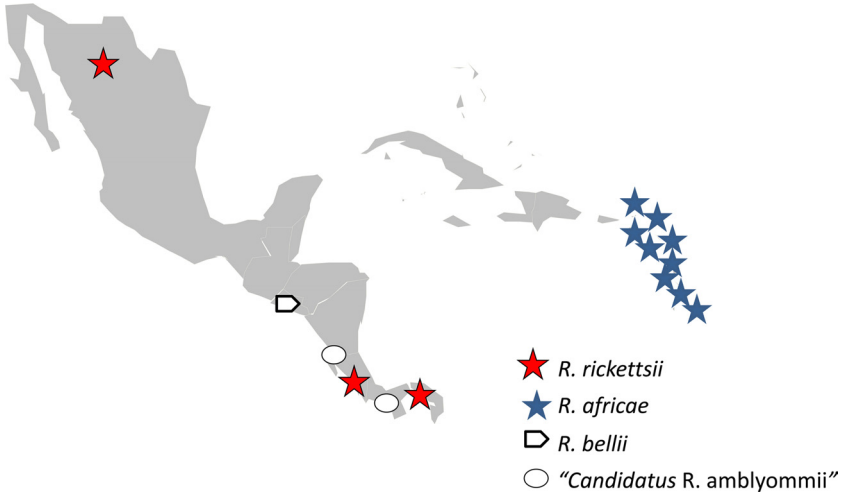

FIG 4 Tick-borne rickettsiae in Mexico and Central America. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

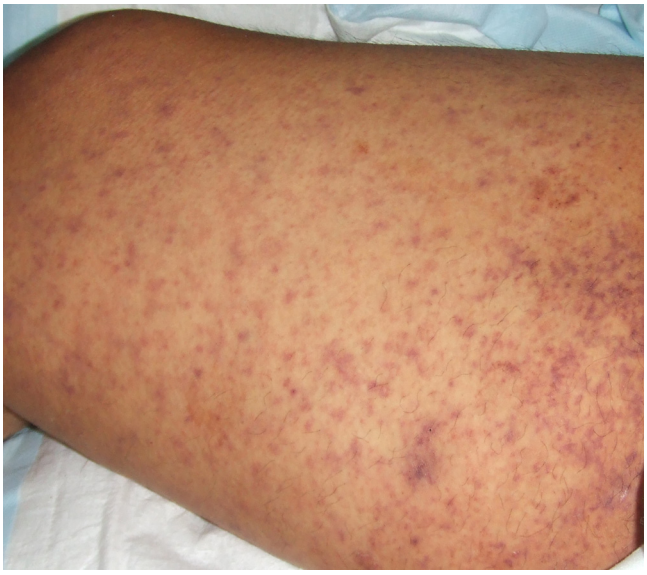

FIG 5 Petechial rash on a patient with Rocky Mountain spotted fever caused by *Rickettsia rickettsii*.

and Central America include the Rocky Mountain wood tick (*Dermacentor andersoni*), the American dog tick (*Dermacentor variabilis*), the Cayenne tick (*Amblyomma cajennense*), and the brown dog tick (*Rhipicephalus sanguineus*) (49, 71); however, *R. rickettsii* is found occasionally in other ticks, including the lone star tick (*Amblyomma americanum*) in the United States, *Amblyomma imitator* in Mexico, *Dermacentor nitens* in Panama, and *Haemaphysalis leporispalustris* in Costa Rica, all of which may occasionally be involved in the transmission of this pathogen to humans and animals (51, 72–75). Contemporary molecular surveys for *R. rickettsii* in North American *Dermacentor* ticks reveal extremely low frequencies of occurrence of these bacteria in ticks, characteristically <0.5% (76–80). However, unusually large numbers of *R. rickettsii*-infected *Rhipicephalus sanguineus* ticks are a hallmark of several hyperendemic foci of RMSF in the United States and Mexico (54, 56, 81–83), suggesting that *Rhipicephalus sanguineus* may be a more important vector of RMSF in North and Central America than previously recognized. To date, *Rhipicephalus sanguineus* has been shown to be an important vector of RMSF only in the southwestern United States and northern Mexico, possibly due to environmental conditions, the presence of a large feral dog population, and/or other animal reservoirs there, and not necessarily an important vector throughout North America. Recent data also indicate that many tick species may be infected simultaneously with multiple SFG rickettsiae, including *R. rickettsii* (74, 84).

Patients with RMSF experience an abrupt onset of high fever that is often accompanied by headache, nausea, vomiting, anorexia, and generalized myalgia. Only rarely is an eschar identified at the infection site (85). A rash begins on the second to fourth day following the appearance of fever. This rash appears as small pink macules, typically on the wrists, ankles, and forearms, and evolves to maculopapules. These lesions evolve into petechiae or purpura in 50% to 60% of patients (Fig. 5). Severe manifestations might include pulmonary edema and hemorrhage, cerebral edema, myocarditis, renal failure, disseminated intravascular coagulopathy, and gangrene (46, 86, 87). Despite the current availability of an effective treatment and advances in medical care, an estimated 5% to 10% of U.S. patients die when infected with *R. rickettsii* (48, 61, 87). For unknown reasons, case-fatality rates in Central America are considerably higher: estimates from recent outbreaks in Mexico are as high as 38% (88–91), and the case-fatality rate of 6 documented RMSF cases in Panama during 2004 to 2007 was 100% (50, 92).

Molecular analysis of 35 historical and contemporary isolates of *R. rickettsii* identified 5 phylogenetic clades based on sequence polymorphisms in several intergenic regions (93). Specific geographical and vector tick associations were identified among these groups, including clades with associated *Amblyomma* ticks from Central and South America and clades characterized by *D. andersoni* ticks in the northwestern United States. These data also suggest that certain isolates, particularly of serotypes Hlp and 364D, are sufficiently different to warrant unique species or subspecies status (94).

(ii) *Rickettsia parkeri*. The first confirmed human infection with *R. parkeri* was reported in 2004, and approximately 15 cases of *R. parkeri* rickettsiosis have been described in the literature since that initial report (66–70). In the United States, *Amblyomma maculatum* (the Gulf Coast tick) is the principal vector for these bacteria, and *R. parkeri* is detected in 8% to 43% of questing adult *A. maculatum* ticks collected in states along the Gulf Coast and the southern Atlantic region (95–101). *R. parkeri* is distributed throughout multiple tissues of infected *A. maculatum* ticks, including the salivary glands, the midgut, the Malpighian tubules, and the ovaries (102). *R. parkeri* is detected infrequently in *A. americanum* (103) and *D. variabilis* (79, 104). Infections of dogs and cows caused by *R. parkeri* have been reported in the southeastern United States (105, 106).

In most cases of *R. parkeri* infection, a necrotic inoculation eschar forms several days following the bite of an infected tick, preceding a low to moderate fever in several days. *R. parkeri* rickettsiosis is milder than RMSF, and no severe systemic manifestations or deaths have been described (67–69). It is likely that some U.S. cases that were previously categorized as RMSF should have been classified as *R. parkeri* rickettsiosis (66, 71, 107, 108). No cases of *R. parkeri* rickettsiosis have been reported in Central America; however, *A. maculatum* occurs throughout this region, and a mild, eschar-associated rickettsiosis that is compatible with *R. parkeri* rickettsiosis was reported recently for a traveler returning from Honduras (109).

(iii) *Rickettsia massiliae*. The first description of *R. massiliae* in North America was reported in 2006, when this SFG rickettsia was detected in adult *Rhipicephalus sanguineus* ticks collected from a hyperendemic focus of RMSF in the southwestern United States (110). This agent was subsequently identified in questing and attached specimens of *Rhipicephalus sanguineus* recovered from dogs in California and North Carolina (99, 111). The distribution and frequency of this bacterial species in brown dog ticks in North and Central America are poorly described; however, preliminary studies suggest that its New World occurrence is somewhat sporadic and focal (82, 111, 112). No confirmed human infections have been documented in the United States or Central America, although *R. massiliae* has been putatively linked to mild to moderately severe illnesses in dogs in California (111).

(iv) *Rickettsia africae*. African tick bite fever (ATBF) caused by *R. africae* is distributed broadly across most of the African conti-

nent (see below). It was first described in the Western Hemisphere in 1998 in a patient from Guadeloupe in the West Indies (113). Since that report, the pathogen has been detected in *Amblyomma variegatum* ticks collected from 8 additional territories and countries in the Caribbean, including Martinique, Dominica, Montserrat, Nevis, St. Kitts, St. Lucia, Antigua, and the U.S. Virgin Islands (113). Tick surveys on these islands revealed *R. africae* infection rates that range from 7% to 62% (114, 115). An important aspect for the epidemiology of ATBF is the acquisition of the disease by North American tourists, hunters, or deployed military members returning from areas where *R. africae* is endemic (116–118). The disease begins approximately 5 to 7 days following a tick bite, with an abrupt onset of fever, fatigue, headache, and myalgia. Inoculation eschars are reported inconsistently and are identified in approximately 50% to 100% of cases; however, the occurrence of multiple eschars is relatively frequent. Other common features include regional lymphadenopathy, a generalized maculopapular or papulovesicular rash, and, occasionally, aphthous stomatitis. No cases of fatal disease resulting from these bacteria have been reported, although more severe manifestations, including myocarditis and neuropathy, are sometimes described.

(v) *Rickettsia philipii* (*Rickettsia* 364D). In 2008, the first human infection with "*Rickettsia* 364D" was confirmed in a patient from northern California. *Rickettsia* 364D, an as-yet-unclassified SFG rickettsia initially described in 1975 from an isolate obtained from *Dermacentor occidentalis* ticks collected in southern California, has been detected in approximately 8% of the questing *D. occidentalis* ticks throughout California (76–80). Because *R. rickettsii* is rarely identified in human-biting ticks in this state, it has been suggested that *Rickettsia* 364D, provisionally named "*Rickettsia philipii*" (94), is responsible for many of the illnesses in this region that resemble and are misdiagnosed as RMSF. In addition to the index patient, three suspected cases have been described, each with an eschar and mild constitutional complaints that variably include fever, headache, myalgia, and fatigue (119).

Species of unknown pathogenicity. (i) *Rickettsia bellii*. *R. bellii* was first isolated in 1966 from *D. variabilis* ticks collected in Arkansas, and many other tick host species for this bacterium were subsequently detected, including *D. andersoni*, *D. occidentalis*, *Dermacentor albipictus*, *Dermacentor parumapertus*, *Haemaphysalis leporispalustris*, and the soft ticks *Ornithodoros concanensis* and *Argas cooleyi* (120). This *Rickettsia* species appears to be distributed sporadically: it has been detected in as many as 80% of the isolates obtained from *D. variabilis* ticks in Ohio and North Carolina but occurs in fewer than 1% of the California *Dermacentor* ticks recently evaluated for SFG rickettsiae by molecular assays. *R. bellii* also occasionally appears in mixed infections of ticks with *R. rickettsii*, *Rickettsia rhipicephali*, or *Rickettsia montanensis* (76, 84). For decades, *R. bellii* was characterized as a nonpathogenic organism; however, subcutaneous inoculation of this rickettsia produces eschars in rabbits and guinea pigs (16), suggesting that its role as a potential pathogen of humans deserves further consideration.

(ii) *Rickettsia canadensis*. *R. canadensis* was initially isolated from a pool of *Haemaphysalis leporispalustris* ticks collected from Ontario, Canada, in 1962 and subsequently from specimens of *Haemaphysalis leporispalustris* collected from California in 1980. Recent phylogenetic analyses suggest that *R. canadensis*, similarly to *R. bellii*, shares some characteristics with both the typhus group and the SFG rickettsiae and may closely resemble ancestral forms of the genus *Rickettsia* (121). *R. canadensis* elicits a febrile response in guinea pigs and produces rickettsemias of several days' duration in meadow mice and baby chicks. Human infections are suggested from several serologic studies of ill patients; however, no confirmed cases of the disease have been identified.

(iii) *Rickettsia montanensis*. *R. montanensis*, first described in 1961 in *Dermacentor* ticks collected in eastern Montana, is identified with various frequencies in *D. variabilis* and *D. andersoni* ticks throughout North America. Its occurrence in populations of *D. variabilis* ticks collected from 15 locations in 4 different provinces of Canada ranged from 0 to 33% (77). In many parts of the eastern United States, *R. montanensis* is the predominant rickettsial species detected in *D. variabilis* ticks (80). Approximately 10% to 17% of questing and attached specimens of *D. variabilis* collected from Florida, Georgia, and Tennessee contain this SFG rickettsia (78, 122). *R. montanensis* has also been reported occasionally in *A. americanum* ticks (78). There are no reports of confirmed disease in humans caused by *R. montanensis*; however, a recent description of a child with an afebrile, rash-associated illness and seroconversion to *R. montanensis* antigens following the bite of an *R. montanensis*-infected *D. variabilis* tick suggests that this SFG *Rickettsia* may cause a mild, spotted-fever-like illness in some patients (123).

(iv) *Rickettsia peacockii*. *R. peacockii*, an endosymbiont of *D. andersoni* ticks in the western United States and Canada, was likely recognized as early as 1925 but was not formally characterized until 1997. The infection frequency of *R. peacockii* in *D. andersoni* is often high: this SFG rickettsia was detected in 76% of 508 ticks collected from 9 localities in Canada (77) and in as many as 80% of *D. andersoni* ticks collected from the eastern side of the Bitterroot Valley of Montana. Also referred to as the East Side agent, *R. peacockii* occurs almost exclusively within the oocytes and interstitial cells of *D. andersoni* ticks, interfering with the ability of *R. rickettsii* to infect these tissues (124). It has been proposed that *R. rickettsii* or another closely related pathogenic SFG rickettsia underwent various changes in its genome to become *R. peacockii*. Potential virulence genes deleted or mutated in *R. peacockii* include those coding for an ankyrin repeat-containing protein, DsbA, RickA, protease II, OmpA, and a putative phosphoenolamine transferase (125, 126).

(v) *Rickettsia rhipicephali*. *R. rhipicephali* was first described in 1975 following its isolation from *Rhipicephalus sanguineus* ticks collected in Mississippi. It has been identified sporadically in *D. occidentalis*, *D. andersoni*, and *D. variabilis* ticks across the United States (76). The pathogenic potential of *R. rhipicephali* in humans is unknown but is suggested by the moderately severe disease elicited in experimentally inoculated meadow voles (66).

Nonvalidated, incompletely described, or uncultivated species. "*Candidatus* Rickettsia amblyommii" was first documented in 1981 and has since been identified as a commonly occurring and widely distributed SFG rickettsia in *A. americanum* ticks (127–129). "*Candidatus* Rickettsia amblyommii" produces a generalized infection in *A. americanum* that is distributed throughout multiple tissues, including the salivary glands, midgut, and ovaries (130). Contemporary surveys of questing adult *A. americanum* ticks collected from several states in the eastern United States reported average infection frequencies of 45% in Georgia, 66% in Maryland, 13% in New Jersey, 42% in New York, and 60% in North Carolina (131–134). Infections have also been detected commonly in larval-stage ticks (78, 127, 135, 136). "*Candidatus*

Rickettsia amblyommii" occurs in several other North American ticks, including *D. variabilis*, *A. maculatum*, and *A. cajennense* (78, 80, 97, 99, 104, 122, 137). In Central America, "*Candidatus* Rickettsia amblyommii" has been identified in *A. cajennense* ticks from Costa Rica and Panama (138, 139) and in *D. nitens*, *Amblyomma oblongoguttatum*, *Amblyomma ovale*, *Rhipicephalus* (*Boophilus*) *microplus*, and *Rhipicephalus sanguineus* ticks in Panama (72, 139, 140). "*Candidatus* Rickettsia amblyommii" has been implicated as a possible cause of mild or subclinical infection in humans in the United States (137, 141); however, neither guinea pigs, meadow voles, nor rabbits exhibit any evidence of disease when inoculated with this SFG rickettsia (130), and there is no evidence of direct detection of "*Candidatus* Rickettsia amblyommii" in human clinical specimens (142).

"*Candidatus* Rickettsia andeanae" was first documented in North America in 2010 in *A. maculatum* ticks collected in Florida and Mississippi (96). Since then, this SFG rickettsia has been identified throughout the U.S. range of *A. maculatum* ticks, occurring sympatrically with but typically at frequencies considerably lower than those of *R. parkeri* (98–101, 143). Coinfections of *A. maculatum* ticks with *R. parkeri* and "*Candidatus* Rickettsia andeanae" have been reported (100, 101). The pathogenic potential of "*Ca.* Rickettsia andeanae" is unknown; however, the recent isolation of this bacterium in cell culture should allow for a more detailed analysis including species characterization and a better understanding of its capacity to elicit disease in vertebrate hosts (144).

"*Candidatus* Rickettsia cooleyi" is commonly encountered in populations of *Ixodes scapularis* ticks across the United States (78, 104, 122). In some areas, it is detected in 90% to 100% of *I. scapularis* ticks (104, 145, 146), suggesting that this species is an endosymbiont. Other incompletely described SFG rickettsiae that have been detected in *I. scapularis* include *Rickettsia* sp. strain Is-1 (GenBank accession number DQ34462) and *Rickettsia* sp. strain TR-39 (accession number DQ480762) (122).

Two unique SFG phylotypes, designated G021 and G022, have been identified in *Ixodes pacificus* ticks collected in California (147). *Rickettsia* sp. G021 forms part of a clade that includes *Rickettsia akari*, *Rickettsia australis*, and the *I. scapularis* endosymbiont TX125 (GenBank accession number EF68975.1). *Rickettsia* sp. G022 appears to be closely related to several pathogenic SFG rickettsiae, including *R. sibirica* subsp. *sibirica*, *R. conorii*, and *R. parkeri*. It is possible that these phylotypes represent the previously described *Rickettsia* strains Tillamook and Grants Pass, which were isolated from *I. pacificus* ticks collected in Oregon and California during the late 1970s and early 1980s, respectively (2, 66). The Tillamook strain causes fever and scrotal swelling in guinea pigs and may be lethal to mice, suggesting that it may play a role as a human pathogen (108).

Rickettsia sp. strain Parumapertus is a SFG rickettsia that is similar to, but distinct from, *R. rickettsii*. It was initially detected in *D. parumapertus* ticks removed from jackrabbits in the Great Basin of the United States in the 1950s. Isolates of this strain no longer exist for genotypic analyses; however, earlier studies documented mild fever and scrotal swelling in guinea pigs inoculated with the agent, suggesting that it holds pathogenic potential for humans (66, 120). '"*Candidatus* Rickettsia" species from *A. tuberculatum* ' was described in 2012 in adult and larval-stage gopher tortoise ticks (*Amblyomma tuberculatum*) collected in Georgia, Florida, and Mississippi. The prevalence of infection among these specimens ranged from 50% to 100%. The pathogenic potential of the "*Candidatus* Rickettsia" species from *A. tuberculatum* in vertebrate hosts is unknown (148).

There are no confirmed reports of natural transmission of a pathogenic *Rickettsia* species to humans by an argasid tick. However, specimens of *Ornithodoros parkeri* and *Ornithodoros rostratus*, when infected experimentally with *R. rickettsii*, are capable of later transmitting the infection to susceptible animals, suggesting a possible role for soft ticks as vectors of one or more SFG rickettsiae. An uncharacterized SFG rickettsia (GenBank accession numbers AY763101 and AY63102), closely related to *Rickettsia peacockii* and *R. rickettsii*, has been detected recently in specimens of the argasid tick *Carios kelleyi* collected in Iowa (149). This SFG agent has not been isolated in culture, and its pathogenic potential is unknown.

South America

Species identified as pathogens. (i) *Rickettsia rickettsii*. *R. rickettsii* is the most important tick-borne zoonotic agent in South America (Fig. 6), where it was first reported in Brazil during the 1920s. Although RMSF is the typical name of the disease caused by *R. rickettsii*, in Brazil, it has been referred to as Brazilian spotted fever since the first half of the past century (150, 151). Human cases of RMSF have also been reported in Argentina and Colombia (152, 153). In Colombia, the disease was first reported as a large outbreak during the 1930s, when 62 (95%) out of 65 affected people succumbed to the infection. Thereafter, it remained unreported for more than 65 years, followed by recent outbreaks during the last 6 years in different parts of Colombia (154). Therefore, it is possible that RMSF remains unreported in other South American countries where diagnostic tools are absent and where the disease is clinically misdiagnosed as several other acute hemorrhagic diseases. Similarly, the clinical illness caused by *R. rickettsii* in domestic dogs may often remain unreported in many parts of South America. Although North American studies have shown for decades that *R. rickettsii* is also pathogenic in dogs, the occurrence of RMSF in dogs was only recently reported in Brazil (155).

General symptoms caused by *R. rickettsii* in South America are similar to those in the United States. Severe clinical manifestations seem to be more frequently reported, usually associated with a higher case-fatality rate, and include jaundice, central nervous system impairment, respiratory distress, and acute renal insufficiency (150, 151). While the general case-fatality rate is currently approximately 20 to 40% (150, 156), the rate may reach 80% in a few areas where diagnostic suspicion and specific antibiotic therapy are delayed (157). Indeed, the higher incidences of other hemorrhagic manifestations endemic to South American countries, such as dengue, leptospirosis, and meningitis, are associated with the lack of diagnostic tools for spotted fever rickettsiosis. This may result in late diagnostic suspicion of rickettsiosis and, consequently, in more severe advanced cases that rapidly cause fatalities (150).

The main vector of *R. rickettsii* in Argentina, Brazil, and Colombia is *A. cajennense*, which is generally the tick that bites humans most frequently in South America (158). Frequently, humans are infested by dozens to hundreds of *A. cajennense* specimens in areas where RMSF is endemic; however, the disease has always had a low incidence, which is related to the low *R. rickettsii* infection rates among ticks under natural conditions, usually ≤1% (159). These low rates may be related to the low ability of *A. cajennense* to sustain *R. rickettsii* infection through

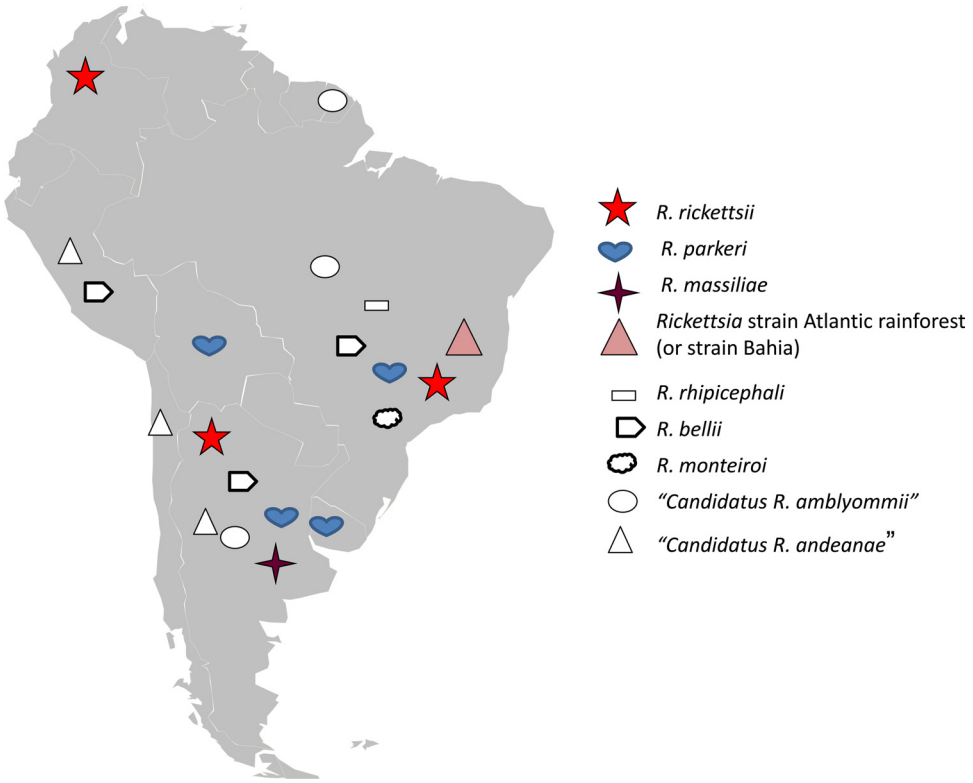

FIG 6 Tick-borne rickettsiae in South America. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

successive generations. One study in Brazil demonstrated that both transstadial and transovarial transmissions of *R. rickettsii* occurred in <50% of infected ticks, in addition to the observed lower reproductive performance of infected female ticks than of uninfected ticks (27). Therefore, it is believed that such areas where RMSF is endemic are highly dependent on the availability of amplifier vertebrate hosts, which are animals that maintain the bacterium in their circulating blood for some days or weeks at levels sufficient to infect new tick cohorts, amplifying rickettsial infection among the tick population. The systematic presence of amplifier hosts would guarantee the establishment of this bacterium in the tick population for successive generations (159). In Brazil, at least two wild vertebrate species, capybaras (*Hydrochoerus hydrochaeris*) and opossums (*Didelphis aurita*), were recently shown to behave as competent amplifier hosts for *A. cajennense* (39, 40).

In a few areas of southeastern Brazil, the tick *Amblyomma aureolatum* replaces *A. cajennense* as the primary vector of *R. rickettsii* (160–162). Interestingly, the transstadial and transovarial transmission rates of *R. rickettsii* in *A. aureolatum* ticks reach 100%. However, because *R. rickettsii* is partially pathogenic for engorged females of this species, tick infection rates under natural conditions are low, approximately 1% (29, 160). In addition, because *A. aureolatum* rarely attacks humans, the incidence of RMSF is also low in these specific areas of endemicity in southeastern Brazil (163). Finally, a number of recent studies from Brazil reported *R. rickettsii* infecting *Rhipicephalus sanguineus* ticks collected from dogs in areas where RMSF is endemic, where dogs are frequently infested by *A. aureolatum* or *A. cajennense* ticks (28, 162, 164–166), and reports have also come from an area where RMSF is not endemic (167). As it has been shown that *R. rickettsii* is maintained by transstadial and transovarial transmission in Brazilian *Rhipicephalus sanguineus* ticks (26, 28) and that the domestic dog is an efficient amplifier host of *R. rickettsii* in *Rhipicephalus sanguineus* ticks (26), studies are needed to elucidate the participation of this tick species in the epidemiology of RMSF in South America. Fortunately, *Rhipicephalus sanguineus* is not considered to be an important human-biting tick in South America (158), which may minimize its role as a primary vector of RMSF in humans.

(ii) *Rickettsia parkeri*. In 2004, *R. parkeri* was reported to infect *Amblyomma triste* ticks in Uruguay (168), at the time when this rickettsia was first confirmed to be a human pathogen in the United States (see above). Several years later, *R. parkeri* was found to infect *A. triste* ticks in Brazil (169) and Argentina (170). Finally, in 2011, Romer et al. reported the first human cases of spotted fever caused by *R. parkeri* in Argentina, which were characterized by fever, rash, inoculation eschar, lymphadenopathy, and no deaths, similar to the clinical illness caused by *R. parkeri* in the United States (68, 171). Similar clinical manifestations, also associated with *A. triste*, have been reported since the 1990s in Uruguay, where at least two of these cases were attributed to *R. parkeri* through cross-absorption (CA) serologic tests (172).

(iii) *Rickettsia massiliae*. In 2004, *R. massiliae* was reported to infect *Rhipicephalus sanguineus* ticks in Buenos Aires, Argentina (173). Several years later, a patient in Spain was diagnosed with an acute spotted fever illness characterized by fever, a palpable purpuric rash on the upper and lower extremities, and an eschar on

the right leg. Molecular analyses confirmed that the spotted fever illness was caused by *R. massiliae* (174). Because this patient had just arrived from Buenos Aires, it was concluded that she had become infected in Argentina, confirming the first case of rickettsiosis caused by *R. massiliae* in South America. Recent studies have shown that the *Rhipicephalus sanguineus* populations from the southern portion of South America are genetically derived from the Mediterranean area (175, 176), where *R. massiliae* has been reported to infect ticks and humans (177). Therefore, it is possible that the distribution of *R. massiliae* in the southern portion of South America is much broader than is currently appreciated.

(iv) *Rickettsia* sp. strain Atlantic rainforest or strain Bahia. Recently, two cases of spotted fever clinically similar to the disease caused by *R. parkeri* were reported in Brazil. However, both cases were confirmed to be caused by a newly recognized SFG rickettsia, strain Atlantic rainforest or strain Bahia, very closely related to *R. parkeri*, *R. africae*, and *R. sibirica* (178, 179). At the same time, the Atlantic rainforest strain was shown to be associated primarily with *Amblyomma ovale* ticks, the presumed vector of transmission to humans (180). In addition, *A. aureolatum* and *Rhipicephalus sanguineus* ticks were also found to be infected by this novel bacterial strain in the same areas as *Rickettsia*-infected *A. ovale* ticks (180, 181). It is possible that the occurrence of spotted fever caused by the Atlantic rainforest strain is much broader than is currently known, as the symptoms of this disease are compatible with the descriptions of clinical illnesses that have been confirmed following seroconversion to spotted fever rickettsial antigens that have been reported in other areas of Brazil, where the agent was found to infect human-biting ticks, namely, *A. ovale* and *A. aureolatum* (151, 181).

Species of unknown pathogenicity. (i) *Rickettsia rhipicephali*. *R. rhipicephali* has been reported to infect the tick *Haemaphysalis juxtakochi* in southeastern and northern Brazil (182, 183). There is serological evidence of canine infection by *R. rhipicephali* in northern Brazil, but the pathogenic role of this infection remains unknown (184).

(ii) *Rickettsia bellii*. Despite having been reported in the United States for more than 50 years, *R. bellii* was first reported in South America in 2004, followed by a number of reports on different tick species. In Brazil, *R. bellii* has been reported to infect 11 tick species, namely, *A. ovale*, *A. oblongoguttatum*, *A. scalpturatum*, *A. humerale*, *A. rotundatum*, *A. aureolatum*, *A. dubitatum*, *Amblyomma incisum*, *A. nodosum*, *Ixodes loricatus*, and *Haemaphysalis juxtakochi*. It was also reported to infect *A. neumanni* and *A. tigrinum* in Argentina and *A. varium* in Peru, totaling 14 tick species for the continent (185, 186). While *R. bellii* has never been associated with human disease, there is serological evidence of animal infection in Brazil (187).

(iii) *Rickettsia monteiroi*. *R. monteiroi* was recently described as having infected the tick *A. incisum* in an Atlantic rainforest reserve in southeastern Brazil (188). *R. monteiroi* is genetically related to the North American species *R. canadensis*, and because *A. incisum* is an important human-biting tick in the Atlantic rainforest biome of southeastern Brazil, the pathogenic role of this rickettsia deserves further investigation.

Nonvalidated, incompletely described, or uncultivated species. "*Candidatus* Rickettsia amblyommii" was reported to infect the tick species *A. cajennense*, *Amblyomma coelebs*, *Amblyomma longirostre*, *Amblyomma geayi*, and *Amblyomma auricularium* in Brazil (32, 189, 190); *Amblyomma neumanni* in Argentina (185); and *A. coelebs* in French Guyana (191). In addition, strains Aranha and AL, which are genetically closely related to "*Candidatus* Rickettsia amblyommii," have been reported to infect *A. longirostre* ticks in Brazil (189, 190, 192). "*Candidatus* Rickettsia amblyommii" was shown to be successfully maintained by transstadial and transovarial transmissions through successive generations in *A. auricularium* ticks, which were able to transmit the bacterium to laboratory rabbits through larval, nymphal, and adult feeding; however, these infections were always asymptomatic (32). Under natural conditions, there is serological evidence of canine infection by "*Candidatus* Rickettsia amblyommii" in Brazil (184, 193); however, there is no evidence that "*Candidatus* Rickettsia amblyommii" is pathogenic for humans or animals.

"*Candidatus* Rickettsia andeanae" was first documented in South America in 2004 in *A. maculatum* and *Ixodes boliviensis* ticks in Peru (194). Several years later, this rickettsia was reported as *Rickettsia* sp. strain Argentina, from *Amblyomma parvum* and *Amblyomma pseudoconcolor* ticks in Argentina (195, 196). More recently, "*Candidatus* Rickettsia andeanae" was reported from an *A. triste* specimen in northern Chile (197). The pathogenic potential of "*Candidatus* Rickettsia andeanae" is unknown.

Three distinct rickettsial strains (COOPERI, NOD, and ApPR) have been reported from different *Amblyomma* ticks in Brazil (162, 198–200). Indeed, these strains are regarded as potential pathogens because they are phylogenetically related to the pathogens *R. parkeri*, *R. africae*, *R. sibirica*, and the Atlantic rainforest strain (200). Further studies are necessary to elucidate their taxonomic status because their genetic relatedness to *R. parkeri*, *R. africae*, and *R. sibirica* could justify a subspecies designation.

The Pampulha strain, recently reported in *A. dubitatum* ticks in Brazil (201–203), and the Colombianensi strain, reported in *Amblyomma dissimile* and *Rhipicephalus* (*Boophilus*) *microplus* ticks in Colombia (204), are two distinct strains that are closely related to the Old World species *Rickettsia tamurae* and *Rickettsia monacensis*. In Brazil, only a few populations of *A. dubitatum* have been found to be infected by the Pampulha strain; however, infection rates are usually very high among the infected populations (203). The pathogenic role of these two South American strains is unknown. Finally, an *R. aeschlimannii*-like strain was reported in the tick *A. tigrinum* in Bolivia (205). Because *R. aeschlimannii* has been reported only in the Old World, further studies are needed to elucidate the taxonomic status of this *R. aeschlimannii*-like strain from Bolivia.

TICK-BORNE RICKETTSIAE IN EUROPE

Species Identified as Pathogens

***Rickettsia conorii* subsp. *conorii*.** *Rickettsia conorii* subsp. *conorii* is the agent responsible for Mediterranean spotted fever (MSF), one of the oldest-recognized vector-borne infectious diseases (2). MSF is endemic in southern Europe, but sporadic cases have been reported in northern and central Europe, sometimes followed by the installation of a local focus of the disease (2). *Rhipicephalus sanguineus* is the vector and a potential reservoir of *R. conorii* subsp. *conorii* in the Mediterranean area (Fig. 2 and 7) (206). However, the excellent fitness of an *R. conorii*-infected tick laboratory colony contrasts with the low prevalence of infected *Rhipicephalus sanguineus* ticks collected in the wild (<1%), even in regions of endemicity such as Southern Europe, with the exception of small foci (25, 177, 207, 208). The influence of extrinsic

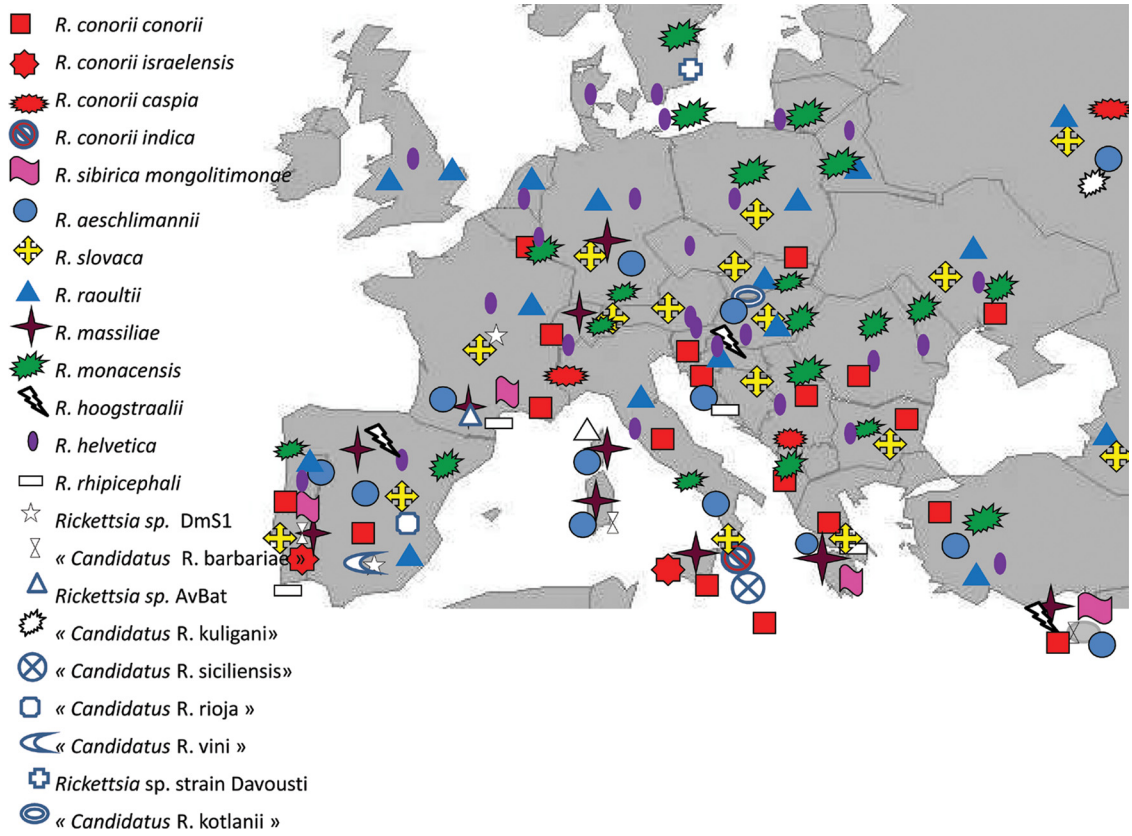

FIG 7 Tick-borne rickettsiae in Europe. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

factors on infections in diapaused *Rhipicephalus sanguineus* ticks has been suggested, and infected quiescent ticks may not survive the winter (25). Vertebrate reservoirs may play a more dominant role in the ecology of *R. conorii* subsp. *conorii* than was previously appreciated (206). The presence of *R. conorii* subsp. *conorii* DNA was reported in blood samples from ill dogs (209, 210). A high seroprevalence rate (15 to 72%) in dogs has been reported in a region where MSF is endemic (211). The proximity to seroreactive dogs has been reported as a risk factor for MSF in humans (210). In addition, hedgehogs were suggested to be a potential reservoir for *R. conorii* subsp. *conorii* (212). However, the animal reservoir of *R. conorii* subsp. *conorii* was never conclusively demonstrated (37, 206), and further studies need to be performed.

In Europe, most MSF cases occur in the summer (2, 213–215). The MSF incidence may increase with higher temperatures, lower rainfall, and a decrease in the number of days of frost during the preceding year (177, 216, 217). Particularly, this higher incidence during warmer months seems to be related to a warming-mediated increase in the aggressiveness of *R. sanguineus* ticks to bite humans (177).

Since 2005, in addition to 14 European countries (2), *R. conorii* was detected in Serbia (218), Romania (219), Slovakia (220), and Malta (221) by serological methods. The seroprevalences of *R. conorii* infection were 3.9% in Italy (222), 4.4% in the Canary Islands (Spain) (223), 8.7 to 11.2% in Spain (224, 225), and up to 23% in the Serbian mountain areas (218). Urban populations are as affected as rural populations, regardless of gender (213).

After an incubation period of approximately 6 days, the onset of MSF is abrupt. Recent studies (213, 226, 227) have confirmed that this disease is characterized by fever (94 to 100%), flu-like symptoms (78%), prostration (64%), an eschar at the tick bite site (53 to 77%), and a rash spreading to the palms and soles (87 to 96%) that is either maculopapular (94%) or petechial (6%) (Fig. 8). In an Italian study of 415 children with MSF, fever, rash, and eschar were present in 93%, 94.5%, and 63.4% of cases, respectively, and 4.6% of the children presented atypical exanthema (petechial, purpuric, papulovesicular, and vesicular) (228). Multiple eschars (177, 213, 228–230) and clusters of MSF cases (177) have been reported, which are novel findings for MSF because the probability of being bitten simultaneously by several infected *Rhipicephalus sanguineus* ticks is considered rare (177). These emerging findings have been linked to the increased aggressiveness and propensity of *Rhipicephalus sanguineus* to bite hosts under warmer conditions, as was shown in animal and human models (177).

In recent years, atypical and serious life-threatening presentations of MSF in Mediterranean countries were reported, with cardiac symptoms (ectasia of the coronary arteries, myocarditis, and atrial fibrillation) (231–233), ocular symptoms (uveitis, retinopathy, and retinal vasculitis) (177, 234–236), neurological symptoms (cerebral infarct, meningoencephalitis, sensorineural hearing loss, acute quadriplegia secondary to an axonal polyneuropathy, and motor and sensory polyneuritis) (228, 236–241), pancreatic involvements (242, 243), splenic rupture (244), acute

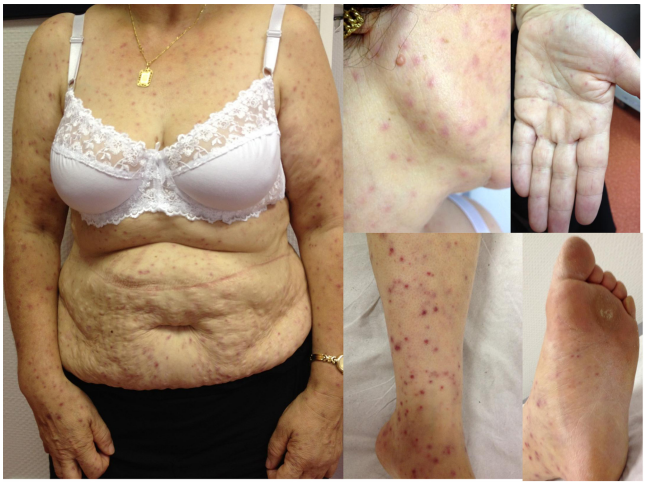

FIG 8 Generalized maculopapular rash including face, palms, and soles on a patient with Mediterranean spotted fever caused by *R. conorii* subsp. *conorii*.

renal failure (245), and the presence of hemophagocytic syndrome (246). In addition to the classical risk factors for malignant MSF (advanced age, immunocompromised situations, chronic alcoholism, glucose-6-phosphate dehydrogenase [G6PD] deficiency, prior prescription of an inappropriate antibiotic, and delay of treatment) (209), alcoholism was definitively confirmed as a risk factor (218), and fluoroquinolone treatment was shown to be associated with increased MSF disease severity and longer hospital stays (238). In a study of Italian children, hospitalization was significantly longer in the group treated with chloramphenicol than in the group treated with clarithromycin (228). Recently, the mortality rate in Portugal reached 13% (9/71) of patients with MSF, including many patients with confusion and obtundation (67%), and a multivariate analysis revealed the following independent predictors associated with fatal outcome: hyperbilirubinemia, acute renal failure, and the absence of rash (226). Other fatal cases were reported in France, Greece, Bulgaria, and Turkey (213, 229, 240, 247).

***Rickettsia conorii* subsp. *israelensis*.** *Rickettsia conorii* subsp. *israelensis* is the agent of Israeli spotted fever (ISF), which was first reported in 1946 in Israel (2). *R. conorii* subsp. *israelensis* was shown to be successfully transmitted transstadially in *Rhipicephalus sanguineus* from nymphs to adults (38). However, the vertical transmission of this bacterium in its host ticks has not yet been demonstrated. Dogs have been suggested to be a competent reservoir of *R. conorii* subsp. *israelensis* (221, 248). Recently, *R. conorii* subsp. *israelensis* DNA was detected in blood samples that were recovered from two clinically ill dogs in Portugal within 48 h of doxycycline administration (209).

In Europe, *R. conorii* subsp. *israelensis* was detected in *Rhipicephalus sanguineus* specimens collected in Sicily and in different regions of Portugal where several clinical cases related to ISF were described (249, 250). The clinical manifestations of ISF are similar to those of MSF. However, a history of tick exposure is reported in 32% of cases, an inoculation eschar is rarely observed (38%), and significantly greater gastrointestinal manifestations, such as nausea (63%) and vomiting (56%), are observed (226). In Portugal, the 29% case-fatality rate among 69 ISF patients suggests that the ISF strain is more virulent than the Malish strain (226). Other fatal cases and severe forms of ISF have been described, especially in children as well as in travelers and those with G6PD deficiency (251–253).

***Rickettsia conorii* subsp. *caspia*.** *Rickettsia conorii* subsp. *caspia* is the agent of Astrakhan fever, a summer spotted fever endemic to the Astrakhan region and nearby regions of the Caspian Sea (2). It is transmitted to humans through the bites of *Rhipicephalus pumilio* ticks. In Europe, this rickettsia was detected in *R. sanguineus* ticks from Kosovo and, recently, from Southern France (2, 254). Thus, Astrakhan fever might be a cause of spotted fever in Europe, and the area of distribution of this *Rickettsia* could be broader than the limits of the Astrakhan region, as was initially believed. In recent years, the increased incidence of Astrakhan fever in Russia is explained by the reconfiguration of natural landscapes as a result of increasing anthropogenic impact (255). Clinically, Astrakhan fever is similar to MSF, but an inoculation eschar is present in only 23% of patients (2). Recently, in a study of 89 Astrakhan fever patients in Russia, maculopapular rash was described for 91% of them, solitary elements of which were transformed into petechiae in 20% of cases. At convalescence (on day 10.2 ± 1.3 of the disease), all eruptions had regressed, as measured by pigmentation (256). At the peak of the fever, there were nasal hemorrhages and bleeding at the injection sites from medication; lowered platelet aggregation was also detected in the presence of thrombocytopenia at the height of the fever (256). To date, no autochthonous cases have been confirmed in other European countries. However, *R. conorii* subsp. *caspia*, detected in 9 of 22 ticks in southern France, was associated with a cluster of cases of SFG rickettsioses that were not identified to the species level (254).

***Rickettsia conorii* subsp. *indica*.** *Rickettsia conorii* subsp. *indica* is the agent of Indian tick typhus, prevalent in India and Pakistan. *R. sanguineus* ticks are considered to be the main vectors. In 2012, the first human case in Europe was reported in Sicily by using molecular tools for detection (257). This patient had not traveled but presented with MSF symptoms, with the presence of an inoculation eschar on the right arm. To date, there are no reports of the detection of this bacterium in ticks collected in European countries.

***Rickettsia massiliae*.** The SFG rickettsia *R. massiliae* was isolated from *R. sanguineus* ticks collected near Marseille, France, in 1992 and then detected in *R. sanguineus*, *Rhipicephalus turanicus*, *Rhipicephalus pusillus*, *Rhipicephalus bursa*, and *Ixodes ricinus* ticks in 8 European countries, including 5 islands: Sardinia and Sicily (Italy), the Canary Islands (Spain), Cephalonia (Greece), and Cyprus (258–263). Dual infections were reported recently in *Rhipicephalus* ticks: *R. massiliae* with *Coxiella burnetii* in Greece and Serbia (264, 265) and *R. massiliae* with *R. conorii* subsp. *caspia* in France (254). *R. massiliae*-infected ticks were collected from animal hosts such as house sparrows, dogs, horses, cats, asymptomatic humans (259, 266), hedgehogs (260), red foxes (261), hares, and goats (258). The reported infection rate of ticks in the wild ranges from 2% to 92% (254, 260). The introduction of *R. massiliae* to the Canary Islands was suggested to have resulted from the translocation of infected *R. pusillus* ticks or from infected wild rabbits migrating from the Iberian Peninsula 600 years ago, the latter of which most likely serves as a natural reservoir host for the pathogen (262). However, no rickettsial DNA was detected in the 150 wild rabbits tested.

In addition to the first Italian human case of *R. massiliae* infection (2), a second case was diagnosed by using serological and

molecular tools in a patient with MSF signs, with complications of acute visual loss and bilateral chorioretinitis. The clinical course was favorable, but 3 months later, the recovery of visual acuity was incomplete (177). The entomological investigation of the house where this patient had been bitten by ticks revealed that 10% of the ticks in the house were infected with a new genotype of *R. massiliae*. Recently, a Polish study (267) showed the presence of specific SFG rickettsial antibodies in 15% of forest workers; among these workers, 79% had species-specific antibodies to *R. massiliae*. These results need to be carefully interpreted because current serological tools cannot precisely determine the exact *Rickettsia* species involved (2).

***Rickettsia sibirica* subsp. *mongolitimonae*.** *Rickettsia sibirica* subsp. *mongolitimonae* causes LAR (lymphangitis-associated rickettsiosis) and was first isolated in Beijing, People's Republic of China, from *Hyalomma asiaticum* ticks collected in Inner Mongolia in 1991 (2). In Europe, *R. sibirica* subsp. *mongolitimonae* was detected in *Hyalomma anatolicum excavatum* ticks (5%) in Greece and Cyprus; in *R. pusillus* ticks (4 to 8%) in France, Portugal, and Spain; and in *R. bursa* ticks (4%) in Spain (258, 263, 268–270).

In addition to the LAR cases reported in France and Greece prior to 2005 (2), two autochthonous cases were reported in Portugal (270, 271), nine were reported in Spain (272–275), and four were reported in France, including a cluster of three cases in the same family (268, 276). To date, a total of 24 cases have been reported in four European countries situated in the Mediterranean region. Most of the cases reported in France and Spain occurred in the spring (11 cases; 46%) and summer, together with one from Portugal (9 cases; 38%), likely corresponding to the abundance and activity of these two tick species (277, 278). Interestingly, a history of tick bites was reported in only 41% (7 cases) of patients. Patients with LAR presented a broad spectrum of clinical syndromes with different degrees of severity. No fatal disease was observed, but complications such as acute renal failure, retinal vasculitis, and lethargy with hyponatriemia have been noted (269, 275, 276). Typical clinical signs, such as fever (100%), headache (86%), myalgia (90%), cutaneous rash (77%), enlarged lymph nodes (71%) and/or lymphangitis (43%), and single or multiple inoculation eschars (92%), in the spring months in the Mediterranean area should guide physicians toward accurate diagnoses of this disease.

***Rickettsia slovaca* and *Rickettsia raoultii*.** *Rickettsia slovaca* and *Rickettsia raoultii* are associated with a syndrome characterized by scalp eschars and neck lymphadenopathy following tick bites, and the term "SENLAT" was proposed for this clinical entity in 2010 (279). Initially, this syndrome was named TIBOLA (tick-borne lymphadenopathy) or DEBONEL (*Dermacentor*-borne necrotic erythema and lymphadenopathy) (Fig. 9). These bacteria have been found in *Dermacentor marginatus* and *Dermacentor reticulatus* ticks in a great majority of European countries, with a high percentage of ticks infected with these bacteria (208, 280–290). *Dermacentor* ticks usually bite hairy domestic and wild animals (291). In a recent study in Spain, the seroprevalences of *R. slovaca* in domestic ruminants were reported to be 16% in sheep, 21% in goats, and 65% in bullfighting cattle. In addition, *R. slovaca* DNA was detected in a goat blood sample, suggesting that *R. slovaca* may be circulating in domestic ruminants (42).

SENLAT occurs most frequently during March to May and September to November, which correspond to the periods of greatest activity of *Dermacentor* adult ticks in Europe (292, 293).

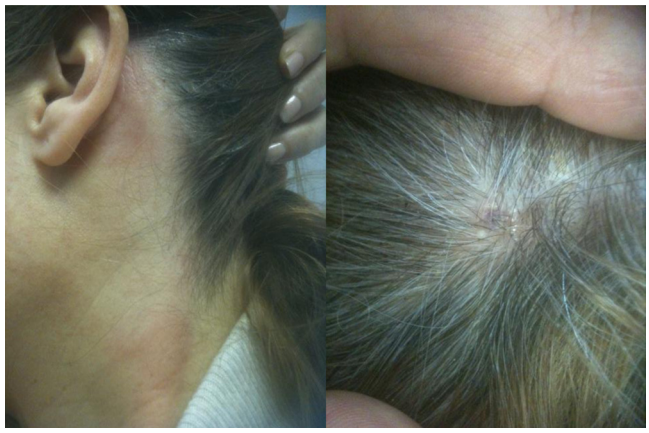

FIG 9 Enlarged cervical lymph nodes (left) and inoculation eschar of the scalp (right) in a patient with *Rickettsia slovaca* infection.

Human infection with *R. slovaca* has been described in France, Slovakia, Italy, Germany, Hungary, Spain, and Poland (292, 294). Infection is most frequent in women (67 to 100%) and children <12 years old (41 to 43%). The median incubation period is 5 to 10 days (range, 1 to 15 days) (293, 295). The clinical description of *R. slovaca* infection includes asthenia (70%); headache (53%); painful adenopathies (69 to 100%); a painful scalp eschar surrounded by a perilesional erythematous halo (64%); and sometimes low fever (36 to 54%), rash (5%), and face edema (291, 292). Antibiotic treatment is successful; however, around the eschar, alopecia (59%) that lasts for several months as well as prolonged (35%) or chronic asthenia (14%) often occur (292). To date, patients with *R. raoultii* infections have been reported in France, Slovakia, and Poland (292, 294, 296), and these patients presented with clinical signs similar to those listed above, except for alopecia. In the Polish case of *R. raoultii* infection, the multiple disseminated small lesions had slightly elevated necrotic centers surrounded by a red area, whereas the single lesions had a vesicular appearance (296).

***Rickettsia monacensis*.** *Rickettsia monacensis* was detected in *I. ricinus* ticks in Spain, Portugal, Italy (including Sardinia), Turkey, Switzerland, Luxembourg, Germany (including Greifswalder Oie Island), Sweden, Slovakia, Albania, Hungary, Bulgaria, Moldova, Ukraine, Serbia, northwestern Russia (Kaliningrad), Belarus, and Poland (208, 280, 283, 289, 297–301). The prevalence of *R. monacensis* in ticks varied between 1% in Germany, 15% in Serbia, 35% Turkey, and 57% in Italy (299, 302). Recently, the DNA of *R. monacensis* was detected in lizard tissue (7%) and in their *I. ricinus* ticks (41%) on Madeira Island (Portugal) (303). Those authors suggested that lizards may be a potential or transitory reservoir for *R. monacensis*.

In 2005, *R. monacensis* was identified as a human pathogen in two patients in Spain (June and September) and in one patient in Sardinia, Italy (April), by using molecular tools (297, 298). A rickettsial strain was isolated from blood samples of Spanish patients by shell vial culture (298). In addition to fever and flu-like symptoms, the inoculation eschar was identified in only one Italian patient (left calf), but a generalized rash including the palms and soles was identified only in Spanish patients. The patients recovered without sequelae following doxycycline treatment.

***Rickettsia aeschlimannii*.** *Rickettsia aeschlimannii* was detected

in *Hyalomma marginatum marginatum* and *Hyalomma marginatum rufipes* ticks in Croatia, Spain, southern France (including Corsica), Portugal, Italy (including Sardinia and Pianosa), Russia, Cyprus, Germany, Turkey, Hungary, and the Greek island of Cephalonia (258, 299, 304–308). This rickettsia may be spread through migratory birds from Africa (308, 309). It was detected in *Hyalomma* ticks collected from several bird species, such as *Acrocephalus schoenbaenus* and *Hirondo rustica* in Corsica (2) and *Luscinia megarhynchos* and *Acrocephalus scirpaceus* in southern France and, in the latter species, in Germany (259, 304). The first human infection caused by *R. aeschlimannii* was reported for a French patient who became ill after returning from Morocco. This patient exhibited symptoms similar to those of MSF. To date, no autochthonous cases of this infection have been reported in Europe (2).

Rickettsia helvetica. *R. helvetica* is transmitted by *I. ricinus*, a sheep tick, which is the main vector and the natural reservoir (2). To date, *R. helvetica* has been detected in *I. ricinus* ticks in at least 24 European countries. In Denmark, the highest infection rate of *R. helvetica* in *I. ricinus* ticks is found in May, followed by July, August, and October (310). In addition, *R. helvetica* was detected in 8% of *Ixodes hexagonus* ticks, hedgehog ticks, in Germany (311); in 44% of larvae and 25% of nymphs of *I. arboricola* that were collected from wild birds in the Czech Republic (312); and in 10% of *D. reticulatus* ticks in Croatia (287). The DNA of *R. helvetica* was detected in hedgehog tissue samples in Germany (311), in lizard tissue on Madeira Island (Portugal) (303), and in whole blood from mice, deer, and wild boar in the Netherlands (311), suggesting that vertebrate hosts play important roles in the geographical dispersion of rickettsiae. The few patients for whom serology-based diagnoses exist had relatively mild, self-limited illnesses associated with headache and myalgias and less frequently with rash and/or an eschar (2). Human infection with *R. helvetica* documented by serology-based diagnoses and sometimes by molecular tools was described only in Austria, France, Italy, Denmark, Switzerland, and Slovakia (2, 294, 313). However, since 2005, no definitive, convincing cases have been published. In particular, recent reports by the same team remain dubious (313–316).

Rickettsia sibirica* subsp. *sibirica. *Rickettsia sibirica* subsp. *sibirica*, responsible for Siberian tick typhus (STT) in Asia (see below), was amplified recently in an *I. ricinus* larva collected from Eurasian blackcaps (*Sylvia atricapilla*) in Spain (317). Those authors suggested that birds play a significant role in the spread of rickettsial agents via infected arthropods.

Species of Unknown Pathogenicity

R. rhipicephali was detected and isolated from *R. sanguineus* ticks collected from dogs in 1975 in Mississippi (2). In Europe, this rickettsia was detected in this tick species collected from France, Portugal, Greece (including the Island of Cephalonia), and Croatia (2, 264). The intradermal injection of *R. rhipicephali* in guinea pigs induced the formation of an inoculation eschar at the infection site, suggesting that this rickettsial species is a potential human pathogen (45). In addition, *R. rhipicephali* induced mononuclear cell inflammation at the site of inoculation, characterized mainly by macrophages and lymphocytes, similarly to *R. conorii* subsp. *conorii*.

In the last 7 years, two *Rickettsia* species within the SFG were isolated: *Rickettsia hoogstraalii* from *Haemaphysalis sulcata* ticks collected from sheep and goats in Croatia, which are closely related to *R. felis* (5), and *Rickettsia* genotype AvBAT from *Argas vespertilionis*, soft bat ticks, collected from southern France (318). In addition, *R. hoogstraalii* was detected in 30% of the *Haemaphysalis punctata* ticks collected in Cyprus (258) and in 3% of *H. punctata* and 16% of *H. sulcata* ticks from Spain (319).

Nonvalidated, Incompletely Described, or Uncultivated Species

Fifteen rickettsial genotypes were detected only by molecular tools in ticks collected in Europe. "*Candidatus* Rickettsia tarasevichiae" was identified in *Ixodes persulcatus* ticks with a high prevalence in Russia (320). This tick replaces *I. ricinus* in northern Russia and Finland (321). "*Candidatus* Rickettsia *barbariae*" was detected in *R. turanicus* and *R. sanguineus* ticks from Portugal, Italy (Sardinia), France, and Cyprus (258, 259, 306). In a study from Cyprus, a new genotype of "*Candidatus* Rickettsia barbariae" was designated "*Candidatus* Rickettsia barbariae" Cretocypriensis (258). "*Candidatus* Rickettsia kulagini" (GenBank accession number DQ365806) was detected in *R. sanguineus* ticks collected from the Crimean Peninsula, Ukraine, and a new *Rickettsia* sp. was detected in *Rhipicephalus turanicus* ticks from Cyprus which is closely related to but distinct from the *R. rhipicephali-R. massiliae* lineage (258). "*Candidatus* Rickettsia siciliensis" was detected in a *R. turanicus* tick that was removed from an asymptomatic 22-month-old female in Sicily (322). "*Candidatus* Rickettsia vini" was proposed as a new *Rickettsia* sp. detected in *I. arboricola* and *I. ricinus* ticks collected from three different bird species in Spain (317). *Rickettsia* sp. strain Davousti, previously found in *Amblyomma tholloni* ticks in Africa, was detected in *Ixodes* species ticks collected from migratory birds in Sweden (323). Furthermore, a sequence with high homology to that of "*Rickettsia limoniae*" was detected in *I. ricinus* ticks from the Italian Alpine zone (324). *Rickettsia* sp. strain DmS1 was detected in *D. marginatus* ticks in France and Spain, and 80% of ticks of this species were positive at the fifth generation of a laboratory-maintained infected colony, attesting to the tick reservoir in the wild (208, 325). "*Candidatus* Rickettsia rioja" was detected in *D. marginatus* ticks collected from patients with SENLAT syndrome in Spain and France (326, 327). A novel *Rickettsia* sp. strain (a sister taxon of *R. bellii*) was detected in *I. ricinus* ticks collected from common nightingales (*Luscinia megarhynchos*) in the Czech Republic (328). "*Candidatus* Rickettsia kotlanii" was detected in ixodid ticks collected from Hungary (329). "*Candidatus* Rickettsia moreli" (GenBank accession numbers Y08784 and Y08785) was detected in *I. ricinus* ticks from Spain; *Rickettsia* sp. strain IXLI1, which was detected in *I. lividus* ticks in the United Kingdom, is closely related to *R. japonica* (330); and *Rickettsia* sp. clone KVH-02-3H7 (GenBank accession number GQ849216) was detected in *I. ricinus* ticks in the Netherlands.

In the last few years, several pathogenic rickettsial species were detected in unusual tick vectors, such as *R. australis*, *R. typhi*, *R. prowazekii*, and 4 other uncharacterized *Rickettsia* spp. related to the typhus group in *I. ricinus* ticks that were collected in the Netherlands (311, 331). Another such example is *R. helvetica* in *D. reticulatus* ticks in Croatia (287). Thus, interpreting the rickettsial data is sometimes difficult, and presenting these findings as new or pathogenic rickettsiae should be performed with prudence (332).

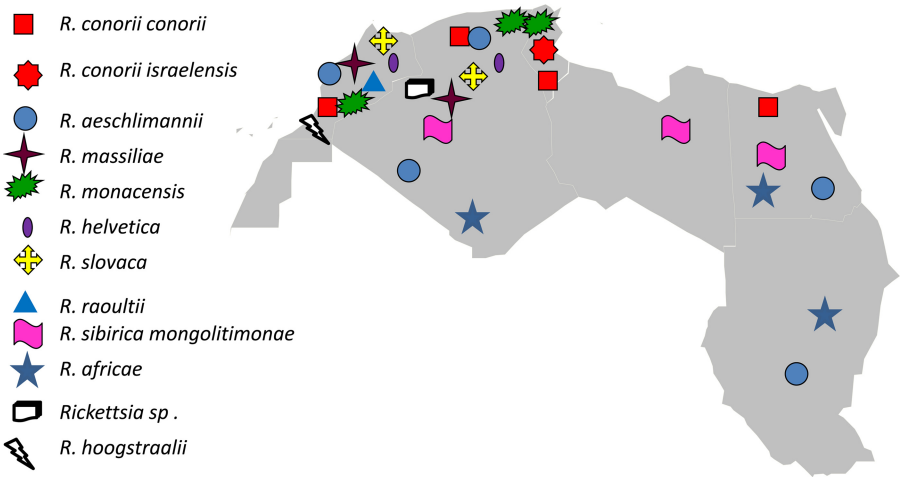

FIG 10 Tick-borne rickettsiae in North Africa. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

TICK-BORNE RICKETTSIAE IN AFRICA

North Africa

North Africa is defined by the United Nations as the northernmost region of the African continent, including eight countries: Algeria, Egypt, Libya, Morocco, South Sudan, Sudan, Tunisia, and Western Sahara (Fig. 10). Despite pioneering work conducted in Tunisia at the beginning of the 20th century, there was an absence of rickettsiosis investigations in North Africa after the 1930s (333). However, thanks to clinicians and entomologists in Oran and Algiers, respectively, 16 new tick-transmitted rickettsiae have been described over the last 25 years, including 8 recognized pathogens (333).

Species identified as pathogens. (i) *Rickettsia conorii* subsp. *conorii*. Several case studies of MSF from North Africa have been published in recent years. In particular, cases have been increasingly reported in Algeria, Tunisia, and Morocco (214, 333). In North Africa, most MSF cases are diagnosed during July and October. Although some aspects of MSF were found to align with the general epidemiology of the disease, uncommon aspects were found, including the increased incidence and the presence of multiple inoculation eschars in 12% of patients. The role of climatic changes in alterations of host-seeking and feeding behaviors of vectors, including *R. sanguineus*, was discussed (177). Additionally, in Algerian cases, 49% of patients were hospitalized with a severe form of the disease. The overall case-fatality rate was 3.6%, but it was 54.5% for patients hospitalized with major neurological manifestations and multiorgan involvement (334, 335). In addition, direct contact with dogs or domestic animals has been reported in 76.5% to 95.2% of the cases, and a history of a tick bite has been found in 38% to 50.3% of the cases (333). *R. conorii* subsp. *conorii* was detected by molecular tools in *R. sanguineus* ticks from Algeria (212), Tunisia (336), and Morocco (337).

(ii) *Rickettsia conorii* subsp. *israelensis*. The agent of the so-called ISF has been found in Sfax (southern Tunisia). Physicians took note of patients with severe forms of MSF and suspected the presence of other species or a virulent *R. conorii* strain. Two cases of ISF that were reported from Sfax were confirmed by the detection of rickettsial DNA in skin biopsy specimens (338).

(iii) *Rickettsia aeschlimannii*. *R. aeschlimannii* was first isolated from *H. marginatum marginatum* ticks collected in Morocco in 1992 (2). The first human infection caused by *R. aeschlimannii* was in a French patient who became ill after returning from a trip to Morocco (339). Recently, two new cases were reported in Algeria (340). *R. aeschlimannii* was detected by molecular tools in *H. marginatum marginatum* from Algeria (212), Morocco (341), and Egypt (342, 343). This rickettsia has also been detected in several *Hyalomma* spp., including *Hyalomma aegyptium* ticks collected from Algerian tortoises and *Hyalomma dromedarii*, *Hyalomma impeltatum*, *H. marginatum rufipes*, and *Hyalomma truncatum* ticks collected from camels and/or cows in Egypt, Sudan, Algeria, and Tunisia (333).

(iv) *Rickettsia sibirica* subsp. *mongolitimonae*. Two cases of *R. sibirica* subsp. *mongolitimonae* infection have been reported in North Africa, in addition to those reported in Europe. The first case reported was an adult female patient who returned to France from a trip to Algeria. She had been in contact with camels, which are highly parasitized by ticks (344, 345). In September 2009, a previously healthy 52-year-old man living in France was admitted with a 10-day history of fever, asthenia, headache, and arthromyalgia after a 2-week trip to Egypt. He had fever, painful axillary lymphadenopathies, and an inoculation eschar surrounded by an inflammatory halo on the left scapular area, but he did not have a rash. During his travel, he had been unsuccessfully treated for headache, arthromyalgia, and diarrhea by amoxicillin-clavulanate, nonsteroidal anti-inflammatory drugs, and gentamicin cream on the eschar for 3 days. He improved and remained well after doxycycline treatment (344, 345).

(v) *Rickettsia slovaca* and *Rickettsia raoultii*. *R. slovaca* and *R. raoultii*, agents of TIBOLA/SENLAT (see the section on Europe above), were detected in *D. marginatus* ticks in 2008 in Morocco (341) and recently in *D. marginatus* tick species collected in northern Algeria (346). However, no human case has been reported in northern Algeria.

(vi) *Rickettsia monacensis*. After the first two human cases of infection due to *R. monacensis* documented in Spain (208), *R. monacensis* was detected in *I. ricinus* ticks in Morocco (341), in Tunisia (347), and twice in Algeria (346, 348). In Algeria, *R. monacensis* was detected in ticks collected in the far-eastern region of

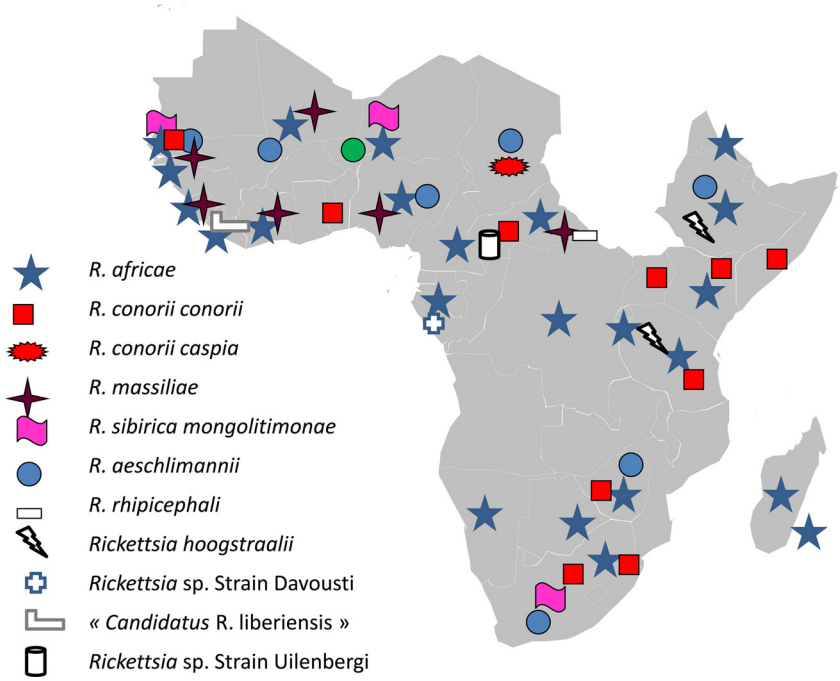

FIG 11 Tick-borne rickettsiae in sub-Saharan Africa. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

Algeria (Tarf) (348) and in the central region (Tizi Ouzou) in 2010 (346). No human case has been reported in northern Africa.

(vii) *Rickettsia massiliae.* *R. massiliae* (see sections on Europe and South America above) has been found in ticks in North Africa. It was isolated from *R. turanicus* and *Rhipicephalus sanguineus* ticks in Algeria (212), and it has been detected in *R. sanguineus* and *R. bursa* ticks in Morocco (337, 341). However, no human case has been reported in northern Algeria.

(viii) *Rickettsia africae.* *R. africae*, the agent of African tick bite fever (ATBF), has very recently been detected in North Africa, including in *H. dromedarii* ticks collected from camels (*Camelus dromedarius*) in Algeria and in Egypt (342, 343). The role of *H. dromedarii* in the epidemiology of *R. africae* requires further investigation. However, no human case of ATBF has been reported in northern Algeria.

(ix) *Rickettsia helvetica.* *R. helvetica* is prevalent in Europe (see above). A small population of *I. ricinus* ticks is present in Tunisia, Algeria, and Morocco. *R. helvetica* is also present in North African countries, including Morocco (341), Tunisia (347), and, very recently, Algeria (346).

Nonvalidated, incompletely described, or uncultivated species. A *Rickettsia* sp. from the SFG was detected in *Rhipicephalus sanguineus* and *Haemaphysalis erinacei* ticks collected from hedgehogs in Algeria (349) and in *Haemaphysalis* ticks from Morocco (341). This *Rickettsia* species is phylogenetically close to *R. heilongjiangensis*.

Sub-Saharan Africa

Species identified as pathogens. (i) *Rickettsia africae.* *R. africae* causes ATBF (2). In southeastern Africa, *A. hebraeum*, known as the South African bont tick, is a recognized vector and reservoir for *R. africae*. Elsewhere in sub-Saharan Africa, *A. variegatum* (350), the tropical bont tick, is a documented vector of *R. africae* (2). In 2009, the transovarial transmission rate of *R. africae* in the third generation of naturally infected *A. variegatum* ticks was estimated to be 100%, and the filial infection rate (the proportion of infected eggs or larvae obtained from an infected female) was estimated to be 93% (30). The infection rate in these tick species in regions of endemicity is high and may reach 100% (13, 351), which suggests an extreme fitness of this rickettsia for its vector (13). Since 2005, *R. africae* has also been detected in *Amblyomma lepidum* ticks (20%) in Djibouti (352); *Rhipicephalus annulatus* ticks (2 to 93%) in Guinea, Senegal, and Nigeria (41, 351, 353); *Rhipicephalus evertsi evertsi* ticks (0.4 to 5%) in Senegal and Nigeria (41, 353); *Rhipicephalus decoloratus* ticks (5 to 77%) in Nigeria and Botswana (354, 355); *Rhipicephalus sanguineus* (5%) and *Hyalomma impeltatum* (10%) ticks in Nigeria (354); *Rhipicephalus geigyi* ticks (14%) in Liberia (356); and *Amblyomma compressum* ticks (10 to 50%) in the Democratic Republic of the Congo and Liberia (356, 357). However, their role in the epidemiology of ATBF is unknown, as the rate of infection in *Rhipicephalus* ticks is always lower and may be considered concomitant, acquired most likely by cofeeding (356) or via a bacteremic animal (355). To date, *R. africae* has been detected in ticks and/or humans in 22 sub-Saharan African countries (Fig. 11).

A high *R. africae* seropositivity rate was detected in indigenous populations in rural areas. For example, the seropositivity rates in Cameroon and Senegal were 12 to 52% (358) and 20.6 to 45.6%, respectively (353). The highest seroprevalence in Cameroon was linked to the presence of cattle, the preferred host of *A. variegatum*, and with lowland rainforest habitats, ideal for the behavior of this tick species (358). However, since 2005 (2), more than 141 acute ATBF cases were reported in international travelers (359–385), but none were reported from native populations. In addition, 197 spotted fever cases, most likely ATBF, in travelers from sub-Sa-

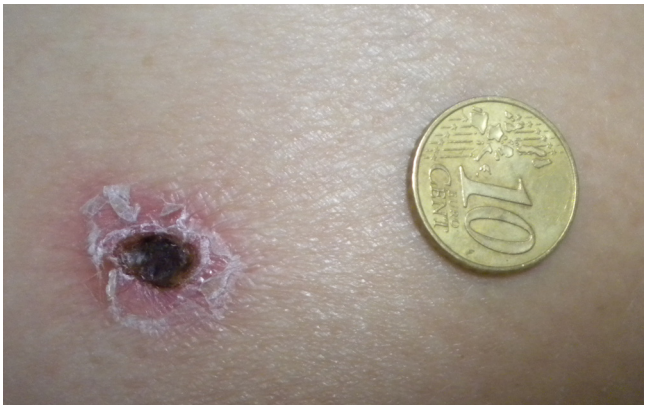

FIG 12 Eschar in a patient with African tick bite fever caused by *R. africae*.

haran Africa have been reported by the GeoSentinel network during June 1996 to December 2008. In 2006, 30 GeoSentinel sites, which are specialized travel or tropical medicine clinics on six continents, compared the frequencies of the occurrence of each diagnosis among travelers (118). ATBF was the second most frequently identified etiology, after malaria, among travelers returning from sub-Saharan Africa (118). This finding was confirmed subsequently by other studies (383, 386). The risk factors for ATBF in travel are male gender, higher age, travel for tourism, and travel during the late summer months in southern Africa (March to May) (385, 387).

Actually, the diagnosis of ATBF, which remained unrecognized for years, is usually based on travel history and clinical presentation with flu-like symptoms associated with one or multiple inoculation eschars (Fig. 12) and grouped cases (attack rate, 33 to 100%), which is explained by the hunting strategy of tick vectors. Ticks attack hosts, emerge from their habitat, and run toward their hosts when these animals appear nearby (367, 379). Recently, more than 100 *A. hebraeum* ticks were identified on the extremities and trunk of one Japanese woman with a confirmed ATBF diagnosis after she traveled to South Africa (374). The rash is observed in 30 to 88% of patients and is mostly maculo- or papulovesicular (364, 367, 373). ATBF is a benign disease; nevertheless, a more severe course was described in elderly populations (364, 365), and some complications, such as subacute cranial or peripheral neuropathy and chronic fatigue (364, 388), internuclear ophthalmoplegia (381), myocarditis (364, 376), and cellulitis, have been reported (365). One coinfection with *Leishmania tropica* was reported after travel to Botswana (389), and one with *Coxiella burnetii*, the agent of Q fever, was reported after a trip to the Gambia (375). Recently, comparative genome analysis may have explained the low virulence level of *R. africae* in humans and its strong adaptation to its tick host. In fact, *R. africae* had 18 fully conserved genes that were either absent or degraded in other species, such as *R. prowazekii*, *R. rickettsii*, or *R. conorii* (13). In addition, analysis of 102 human and tick strains suggested that *R. africae* is clonal, a unique characteristic among the SFG rickettsia species (13).

(ii) *Rickettsia conorii* subsp. *conorii*. *Rickettsia conorii* subsp. *conorii*, the agent of MSF, has been reported in 9 sub-Saharan African countries to date (Fig. 11). Although the recognized vector of *R. conorii* is *R. sanguineus*, this rickettsia has been detected in *Rhipicephalus mushamae* ticks from cattle in the Central African Republic and has been isolated from *Haemaphysalis leachi* and *Rhipicephalus simus* ticks from dogs in Zimbabwe. All of these ticks are suspected to be potential vectors in sub-Saharan Africa (2). Recently, *R. conorii* was detected in a *Rhipicephalus evertsi evertsi* tick (1/268) collected from a horse in rural Senegal (353) and in a *Haemaphysalis punctaleachi* ticks (1/9) from a dog in Uganda (352). These ticks seldom feed on humans, and their role as vectors of *R. conorii* subsp. *conorii* in these areas has not been demonstrated.

R. conorii DNA was detected in a blood sample collected from a febrile 4-year-old girl with tachycardia, who was among 134 other febrile patients from Sine-Saloum, Senegal, who were analyzed (353). This patient recovered without antibiotics (353), but another MSF case mimicking a hemorrhagic viral fever had a fatal outcome for a South African man (390). In all these cases (353, 390, 391), the lack of a tick exposure report and the lack of pathognomonic signs such as an inoculation eschar or skin rash have contributed to the lack of any clinical suspicion. This absence of suspicion potentially led to the delayed introduction of a specific antimicrobial therapy. In MSF, the absence of an inoculation eschar has been described in 14 to 40% of MSF cases (215), and the absence of maculopapular rash has been described in 1 to 4% of cases (226). However, this rash may be imperceptible in patients with pigmented skin (215). Seven more benign MSF cases were reported in international travelers from sub-Saharan Africa, including one from South Africa, one from Swaziland, and one from Kenya (373, 383, 392, 393). As MSF and ATBF are the most endemic rickettsioses in these areas, clinicians are encouraged to contact a specialized laboratory to better identify the rickettsial agent.

(iii) *Rickettsia conorii* subsp. *caspia*. *Rickettsia conorii* subsp. *caspia* is the agent of Astrakhan fever. Since the isolation of this bacterium from a patient returning from Chad with fever and a maculopapulous rash (2), no other reports of isolation in humans or ticks were reported from sub-Saharan Africa.

(iv) *Rickettsia aeschlimannii*. *R. aeschlimannii* caused a spotted fever in one case in South Africa after a *Rhipicephalus appendiculatus* tick bite (2). However, *Hyalomma* ticks seem to be the main vectors and reservoirs of *R. aeschlimannii*. Recently, it was detected in 45 to 51% of *H. marginatum rufipes* specimens and 6 to 7% of *H. truncatum* specimens collected from cows, donkeys, sheep, goats, and horses in Senegal (353). In addition, one *R. aeschlimannii* strain, RH15, was isolated from an *H. truncatum* specimen collected in Senegal (353). *H. marginatum rufipes* is widely distributed in much of Africa, commonly in the drier areas, and the infestation of birds by the immature stages of this tick contributes to its extensive distribution and the spread of infected ticks.

Unexpectedly, *R. aeschlimannii* was detected in 0.7 to 5% of the *R. evertsi evertsi* specimens from Senegal and Nigeria (41, 353) and in 2% of the *R. annulatus* specimens and 2% of the *A. variegatum* specimens from Nigeria (41). In one Nigerian study (41), it was detected only in feeding ticks, suggesting that cattle may play a role as an animal reservoir. To date, this bacterium has been detected in 8 sub-Saharan African countries.

(v) *Rickettsia sibirica* subsp. *mongolitimonae*. *R. sibirica* subsp. *mongolitimonae*, the agent of LAR, was described in a febrile man from South Africa with a toe eschar and lymphangitis (2). Recently, in Senegal, *R. sibirica* subsp. *mongolitimonae* was detected in 14% of *H. truncatum* ticks, with the isolation of one strain, RH05, in cell culture (353). The infected *H. truncatum* ticks

were collected from cattle, donkeys, sheep, goats, and horses (353). *H. truncatum* ticks are common in sub-Saharan Africa, and their abundance is influenced by the hare population, the host during the immature stages. As immature ticks can attach to humans, LAR is most likely distributed across almost all of these countries.

(vi) *Rickettsia massiliae*. *R. massiliae* is a pathogenic rickettsia that is epidemiologically associated with the hard ticks of the genus *Rhipicephalus*. It was described as a human pathogen in Europe and South America (see above), but there has been no report from Africa. However, a high infection rate was detected in *Rhipicephalus guilhoni* ticks (22%) that were collected from donkeys and cows in Senegal (353) and in *Rhipicephalus senegalensis* ticks (8%) in Guinea (356). Recently, *R. massiliae* was detected while searching for *R. evertsi* ticks (3%) collected from the vegetation at seven Nigerian locations by cloth dragging and by direct hand picking, suggesting that these bacteria are surviving and easily being perpetuated in the wild (41). In addition, the *R. massiliae* Guinean genotype was detected by molecular tools in 16% of *Rhipicephalus senegalensis* and in 2% of *Haemaphysalis paraleachi* ticks collected from dogs in Guinea (356).

Species of unknown pathogenicity. Two rickettsial species of unknown pathogenicity were detected in ticks in sub-Saharan Africa. *R. rhipicephali* was detected for the first time in the Central African Republic in 1994 in *Rhipicephalus lunulatus* and *Rhipicephalus composites* group ticks (2). Since then, it has not been detected in ticks in these geographical areas. In 2012, *R. hoogstraalii* was detected in *Argas persicus* ticks from Ethiopia (394).

Nonvalidated, incompletely described, or uncultivated species. "*Candidatus* Rickettsia liberiensis," which is genetically close to *R. raoultii*, was detected in *Ixodes muniensis* ticks collected from dogs in Liberia (356). In Gabon, *Rickettsia* sp. strain Davousti, which is phylogenetically close to *R. heilongjiangensis*, and in the Central African Republic, *Rickettsia* sp. strain Uilenbergi, which is phylogenetically close to the *R. massiliae* group, were detected in *Amblyomma tholloni* ticks, both of which were collected from elephants (395). *A. tholloni* ticks rarely feed on humans and occur widely in Africa, following the distribution of the African elephant: from South Africa in the south to the Sudan in the north and from Sierra Leone in the west to Somalia in the east. In addition, one *Rickettsia* species belonging to the *R. rickettsii* group was detected in *R. evertsi* ticks in Nigeria (41), and another rickettsial species (GenBank accession numbers DQ092217 and DQ092215) that is closely related to *R. felis* based on their 17-kDa antigen sequences and is closely related to *Rickettsia cooleyi* based on their citrate synthase genes was detected in *Ornithodoros moubata*, a soft tick from Tanzania (396).

TICK-BORNE RICKETTSIAE IN ASIA

Species Identified as Pathogens

***Rickettsia sibirica* subsp. *sibirica*.** Siberian tick typhus (STT), caused by *R. sibirica* subsp. *sibirica*, was described in Russia in the 1930s (2). Since then, STT has been found across a large territory from the Pacific coast to western Siberia in Russia, China, Mongolia, and Kazakhstan (120, 397) (Fig. 13). Recent studies describe several serologically confirmed cases from South Korea (398). At least some of the STT cases reported previously in the Russian Far East were most likely misdiagnosed Far-Eastern spotted fever (FESF) caused by *Rickettsia heilongjiangensis* (see below) (399). In spite of some clinical and epidemiological differences, the distinction between these two rickettsiae is possible only by molecular methods. The incidence of STT in Russia is continuously increasing, varying between 2.5 and 4.0 per thousand officially registered cases per year (400) and reaching 50 to 55 per thousand in regions of endemicity, especially Altay and Krasnoyarsk (2, 401). It is most likely the most prevalent rickettsiosis in Asia.

The most important vectors are *Dermacentor* ticks; however, *Haemaphysalis* and even *Ixodes* ticks have also been implicated (402). The infection rate in *Dermacentor* ticks may vary from 8.3 to 13.0% (403, 404). The morbidity is strongly seasonal, with peaks in April and May (120), corresponding to the peaks in activity of *Dermacentor* ticks in Siberia. Children younger than 14 years of age comprise up to 75% of patients (399).

The mean incubation period is 4 days, and the clinical features are typical for a spotted fever, including a high fever associated with an inoculation eschar that is often accompanied by regional lymphadenopathy and a maculopapular (rarely with a hemorrhagic component) rash. This disease is usually mild and is seldom associated with severe complications (2).

***Rickettsia heilongjiangensis*.** The first cases of FESF caused by *R. heilongjiangensis*, exhibiting mild rash associated with fever and an eschar, have been reported in the Russian Far East and the People's Republic of China (2). In both countries, FESF cases were most likely misdiagnosed as STT before molecular tools became available (120, 399). Recently, the first case from Japan was also reported (405). In Russia and China, *R. heilongjiangensis* was isolated from *Haemaphysalis concinna* and *Dermacentor silvarum* ticks (402, 406). The rate of infection in *H. concinna* ticks may reach up to 28% (406). *R. heilongjiangensis* was also identified in *Haemaphysalis flava* ticks (407) in central China. Wild animals, usually *Rattus edwardsii*, *Rattus fulvescens*, *Rattus nivivente*, *Rattus flavipectus*, and *Berylmys bowersi*, are considered reservoirs for this bacterium in nature (408). However, recently, the DNA of this rickettsia was identified in the blood of goats in China (409).

It was recently shown that, compared to STT, the peak of morbidity of FESF in the Russian Far East is much later, in July. This peak corresponds to the month exhibiting the highest level of activity of *Haemaphysalis* ticks. Moreover, the affected population is much older, especially the 50-and-older age group (399, 406). The pathogenicity of *R. heilongjiangensis* was not studied until recently, when the pathological inflammatory effects were described in a mouse model (410).

The distribution of *R. heilongjiangensis* is most likely much larger than the Russian Far East and northern China, as a phylogenetically related strain, PMK94, was isolated from a patient with septic shock in Thailand (411, 412).

***Rickettsia japonica*.** *R. japonica* is the etiological agent of Japanese spotted fever (JSF), the typical spotted fever identified in southwestern Japan. It is characterized by fever, headache, and the appearance of an eschar and a rash (413). The main vectors are *H. flava*, *Haemaphysalis hystricis*, *Haemaphysalis longicornis*, *Haemaphysalis cornigera*, *Haemaphysalis formosensis*, *Ixodes ovatus*, and *Dermacentor taiwanensis* (2, 414). The reservoirs may be wild rodents and small carnivores such as feral raccoons (415). Until recently, JSF was thought to be restricted to Japan. Recently, however, a large amount of data to the contrary have become available. Closely related *Rickettsia* spp. were detected in *H. longicornis* ticks by PCR in South Korea (416). In northern Thailand (Chiang Mai), strain TCM1 was isolated from *H. hystricis* ticks; phylogenetic

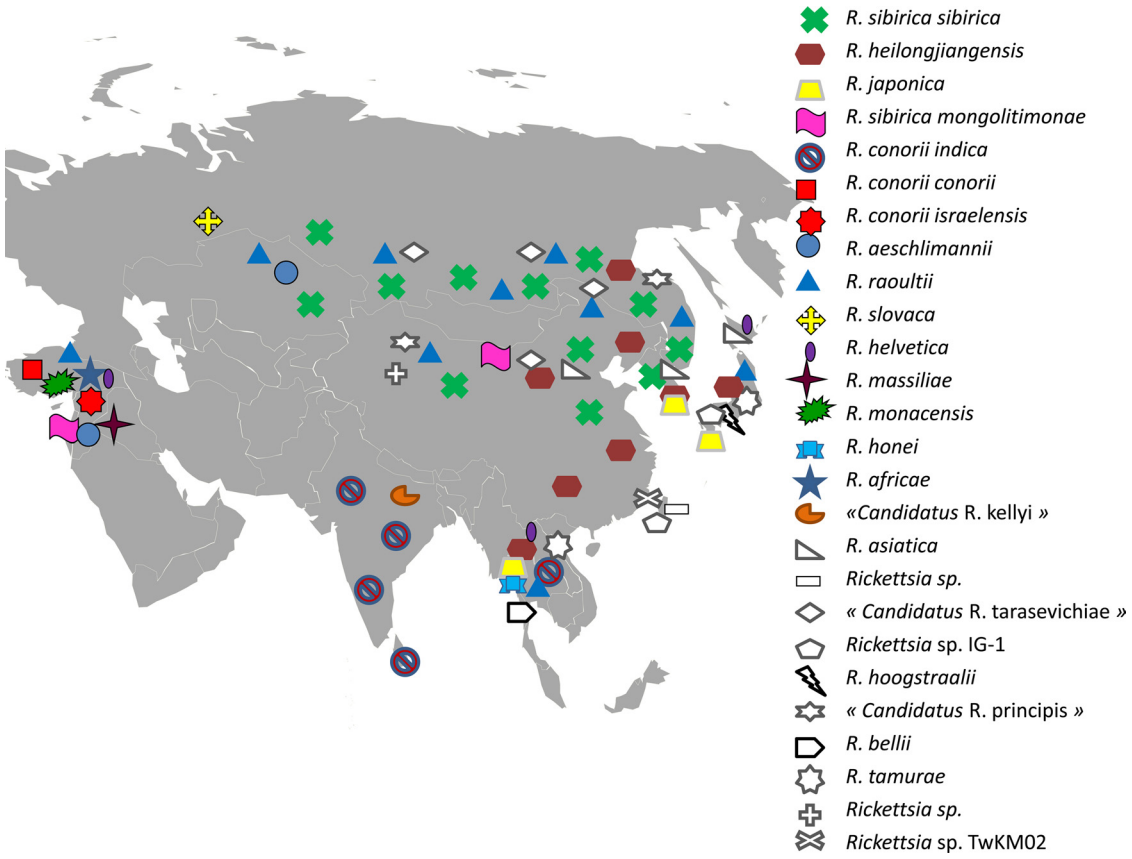

FIG 13 Tick-borne rickettsiae in Asia. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

analysis showed that it is most closely related to Japanese strains (412). The complete genome of this rickettsia was recently published (417).

***Rickettsia sibirica* subsp. *mongolitimonae*.** First described in Inner Mongolia, China, *Rickettsia sibirica* subsp. *mongolitimonae* is widely distributed in *Hyalomma* ticks in Southern Europe and Africa (418). The presence of the DNA of this rickettsia in *Hyalomma* sp. ticks from Israel was also reported (419). Despite a number of human cases reported in Europe and Africa (see above), no report of morbidity from Asia is currently available.

***Rickettsia conorii* subsp. *conorii*.** The only place in Asia in which MSF was reported is a Bursa province in Turkey (236). The disease is transmitted by brown dog ticks, *R. sanguineus* (2); however, other species, such as *R. bursa*, may also be implicated (299).

***Rickettsia conorii* subsp. *indica*.** *R. conorii* subsp. *indica* is the agent of Indian tick typhus, a tick-borne rickettsiosis prevalent in India (420, 421), with solitary cases reported from Laos (422) and Sri Lanka (423). Clinically, the disease resembles MSF; however, a series of three severe cases complicated by gangrene were reported recently (424). It was isolated in 1950 from *R. sanguineus* ticks collected in that country, although it has never been isolated in patients there (2). Indian tick typhus also differs from MSF, the disease caused by the *R. conorii* strain type, in that the rash is often purpuric, and an inoculation eschar at the bite site is seldom identified (425). The genome of *R. conorii* subsp. *indica* was recently published (425).

***Rickettsia conorii* subsp. *israelensis*.** *Rickettsia conorii* subsp. *israelensis* was first isolated in 1974 in Israel, and its genome was recently sequenced (2, 426). It is the agent of ISF (2). Like MSF, ISF is transmitted by infected *R. sanguineus* ticks. Human cases of spotted fever have been reported since the late 1940s in Israel; however, recently, disease caused by *R. conorii* subsp. *israelensis* was reported in Italy, Portugal, and Tunisia (253, 426). The eschar at the inoculation site typical of MSF is usually lacking.

***Rickettsia honei*.** *R. honei* is another SFG rickettsia that was described as a new species in 1998 and as the cause of Flinders Island spotted fever (FISF) in Australia (427). The original Thai tick typhus isolate, TT-118, was obtained from a mixed pool of *Ixodes* sp. and *Rhipicephalus* sp. larval ticks from *Rattus rattus* trapped in Chiangmai Province, Thailand, in 1962 and has recently been determined to be a strain of *R. honei* (428). This discovery significantly enlarged the geographical distribution of this pathogenic rickettsia. The first molecularly confirmed case in Thailand was reported in 2005 (428); however, many serologically verified spotted fever cases have been reported in Thailand (429). Recently, a severe case of tick-borne rickettsiosis caused by *R. honei* was reported in Nepal (430). The typical clinical picture of spotted fever was associated with encephalitis, pneumonitis, tinnitus, and deafness. The complete genome of the RB(T) strain of *R. honei* was recently sequenced and published (431).

***Rickettsia tamurae*.** *R. tamurae* was isolated from *Amblyomma testudinarium* ticks in Japan (7). The typical hosts of this tick are wild and domestic pigs, but the tick also infests deer, cattle, other livestock, and humans. Wild boars in Japan may be infected by *R.*

tamurae, which is found in skin biopsy specimens and ticks (432). Until recently, it was not thought to be pathogenic, but the first human case was reported in 2011 in Japan (433). However, a spotted fever case reported from Laos was seroreactive for the *R. tamurae* antigen (422).

"*Candidatus* Rickettsia kellyi." "*Candidatus* Rickettsia kellyi" is phylogenetically very distant from all known species to date. No isolates exist; however, the *ompA* gene of this rickettsia was sequenced from the skin biopsy specimen of a 1-year-old child with clinical signs of spotted fever in India (434). Several closely related sequences (GenBank accession numbers HM587248 to HM587251) without a supporting published manuscript were recently deposited in GenBank; they were also amplified from skin biopsy samples of Indian patients.

Rickettsia aeschlimannii. No cases of *R. aeschlimannii* infection in Asia have yet been reported. This species is thought to be associated mostly with *Hyalomma* species ticks in Africa, Europe, and Asia, where it was identified in *H. punctata* ticks in Kazakhstan (120) and *H. sulcata* ticks in Georgia (290). It was also detected in *Hyalomma marginatum* and *Hyalomma detritum* ticks in Israel (435).

Rickettsia raoultii. *R. raoultii* was described as a new species in 2008 (292). The type strain, Kharbarovsk, was isolated from *D. silvarum* ticks in the Russian Far East (6). Since then, this rickettsia has been identified in different parts of Asiatic Russia (Omsk, Novosibirsk, and Buryatiaya) and Kazakhstan in different species of *Dermacentor* ticks, including *D. reticulatus*, *D. marginatus*, and *D. nuttalli*. The most recent report also shows that this rickettsia is widely distributed in northern China (436) and Mongolia (404). Similar rickettsiae were also identified in *D. niveus* ticks in China (GenBank accession numbers JQ664721 and JQ664722); *H. hystricis* ticks in Japan (accession number JQ697956); and *Haemaphysalis ornithophila*, *Haemaphysalis shimoga*, *Haemaphysalis lagrangei*, and *A. testudinarium* ticks in Thailand (437). It was also detected in *D. marginatus* ticks in Turkey (299) and Georgia (290). No cases from Asia have been reported to date.

Rickettsia slovaca. *R. slovaca* is responsible for at least two-thirds of all TIBOLA cases in Europe (see above) (292). The geographical distribution of *R. slovaca* and *R. raoultii* most likely corresponds to the geographical distribution of Palearctic *Dermacentor* spp.: *R. slovaca* was also found in *D. marginatus* ticks in the Kurgan region (Ural) of Russia (402) and in Georgia (290) and in 6.5% of *D. silvarum* ticks in China (436). Human cases have not been reported in Asia.

Rickettsia helvetica. In Asia, *R. helvetica* was identified in *Ixodes persulcatus* ticks in Hokkaido, Japan (438), as well as in *Ixodes ovatus* and *Ixodes monospinosus* ticks (2). It was also reported in Turkey, where the distribution area of *I. ricinus* ticks touches Asia. Serologically confirmed human cases were reported from Laos (422) and Thailand (2). DNA of *R. helvetica* was also identified in the blood of wild feral raccoons (*Procyon lotor*) in Japan (415).

Rickettsia massiliae. *R. massiliae* has been regularly identified in *R. turanicus* and *R. sanguineus* ticks all over their distribution areas, including Israel (419, 435). Additionally, both *Rhipicephalus* species are widely distributed in Middle and Central Asia (439). The distribution area of *R. massiliae* may also include these regions; however, no recent reports from these regions are available.

Rickettsia monacensis. *R. monacensis*, recently considered pathogenic, was identified in *I. ricinus* ticks in Turkey (299).

Rickettsia africae. *R. africae*, the agent of ATBF, is usually associated with *Amblyomma* ticks. However, it has been detected in several species of *Hyalomma* ticks, including *H. dromedarii* in Egypt (342). Similarly, *R. africae* was reported in *H. aegyptium* ticks from Turkey (299). No human cases from Asia have been reported to date.

Species of Unknown Pathogenicity

Rickettsia asiatica was isolated from *I. ovatus* ticks in Japan (3). Some closely related species were also reported in China and South Korea in *I. ovatus* and *I. pomerantzevi* ticks (GenBank accession numbers AB297812 and AB297808). Up to 63% of wild sika deer may have the DNA of this rickettsia in their blood, indicating that they could be a potential reservoir (440).

Nonvalidated, Incompletely Described, or Uncultivated Species

Three strains of rickettsia closely related to *R. rhipicephali* were isolated from *Rhipicephalus haemaphysaloides* ticks in Taiwan (441). "*Candidatus* Rickettsia tarasevichiae" was identified in *I. persulcatus* ticks almost everywhere in Asiatic Russia (2, 406). It was also identified in *I. persulcatus* ticks in Hokkaido (438). The pathogenicity of this rickettsia for humans is not yet known. A strain that has yet to be named, IG-1, was isolated from *Ixodes granulatus* ticks from Taiwan. Phylogenetic analysis showed that this strain may belong to a new species (442). Identical rickettsiae were later found in *I. granulatus* ticks in Japan (443). *R. hoogstraalii* was originally isolated in 2006 from *H. sulcata* ticks from Croatia and *Carios capensis* ticks from the United States (5). However, a detailed search showed that in 2006, this rickettsia was already identified in *C. capensis* soft ticks in Japan (444). "*Candidatus* Rickettsia principis" was identified in 1.5% of *Haemaphysalis japonica douglasi* ticks from the Russian Far East (406). A closely related species was soon identified in *Haemaphysalis danieli* ticks recovered from cattle in the Xinjiang Uygur Autonomous Region Area, China (445).

TICK-BORNE RICKETTSIAE IN AUSTRALIA AND THE PACIFIC

In the Oceanic region, there are a number of recognized tick-transmitted SFG rickettsiae, but they are limited mostly to Australia (Fig. 14). Investigation of the presence of rickettsiae in regions outside Australia has just started, and anecdotal evidence suggests that SFG rickettsioses are underreported and more widespread than is currently known. Tick-borne SFG rickettsiae have yet to be reported from New Zealand or any of the 20 other major Pacific Island nations; however, further research is required to verify their presence or absence from these regions.

Species Identified as Pathogens

Rickettsia australis. The first cases of tick-borne rickettsiosis in Australia were reported in 1946 from Queensland, with two isolates from the reported cases (2). Caused by tick bites and with a clinical presentation similar to that of murine typhus, the disease was named Queensland tick typhus (QTT). Serological analysis of isolates demonstrated its uniqueness relative to other known rickettsiae, which led to it being named *R. australis*. The three tick species that have been identified as vectors of *R. australis* are *Ixodes tasmani*, *Ixodes holocyclus*, and *Ixodes cornuatus*. The distributions of the ticks that have been found to harbor *R. australis* are located along the eastern states ranging from the Torres Strait islands to

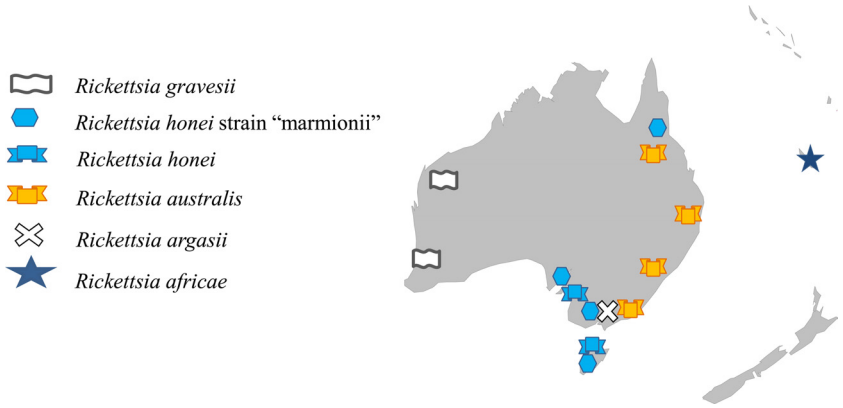

FIG 14 Tick-borne rickettsiae in Australia. Colored symbols indicate pathogenic rickettsiae. White symbols indicate rickettsiae of possible pathogenicity and rickettsiae of unknown pathogenicity. (Adapted from reference 2.)

northern Queensland through to Wilsons Promontory, Victoria (446, 447).

Symptoms associated with QTT include headache, chills, malaise, fever, maculopapular rash (Fig. 15), and an eschar that is found at the tick bite site. Cases of *R. australis* infection are seldom reported in the literature but do occur, with the severity of disease ranging from very mild to life threatening. Fatalities linked to *R. australis* infection are rare, and severe disease in patients with underlying problems is uncommon (448–450).

Rickettsia honei. The first cases of *R. honei* infections were reported by Stewart in 1991, and the rickettsia-like symptoms were initially mistakenly attributed to *R. australis* (2). The comparatively different clinical presentation (the rash was maculopapular, and there was no vesiculation), seasonality (December through January instead of June through November), and geographical location compared to that of QTT warranted the newly discovered rickettsial disease to be named FISF. The rickettsiosis is generally mild, with symptoms such as fever, myalgia, headache, cough, and rash (2). Although *R. honei* was first discovered in Australia, it was subsequently described in Thailand (428) and, most recently, Nepal (430). The tick vector for *R. honei* in Australia is *Bothriocroton hydrosauri*, previously known as *Aponomma hydrosauri* (451). Geographically, human cases of FISF and ticks harboring *R. honei* have thus far been limited to the states of South Australia and Tasmania (452–454). However, *B. hydrosauri* has been observed in other states, including Victoria and New South Wales; no evidence of *R. honei* has been reported from these areas.

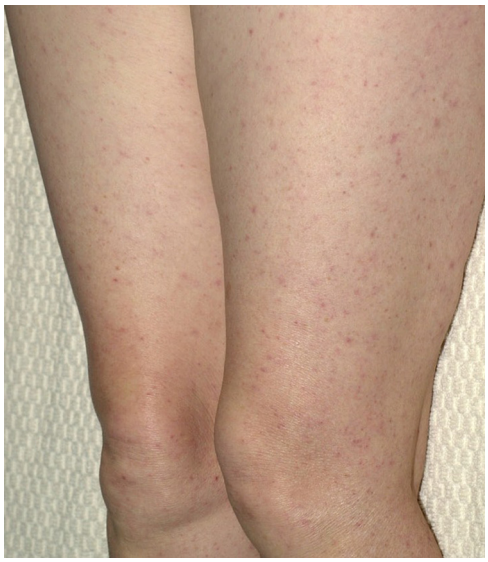

FIG 15 Maculopapular rash on the legs of a patient with Queensland tick typhus caused by *Rickettsia australis*.

***Rickettsia honei* strain marmionii.** The rickettsia described by Lane et al. (455) was most likely the first description of *Rickettsia honei* strain "marmionii" in Australia. This strain is similar to *R. honei*, with some slight genetic variations that are not distinct enough to warrant classification as a new species. Due to its expanded geographic range in four states (South Australia, Victoria, Tasmania, and Queensland) and its different tick hosts, recognition was given to its uniqueness from *R. honei* (456). The *Haemaphysalis novaeguineae* ticks that harbor *R. honei* strain marmionii typically infest macropods and are prevalent in northern Australia and Papua New Guinea. The tick vectors responsible for the transmission of *R. honei* strain marmionii in the southern states are unknown. It has been detected in infected patients only by molecular techniques (456, 457). The rickettsiosis caused by *R. honei* strain marmionii has a clinical presentation similar to that of FISF, with fever, headache, arthralgia, myalgia, cough, maculopapular/petechial rash, nausea, pharyngitis, lymphadenopathy, and eschar (456). However, given the large geographical distribution of this agent, the disease would be more appropriately described as Australian spotted fever.

Rickettsia africae. Cases of *R. africae* in Australia and the oceanic region are commonly reported in travelers returning from sub-Saharan Africa (458). However, a recent report of *R. africae* in *Amblyomma loculosum* ticks in New Caledonia provides evidence that the geographic endemicity of this organism goes well beyond its traditional location in continental Africa (459). *A. loculosum* is endemic to the islands in the Indian Ocean and South Pacific and has been found on various vertebrates, including marine birds, local mammals, and reptiles (452). It is believed that *R. africae* may have been introduced to New Caledonia by migrating birds rather than with the importation of cattle, as was the case in the West Indies (2). Although there are no reports of rickettsiosis transmitted by tick bites or linked to locally acquired African tick typhus in

Australia or New Caledonia, the presence of the disease cannot be excluded.

Species of Unknown Pathogenicity

Rickettsia gravesii. Evidence of SFG rickettsiosis in Western Australia has been established for several years with the use of serological assays; however, no rickettsial agents have ever been characterized in human specimens. The clinical presentation of this disease must be relatively mild, as it is generally not detected. *Rickettsia gravesii* is a recently described species with a close genotypic association with *R. raoultii* and *R. aeschlimannii* but distinct enough to warrant its acceptance as a novel rickettsial species (460, 461). It has been found to be highly prevalent among tick populations in Western Australia. The prevalence has been shown to be >70% in *Amblyomma triguttatum* ticks (462), which are widely known to bite large vertebrate mammals, including humans (463). These ticks are found in all states and territories of Australia and are aggressive feeders, which implies that *R. gravesii* has a potential vector that can transmit this agent across Australia.

Rickettsia argasii. "*R. argasii*" (GenBank accession numbers JQ727682 and JQ727683) was recently isolated from the soft tick *Argas dewae* from bat roosting boxes in Victoria, Australia. These ticks are found primarily on the microbats *Chalinolobus gouldii* and *Vespadelus* sp. The potential for geographical spread of this agent is high, as bats are known to travel great distances. No rickettsiosis has so far been attributed to *R. argasii*, nor has the rickettsia been found in other tick species. The potential for human rickettsiosis is believed to be extremely low due to the host-specific nature of this tick.

Nonvalidated, Incompletely Described, or Uncultivated Species

Six other rickettsiae determined to be highly divergent from other known rickettsiae worldwide have been mentioned in the literature; however, culture isolation has thus far been unsuccessful. These six rickettsiae have been tentatively named "Rickettsia antechini" (detected in *Ixodes antechini*) (427), "Rickettsia derrickii" (in *Bothriocroton hydrosauri*) (427), "Rickettsia guntherii" (in *Haemaphysalis humerosa*) (427), "Rickettsia sauri" (in *Bothriocroton hydrosauri*) (427), "Rickettsia tasmanensis" (in *Ixodes tasmani*) (464), and koala rickettsia (in *Bothriocroton concolor*) (427, 465). Their pathogenic potential is unknown, their presence in ticks was detected by PCR assays, and their novelty was determined by genotypic analysis of PCR amplicons.

NEW APPROACHES TO DIAGNOSIS

Generally, the clinical symptoms of tick-borne SFG rickettsioses begin 4 to 10 days after a bite and typically include fever, headache, muscle pain, rash, local lymphadenopathy, and, for most of these diseases, a characteristic inoculation eschar at the bite site. However, these signs vary depending on the rickettsial species involved, and typical signs may be absent or unnoticed by an undirected clinical examination. Therefore, the diagnosis of rickettsioses has been characterized as a challenge because many physicians are unfamiliar with the nonspecific symptoms found during the early stages of the illness. Common nonspecific laboratory methods and specific methods for the diagnosis of rickettsioses were reviewed in 2005, including serology, culture, histochemical, and immunohistochemical methods and molecular tools available at that time (2). New approaches have emerged in recent years.

Serological tests are still the easiest, most frequently used, and most widely available method for the diagnosis of rickettsiosis. However, even when using the immunofluorescence reference method, seroconversion is usually detected 7 to 15 days after the onset of disease (25 to 28 days for *R. africae* infection). Most commercially available MIF assays and even national reference centers offer a very limited selection of antigens that cross-react with different rickettsiae.

In this context, it is important for practicing physicians to remember that MIF may be adequate for diagnosis of spotted fever rickettsiosis but that it is likely to be insufficient for definitive identification of the etiologic agent. More sophisticated serologic assays, such as cross-absorption (CA) techniques and Western blotting (WB), can be used to help to differentiate rickettsial infections by antibody evaluation, but these methods are only now becoming available at the WHO collaborative center in Marseille, France.

In cell culture, rickettsiae may be detectable as early as 48 to 72 h postinoculation. Additionally, the isolation of *Rickettsia* species from samples using cell culture, particularly the shell vial technique, remains critical for the description of new species, enabling genetic descriptions, physiological analyses, improvement of diagnostic tools, and antibiotic susceptibility testing of bacteria. Although the development of cell culture systems for viral isolation has led to an increase in the number of laboratories suitably equipped to isolate rickettsiae, the isolation of rickettsial organisms remains difficult, and few reference centers are able to do so. To be suitable for culture, samples must be collected prior to the initiation of an antibiotic regimen and as early as possible in the course of the disease.

To reduce the delay in diagnosis, molecular tools for the diagnosis of human rickettsiosis allow both convenient and rapid detection and identification of rickettsiae.

Although culture is less sensitive than serology and quantitative PCR (qPCR) for the diagnosis of tick-borne rickettsiosis, it has recently been shown that skin biopsy specimens (from rash and/or eschar) cultivated in a reference center can be positive even when molecular tests are negative and that a negative result by the use of molecular assays does not exclude the diagnosis of rickettsiosis. A positive correlation between the bacterial copies and isolation success in skin biopsy specimens and ticks was also found. To increase the sensitivity of the culture, skin biopsy specimens should be sampled before treatment and early in the course of the disease and should be inoculated as soon as possible (466).

A new step for the diagnosis of tick-borne rickettsioses has been achieved recently with the emergence of the use of quantitative real-time PCR (467–469). Genomic approaches have recently increased our knowledge of the genus *Rickettsia*, and massive amounts of genomic data have become available (1, 470). These sequence data have been used to develop specific qPCR primers and probes. In 2012, the WHO Collaborative Center for Rickettsioses and Other Arthropod-Borne Bacterial Diseases reported 2 years of experience with rickettsial molecular detection using qPCR. All *Rickettsia* genomes available were compared to discover specific sequences to design new sets of primers and probes. The specificity was verified *in silico* and against a panel of 30 rickettsial species. Sensitivity was determined by using 10-fold serial dilutions. Primers and probes that were both specific and sensitive were routinely used for the diagnosis of rickettsial infections from clinical specimens. Sets of primers and probes that could detect *R.*

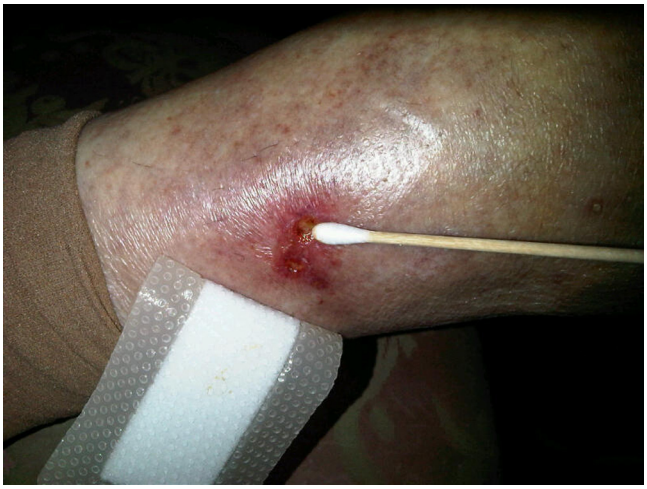

FIG 16 Use of swabs of skin eschar in the diagnosis of a case of *Rickettsia sibirica mongolitimonae* by qPCR.

conorii, *R. slovaca*, *R. africae*, and *R. australis* were retained; 643 clinical samples were screened for the presence of *Rickettsia* DNA. Compared to traditional detection methods, qPCR assays improved the management of patients with suspected cases of rickettsiosis, with 45 positive samples being detected mainly from cutaneous biopsy specimens and swabs (31/45) (469).

In fact, the use of cutaneous swabs from patients rather than cutaneous biopsy specimens for qPCR testing is most likely the second major innovation in the diagnosis of tick-borne rickettsioses (Fig. 16). Skin biopsy specimens, particularly eschar biopsy specimens, are used for detection of *Rickettsia* spp. by molecular tools, but this technique is invasive and painful for patients and is difficult to perform on certain areas of the body. The sample cannot be obtained by a general practitioner or a family doctor in a consulting room or in a patient's home. In addition, the sample cannot be obtained for epidemiological and clinical research in developing countries. In 2009, one study reported the usefulness of swabs of skin lesions in the diagnosis of 3 cases of Queensland tick typhus and 1 case of ATBF (359). To determine the usefulness of the noninvasive cutaneous swab specimens for detecting rickettsiae, skin eschars of 6 guinea pigs and 9 humans were tested in 2011. Specimens from eschars in guinea pigs were positive for rickettsiae as long as lesions were present, and the efficacy and reliability of the skin lesion swabs were shown for the molecular detection of 6 *Rickettsia* species. The optimal storage temperature for specimens was 4°C for 3 days (248).

Eschar swabbing has also been successfully used when a total of 39 patients were sampled in Oran, Algeria (471). Swabs were then sent to and tested in Marseille, France. In this prospective study, *R. conorii* was identified in 64% of patients with eschars and rash by using this procedure. The opinions of health care providers and patients were evaluated. As expected, most health professionals preferred collecting swab samples over biopsy samples for patients and for themselves. Patients also preferred having a swab sample taken over a skin biopsy sample (471). Swabbing of an eschar is easy and painless. Any practitioner at the bedside needs only a classic dry sterile swab. It needs to be directed, while rotating vigorously, to the base of the eschar, after removing the crust. If the eschar lesion appears very dry, a wet compress, previously humidified with sterile water and placed onto the inoculation eschar for 1 min before swabbing, will increase the quantity of material swabbed. Also, the crust eschar can also be used for rickettsial diagnosis. In 2012, the usefulness of eschar swabs and/or eschar crust samples was reported for the diagnosis of *R. africae* infection in returning travelers (472). Finally, in 2013, the use of a swab technique to diagnose *R. parkeri* infection was reported (473).

NEW TOOLS TO IDENTIFY TICKS

The removal of a tick from the human body is commonplace. Certain tick species are well-known vectors of human diseases, particularly rickettsioses (Fig. 2). Therefore, identifying the tick species is clinically helpful, as it will alert the physician to the diseases that may have been transmitted. Such information must be obtained quickly. Tick species can be morphologically identified by using taxonomic keys for local species in several geographic regions (474). However, morphological identification can be difficult because it requires some entomological expertise. Additionally, a specimen that is damaged or immature is difficult to identify. Molecular methods, such as the sequencing of mitochondrial DNA, could be used to improve identification; however, there is currently no PCR assay that can distinguish tick species, and ideal PCR primer pairs that can amplify the relevant gene fragments are not available. Protein profiling by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) is now increasingly common for the routine identification of microorganisms in clinical microbiology (475). The MALDI-TOF MS approach was recently applied for the differentiation of arthropods. Recently, a MALDI-TOF MS study of 7 ticks reported that whole ticks or body parts can generate spectra that are sufficient for species identification (476). More recently, we found that the use of tick legs appears to be an effective means to rapidly identify tick vectors by MALDI-TOF MS if a reference database is available. The remainder of the body can be reserved for other purposes, such as the detection of pathogens (477). The benefits for clinicians include more targeted surveillance of patients for symptoms of potentially transmitted diseases and the ability to make decisions that are more informed as to whether postexposure prophylactic treatment should be administered.

TREATMENT PERSPECTIVE

Little new data describing antimicrobial therapy of tick-borne SFG rickettsioses have been published since 2005, and doxycycline remains the standard treatment for these infections. This regimen is associated with better outcomes than other regimens (478). It is also evident that doxycycline should be used in children presenting with severe rickettsial disease and should be considered by all physicians in light of its good tolerance. Fluoroquinolones have been presented as an alternative to doxycycline; however, recent studies have shown that fluoroquinolones are associated with a deleterious outcome during *R. conorii* infection in humans and in a cell culture model, potentially due to the upregulation of a toxin-antitoxin module (479, 480). In the future, the impact of fluoroquinolones in retrospective studies of other rickettsioses should be assessed. However, because we do not recommend the use of fluoroquinolones for the treatment of MSF, prospective studies of other rickettsial diseases seem imprudent. Josamycin and new macrolide compounds, such as clarithromycin and azithromycin, may represent alternatives for the treatment of some rickettsioses, particularly in pregnant women, under strict follow-up and in the

absence of severe disease (478). Telithromycin also seems to be highly active *in vitro*, but *in vivo* data are lacking; therefore, these drugs should be evaluated further (478). In any case, early empirical antibiotic therapy should be prescribed for any suspected tick-transmitted rickettsiosis before confirmation of the diagnosis.

CONCLUSION

Tick-borne rickettsioses are truly a paradigm for emerging infectious diseases. Efforts to characterize distinct tick-borne rickettsioses are occurring in regions for which a single pathogenic rickettsial species has been previously described. Collaborations with investigators in the tropics and the curiosity of clinicians, combined with powerful diagnostic methods, have continued to increase the recognition of rickettsial organisms, including pathogenic organisms. Because ecotourism and adventure travel are increasingly popular worldwide, the incidence of travel-associated tick-borne emerging rickettsioses is likely to increase in the future (385, 387, 481).

Rickettsiae are difficult to grow, and serological techniques lead to cross-reactions that often cannot differentiate *Rickettsia* species. Only the serological technique of Western blotting with cross-absorption can help in this situation, and this technique is limited in routine practice to the laboratory of the WHO Collaborative Center for Rickettsioses and Other Arthropod-Borne Bacterial Diseases in Marseille, France.

A diagnostic revolution has resulted from the introduction of molecular methods. The use of qPCR is widespread and inexpensive and reduces the delay in the diagnosis of rickettsial infections. These real-time PCR assays could be implemented easily in laboratories that have molecular biology facilities and may be added to existing molecular tools as a point-of-care strategy (482).

Another major step forward in recent years has been the practice of swabbing eschars rather than excisional biopsy techniques. This method has proved effective in the diagnosis of infections by *R. australis*, *R. parkeri*, *R. africae*, *R. conorii*, and *R. sibirica* subsp. *mongolitimonae*. This nontraumatic approach can be used to sample lesional material even in sensitive sites such as eyes or genitalia and ultimately may contribute to an increase in the recognized spectrum of infections associated with *Rickettsia* species. This technique has a high acceptance rate for clinicians and patients because the test is easily performed and is considerably less invasive than a conventional skin biopsy. Moreover, this test can be applied in large epidemiological and clinical studies in developing countries.

Regarding ticks and rickettsioses, many points remain to be clarified. It appears that in humans, most rickettsioses are associated with clinical and epidemiological features that skillful clinicians should be able to identify. Among these features are skin manifestations that include the type and location of the rash, inoculation eschars, and lymphangitis. The seasonality of infection and the number of tick bites change depending on the geographic location and the degree of aggression exhibited by the ticks, the degree of host specificity, and environmental factors such as temperature and humidity. *Rhipicephalus sanguineus* ticks appear to be more prone to biting humans when ambient temperatures are relatively warm and rarely bite humans when temperatures are cooler. The reason why certain ticks, such as *Dermacentor* species, bite more readily during the cool season in Europe remains unknown.

Recent articles describing the detection of rickettsiae in ticks have generated new questions regarding tick-rickettsia associations and interactions and have led to a growing realization that classical tools, particularly microbiological isolation and animal transmission studies, will be needed to better define the roles of ticks as potential reservoirs and vectors. The role as reservoirs would imply that maintenance of rickettsiae relies on both efficient transstadial and transovarial transmission and that rickettsiae have no effect on the reproductive fitness or viability of the tick host.

It is difficult to speculate on if there are still many species and subspecies of rickettsiae to discover, including human pathogens, or if the field is approaching the upper limit of that list. There are probably as many as the arthropods in which they reside.

In the past, it was clear that many rickettsiae were identified in ticks long before they were found in humans because the number of DNA copies and the bacterial loads are higher in arthropods than in human blood. This search for additional pathogens in arthropods remains an essential element of the discovery of the next pathogenic rickettsioses in humans.

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REFERENCES

1. **Merhej V, Raoult D.** 2011. Rickettsial evolution in the light of comparative genomics. Biol. Rev. Camb. Philos. Soc. **86:**379–405.
2. **Parola P, Paddock CD, Raoult D.** 2005. Tick-borne rickettsioses around the world: emerging diseases challenging old concepts. Clin. Microbiol. Rev. **18:**719–756.
3. **Fujita H, Fournier PE, Takada N, Saito T, Raoult D.** 2006. *Rickettsia asiatica* sp. nov., isolated in Japan. Int. J. Syst. Evol. Microbiol. **56:**2365–2368.
4. **Euzéby J.** 2006. Validation list no. 108. Int. J. Syst. Evol. Microbiol. **56:**499–500.
5. **Duh D, Punda-Polic V, Avsic-Zupanc T, Bouyer D, Walker DH, Popov VL, Jelovsek M, Gracner M, Trilar T, Bradaric N, Kurtti TJ, Strus J.** 2010. *Rickettsia hoogstraalii* sp. nov., isolated from hard- and soft-bodied ticks. Int. J. Syst. Evol. Microbiol. **60:**977–984.
6. **Mediannikov O, Matsumoto K, Samoylenko I, Drancourt M, Roux V, Rydkina E, Davoust B, Tarasevich I, Brouqui P, Fournier PE.** 2008. *Rickettsia raoultii* sp. nov., a spotted fever group rickettsia associated with *Dermacentor* ticks in Europe and Russia. Int. J. Syst. Evol. Microbiol. **58:**1635–1639.
7. **Fournier PE, Takada N, Fujita H, Raoult D.** 2006. *Rickettsia tamurae* sp. nov., isolated from *Amblyomma testudinarium* ticks. Int. J. Syst. Evol. Microbiol. **56:**1673–1675.
8. **Zhu Y, Fournier PE, Eremeeva M, Raoult D.** 2005. Proposal to create subspecies of *Rickettsia conorii* based on multi-locus sequence typing and an emended description of *Rickettsia conorii*. BMC Microbiol. **5:**11. doi:10.1186/1471-2180-5-11.
9. **Fournier PE, Zhu Y, Yu X, Raoult D.** 2006. Proposal to create subspecies of *Rickettsia sibirica* and an emended description of *Rickettsia sibirica*. Ann. N. Y. Acad. Sci. **1078:**597–606.
10. **Fournier PE, Dumler JS, Greub G, Zhang J, Wu Y, Raoult D.** 2003. Gene sequence-based criteria for identification of new rickettsia isolates and description of *Rickettsia heilongjiangensis* sp. nov. J. Clin. Microbiol. **41:**5456–5465.
11. **Klenk HP, Goker M.** 2010. En route to a genome-based classification of Archaea and Bacteria? Syst. Appl. Microbiol. **33:**175–182.
12. **Merhej V, Royer-Carenzi M, Pontarotti P, Raoult D.** 2009. Massive comparative genomic analysis reveals convergent evolution of specialized bacteria. Biol. Direct **4:**13. doi:10.1186/1745-6150-4-13.
13. **Fournier PE, El Karkouri K, Leroy Q, Robert C, Giumelli B, Renesto P, Socolovschi C, Parola P, Audic S, Raoult D.** 2009. Analysis of the

Rickettsia africae genome reveals that virulence acquisition in *Rickettsia* species may be explained by genome reduction. BMC Genomics **10:**166. doi:10.1186/1471-2164-10-166.
14. **Baldridge GD, Burkhardt NY, Felsheim RF, Kurtti TJ, Munderloh UG.** 2008. Plasmids of the pRM/pRF family occur in diverse *Rickettsia* species. Appl. Environ. Microbiol. **74:**645–652.
15. **Fournier PE, Belghazi L, Robert C, Elkarkouri K, Richards AL, Greub G, Collyn F, Ogawa M, Portillo A, Oteo JA, Psaroulaki A, Bitam I, Raoult D.** 2008. Variations of plasmid content in *Rickettsia felis*. PLoS One **3:**e2289. doi:10.1371/journal.pone.0002289.
16. **Ogata H, La Scola B, Audic S, Renesto P, Blanc G, Robert C, Fournier PE, Claverie JM, Raoult D.** 2006. Genome sequence of *Rickettsia bellii* illuminates the role of amoebae in gene exchanges between intracellular pathogens. PLoS Genet. **2:**e76. doi:10.1371/journal.pgen.0020076.
17. **Ogata H, Renesto P, Audic S, Robert C, Blanc G, Fournier PE, Parinello H, Claverie JM, Raoult D.** 2005. The genome sequence of *Rickettsia felis* identifies the first putative conjugative plasmid in an obligate intracellular parasite. PLoS Biol. **3:**e248. doi:10.1371/journal.pbio.0030248.
18. **Merhej V, Notredame C, Royer-Carenzi M, Pontarotti P, Raoult D.** 2011. The rhizome of life: the sympatric *Rickettsia felis* paradigm demonstrates the random transfer of DNA sequences. Mol. Biol. Evol. **28:**3213–3223.
19. **Socolovschi C, Mediannikov O, Raoult D, Parola P.** 2009. The relationship between spotted fever group *Rickettsiae* and ixodid ticks. Vet. Res. **40:**34. doi:10.1051/vetres/2009017.
20. **Socolovschi C, Matsumoto K, Brouqui P, Raoult D, Parola P.** 2009. Experimental infection of *Rhipicephalus sanguineus* with *Rickettsia conorii conorii*. Clin. Microbiol. Infect. **15**(Suppl 2):324–325.
21. **Levin ML, Killmaster L, Eremeeva ME, Dasch GA.** 2009. Effects of *Rickettsia conorii* infection on the survival of *Rhipicephalus sanguineus* ticks. Clin. Microbiol. Infect. **15**(Suppl 2):277–278.
22. **Matsumoto K, Brouqui P, Raoult D, Parola P.** 2005. Experimental infection models of ticks of the *Rhipicephalus sanguineus* group with *Rickettsia conorii*. Vector Borne Zoonotic Dis. **5:**363–372.
23. **Levin ML, Killmaster L, Zemtsova G, Grant D, Mumcuoglu KY, Eremeeva ME, Dasch GA.** 2009. Incongruent effects of two isolates of *Rickettsia conorii* on the survival of *Rhipicephalus sanguineus* ticks. Exp. Appl. Acarol. **49:**347–359.
24. **Socolovschi C, Bitam I, Raoult D, Parola P.** 2009. Transmission of *Rickettsia conorii conorii* in naturally infected *Rhipicephalus sanguineus*. Clin. Microbiol. Infect. **15**(Suppl 2):319–321.
25. **Socolovschi C, Gaudart J, Bitam I, Huynh TP, Raoult D, Parola P.** 2012. Why are there so few *Rickettsia conorii conorii*-infected *Rhipicephalus sanguineus* ticks in the wild? PLoS Negl. Trop. Dis. **6:**e1697. doi:10.1371/journal.pntd.0001697.
26. **Piranda EM, Faccini JL, Pinter A, Pacheco RC, Cancado PH, Labruna MB.** 2011. Experimental infection of *Rhipicephalus sanguineus* ticks with the bacterium *Rickettsia rickettsii*, using experimentally infected dogs. Vector Borne Zoonotic Dis. **11:**29–36.
27. **Soares JF, Soares HS, Barbieri AM, Labruna MB.** 2012. Experimental infection of the tick *Amblyomma cajennense*, Cayenne tick, with *Rickettsia rickettsii*, the agent of Rocky Mountain spotted fever. Med. Vet. Entomol. **26:**139–151.
28. **Pacheco RC, Moraes-Filho J, Guedes E, Silveira I, Richtzenhain LJ, Leite RC, Labruna MB.** 2011. Rickettsial infections of dogs, horses and ticks in Juiz de Fora, southeastern Brazil, and isolation of *Rickettsia rickettsii* from *Rhipicephalus sanguineus* ticks. Med. Vet. Entomol. **25:**148–155.
29. **Labruna MB, Ogrzewalska M, Soares JF, Martins TF, Soares HS, Moraes-Filho J, Nieri-Bastos FA, Almeida AP, Pinter A.** 2011. Experimental infection of *Amblyomma aureolatum* ticks with *Rickettsia rickettsii*. Emerg. Infect. Dis. **17:**829–834.
30. **Socolovschi C, Huynh TP, Davoust B, Gomez J, Raoult D, Parola P.** 2009. Transovarial and trans-stadial transmission of *Rickettsiae africae* in *Amblyomma variegatum* ticks. Clin. Microbiol. Infect. **15**(Suppl 2):317–318.
31. **Horta MC, Pinter A, Schumaker TT, Labruna MB.** 2006. Natural infection, transovarial transmission, and transstadial survival of *Rickettsia bellii* in the tick *Ixodes loricatus* (Acari: Ixodidae) from Brazil. Ann. N. Y. Acad. Sci. **1078:**285–290.
32. **Saraiva DG, Nieri-Bastos FA, Horta MC, Soares HS, Nicola PA, Pereira LCM, Labruna MB.** 24 May 2013. *Rickettsia amblyommii* infecting *Amblyomma auricularium* ticks in Pernambuco, northeastern Brazil: isolation, transovarial transmission, and transstadial perpetuation. Vector Borne Zoonotic Dis. [Epub ahead of print.] doi:10.1089/vbz.2012.1223.
33. **Medina-Sanchez A, Bouyer DH, Alcantara-Rodriguez V, Mafra C, Zavala-Castro J, Whitworth T, Popov VL, Fernandez-Salas I, Walker DH.** 2005. Detection of a typhus group *Rickettsia* in *Amblyomma* ticks in the state of Nuevo Leon, Mexico. Ann. N. Y. Acad. Sci. **1063:**327–332.
34. **Parola P.** 2011. *Rickettsia felis*: from a rare disease in the USA to a common cause of fever in sub-Saharan Africa. Clin. Microbiol. Infect. **17:**996–1000.
35. **Socolovschi C, Audoly G, Raoult D.** 2013. Connection of toxin-antitoxin modules to inoculation eschar and arthropod vertical transmission in Rickettsiales. Comp. Immunol. Microbiol. Infect. Dis. **36:**199–209.
36. **Davoust B, Mediannikov O, Marie JL, Socolovschi C, Parola P, Raoult D.** 2010. Are vertebrates reservoir hosts for *Rickettsia*? Bull. Acad. Vet. France **163:**291–302.
37. **Levin ML, Killmaster LF, Zemtsova GE.** 2012. Domestic dogs (*Canis familiaris*) as reservoir hosts for *Rickettsia conorii*. Vector Borne Zoonotic Dis. **12:**28–33.
38. **Zemtsova G, Killmaster LF, Mumcuoglu KY, Levin ML.** 2010. Co-feeding as a route for transmission of *Rickettsia conorii israelensis* between *Rhipicephalus sanguineus* ticks. Exp. Appl. Acarol. **52:**383–392.
39. **Horta MC, Moraes-Filho J, Casagrande RA, Saito TB, Rosa SC, Ogrzewalska M, Matushima ER, Labruna MB.** 2009. Experimental infection of opossums *Didelphis aurita* by *Rickettsia rickettsii* and evaluation of the transmission of the infection to ticks *Amblyomma cajennense*. Vector Borne Zoonotic Dis. **9:**109–118.
40. **Souza CE, Moraes-Filho J, Ogrzewalska M, Uchoa FC, Horta MC, Souza SS, Borba RC, Labruna MB.** 2009. Experimental infection of capybaras *Hydrochoerus hydrochaeris* by *Rickettsia rickettsii* and evaluation of the transmission of the infection to ticks *Amblyomma cajennense*. Vet. Parasitol. **161:**116–121.
41. **Reye AL, Arinola OG, Hubschen JM, Muller CP.** 2012. Pathogen prevalence in ticks collected from the vegetation and livestock in Nigeria. Appl. Environ. Microbiol. **78:**2562–2568.
42. **Ortuno A, Pons I, Quesada M, Lario S, Anton E, Gil A, Castella J, Segura F.** 2012. Evaluation of the presence of *Rickettsia slovaca* infection in domestic ruminants in Catalonia, Northeastern Spain. Vector Borne Zoonotic Dis. **12:**1019–1022.
43. **Ortuno A, Quesada M, Lopez-Claessens S, Castella J, Sanfeliu I, Anton E, Segura-Porta F.** 2007. The role of wild boar (*Sus scrofa*) in the eco-epidemiology of *R. slovaca* in Northeastern Spain. Vector Borne Zoonotic Dis. **7:**59–64.
44. **Inokuma H, Seino N, Suzuki M, Kaji K, Takahashi H, Igota H, Inoue S.** 2008. Detection of *Rickettsia helvetica* DNA from peripheral blood of sika deer (*Cervus nippon yesoensis*) in Japan. J. Wildl. Dis. **44:**164–167.
45. **La Scola B, Bechah Y, Lepidi H, Raoult D.** 2009. Prediction of rickettsial skin eschars in humans using an experimental guinea pig model. Microb. Pathog. **47:**128–133.
46. **Chapman AS, Murphy SM, Demma LJ, Holman RC, Curns AT, McQuiston JH, Krebs JW, Swerdlow DL.** 2006. Rocky Mountain spotted fever in the United States, 1997-2002. Vector Borne Zoonotic Dis. **6:**170–178.
47. **Chen LF, Sexton DJ.** 2008. What's new in Rocky Mountain spotted fever? Infect. Dis. Clin. North Am. **22:**415–432.
48. **Childs JE, Paddock CD.** 2007. Rocky Mountain spotted fever, p 97–116. *In* Raoult D, Parola P (ed), Rickettsial diseases. Informa Healthcare, New York, NY.
49. **Dantas-Torres F.** 2007. Rocky Mountain spotted fever. Lancet Infect. Dis. **7:**724–732.
50. **Estripeaut D, Aramburu MG, Saez-Llorens X, Thompson HA, Dasch GA, Paddock CD, Zaki S, Eremeeva ME.** 2007. Rocky Mountain spotted fever, Panama. Emerg. Infect. Dis. **13:**1763–1765.
51. **Hun L, Cortes X, Taylor L.** 2008. Molecular characterization of *Rickettsia rickettsii* isolated from human clinical samples and from the rabbit tick *Haemaphysalis leporispalustris* collected at different geographic zones in Costa Rica. Am. J. Trop. Med. Hyg. **79:**899–902.
52. **Eremeeva ME, Berganza E, Suarez G, Gobern L, Dueger E, Castillo L, Reyes L, Wikswo ME, Abramowicz KF, Dasch GA, Lindblade KA.** 2013. Investigation of an outbreak of rickettsial febrile illness in Guate-

mala, 2007. Int. J. Infect. Dis. **17:**e304–e311. doi:10.1016/j.ijid.2012.11.011.
53. **Openshaw JJ, Swerdlow DL, Krebs JW, Holman RC, Mandel E, Harvey A, Haberling D, Massung RF, McQuiston JH.** 2010. Rocky mountain spotted fever in the United States, 2000-2007: interpreting contemporary increases in incidence. Am. J. Trop. Med. Hyg. **83:**174–182.
54. **Demma LJ, Traeger MS, Nicholson WL, Paddock CD, Blau DM, Eremeeva ME, Dasch GA, Levin ML, Singleton J, Jr, Zaki SR, Cheek JE, Swerdlow DL, McQuiston JH.** 2005. Rocky Mountain spotted fever from an unexpected tick vector in Arizona. N. Engl. J. Med. **353:**587–594.
55. **Demma LJ, Holman RC, Mikosz CA, Curns AT, Swerdlow DL, Paisano EL, Cheek JE.** 2006. Rocky Mountain spotted fever hospitalizations among American Indians. Am. J. Trop. Med. Hyg. **75:**537–541.
56. **Nicholson WL, Paddock CD, Demma L, Traeger M, Johnson B, Dickson J, McQuiston J, Swerdlow D.** 2006. Rocky Mountain spotted fever in Arizona: documentation of heavy environmental infestations of *Rhipicephalus sanguineus* at an endemic site. Ann. N. Y. Acad. Sci. **1078:**338–341.
57. **Nicholson WL, Gordon R, Demma LJ.** 2006. Spotted fever group rickettsial infection in dogs from eastern Arizona: how long has it been there? Ann. N. Y. Acad. Sci. **1078:**519–522.
58. **McQuiston JH, Guerra MA, Watts MR, Lawaczeck E, Levy C, Nicholson WL, Adjemian J, Swerdlow DL.** 2011. Evidence of exposure to spotted fever group rickettsiae among Arizona dogs outside a previously documented outbreak area. Zoonoses Public Health **58:**85–92.
59. **Bustamente Moreno JG, Pon Méndez A.** 2010. Actualización en la vigilancia epidemiológica de "rickettsiosis." Part I. Epidemiol. Bol. **6:**1–4.
60. **Bustamente Moreno JG, Pon Méndez A.** 2010. Actualización en la vigilancia epidemiológica de "rickettsiosis." Part II. Epidemiol. Bol. **7:**1–3.
61. **Baty S, McElroy K, Levy C, Nicholson W, McQuiston J.** 2011. Emergence of a new focus of Rocky Mountain spotted fever—south central Arizona, 2009-2010, p 121. Abstr. 60th Annu. Epidemic Intell. Serv. Conf., Atlanta, GA.
62. **Holman RC, McQuiston JH, Haberling DL, Cheek JE.** 2009. Increasing incidence of Rocky Mountain spotted fever among the American Indian population in the United States. Am. J. Trop. Med. Hyg. **80:**601–605.
63. **Dahlgren FS, Holman RC, Paddock CD, Callinan LS, McQuiston JH.** 2012. Fatal Rocky Mountain spotted fever in the United States, 1999-2007. Am. J. Trop. Med. Hyg. **86:**713–719.
64. **Folkema AM, Holman RC, McQuiston JH, Cheek JE.** 2012. Trends in clinical diagnoses of Rocky Mountain spotted fever among American Indians, 2001-2008. Am. J. Trop. Med. Hyg. **86:**152–158.
65. **Paddock CD, Telford SRI.** 2011. Through a glass, darkly: the global incidence of tick-borne diseases, p 221–266. *In* Institute of Medicine (ed), Critical needs and gaps in understanding prevention, amelioration, and resolution of Lyme and other tick-borne diseases: the short-term and long-term outcomes. National Academies Press, Washington, DC.
66. **Paddock CD.** 2005. *Rickettsia parkeri* as a paradigm for multiple causes of tick-borne spotted fever in the Western Hemisphere. Ann. N. Y. Acad. Sci. **1063:**315–326.
67. **Whitman TJ, Richards AL, Paddock CD, Tamminga CL, Sniezek PJ, Jiang J, Byers DK, Sanders JW.** 2007. *Rickettsia parkeri* infection after tick bite, Virginia. Emerg. Infect. Dis. **13:**334–336.
68. **Paddock CD, Finley RW, Wright CS, Robinson HN, Schrodt BJ, Lane CC, Ekenna O, Blass MA, Tamminga CL, Ohl CA, McLellan SL, Goddard J, Holman RC, Openshaw JJ, Sumner JW, Zaki SR, Eremeeva ME.** 2008. *Rickettsia parkeri* rickettsiosis and its clinical distinction from Rocky Mountain spotted fever. Clin. Infect. Dis. **47:**1188–1196.
69. **Cragun WC, Bartlett BL, Ellis MW, Hoover AZ, Tyring SK, Mendoza N, Vento TJ, Nicholson WL, Eremeeva ME, Olano JP, Rapini RP, Paddock CD.** 2010. The expanding spectrum of eschar-associated rickettsioses in the United States. Arch. Dermatol. **146:**641–648.
70. **Centers for Disease Control and Prevention.** 2010. Spotted fever rickettsioses 2010 case definition. Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/spottedfever_current.htm. Accessed 5 October 2012.
71. **Parola P, Labruna MB, Raoult D.** 2009. Tick-borne rickettsioses in America: unanswered questions and emerging diseases. Curr. Infect. Dis. Rep. **11:**40–50.
72. **Bermudez SE, Eremeeva ME, Karpathy SE, Samudio F, Zambrano ML, Zaldivar Y, Motta JA, Dasch GA.** 2009. Detection and identification of rickettsial agents in ticks from domestic mammals in eastern Panama. J. Med. Entomol. **46:**856–861.
73. **Oliveira KA, Pinter A, Medina-Sanchez A, Boppana VD, Wikel SK, Saito TB, Shelite T, Blanton L, Popov V, Teel PD, Walker DH, Galvao MA, Mafra C, Bouyer DH.** 2010. *Amblyomma imitator* ticks as vectors of *Rickettsia rickettsii*, Mexico. Emerg. Infect. Dis. **16:**1282–1284.
74. **Berrada ZL, Goethert HK, Cunningham J, Telford SR, III.** 2011. *Rickettsia rickettsii* (Rickettsiales: Rickettsiaceae) in *Amblyomma americanum* (Acari: Ixodidae) from Kansas. J. Med. Entomol. **48:**461–467.
75. **Breitschwerdt EB, Hegarty BC, Maggi RG, Lantos PM, Aslett DM, Bradley JM.** 2011. *Rickettsia rickettsii* transmission by a lone star tick, North Carolina. Emerg. Infect. Dis. **17:**873–875.
76. **Wikswo ME, Hu R, Dasch GA, Krueger L, Arugay A, Jones K, Hess B, Bennett S, Kramer V, Eremeeva ME.** 2008. Detection and identification of spotted fever group rickettsiae in *Dermacentor* species from southern California. J. Med. Entomol. **45:**509–516.
77. **Dergousoff SJ, Gajadhar AJ, Chilton NB.** 2009. Prevalence of *Rickettsia* species in Canadian populations of *Dermacentor andersoni* and *D. variabilis*. Appl. Environ. Microbiol. **75:**1786–1789.
78. **Moncayo AC, Cohen SB, Fritzen CM, Huang E, Yabsley MJ, Freye JD, Dunlap BG, Huang J, Mead DG, Jones TF, Dunn JR.** 2010. Absence of *Rickettsia rickettsii* and occurrence of other spotted fever group rickettsiae in ticks from Tennessee. Am. J. Trop. Med. Hyg. **83:**653–657.
79. **Fritzen CM, Huang J, Westby K, Freye JD, Dunlap B, Yabsley MJ, Schardein M, Dunn JR, Jones TF, Moncayo AC.** 2011. Infection prevalences of common tick-borne pathogens in adult lone star ticks (*Amblyomma americanum*) and American dog ticks (*Dermacentor variabilis*) in Kentucky. Am. J. Trop. Med. Hyg. **85:**718–723.
80. **Stromdahl EY, Jiang J, Vince M, Richards AL.** 2011. Infrequency of *Rickettsia rickettsii* in *Dermacentor variabilis* removed from humans, with comments on the role of other human-biting ticks associated with spotted fever group rickettsiae in the United States. Vector Borne Zoonotic Dis. **11:**969–977.
81. **Eremeeva ME, Bosserman E, Zambrano M, Demma L, Dasch GA.** 2006. Molecular typing of novel *Rickettsia rickettsii* isolates from Arizona. Ann. N. Y. Acad. Sci. **1078:**573–577.
82. **Garrison LE, Kelly R, Nicholson WL, Eremeeva ME.** 2007. Tick surveillance notes: *Rickettsia rickettsii* in *Rhipicephalus sanguineus* from Gordon County. Georgia Epidemiol. Rep. **23:**1–2.
83. **Eremeeva ME, Zambrano ML, Anaya L, Beati L, Karpathy SE, Santos-Silva MM, Salceda B, MacBeth D, Olguin H, Dasch GA, Aranda CA.** 2011. *Rickettsia rickettsii* in *Rhipicephalus* ticks, Mexicali, Mexico. J. Med. Entomol. **48:**418–421.
84. **Carmichael JR, Fuerst PA.** 2006. A rickettsial mixed infection in a *Dermacentor variabilis* tick from Ohio. Ann. N. Y. Acad. Sci. **1078:**334–337.
85. **Arguello AP, Hun L, Rivera P, Taylor L.** 2012. A fatal urban case of Rocky Mountain spotted fever presenting an eschar in San Jose, Costa Rica. Am. J. Trop. Med. Hyg. **87:**345–348.
86. **Minniear TD, Buckingham SC.** 2009. Managing Rocky Mountain spotted fever. Expert Rev. Anti Infect. Ther. **7:**1131–1137.
87. **Buckingham SC, Marshall GS, Schutze GE, Woods CR, Jackson MA, Patterson LE, Jacobs RF.** 2007. Clinical and laboratory features, hospital course, and outcome of Rocky Mountain spotted fever in children. J. Pediatr. **150:**180–184.
88. **Martinez-Medina MA, Alvarez-Hernandez G, Padilla-Zamudioa JG, Rojas-Guerra MG.** 2007. Rocky Mountain spotted fever in children: clinical and epidemiological features. Gac. Med. Mex. **143:**137–140. (In Spanish.)
89. **Zavala-Castro JE, Dzul-Rosado KR, Leon JJ, Walker DH, Zavala-Velazquez JE.** 2008. An increase in human cases of spotted fever rickettsiosis in Yucatan, Mexico, involving children. Am. J. Trop. Med. Hyg. **79:**907–910.
90. **Sanchez R, Alpuche C, Lopez-Gatell H, Soria C, Estrada J, Olguin H, Lezana MA, Nicholson W, Eremeeva M, CDC Infectious Disease Pathology Branch, Dasch G, Fonseca M, Montiel S, Waterman S, McQuiston J.** 2009. *Rhipicephalus sanguineus*-associated Rocky Mountain spotted fever in Mexicali, Mexico: observations from an outbreak in 2008-2009, abstr 75. Abstr. 23rd Meet. Am. Soc. Rickettsiol., Hilton Head, SC, 15 to 18 August 2009.
91. **Alvarez-Hernandez G.** 2010. Rocky Mountain spotted fever, a forgotten epidemic. Salud Publica Mex. **52**(1)**:**1–3. (In Spanish.)
92. **Tribaldos M, Zaldivar Y, Bermudez S, Samudio F, Mendoza Y, Mar-**

tinez AA, Villalobos R, Eremeeva ME, Paddock CD, Page K, Smith RE, Pascale JM. 2011. Rocky Mountain spotted fever in Panama: a cluster description. J. Infect. Dev. Ctries. **5:**737–741.
93. **Karpathy SE, Dasch GA, Eremeeva ME.** 2007. Molecular typing of isolates of *Rickettsia rickettsii* by use of DNA sequencing of variable intergenic regions. J. Clin. Microbiol. **45:**2545–2553.
94. **Eremeeva ME, Dasch GA.** 2009. Closing the gaps between genotype and phenotype in *Rickettsia rickettsii*. Ann. N. Y. Acad. Sci. **1166:**12–26.
95. **Sumner JW, Durden LA, Goddard J, Stromdahl EY, Clark KL, Reeves WK, Paddock CD.** 2007. Gulf Coast ticks (*Amblyomma maculatum*) and *Rickettsia parkeri*, United States. Emerg. Infect. Dis. **13:**751–753.
96. **Paddock CD, Fournier PE, Sumner JW, Goddard J, Elshenawy Y, Metcalfe MG, Loftis AD, Varela-Stokes A.** 2010. Isolation of *Rickettsia parkeri* and identification of a novel spotted fever group *Rickettsia* sp. from Gulf Coast ticks (*Amblyomma maculatum*) in the United States. Appl. Environ. Microbiol. **76:**2689–2696.
97. **Trout R, Steelman CD, Szalanski AL, Williamson PC.** 2010. Rickettsiae in Gulf Coast ticks, Arkansas, USA. Emerg. Infect. Dis. **16:**830–832.
98. **Wright CL, Nadolny RM, Jiang J, Richards AL, Sonenshine DE, Gaff HD, Hynes WL.** 2011. *Rickettsia parkeri* in Gulf Coast ticks, southeastern Virginia, USA. Emerg. Infect. Dis. **17:**896–898.
99. **Fornadel CM, Zhang X, Smith JD, Paddock CD, Arias JR, Norris DE.** 2011. High rates of *Rickettsia parkeri* infection in Gulf Coast ticks (*Amblyomma maculatum*) and identification of "*Candidatus* Rickettsia andeanae" from Fairfax County, Virginia. Vector Borne Zoonotic Dis. **11:**1535–1539.
100. **Varela-Stokes AS, Paddock CD, Engber B, Toliver M.** 2011. *Rickettsia parkeri* in *Amblyomma maculatum* ticks, North Carolina, USA, 2009-2010. Emerg. Infect. Dis. **17:**2350–2353.
101. **Ferrari FA, Goddard J, Paddock CD, Varela-Stokes AS.** 2012. *Rickettsia parkeri* and *Candidatus Rickettsia andeanae* in Gulf Coast ticks, Mississippi, USA. Emerg. Infect. Dis. **18:**1705–1707.
102. **Edwards KT, Goddard J, Varela-Stokes A.** 2011. Distribution of spotted fever group rickettsiae in select tissues of experimentally infected and field-collected Gulf Coast ticks. J. Med. Entomol. **48:**687–690.
103. **Cohen SB, Yabsley MJ, Garrison LE, Freye JD, Dunlap BG, Dunn JR, Mead DG, Jones TF, Moncayo AC.** 2009. *Rickettsia parkeri* in *Amblyomma americanum* ticks, Tennessee and Georgia, USA. Emerg. Infect. Dis. **15:**1471–1473.
104. **Williamson PC, Billingsley PM, Teltow GJ, Seals JP, Turnbough MA, Atkinson SF.** 2010. *Borrelia*, *Ehrlichia*, and *Rickettsia* spp. in ticks removed from persons, Texas, USA. Emerg. Infect. Dis. **16:**441–446.
105. **Edwards KT, Goddard J, Jones TL, Paddock CD, Varela-Stokes AS.** 2011. Cattle and the natural history of *Rickettsia parkeri* in Mississippi. Vector Borne Zoonotic Dis. **11:**485–491.
106. **Grasperge BJ, Wolfson W, Macaluso KR.** 2012. *Rickettsia parkeri* infection in domestic dogs, Southern Louisiana, USA, 2011. Emerg. Infect. Dis. **18:**995–997.
107. **Raoult D, Paddock CD.** 2005. *Rickettsia parkeri* infection and other spotted fevers in the United States. N. Engl. J. Med. **353:**626–627.
108. **Paddock CD.** 2009. The science and fiction of emerging rickettsioses. Ann. N. Y. Acad. Sci. **1166:**133–143.
109. **Chen LH, Wilson ME.** 2009. Tick-borne rickettsiosis in traveler returning from Honduras. Emerg. Infect. Dis. **15:**1321–1323.
110. **Eremeeva ME, Bosserman EA, Demma LJ, Zambrano ML, Blau DM, Dasch GA.** 2006. Isolation and identification of *Rickettsia massiliae* from *Rhipicephalus sanguineus* ticks collected in Arizona. Appl. Environ. Microbiol. **72:**5569–5577.
111. **Beeler E, Abramowicz KF, Zambrano ML, Sturgeon MM, Khalaf N, Hu R, Dasch GA, Eremeeva ME.** 2011. A focus of dogs and *Rickettsia massiliae*-infected *Rhipicephalus sanguineus* in California. Am. J. Trop. Med. Hyg. **84:**244–249.
112. **Wikswo ME, Hu R, Metzger ME, Eremeeva ME.** 2007. Detection of *Rickettsia rickettsii* and *Bartonella henselae* in *Rhipicephalus sanguineus* ticks from California. J. Med. Entomol. **44:**158–162.
113. **Kelly PJ.** 2006. *Rickettsia africae* in the West Indies. Emerg. Infect. Dis. **12:**224–226.
114. **Robinson JB, Eremeeva ME, Olson PE, Thornton SA, Medina MJ, Sumner JW, Daschi GA.** 2009. New approaches to detection and identification of *Rickettsia africae* and *Ehrlichia ruminantium* in *Amblyomma variegatum* (Acari: Ixodidae) ticks from the Caribbean. J. Med. Entomol. **46:**942–951.
115. **Kelly P, Lucas H, Beati L, Yowell C, Mahan S, Dame J.** 2010. *Rickettsia africae* in *Amblyomma variegatum* and domestic ruminants on eight Caribbean islands. J. Parasitol. **96:**1086–1088.
116. **Owen CE, Bahrami S, Malone JC, Callen JP, Kulp-Shorten CL.** 2006. African tick bite fever: a not-so-uncommon illness in international travelers. Arch. Dermatol. **142:**1312–1314.
117. **McQuade J, Cather JC.** 2006. Fever and malaise associated with a painful papule on the ankle. Proc. Bayl. Univ. Med. Cent. **19:**49–51.
118. **Freedman DO, Weld LH, Kozarsky PE, Fisk T, Robins R, von Sonnenburg F, Keystone JS, Pandey P, Cetron MS.** 2006. Spectrum of disease and relation to place of exposure among ill returned travelers. N. Engl. J. Med. **354:**119–130.
119. **Shapiro MR, Fritz CL, Tait K, Paddock CD, Nicholson WL, Abramowicz KF, Karpathy SE, Dasch GA, Sumner JW, Adem PV, Scott JJ, Padgett KA, Zaki SR, Eremeeva ME.** 2010. *Rickettsia* 364D: a newly recognized cause of eschar-associated illness in California. Clin. Infect. Dis. **50:**541–548.
120. **Mediannikov O, Parola P, Raoult D.** 2007. Other tick-borne rickettsioses, p 139–163. *In* Raoult D, Parola P (ed), Rickettsial diseases. Informa Healthcare, New York, NY.
121. **Eremeeva ME, Madan A, Shaw CD, Tang K, Dasch GA.** 2005. New perspectives on rickettsial evolution from new genome sequences of rickettsia, particularly *R. canadensis*, and *Orientia tsutsugamushi*. Ann. N. Y. Acad. Sci. **1063:**47–63.
122. **Yabsley MJ, Nims TN, Savage MY, Durden LA.** 2009. Ticks and tick-borne pathogens and putative symbionts of black bears (*Ursus americanus floridanus*) from Georgia and Florida. J. Parasitol. **95:**1125–1128.
123. **McQuiston JH, Zemtsova G, Perniciaro J, Hutson M, Singleton J, Nicholson WL, Levin ML.** 2012. Afebrile spotted fever group *Rickettsia* infection after a bite from a *Dermacentor variabilis* tick infected with *Rickettsia montanensis*. Vector Borne Zoonotic. Dis. **12:**1059–1061.
124. **Kurtti TJ, Simser JA, Baldridge GD, Palmer AT, Munderloh UG.** 2005. Factors influencing in vitro infectivity and growth of *Rickettsia peacockii* (Rickettsiales: Rickettsiaceae), an endosymbiont of the Rocky Mountain wood tick, *Dermacentor andersoni* (Acari, Ixodidae). J. Invertebr. Pathol. **90:**177–186.
125. **Simser JA, Rahman MS, Dreher-Lesnick SM, Azad AF.** 2005. A novel and naturally occurring transposon, ISRpe1 in the *Rickettsia peacockii* genome disrupting the rickA gene involved in actin-based motility. Mol. Microbiol. **58:**71–79.
126. **Felsheim RF, Kurtti TJ, Munderloh UG.** 2009. Genome sequence of the endosymbiont *Rickettsia peacockii* and comparison with virulent *Rickettsia rickettsii*: identification of virulence factors. PLoS One **4:**e8361. doi: 10.1371/journal.pone.0008361.
127. **Clay K, Klyachko O, Grindle N, Civitello D, Oleske D, Fuqua C.** 2008. Microbial communities and interactions in the lone star tick, *Amblyomma americanum*. Mol. Ecol. **17:**4371–4381.
128. **Heise SR, Elshahed MS, Little SE.** 2010. Bacterial diversity in *Amblyomma americanum* (Acari: Ixodidae) with a focus on members of the genus *Rickettsia*. J. Med. Entomol. **47:**258–268.
129. **Jiang J, Yarina T, Miller MK, Stromdahl EY, Richards AL.** 2010. Molecular detection of *Rickettsia amblyommii* in *Amblyomma americanum* parasitizing humans. Vector Borne Zoonotic Dis. **10:**329–340.
130. **Zanettii AS, Pornwiroon W, Kearney MT, Macaluso KR.** 2008. Characterization of rickettsial infection in *Amblyomma americanum* (Acari: Ixodidae) by quantitative real-time polymerase chain reaction. J. Med. Entomol. **45:**267–275.
131. **Mixson TR, Campbell SR, Gill JS, Ginsberg HS, Reichard MV, Schulze TL, Dasch GA.** 2006. Prevalence of *Ehrlichia*, *Borrelia*, and rickettsial agents in *Amblyomma americanum* (Acari: Ixodidae) collected from nine states. J. Med. Entomol. **43:**1261–1268.
132. **Smith MP, Ponnusamy L, Jiang J, Ayyash LA, Richards AL, Apperson CS.** 2010. Bacterial pathogens in Ixodid ticks from a Piedmont County in North Carolina: prevalence of rickettsial organisms. Vector Borne Zoonotic Dis. **10:**939–952.
133. **Schulze TL, Jordan RA, White JC, Roegner VE, Healy SP.** 2011. Geographical distribution and prevalence of selected *Borrelia*, *Ehrlichia*, and *Rickettsia* infections in *Amblyomma americanum* (Acari: Ixodidae) in New Jersey. J. Am. Mosq. Control Assoc. **27:**236–244.
134. **Zhang X, Ren X, Norris DE, Rasgon JL.** 2012. Distribution and infection frequency of '*Candidatus Rickettsia amblyommii*' in Maryland populations of the lone star tick (*Amblyomma americanum*) and culture in an *Anopheles gambiae* mosquito cell line. Ticks Tick Borne Dis. **3:**38–42.

135. **Stromdahl EY, Vince MA, Billingsley PM, Dobbs NA, Williamson PC.** 2008. *Rickettsia amblyommii* infecting *Amblyomma americanum* larvae. Vector Borne Zoonotic Dis. **8:**15–24.
136. **Castellaw AH, Showers J, Goddard J, Chenney EF, Varela-Stokes AS.** 2010. Detection of vector-borne agents in lone star ticks, Amblyomma americanum (Acari: Ixodidae), from Mississippi. J. Med. Entomol. **47:** 473–476.
137. **Apperson CS, Engber B, Nicholson WL, Mead DG, Engel J, Yabsley MJ, Dail K, Johnson J, Watson DW.** 2008. Tick-borne diseases in North Carolina: is "Rickettsia amblyommii" a possible cause of rickettsiosis reported as Rocky Mountain spotted fever? Vector Borne Zoonotic Dis. **8:**597–606.
138. **Hun L, Troyo A, Taylor L, Barbieri AM, Labruna MB.** 2011. First report of the isolation and molecular characterization of *Rickettsia amblyommii* and *Rickettsia felis* in Central America. Vector Borne Zoonotic Dis. **11:**1395–1397.
139. **Bermudez CS, Zaldivar AY, Spolidorio MG, Moraes-Filho J, Miranda RJ, Caballero CM, Mendoza Y, Labruna MB.** 2011. Rickettsial infection in domestic mammals and their ectoparasites in El Valle de Anton, Cocle, Panama. Vet. Parasitol. **177:**134–138.
140. **Eremeeva ME, Karpathy SE, Levin ML, Caballero CM, Bermudez S, Dasch GA, Motta JA.** 2009. Spotted fever rickettsiae, *Ehrlichia* and *Anaplasma*, in ticks from peridomestic environments in Panama. Clin. Microbiol. Infect. **15**(Suppl 2):12–14.
141. **Billeter SA, Blanton HL, Little SE, Levy MG, Breitschwerdt EB.** 2007. Detection of *Rickettsia amblyommii* in association with a tick bite rash. Vector Borne Zoonotic Dis. **7:**607–610.
142. **Nicholson WL, Masters E, Wormser GP.** 2009. Preliminary serologic investigation of '*Rickettsia amblyommii*' in the aetiology of Southern tick associated rash illness (STARI). Clin. Microbiol. Infect. **15**(Suppl 2):235–236.
143. **Jiang J, Stromdahl EY, Richards AL.** 2012. Detection of *Rickettsia parkeri* and *Candidatus Rickettsia andeanae* in *Amblyomma maculatum* Gulf Coast ticks collected from humans in the United States. Vector Borne Zoonotic Dis. **12:**175–182.
144. **Luce-Fedrow A, Wright C, Gaff HD, Sonenshine DE, Hynes WL, Richards AL.** 2012. In vitro propagation of *Candidatus Rickettsia andeanae* isolated from *Amblyomma maculatum*. FEMS Immunol. Med. Microbiol. **64:**74–81.
145. **Moreno CX, Moy F, Daniels TJ, Godfrey HP, Cabello FC.** 2006. Molecular analysis of microbial communities identified in different developmental stages of *Ixodes scapularis* ticks from Westchester and Dutchess Counties, New York. Environ. Microbiol. **8:**761–772.
146. **Rounds MA, Crowder CD, Matthews HE, Philipson CA, Scoles GA, Ecker DJ, Schutzer SE, Eshoo MW.** 2012. Identification of endosymbionts in ticks by broad-range polymerase chain reaction and electrospray ionization mass spectrometry. J. Med. Entomol. **49:**843–850.
147. **Phan JN, Lu CR, Bender WG, Smoak RM, Zhong J, III.** 2011. Molecular detection and identification of *Rickettsia* species in *Ixodes pacificus* in California. Vector Borne Zoonotic Dis. **11:**957–961.
148. **Zemtsova GE, Gleim E, Yabsley MJ, Conner LM, Mann T, Brown MD, Wendland L, Levin ML.** 2012. Detection of a novel spotted fever group *Rickettsia* in the gophertortoise tick. J. Med. Entomol. **49:**783–786.
149. **Loftis AD, Gill JS, Schriefer ME, Levin ML, Eremeeva ME, Gilchrist MJ, Dasch GA.** 2005. Detection of *Rickettsia*, *Borrelia*, and *Bartonella* in Carios kelleyi (Acari: Argasidae). J. Med. Entomol. **42:**473–480.
150. **Angerami RN, Resende MR, Feltrin AF, Katz G, Nascimento EM, Stucchi RS, Silva LJ.** 2006. Brazilian spotted fever: a case series from an endemic area in southeastern Brazil: clinical aspects. Ann. N. Y. Acad. Sci. **1078:**252–254.
151. **Angerami RN, da Silva AM, Nascimento EM, Colombo S, Wada MY, dos Santos FC, Mancini DM, de Oliveira RC, Katz G, Martins EC, da Silva LJ.** 2009. Brazilian spotted fever: two faces of a same disease? A comparative study of clinical aspects between an old and a new endemic area in Brazil. Clin. Microbiol. Infect. **15**(Suppl 2):207–208.
152. **Hidalgo M, Orejuela L, Fuya P, Carrillo P, Hernandez J, Parra E, Keng C, Small M, Olano JP, Bouyer D, Castaneda E, Walker D, Valbuena G.** 2007. Rocky Mountain spotted fever, Colombia. Emerg. Infect. Dis. **13:** 1058–1060.
153. **Paddock CD, Fernandez S, Echenique GA, Sumner JW, Reeves WK, Zaki SR, Remondegui CE.** 2008. Rocky Mountain spotted fever in Argentina. Am. J. Trop. Med. Hyg. **78:**687–692.
154. **Hidalgo M, Miranda J, Heredia D, Zambrano P, Vesga JF, Lizarazo D, Mattar S, Valbuena G.** 2011. Outbreak of Rocky Mountain spotted fever in Cordoba, Colombia. Mem. Inst. Oswaldo Cruz **106:**117–118.
155. **Labruna MB, Kamakura O, Moraes-Filho J, Horta MC, Pacheco RC.** 2009. Rocky Mountain spotted fever in dogs, Brazil. Emerg. Infect. Dis. **15:**458–460.
156. **de Sa Del Fiol F, Junqueira FM, da Rocha MCP, de Toledo MI, Barberato Filho S.** 2010. A febre maculosa no Brasil. Rev. Panam. Salud Publica **27:**461–466.
157. **Horta MC, Labruna MB, Pinter A, Linardi PM, Schumaker TT.** 2007. *Rickettsia* infection in five areas of the state of Sao Paulo, Brazil. Mem. Inst. Oswaldo Cruz **102:**793–801.
158. **Guglielmone AA, Beati L, Barros-Battesti DM, Labruna MB, Nava S, Venzal JM, Mangold AJ, Szabo MP, Martins JR, Gonzalez-Acuna D, Estrada-Pena A.** 2006. Ticks (Ixodidae) on humans in South America. Exp. Appl. Acarol. **40:**83–100.
159. **Labruna MB.** 2009. Ecology of rickettsia in South America. Ann. N. Y. Acad. Sci. **1166:**156–166.
160. **Pinter A, Labruna MB.** 2006. Isolation of *Rickettsia rickettsii* and *Rickettsia bellii* in cell culture from the tick *Amblyomma aureolatum* in Brazil. Ann. N. Y. Acad. Sci. **1078:**523–529.
161. **Katz G, Neves VLFC, Angerami RN, Nascimento EMM, Colombo S.** 2009. Statistics and epidemiology of Brazilian spotted fever in São Paulo, Brazil. Bol. Epidemiol. Paulista **6:**4–13.
162. **Ogrzewalska M, Saraiva DG, Moraes-Filho J, Martins TF, Costa FB, Pinter A, Labruna MB.** 2012. Epidemiology of Brazilian spotted fever in the Atlantic Forest, state of Sao Paulo, Brazil. Parasitology **139:**1283–1300.
163. **Labruna MB, Ogrzewalska M, Martins TF, Pinter A, Horta MC.** 2008. Comparative susceptibility of larval stages of *Amblyomma aureolatum*, *Amblyomma cajennense*, and *Rhipicephalus sanguineus* to infection by *Rickettsia rickettsii*. J. Med. Entomol. **45:**1156–1159.
164. **Moraes-Filho J, Pinter A, Pacheco RC, Gutmann TB, Barbosa SO, Gonzales MA, Muraro MA, Cecilio SR, Labruna MB.** 2009. New epidemiological data on Brazilian spotted fever in an endemic area of the state of Sao Paulo, Brazil. Vector Borne Zoonotic Dis. **9:**73–78.
165. **Cunha NC, Fonseca AH, Rezende J, Rozental T, Favacho ARM, Barreira JD, Massard CL, Lemos ERS.** 2009. First identification of natural infection of *Rickettsia rickettsii* in the *Rhipicephalus sanguineus* tick, in the State of Rio de Janeiro. Pesqui. Vet. Bras. **29:**105–108.
166. **Gehrke FS, Gazeta GS, Souza ER, Ribeiro A, Marrelli MT, Schumaker TT.** 2009. *Rickettsia rickettsii*, *Rickettsia felis* and *Rickettsia* sp. TwKM03 infecting *Rhipicephalus sanguineus* and *Ctenocephalides felis* collected from dogs in a Brazilian spotted fever focus in the State of Rio De Janeiro/ Brazil. Clin. Microbiol. Infect. **15**(Suppl 2):267–268.
167. **de Almeida RF, Garcia MV, Cunha RC, Matias J, Araujo e Silva E, de Fatima Cepa Matos M, Andreotti R.** 2013. Ixodid fauna and zoonotic agents in ticks from dogs: first report of *Rickettsia rickettsii* in *Rhipicephalus sanguineus* in the state of Mato Grosso do Sul, mid-western Brazil. Exp. Appl. Acarol. **60:**63–72.
168. **Venzal JM, Estrada-Pena A, Portillo A, Mangold AJ, Castro O, De Souza CG, Felix ML, Perez-Martinez L, Santibanez S, Oteo JA.** 2012. *Rickettsia parkeri*: a rickettsial pathogen transmitted by ticks in endemic areas for spotted fever rickettsiosis in southern Uruguay. Rev. Inst. Med. Trop. Sao Paulo **54:**131–134.
169. **Silveira I, Pacheco RC, Szabo MP, Ramos HG, Labruna MB.** 2007. *Rickettsia parkeri* in Brazil. Emerg. Infect. Dis. **13:**1111–1113.
170. **Nava S, Elshenawy Y, Eremeeva ME, Sumner JW, Mastropaolo M, Paddock CD.** 2008. *Rickettsia parkeri* in Argentina. Emerg. Infect. Dis. **14:**1894–1897.
171. **Romer Y, Seijo AC, Crudo F, Nicholson WL, Varela-Stokes A, Lash RR, Paddock CD.** 2011. *Rickettsia parkeri* rickettsiosis, Argentina. Emerg. Infect. Dis. **17:**1169–1173.
172. **Conti-Diaz IA, Moraes-Filho J, Pacheco RC, Labruna MB.** 2009. Serological evidence of *Rickettsia parkeri* as the etiological agent of rickettsiosis in Uruguay. Rev. Inst. Med. Trop. Sao Paulo **51:**337–339.
173. **Cicuttin GL, Rodríguez VM, Jado I, Anda P.** 2004. Primera detección de *Rickettsia massiliae* en la Ciudad de Buenos Aires. Resultados preliminares. Rev. Argent. Zoonosis **1:**8–10.
174. **Garcia-Garcia JC, Portillo A, Nunez MJ, Santibanez S, Castro B, Oteo JA.** 2010. A patient from Argentina infected with *Rickettsia massiliae*. Am. J. Trop. Med. Hyg. **82:**691–692.
175. **Moraes-Filho J, Marcili A, Nieri-Bastos FA, Richtzenhain LJ, Labruna**

MB. 2011. Genetic analysis of ticks belonging to the *Rhipicephalus sanguineus* group in Latin America. Acta Trop. **117:**51–55.
176. **Nava S, Mastropaolo M, Venzal JM, Mangold AJ, Guglielmone AA.** 2012. Mitochondrial DNA analysis of *Rhipicephalus sanguineus* sensu lato (Acari: Ixodidae) in the Southern Cone of South America. Vet. Parasitol. **190:**547–555.
177. **Parola P, Socolovschi C, Jeanjean L, Bitam I, Fournier PE, Sotto A, Labauge P, Raoult D.** 2008. Warmer weather linked to tick attack and emergence of severe rickettsioses. PLoS Negl. Trop. Dis. **2:**e338. doi:10.1371/journal.pntd.0000338.
178. **Spolidorio MG, Labruna MB, Mantovani E, Brandao PE, Richtzenhain LJ, Yoshinari NH.** 2010. Novel spotted fever group rickettsiosis, Brazil. Emerg. Infect. Dis. **16:**521–523.
179. **Silva N, Eremeeva ME, Rozental T, Ribeiro GS, Paddock CD, Ramos EA, Favacho AR, Reis MG, Dasch GA, de Lemos ER, Ko AI.** 2011. Eschar-associated spotted fever rickettsiosis, Bahia, Brazil. Emerg. Infect. Dis. **17:**275–278.
180. **Sabatini GS, Pinter A, Nieri-Bastos FA, Marcili A, Labruna MB.** 2010. Survey of ticks (Acari: Ixodidae) and their rickettsia in an Atlantic rain forest reserve in the State of Sao Paulo, Brazil. J. Med. Entomol. **47:**913–916.
181. **Medeiros AP, Souza AP, Moura AB, Lavina MS, Bellato V, Sartor AA, Nieri-Bastos FA, Richtzenhain LJ, Labruna MB.** 2011. Spotted fever group *Rickettsia* infecting ticks (Acari: Ixodidae) in the state of Santa Catarina, Brazil. Mem. Inst. Oswaldo Cruz **106:**926–930.
182. **Labruna MB, Camargo LM, Camargo EP, Walker DH.** 2005. Detection of a spotted fever group *Rickettsia* in the tick *Haemaphysalis juxtakochi* in Rondonia, Brazil. Vet. Parasitol. **127:**169–174.
183. **Labruna MB, Pacheco RC, Richtzenhain LJ, Szabo MP.** 2007. Isolation of *Rickettsia rhipicephali* and *Rickettsia bellii* from *Haemaphysalis juxtakochi* ticks in the state of Sao Paulo, Brazil. Appl. Environ. Microbiol. **73:**869–873.
184. **Labruna MB, Horta MC, Aguiar DM, Cavalcante GT, Pinter A, Gennari SM, Camargo LM.** 2007. Prevalence of *Rickettsia* infection in dogs from the urban and rural areas of Monte Negro municipality, western Amazon, Brazil. Vector Borne Zoonotic Dis. **7:**249–255.
185. **Labruna MB, Pacheco RC, Nava S, Brandao PE, Richtzenhain LJ, Guglielmone AA.** 2007. Infection by *Rickettsia bellii* and *Candidatus* "*Rickettsia amblyommii*" in *Amblyomma neumanni* ticks from Argentina. Microb. Ecol. **54:**126–133.
186. **Ogrzewalska M, Literak I, Cardenas-Callirgos JM, Capek M, Labruna MB.** 2012. *Rickettsia bellii* in ticks *Amblyomma varium* Koch, 1844, from birds in Peru. Ticks Tick Borne Dis. **3:**254–256.
187. **Pacheco RC, Horta MC, Moraes-Filho J, Ataliba AC, Pinter A, Labruna MB.** 2007. Rickettsial infection in capybaras (*Hydrochoerus hydrochaeris*) from Sao Paulo, Brazil: serological evidence for infection by *Rickettsia bellii* and *Rickettsia parkeri*. Biomedica **27:**364–371.
188. **Pacheco RC, Moraes-Filho J, Marcili A, Richtzenhain LJ, Szabo MP, Catroxo MH, Bouyer DH, Labruna MB.** 2011. *Rickettsia monteiroi* sp. nov., infecting the tick *Amblyomma incisum* in Brazil. Appl. Environ. Microbiol. **77:**5207–5211.
189. **Labruna MB, Mattar S, Nava S, Bermudez S, Venzal JM, Dolz G, Abarca K, Romero L, de Sousa R, Oteo J, Zavala-Castro J.** 2011. Rickettsioses in Latin America, Caribbean, Spain and Portugal. Rev. MVZ Cordoba **16:**2435–2457.
190. **Ogrzewalska M, Uezu A, Labruna MB.** 2010. Ticks (Acari: Ixodidae) infesting wild birds in the eastern Amazon, northern Brazil, with notes on rickettsial infection in ticks. Parasitol. Res. **106:**809–816.
191. **Parola P, Matsumoto K, Socolovschi C, Parzy D, Raoult D.** 2007. A tick-borne rickettsia of the spotted-fever group, similar to *Rickettsia amblyommii*, in French Guyana. Ann. Trop. Med. Parasitol. **101:**185–188.
192. **Ogrzewalska M, Pacheco RC, Uezu A, Ferreira F, Labruna MB.** 2008. Ticks (Acari: Ixodidae) infesting wild birds in an Atlantic forest area in the state of Sao Paulo, Brazil, with isolation of rickettsia from the tick *Amblyomma longirostre*. J. Med. Entomol. **45:**770–774.
193. **Melo AL, Martins TF, Horta MC, Moraes-Filho J, Pacheco RC, Labruna MB, Aguiar DM.** 2011. Seroprevalence and risk factors to *Ehrlichia* spp. and *Rickettsia* spp. in dogs from the Pantanal Region of Mato Grosso State, Brazil. Ticks Tick Borne Dis. **2:**213–218.
194. **Jiang J, Blair PJ, Felices V, Moron C, Cespedes M, Anaya E, Schoeler GB, Sumner JW, Olson JG, Richards AL.** 2005. Phylogenetic analysis of a novel molecular isolate of spotted fever group rickettsiae from northern Peru: Candidatus *Rickettsia andeanae*. Ann. N. Y. Acad. Sci. **1063:**337–342.
195. **Pacheco RC, Moraes-Filho J, Nava S, Brandao PE, Richtzenhain LJ, Labruna MB.** 2007. Detection of a novel spotted fever group rickettsia in *Amblyomma parvum* ticks (Acari: Ixodidae) from Argentina. Exp. Appl. Acarol. **43:**63–71.
196. **Tomassone L, Nunez P, Ceballos LA, Gurtler RE, Kitron U, Farber M.** 2010. Detection of "*Candidatus Rickettsia* sp. strain Argentina" and *Rickettsia bellii* in *Amblyomma* ticks (Acari: Ixodidae) from Northern Argentina. Exp. Appl. Acarol. **52:**93–100.
197. **Abarca K, Lopez J, Acosta-Jamett G, Lepe P, Soares JF, Labruna MB.** 2012. A third *Amblyomma* species and the first tick-borne rickettsia in Chile. J. Med. Entomol. **49:**219–222.
198. **Ogrzewalska M, Pacheco RC, Uezu A, Richtzenhain LJ, Ferreira F, Labruna MB.** 2009. Rickettsial infection in *Amblyomma nodosum* ticks (Acari: Ixodidae) from Brazil. Ann. Trop. Med. Parasitol. **103:**413–425.
199. **Almeida RF, Garcia MV, Cunha RC, Matias J, Labruna MB, Andreotti R.** 2013. The first report of *Rickettsia* spp. in *Amblyomma nodosum* in the State of Mato Grosso do Sul, Brazil. Ticks Tick Borne Dis. **4:**156–159.
200. **Pacheco RC, Arzua M, Nieri-Bastos FA, Moraes-Filho J, Marcili A, Richtzenhain LJ, Barros-Battesti DM, Labruna MB.** 2012. Rickettsial infection in ticks (Acari: Ixodidae) collected on birds in southern Brazil. J. Med. Entomol. **49:**710–716.
201. **Guedes E, Leite RC, Pacheco RC, Silveira I, Labruna MB.** 2011. *Rickettsia* species infecting *Amblyomma* ticks from an area endemic for Brazilian spotted fever in Brazil. Rev. Bras. Parasitol. Vet. **20:**308–311.
202. **Almeida AP, Cunha LM, Bello AC, da Cunha AP, Domingues LN, Leite RC, Labruna MB.** 2011. A novel *Rickettsia* infecting *Amblyomma dubitatum* ticks in Brazil. Ticks Tick Borne Dis. **2:**209–212.
203. **Spolidorio MG, Andreoli GS, Martins TF, Brandao PE, Labruna MB.** 2012. Rickettsial infection in ticks collected from road-killed wild animals in Rio de Janeiro, Brazil. J. Med. Entomol. **49:**1510–1514.
204. **Miranda J, Portillo A, Oteo JA, Mattar S.** 2012. *Rickettsia* sp. strain colombianensi (Rickettsiales: Rickettsiaceae): a new proposed *Rickettsia* detected in *Amblyomma dissimile* (Acari: Ixodidae) from iguanas and free-living larvae ticks from vegetation. J. Med. Entomol. **49:**960–965.
205. **Tomassone L, Conte V, Parrilla G, De Meneghi D.** 2010. *Rickettsia* infection in dogs and *Rickettsia parkeri* in *Amblyomma tigrinum* ticks, Cochabamba Department, Bolivia. Vector Borne Zoonotic Dis. **10:**953–958.
206. **Parola P, Socolovschi C, Raoult D.** 2009. Deciphering the relationships between *Rickettsia conorii conorii* and *Rhipicephalus sanguineus* in the ecology and epidemiology of Mediterranean spotted fever. Ann. N. Y. Acad. Sci. **1166:**49–54.
207. **Marquez FJ, Rodriguez-Liebana JJ, Soriguer RC, Muniain MA, Bernabeu-Wittel M, Caruz A, Contreras-Chova F.** 2008. Spotted fever group *Rickettsia* in brown dog ticks *Rhipicephalus sanguineus* in southwestern Spain. Parasitol. Res. **103:**119–122.
208. **Fernandez-Soto P, Perez-Sanchez R, Alamo-Sanz R, Encinas-Grandes A.** 2006. Spotted fever group rickettsiae in ticks feeding on humans in northwestern Spain: is *Rickettsia conorii* vanishing? Ann. N. Y. Acad. Sci. **1078:**331–333.
209. **Alexandre N, Santos AS, Bacellar F, Boinas FJ, Nuncio MS, de Sousa R.** 2011. Detection of *Rickettsia conorii* strains in Portuguese dogs (*Canis familiaris*). Ticks Tick Borne Dis. **2:**119–122.
210. **Solano-Gallego L, Kidd L, Trotta M, Di Marco M, Caldin M, Furlanello T, Breitschwerdt E.** 2006. Febrile illness associated with *Rickettsia conorii* infection in dogs from Sicily. Emerg. Infect. Dis. **12:**1985–1988.
211. **Pennisi MG, Capri A, Solano-Gallego L, Lombardo G, Torina A, Masucci M.** 2012. Prevalence of antibodies against *Rickettsia conorii*, *Babesia canis*, *Ehrlichia canis*, and *Anaplasma phagocytophilum* antigens in dogs from the Stretto di Messina area (Italy). Ticks Tick Borne Dis. **3:**315–318.
212. **Bitam I, Parola P, Matsumoto K, Rolain JM, Baziz B, Boubidi SC, Harrat Z, Belkaid M, Raoult D.** 2006. First molecular detection of *R. conorii*, *R. aeschlimannii*, and *R. massiliae* in ticks from Algeria. Ann. N. Y. Acad. Sci. **1078:**368–372.
213. **Baltadzhiev IG, Popivanova NI.** 2012. Some epidemiological features of the Mediterranean spotted fever re-emerging in Bulgaria. Folia Med. (Plovdiv.) **54:**36–43.
214. **Rovery C, Raoult D.** 2008. Mediterranean spotted fever. Infect. Dis. Clin. North Am. **22:**515–530.

215. **Rovery C, Brouqui P, Raoult D.** 2008. Questions on Mediterranean spotted fever a century after its discovery. Emerg. Infect. Dis. **14:**1360–1367.
216. **de Sousa R, Luz T, Parreira P, Santos-Silva M, Bacellar F.** 2006. Boutonneuse fever and climate variability. Ann. N. Y. Acad. Sci. **1078:**162–169.
217. **Vescio MF, Piras MA, Ciccozzi M, Carai A, Farchi F, Maroli M, Mura MS, Rezza G.** 2008. Socio-demographic and climatic factors as correlates of Mediterranean spotted fever (MSF) in northern Sardinia. Am. J. Trop. Med. Hyg. **78:**318–320.
218. **Samardzic S, Marinkovic T, Marinkovic D, Djuricic B, Ristanovic E, Simovic T, Lako B, Vukov B, Bozovic B, Gligic A.** 2008. Prevalence of antibodies to rickettsiae in different regions of Serbia. Vector Borne Zoonotic Dis. **8:**219–224.
219. **Serban R, Pistol A, Negut M, Cucuiu R.** 2009. *Rickettsia conorii* infection in Romania, 2000-2008. Bacteriol. Virusol. Parazitol. Epidemiol. **54:**177–183. (In Romanian.)
220. **Kovacova E, Sekeyova Z, Travnicek M, Bhide MR, Mardzinova S, Curlik J, Spanelova D.** 2006. Monitoring of humans and animals for the presence of various *Rickettsiae* and *Coxiella burnetii* by serological methods. Ann. N. Y. Acad. Sci. **1078:**587–589.
221. **Tonna I, Mallia AC, Piscopo T, Cuschieri P, Fenollar F, Raoult D.** 2006. Characterisation of rickettsial diseases in a hospital-based population in Malta. J. Infect. **53:**394–402.
222. **Cinco M, Luzzati R, Mascioli M, Floris R, Brouqui P.** 2006. Serological evidence of *Rickettsia* infections in forestry rangers in north-eastern Italy. Clin. Microbiol. Infect. **12:**493–495.
223. **Bolanos-Rivero M, Santana-Rodriguez E, Angel-Moreno A, Hernandez-Cabrera M, Liminana-Canal JM, Carranza-Rodriguez C, Martin-Sanchez AM, Perez-Arellano JL.** 2011. Seroprevalence of *Rickettsia typhi* and *Rickettsia conorii* infections in the Canary Islands (Spain). Int. J. Infect. Dis. **15:**e481–e485. doi:10.1016/j.ijid.2011.03.019.
224. **Lledo L, Gonzalez R, Gegundez MI, Beltran M, Saz JV.** 2009. Epidemiological study of rickettsial infections in patients with hypertransaminemia in Madrid (Spain). Int. J. Environ. Res. Public Health **6:**2526–2533.
225. **Bernabeu-Wittel M, del Toro MD, Nogueras MM, Muniain MA, Cardenosa N, Marquez FJ, Segura F, Pachon J.** 2006. Seroepidemiological study of *Rickettsia felis*, *Rickettsia typhi*, and *Rickettsia conorii* infection among the population of southern Spain. Eur. J. Clin. Microbiol. Infect. Dis. **25:**375–381.
226. **Sousa R, Franca A, Doria NS, Belo A, Amaro M, Abreu T, Pocas J, Proenca P, Vaz J, Torgal J, Bacellar F, Ismail N, Walker DH.** 2008. Host- and microbe-related risk factors for and pathophysiology of fatal *Rickettsia conorii* infection in Portuguese patients. J. Infect. Dis. **198:**576–585.
227. **Germanakis A, Psaroulaki A, Gikas A, Tselentis Y.** 2006. Mediterranean spotted fever in Crete, Greece: clinical and therapeutic data of 15 consecutive patients. Ann. N. Y. Acad. Sci. **1078:**263–269.
228. **Colomba C, Saporito L, Polara VF, Rubino R, Titone L.** 2006. Mediterranean spotted fever: clinical and laboratory characteristics of 415 Sicilian children. BMC Infect. Dis. **6:**60. doi:10.1186/1471-2334-6-60.
229. **Kuloglu F, Rolain JM, Aydoslu B, Akata F, Tugrul M, Raoult D.** 2006. Prospective evaluation of rickettsioses in the Trakya (European) region of Turkey and atypic presentations of *Rickettsia conorii*. Ann. N. Y. Acad. Sci. **1078:**173–175.
230. **Bartolome J, Lorente S, Hernandez-Perez N, Martinez-Alfaro E, Marin-Ors A, Crespo MD.** 2005. Clinical and epidemiological study of spotted fever group rickettsiosis in Albacete, Spain. Enferm. Infecc. Microbiol. Clin. **23:**194–196. (In Spanish.)
231. **Cascio A, Maggio MC, Cardella F, Zangara V, Accomando S, Costa A, Iaria C, Mansueto P, Giordano S.** 2011. Coronary involvement in Mediterranean spotted fever. New Microbiol. **34:**421–424.
232. **Ben Mansour N, Barakett N, Hajlaoui N, Haggui A, Filali T, Dahmen R, Fehri W, Haouala H.** 2011. Acute myocarditis complicating Mediterranean spotted fever. A case report. Ann. Cardiol. Angeiol. (Paris) doi:10.1016/j.ancard.2011.05.003. (In French.)
233. **Colomba C, Saporito L, Colletti P, Mazzola G, Rubino R, Pampinella D, Titone L.** 2008. Atrial fibrillation in Mediterranean spotted fever. J. Med. Microbiol. **57:**1424–1426.
234. **Agahan AL, Torres J, Fuentes-Paez G, Martinez-Osorio H, Orduna A, Calonge M.** 2011. Intraocular inflammation as the main manifestation of *Rickettsia conorii* infection. Clin. Ophthalmol. **5:**1401–1407.
235. **Leone S, De Marco M, Ghirga P, Nicastri E, Lazzari R, Narciso P.** 2008. Retinopathy in *Rickettsia conorii* infection: case report in an immunocompetent host. Infection **36:**384–386.
236. **Kuloglu F, Rolain JM, Akata F, Eroglu C, Celik AD, Parola P.** 2012. Mediterranean spotted fever in the Trakya region of Turkey. Ticks Tick Borne Dis. **3:**298–304.
237. **Tsiachris D, Deutsch M, Vassilopoulos D, Zafiropoulou R, Archimandritis AJ.** 2008. Sensorineural hearing loss complicating severe rickettsial diseases: report of two cases. J. Infect. **56:**74–76.
238. **Caroleo S, Longo C, Pirritano D, Nistico R, Valentino P, Iocco M, Santangelo E, Amantea B.** 2007. A case of acute quadriplegia complicating Mediterranean spotted fever. Clin. Neurol. Neurosurg. **109:**463–465.
239. **Tzavella K, Chatzizisis YS, Vakali A, Mandraveli K, Zioutas D, Alexiou-Daniel S.** 2006. Severe case of Mediterranean spotted fever in Greece with predominantly neurological features. J. Med. Microbiol. **55:**341–343.
240. **Botelho-Nevers E, Foucault C, Lepidi H, Brouqui P.** 2005. Cerebral infarction: an unusual complication of Mediterranean spotted fever. Eur. J. Intern. Med. **16:**525–527.
241. **Spengos K, Stouraitis G, Voumvourakis K, Zambelis T, Karandreas N.** 2005. Motor and sensory polyneuritis with distal conduction failure as uncommon complication of an acute *Rickettsia conorii* infection. J. Neurol. Sci. **234:**113–116.
242. **Rombola F.** 2011. Mediterranean spotted fever presenting as an acute pancreatitis. Acta Gastroenterol. Belg. **74:**91–92.
243. **Tikare NV, Shahapur PR, Bidari LH, Mantur BG.** 2010. Rickettsial meningoencephalitis in a child—a case report. J. Trop. Pediatr. **56:**198–200.
244. **Schmulewitz L, Moumile K, Patey-Mariaud de Serre N, Poiree S, Gouin E, Mechai F, Cocard V, Mamzer-Bruneel MF, Abachin E, Berche P, Lortholary O, Lecuit M.** 2008. Splenic rupture and malignant Mediterranean spotted fever. Emerg. Infect. Dis. **14:**995–997.
245. **Montasser DI, Zajjari Y, Alayoud A, Bahadi A, Aatif T, Hassani K, Hamzi A, Allam M, Benyahia M, Oualim Z.** 2011. Acute renal failure as a complication of Mediterranean spotted fever. Nephrol. Ther. **7:**245–247. (In French.)
246. **Perez-De Pedro I, Macias-Vega IN, Miranda-Candon I, Camps-Garcia MT.** 2008. Severe *Rickettsia conorii* infection associated with hemophagocytic syndrome. Enferm. Infecc. Microbiol. Clin. **26:**597–598. (In French.)
247. **Papa A, Dalla V, Petala A, Maltezou HC, Maltezos E.** 2010. Fatal Mediterranean spotted fever in Greece. Clin. Microbiol. Infect. **16:**589–592.
248. **Bechah Y, Socolovschi C, Raoult D.** 2011. Identification of rickettsial infections by using cutaneous swab specimens and PCR. Emerg. Infect. Dis. **17:**83–86.
249. **de Sousa R, Santos-Silva M, Santos AS, Barros SC, Torgal J, Walker DH, Bacellar F.** 2007. *Rickettsia conorii israeli* tick typhus strain isolated from *Rhipicephalus sanguineus* ticks in Portugal. Vector Borne Zoonotic Dis. **7:**444–447.
250. **Giammanco GM, Di Rosa S, Ammatuna P, Mansueto P, Micalizzi A, Vitale G.** 2005. Continous [*sic*] alert for rickettsiosis in Sicily: molecular characterization of *Rickettsia* sp. obtained from ticks and human beings (1986-2001). New Microbiol. **28:**377–379.
251. **Boillat N, Genton B, D'Acremont V, Raoult D, Greub G.** 2008. Fatal case of Israeli spotted fever after Mediterranean cruise. Emerg. Infect. Dis. **14:**1944–1946.
252. **Chai JT, Eremeeva ME, Borland CD, Karas JA.** 2008. Fatal Israeli spotted fever in a UK traveler to South Portugal. J. Travel Med. **15:**122–123.
253. **Giammanco GM, Vitale G, Mansueto S, Capra G, Caleca MP, Ammatuna P.** 2005. Presence of *Rickettsia conorii* subsp. *israelensis*, the causative agent of Israeli spotted fever, in Sicily, Italy, ascertained in a retrospective study. J. Clin. Microbiol. **43:**6027–6031.
254. **Renvoise A, Delaunay P, Blanchouin E, Cannavo I, Cua E, Socolovschi C, Parola P, Raoult D.** 2012. Urban family cluster of spotted fever rickettsiosis linked to *Rhipicephalus sanguineus* infected with *Rickettsia conorii* subsp. caspia and *Rickettsia massiliae*. Ticks Tick Borne Dis. **3:**389–392.
255. **Pokrovsky VI, Ugleva SV, Shabalina SV.** 2011. Comparative characteristics of transmissive fevers in the territory of Astrakhan region (clinicoepidemiological evidence). Ter. Arkh. **83**(11)**:**55–59. (In Russian.)

256. **Maleev VV, Galimzianov K, Lazareva EN, Poliakova AM, Astrina OS, Kudriavtsev VA, Arshba TE.** 2009. Hemostatic disorders and their implication in the pathogenesis of Astrakhan rickettsial fever. Ter. Arkh. **81**(11):32–35. (In Russian.)
257. **Torina A, Fernandez de Mera IG, Alongi A, Mangold AJ, Blanda V, Scarlata F, Di Marco V, de la Fuente J.** 2012. *Rickettsia conorii* Indian tick typhus strain and *R. slovaca* in humans, Sicily. Emerg. Infect. Dis. **18:**1008–1010.
258. **Chochlakis D, Ioannou I, Sandalakis V, Dimitriou T, Kassinis N, Papadopoulos B, Tselentis Y, Psaroulaki A.** 2012. Spotted fever group rickettsiae in ticks in Cyprus. Microb. Ecol. **63:**314–323.
259. **Socolovschi C, Reynaud P, Kernif T, Raoult D, Parola P.** 2012. Rickettsiae of spotted fever group, *Borrelia valaisiana*, and *Coxiella burnetii* in ticks on passerine birds and mammals from the Camargue in the south of France. Ticks Tick Borne Dis. **3:**355–360.
260. **Marie JL, Davoust B, Socolovschi C, Raoult D, Parola P.** 2012. Molecular detection of rickettsial agents in ticks and fleas collected from a European hedgehog (*Erinaceus europaeus*) in Marseilles, France. Comp. Immunol. Microbiol. Infect. Dis. **35:**77–79.
261. **Marie JL, Davoust B, Socolovschi C, Mediannikov O, Roqueplo C, Beaucournu JC, Raoult D, Parola P.** 2012. Rickettsiae in arthropods collected from red foxes (*Vulpes vulpes*) in France. Comp. Immunol. Microbiol. Infect. Dis. **35:**59–62.
262. **Fernandez de Mera IG, Zivkovic Z, Bolanos M, Carranza C, Perez-Arellano JL, Gutierrez C, de la Fuente J.** 2009. *Rickettsia massiliae* in the Canary Islands. Emerg. Infect. Dis. **15:**1869–1870.
263. **Toledo A, Olmeda AS, Escudero R, Jado I, Valcarcel F, Casado-Nistal MA, Rodriguez-Vargas M, Gil H, Anda P.** 2009. Tick-borne zoonotic bacteria in ticks collected from central Spain. Am. J. Trop. Med. Hyg. **81:**67–74.
264. **Psaroulaki A, Ragiadakou D, Kouris G, Papadopoulos B, Chaniotis B, Tselentis Y.** 2006. Ticks, tick-borne rickettsiae, and *Coxiella burnetii* in the Greek Island of Cephalonia. Ann. N. Y. Acad. Sci. **1078:**389–399.
265. **Tomanovic S, Chochlakis D, Radulovic Z, Milutinovic M, Cakic S, Mihaljica D, Tselentis Y, Psaroulaki A.** 2013. Analysis of pathogen co-occurrence in host-seeking adult hard ticks from Serbia. Exp. Appl. Acarol. **59:**367–376.
266. **Trotta M, Nicetto M, Fogliazza A, Montarsi F, Caldin M, Furlanello T, Solano-Gallego L.** 2012. Detection of *Leishmania infantum*, *Babesia canis*, and rickettsiae in ticks removed from dogs living in Italy. Ticks Tick Borne Dis. **3:**294–297.
267. **Podsiadly E, Chmielewski T, Karbowiak G, Kedra E, Tylewska-Wierzbanowska S.** 2011. The occurrence of spotted fever rickettsioses and other tick-borne infections in forest workers in Poland. Vector Borne Zoonotic Dis. **11:**985–989.
268. **Edouard S, Parola P, Socolovschi C, Davoust B, La Scola B, Raoult D.** 2013. Clustered cases of *Rickettsia sibirica mongolitimonae* infection, France. Emerg. Infect. Dis. **19:**337–338.
269. **Psaroulaki A, Germanakis A, Gikas A, Scoulica E, Tselentis Y.** 2005. Simultaneous detection of "*Rickettsia mongolotimonae*" in a patient and in a tick in Greece. J. Clin. Microbiol. **43:**3558–3559.
270. **de Sousa R, Barata C, Vitorino L, Santos-Silva M, Carrapato C, Torgal J, Walker D, Bacellar F.** 2006. *Rickettsia sibirica* isolation from a patient and detection in ticks, Portugal. Emerg. Infect. Dis. **12:**1103–1108.
271. **de Sousa R, Duque L, Anes M, Pocas J, Torgal J, Bacellar F, Olano JP, Walker DH.** 2008. Lymphangitis in a Portuguese patient infected with *Rickettsia sibirica*. Emerg. Infect. Dis. **14:**529–530.
272. **Ibarra V, Portillo A, Palomar AM, Sanz MM, Metola L, Blanco JR, Oteo JA.** 2012. Septic shock in a patient infected with *Rickettsia sibirica mongolitimonae*, Spain. Clin. Microbiol. Infect. **18:**E283–E285. doi:10.1111/j.1469-0691.2012.03887.x.
273. **Aguirrebengoa K, Portillo A, Santibanez S, Marin JJ, Montejo M, Oteo JA.** 2008. Human *Rickettsia sibirica mongolitimonae* infection, Spain. Emerg. Infect. Dis. **14:**528–529.
274. **Fleta-Asin B, Alonso-Castro L, Jado-Garcia I, Anda-Fernandez P.** 2011. Detection by polymerase chain reaction of *Rickettsia sibirica mongolotimonae* in the skin biopsy of a rash: a case report. Enferm. Infecc. Microbiol. Clin. **29:**778–779. (In Spanish.)
275. **Ramos JM, Jado I, Padilla S, Masia M, Anda P, Gutierrez F.** 2013. Human infection with *Rickettsia sibirica mongolitimonae*, Spain, 2007-2011. Emerg. Infect. Dis. **19:**267–269.
276. **Caron J, Rolain JM, Mura F, Guillot B, Raoult D, Bessis D.** 2008. *Rickettsia sibirica* subsp. *mongolitimonae* infection and retinal vasculitis. Emerg. Infect. Dis. **14:**683–684.
277. **Gilot B, Laforge ML, Pichot J, Raoult D.** 1990. Relationships between the *Rhipicephalus sanguineus* complex ecology and Mediterranean spotted fever epidemiology in France. Eur. J. Epidemiol. **6:**357–362.
278. **Walker AR, Bouattour A, Camicas J-L, Estrada-Peña A, Horak IG, Latif AA, Pegram RG, Reston PM.** 2003. Ticks of domestic animals in Africa. A guide to identification of species. Bioscience Reports, Edinburgh, United Kingdom.
279. **Angelakis E, Pulcini C, Waton J, Imbert P, Socolovschi C, Edouard S, Dellamonica P, Raoult D.** 2010. Scalp eschar and neck lymphadenopathy caused by *Bartonella henselae* after tick bite. Clin. Infect. Dis. **50:**549–551.
280. **Maioli G, Pistone D, Bonilauri P, Pajoro M, Barbieri I, Mulatto P, Vicari N, Dottori M.** 2012. Ethiological [*sic*] agents of rickettsiosis and anaplasmosis in ticks collected in Emilia-Romagna region (Italy) during 2008 and 2009. Exp. Appl. Acarol. **57:**199–208.
281. **Spitalska E, Stefanidesova K, Kocianova E, Boldis V.** 2012. *Rickettsia slovaca* and *Rickettsia raoultii* in *Dermacentor marginatus* and *Dermacentor reticulatus* ticks from Slovak Republic. Exp. Appl. Acarol. **57:**189–197.
282. **Dobler G, Wolfel R.** 2009. Typhus and other rickettsioses: emerging infections in Germany. Dtsch. Arztebl. Int. **106:**348–354.
283. **Milhano N, de Carvalho IL, Alves AS, Arroube S, Soares J, Rodriguez P, Carolino M, Nuncio MS, Piesman J, de Sousa R.** 2010. Coinfections of *Rickettsia slovaca* and *Rickettsia helvetica* with *Borrelia lusitaniae* in ticks collected in a Safari Park, Portugal. Ticks Tick Borne Dis. **1:**172–177.
284. **Masala G, Chisu V, Satta G, Socolovschi C, Raoult D, Parola P.** 2012. *Rickettsia slovaca* from *Dermacentor marginatus* ticks in Sardinia, Italy. Ticks Tick Borne Dis. **3:**393–395.
285. **Kachrimanidou M, Souliou E, Pavlidou V, Antoniadis A, Papa A.** 2010. First detection of *Rickettsia slovaca* in Greece. Exp. Appl. Acarol. **50:**93–96.
286. **Chmielewski T, Podsiadly E, Karbowiak G, Tylewska-Wierzbanowska S.** 2009. *Rickettsia* spp. in ticks, Poland. Emerg. Infect. Dis. **15:**486–488.
287. **Dobec M, Golubic D, Punda-Polic V, Kaeppeli F, Sievers M.** 2009. *Rickettsia helvetica* in *Dermacentor reticulatus* ticks. Emerg. Infect. Dis. **15:**98–100.
288. **Selmi M, Bertolotti L, Tomassone L, Mannelli A.** 2008. *Rickettsia slovaca* in *Dermacentor marginatus* and tick-borne lymphadenopathy, Tuscany, Italy. Emerg. Infect. Dis. **14:**817–820.
289. **Reye AL, Stegniy V, Mishaeva NP, Velhin S, Hubschen JM, Ignatyev G, Muller CP.** 2013. Prevalence of tick-borne pathogens in *Ixodes ricinus* and *Dermacentor reticulatus* ticks from different geographical locations in Belarus. PLoS One **8:**e54476. doi:10.1371/journal.pone.0054476.
290. **Jiang J, You BJ, Liu E, Apte A, Yarina TR, Myers TE, Lee JS, Francesconi SC, O'Guinn ML, Tsertsvadze N, Vephkhvadze N, Babuadze G, Sidamonidze K, Kokhreidze M, Donduashvili M, Onashvili T, Ismayilov A, Agayev N, Aliyev M, Muttalibov N, Richards AL.** 2012. Development of three quantitative real-time PCR assays for the detection of *Rickettsia raoultii*, *Rickettsia slovaca*, and *Rickettsia aeschlimannii* and their validation with ticks from the country of Georgia and the Republic of Azerbaijan. Ticks Tick Borne Dis. **3:**327–331.
291. **Porta FS, Nieto EA, Creus BF, Espin TM, Casanova FJ, Sala IS, Garcia SL, Aguilar JL, Vilaseca MQ.** 2008. Tick-borne lymphadenopathy: a new infectious disease in children. Pediatr. Infect. Dis. J. **27:**618–622.
292. **Parola P, Rovery C, Rolain JM, Brouqui P, Davoust B, Raoult D.** 2009. *Rickettsia slovaca* and *R. raoultii* in tick-borne rickettsioses. Emerg. Infect. Dis. **15:**1105–1108.
293. **Gouriet F, Rolain JM, Raoult D.** 2006. *Rickettsia slovaca* infection, France. Emerg. Infect. Dis. **12:**521–523.
294. **Sekeyova Z, Subramanian G, Mediannikov O, Diaz MQ, Nyitray A, Blaskovicova H, Raoult D.** 2012. Evaluation of clinical specimens for *Rickettsia*, *Bartonella*, *Borrelia*, *Coxiella*, *Anaplasma*, *Francisella* and *Diplorickettsia* positivity using serological and molecular biology methods. FEMS Immunol. Med. Microbiol. **64:**82–91.
295. **Ibarra V, Oteo JA, Portillo A, Santibanez S, Blanco JR, Metola L, Eiros JM, Perez-Martinez L, Sanz M.** 2006. *Rickettsia slovaca* infection: DEBONEL/TIBOLA. Ann. N. Y. Acad. Sci. **1078:**206–214.
296. **Switaj K, Chmielewski T, Borkowski P, Tylewska-Wierzbanowska S, Olszynska-Krowicka M.** 2012. Spotted fever rickettsiosis caused by *Rickettsia raoultii*—case report. Przegl. Epidemiol. **66:**347–350.

297. **Madeddu G, Mancini F, Caddeo A, Ciervo A, Babudieri S, Maida I, Fiori ML, Rezza G, Mura MS.** 2012. *Rickettsia monacensis* as cause of Mediterranean spotted fever-like illness, Italy. Emerg. Infect. Dis. **18:** 702–704.
298. **Jado I, Oteo JA, Aldamiz M, Gil H, Escudero R, Ibarra V, Portu J, Portillo A, Lezaun MJ, Garcia-Amil C, Rodriguez-Moreno I, Anda P.** 2007. *Rickettsia monacensis* and human disease, Spain. Emerg. Infect. Dis. **13:**1405–1407.
299. **Gargili A, Palomar AM, Midilli K, Portillo A, Kar S, Oteo JA.** 2012. *Rickettsia* species in ticks removed from humans in Istanbul, Turkey. Vector Borne Zoonotic Dis. **12:**938–941.
300. **Reye AL, Hubschen JM, Sausy A, Muller CP.** 2010. Prevalence and seasonality of tick-borne pathogens in questing *Ixodes ricinus* ticks from Luxembourg. Appl. Environ. Microbiol. **76:**2923–2931.
301. **Rymaszewska A, Piotrowski M.** 2013. Use of DNA sequences for *Rickettsia* identification in *Ixodes ricinus* ticks: the first detection of *Rickettsia monacensis* in Poland. Microbes Infect. **15:**140–146.
302. **Radulovic Z, Chochlakis D, Tomanovic S, Milutinovic M, Tselentis Y, Psaroulaki A.** 2011. First detection of spotted fever group rickettsiae in ticks in Serbia. Vector Borne Zoonotic Dis. **11:**111–115.
303. **de Sousa R, Lopes de Carvalho I, Santos AS, Bernardes C, Milhano N, Jesus J, Menezes D, Nuncio MS.** 2012. Role of the lizard *Teira dugesii* as a potential host for *Ixodes ricinus* tick-borne pathogens. Appl. Environ. Microbiol. **78:**3767–3769.
304. **Rumer L, Graser E, Hillebrand T, Talaska T, Dautel H, Mediannikov O, Roy-Chowdhury P, Sheshukova O, Donoso MO, Niedrig M.** 2011. *Rickettsia aeschlimannii* in *Hyalomma marginatum* ticks, Germany. Emerg. Infect. Dis. **17:**325–326.
305. **Shpynov S, Rudakov N, Tohkov Y, Matushchenko A, Tarasevich I, Raoult D, Fournier PE.** 2009. Detection of *Rickettsia aeschlimannii* in *Hyalomma marginatum* ticks in western Russia. Clin. Microbiol. Infect. **15**(Suppl 2):315–316.
306. **Mura A, Masala G, Tola S, Satta G, Fois F, Piras P, Rolain JM, Raoult D, Parola P.** 2008. First direct detection of rickettsial pathogens and a new rickettsia, '*Candidatus* Rickettsia barbariae', in ticks from Sardinia, Italy. Clin. Microbiol. Infect. **14:**1028–1033.
307. **Fernandez-Soto P, Encinas-Grandes A, Perez-Sanchez R.** 2003. *Rickettsia aeschlimannii* in Spain: molecular evidence in *Hyalomma marginatum* and five other tick species that feed on humans. Emerg. Infect. Dis. **9:**889–890.
308. **Hornok S, Csorgo T, de la Fuente J, Gyuranecz M, Privigyei C, Meli ML, Kreizinger Z, Gonczi E, Fernandez de Mera IG, Hofmann-Lehmann R.** 2013. Synanthropic birds associated with high prevalence of tick-borne rickettsiae and with the first detection of *Rickettsia aeschlimannii* in Hungary. Vector Borne Zoonotic Dis. **13:**77–83.
309. **Tomassone L, Grego E, Auricchio D, Iori A, Giannini F, Rambozzi L.** 2013. Lyme borreliosis spirochetes and spotted fever group rickettsiae in ixodid ticks from Pianosa Island, Tuscany Archipelago, Italy. Vector Borne Zoonotic Dis. **13:**84–91.
310. **Kantso B, Svendsen CB, Jensen PM, Vennestrom J, Krogfelt KA.** 2010. Seasonal and habitat variation in the prevalence of *Rickettsia helvetica* in *Ixodes ricinus* ticks from Denmark. Ticks Tick Borne Dis. **1:**101–103.
311. **Sprong H, Wielinga PR, Fonville M, Reusken C, Brandenburg AH, Borgsteede F, Gaasenbeek C, van der Giessen JW.** 2009. *Ixodes ricinus* ticks are reservoir hosts for *Rickettsia helvetica* and potentially carry flea-borne *Rickettsia* species. Parasit. Vectors **2:**41. doi:10.1186/1756-3305-2-41.
312. **Spitalska E, Literak I, Kocianova E, Taragel'ova V.** 2011. The importance of *Ixodes arboricola* in transmission of *Rickettsia* spp., *Anaplasma phagocytophilum*, and *Borrelia burgdorferi* sensu lato in the Czech Republic, Central Europe. Vector Borne Zoonotic Dis. **11:**1235–1241.
313. **Nilsson K.** 2009. Septicaemia with *Rickettsia helvetica* in a patient with acute febrile illness, rash and myasthenia. J. Infect. **58:**79–82.
314. **Nilsson K, Elfving K, Pahlson C.** 2010. *Rickettsia helvetica* in patient with meningitis, Sweden, 2006. Emerg. Infect. Dis. **16:**490–492.
315. **Nilsson K, Wallmenius K, Pahlson C.** 2011. Coinfection with *Rickettsia helvetica* and herpes simplex virus 2 in a young woman with meningoencephalitis. Case Rep. Infect. Dis. **2011:**469194. doi:10.1155/2011/469194.
316. **Svendsen CB, Milman N, Andersen CB, Rasmussen EM, Thomsen VO, Krogfelt KA.** 2011. Is sarcoidosis a rickettsiosis? An archival study. Scand. J. Infect. Dis. **43:**349–353.
317. **Palomar AM, Santibanez P, Mazuelas D, Roncero L, Santibanez S, Portillo A, Oteo JA.** 2012. Role of birds in dispersal of etiologic agents of tick-borne zoonoses, Spain, 2009. Emerg. Infect. Dis. **18:**1188–1191.
318. **Socolovschi C, Kernif T, Raoult D, Parola P.** 2012. *Borrelia*, *Rickettsia*, and *Ehrlichia* species in bat ticks, France, 2010. Emerg. Infect. Dis. **18:** 1966–1975.
319. **Marquez FJ.** 2008. Spotted fever group *Rickettsia* in ticks from southeastern Spain natural parks. Exp. Appl. Acarol. **45:**185–194.
320. **Eremeeva ME, Oliveira A, Robinson JB, Ribakova N, Tokarevich NK, Dasch GA.** 2006. Prevalence of bacterial agents in *Ixodes persulcatus* ticks from the Vologda Province of Russia. Ann. N. Y. Acad. Sci. **1078:**291–298.
321. **Jaaskelainen AE, Tikkakoski T, Uzcategui NY, Alekseev AN, Vaheri A, Vapalahti O.** 2006. Siberian subtype tickborne encephalitis virus, Finland. Emerg. Infect. Dis. **12:**1568–1571.
322. **Eremeeva ME, Stromdahl EY.** 2011. New spotted fever group *Rickettsia* in a *Rhipicephalus turanicus* tick removed from a child in eastern Sicily, Italy. Am. J. Trop. Med. Hyg. **84:**99–101.
323. **Elfving K, Olsen B, Bergstrom S, Waldenstrom J, Lundkvist A, Sjostedt A, Mejlon H, Nilsson K.** 2010. Dissemination of spotted fever rickettsia agents in Europe by migrating birds. PLoS One **5:**e8572. doi:10.1371/journal.pone.0008572.
324. **Floris R, Yurtman AN, Margoni EF, Mignozzi K, Boemo B, Altobelli A, Cinco M.** 2008. Detection and identification of *Rickettsia* species in the northeast of Italy. Vector Borne Zoonotic Dis. **8:**777–782.
325. **Socolovschi C, Matsumoto K, Phong HT, Davoust B, Raoult D, Parola P.** 2009. Transmission of *Rickettsia* sp. DmS1 in the tick, *Dermacentor marginatus*. Clin. Microbiol. Infect. **15**(Suppl 2):322–323.
326. **Portillo A, Ibarra V, Santibanez S, Perez-Martinez L, Blanco JR, Oteo JA.** 2009. Genetic characterisation of *omp*A, *omp*B and *glt*A genes from *Candidatus Rickettsia rioja*. Clin. Microbiol. Infect. **15**(Suppl 2):307–308.
327. **Perez-Perez L, Portillo A, Allegue F, Zulaica A, Oteo JA, Caeiro JL, Fabeiro JM.** 2010. *Dermacentor*-borne necrosis erythema and lymphadenopathy (DEBONEL): a case associated with *Rickettsia rioja*. Acta Derm. Venereol. **90:**214–215.
328. **Dubska L, Literak I, Kverek P, Roubalova E, Kocianova E, Taragelova V.** 2012. Tick-borne zoonotic pathogens in ticks feeding on the common nightingale including a novel strain of *Rickettsia* sp. Ticks Tick Borne Dis. **3:**265–268.
329. **Sreter-Lancz Z, Szell Z, Kovacs G, Egyed L, Marialigeti K, Sreter T.** 2006. Rickettsiae of the spotted-fever group in ixodid ticks from Hungary: identification of a new genotype ('*Candidatus* Rickettsia kotlanii'). Ann. Trop. Med. Parasitol. **100:**229–236.
330. **Graham RI, Mainwaring MC, Du Feu R.** 2010. Detection of spotted fever group *Rickettsia* spp. from bird ticks in the U.K. Med. Vet. Entomol. **24:**340–343.
331. **van Overbeek L, Gassner F, van der Plas CL, Kastelein P, Nunes-da Rocha U, Takken W.** 2008. Diversity of *Ixodes ricinus* tick-associated bacterial communities from different forests. FEMS Microbiol. Ecol. **66:** 72–84.
332. **Tijsse-Klasen E, Fonville M, van Overbeek L, Reimerink JH, Sprong H.** 2010. Exotic rickettsiae in *Ixodes ricinus*: fact or artifact? Parasit. Vectors **3:**54. doi:10.1186/1756-3305-3-54.
333. **Kernif T, Socolovschi C, Bitam I, Raoult D, Parola P.** 2012. Vector-borne rickettsioses in North Africa. Infect. Dis. Clin. North Am. **26:**455–478.
334. **Kaabia N, Bellazreg F, Hachfi W, Khalifa M, Ghanouchi N, Bahri F, Letaief A.** 2009. Rickettsial infection in hospitalised patients in central Tunisia: report of 119 cases. Clin. Microbiol. Infect. **15**(Suppl 2):216–217.
335. **Mouffok N, Parola P, Lepidi H, Raoult D.** 2009. Mediterranean spotted fever in Algeria—new trends. Int. J. Infect. Dis. **13:**227–235.
336. **Sfar N, Kaabia N, Letaief A, Rolain JM, Parola P, Bouattour A, Raoult D.** 2009. First molecular detection of *R. conorii* subsp. *conorii* 99 years after the Conor description of Mediterranean spotted fever, in Tunisia. Clin. Microbiol. Infect. **15**(Suppl 2):309–310.
337. **Boudebouch N, Sarih M, Socolovschi C, Amarouch H, Hassar M, Raoult D, Parola P.** 2009. Molecular survey for spotted fever group rickettsiae in ticks from Morocco. Clin. Microbiol. Infect. **15**(Suppl 2): 259–260.
338. **Znazen A, Hammami B, Lahiani D, Ben Jemaa M, Hammami A.** 2011. Israeli spotted fever, Tunisia. Emerg. Infect. Dis. **17:**1328–1330.
339. **Raoult D, Fournier PE, Abboud P, Caron F.** 2002. First documented human *Rickettsia aeschlimannii* infection. Emerg. Infect. Dis. **8:**748–749.

340. **Mokrani N, Parola P, Tebbal S, Dalichaouche M, Aouati A, Raoult D.** 2008. *Rickettsia aeschlimannii* infection, Algeria. Emerg. Infect. Dis. **14:** 1814–1815.
341. **Sarih M, Socolovschi C, Boudebouch N, Hassar M, Raoult D, Parola P.** 2008. Spotted fever group rickettsiae in ticks, Morocco. Emerg. Infect. Dis. **14:**1067–1073.
342. **Abdel-Shafy S, Allam NA, Mediannikov O, Parola P, Raoult D.** 2012. Molecular detection of spotted fever group rickettsiae associated with ixodid ticks in Egypt. Vector Borne Zoonotic Dis. **12:**346–359.
343. **Kernif T, Djerbouh A, Mediannikov O, Ayach B, Rolain JM, Raoult D, Parola P, Bitam I.** 2012. *Rickettsia africae* in *Hyalomma dromedarii* ticks from sub-Saharan Algeria. Ticks Tick Borne Dis. **3:**377–379.
344. **Fournier PE, Gouriet F, Brouqui P, Lucht F, Raoult D.** 2005. Lymphangitis-associated rickettsiosis, a new rickettsiosis caused by *Rickettsia sibirica mongolotimonae*: seven new cases and review of the literature. Clin. Infect. Dis. **40:**1435–1444.
345. **Socolovschi C, Barbarot S, Lefebvre M, Parola P, Raoult D.** 2010. *Rickettsia sibirica mongolitimonae* in traveler from Egypt. Emerg. Infect. Dis. **16:**1495–1496.
346. **Kernif T, Messaoudene D, Ouahioune S, Parola P, Raoult D, Bitam I.** 2012. Spotted fever group rickettsiae identified in *Dermacentor marginatus* and *Ixodes ricinus* ticks in Algeria. Ticks Tick Borne Dis. **3:**380–381.
347. **Sfar N, M'ghirbi Y, Letaief A, Parola P, Bouattour A, Raoult D.** 2008. First report of *Rickettsia monacensis* and *Rickettsia helvetica* from Tunisia. Ann. Trop. Med. Parasitol. **102:**561–564.
348. **Dib L, Bitam I, Bensouilah M, Parola P, Raoult D.** 2009. First description of *Rickettsia monacensis* in *Ixodes ricinus* in Algeria. Clin. Microbiol. Infect. **15**(Suppl 2):261–262.
349. **Khaldi M, Socolovschi C, Benyettou M, Barech G, Biche M, Kernif T, Raoult D, Parola P.** 2012. Rickettsiae in arthropods collected from the North African hedgehog (*Atelerix algirus*) and the desert hedgehog (*Paraechinus aethiopicus*) in Algeria. Comp. Immunol. Microbiol. Infect. Dis. **35:**117–122.
350. **Beati L, Patel J, Lucas-Williams H, Adakal H, Kanduma EG, Tembo-Mwase E, Krecek R, Mertins JW, Alfred JT, Kelly S, Kelly P.** 2012. Phylogeography and demographic history of *Amblyomma variegatum* (Fabricius) (Acari: Ixodidae), the tropical bont tick. Vector Borne Zoonotic Dis. **12:**514–525.
351. **Mediannikov O, Trape JF, Diatta G, Parola P, Fournier PE, Raoult D.** 2010. *Rickettsia africae*, Western Africa. Emerg. Infect. Dis. **16:**571–573.
352. **Socolovschi C, Matsumoto K, Marie JL, Davoust B, Raoult D, Parola P.** 2007. Identification of rickettsiae, Uganda and Djibouti. Emerg. Infect. Dis. **13:**1508–1510.
353. **Mediannikov O, Diatta G, Fenollar F, Sokhna C, Trape JF, Raoult D.** 2010. Tick-borne rickettsioses, neglected emerging diseases in rural Senegal. PLoS Negl. Trop. Dis. **4:**e821. doi:10.1371/journal.pntd.0000821.
354. **Ogo NI, de Mera IG, Galindo RC, Okubanjo OO, Inuwa HM, Agbede RI, Torina A, Alongi A, Vicente J, Gortazar C, de la Fuente J.** 2012. Molecular identification of tick-borne pathogens in Nigerian ticks. Vet. Parasitol. **187:**572–577.
355. **Portillo A, Perez-Martinez L, Santibanez S, Blanco JR, Ibarra V, Oteo JA.** 2007. Detection of *Rickettsia africae* in *Rhipicephalus* (*Boophilus*) *decoloratus* ticks from the Republic of Botswana, South Africa. Am. J. Trop. Med. Hyg. **77:**376–377.
356. **Mediannikov O, Diatta G, Zolia Y, Balde MC, Kohar H, Trape JF, Raoult D.** 2012. Tick-borne rickettsiae in Guinea and Liberia. Ticks Tick Borne Dis. **3:**43–48.
357. **Mediannikov O, Davoust B, Socolovschi C, Tshilolo L, Raoult D, Parola P.** 2012. Spotted fever group rickettsiae in ticks and fleas from the Democratic Republic of the Congo. Ticks Tick Borne Dis. **3:**371–373.
358. **Ndip LM, Biswas HH, Nfonsam LE, LeBreton M, Ndip RN, Bissong MA, Mpoudi-Ngole E, Djoko C, Tamoufe U, Prosser AT, Burke DS, Wolfe ND.** 2011. Risk factors for African tick-bite fever in rural central Africa. Am. J. Trop. Med. Hyg. **84:**608–613.
359. **Wang JM, Hudson BJ, Watts MR, Karagiannis T, Fisher NJ, Anderson C, Roffey P.** 2009. Diagnosis of Queensland tick typhus and African tick bite fever by PCR of lesion swabs. Emerg. Infect. Dis. **15:**963–965.
360. **Kibsgaard L, Lindberg J, Villumsen S, Larsen CS.** 2012. Rickettsiosis is a neglected cause of fever in returned travellers. Ugeskr. Laeger. **174:** 1529–1530. (In Danish.)
361. **Stephany D, Buffet P, Rolain JM, Raoult D, Consigny PH.** 2009. *Rickettsia africae* infection in man after travel to Ethiopia. Emerg. Infect. Dis. **15:**1867–1869.
362. **Mechai F, Han Y, Gachot B, Consigny PH, Viard JP, Lecuit M, Lortholary O.** 2009. Pristinamycin for *Rickettsia africae* infection. J. Travel Med. **16:**136–137.
363. **Consigny PH, Schuett I, Fraitag S, Rolain JM, Buffet P.** 2009. Unusual location of an inoculation lesion in a traveler with African tick-bite fever returning from South Africa. J. Travel Med. **16:**439–440.
364. **Roch N, Epaulard O, Pelloux I, Pavese P, Brion JP, Raoult D, Maurin M.** 2008. African tick bite fever in elderly patients: 8 cases in French tourists returning from South Africa. Clin. Infect. Dis. **47:**e28–e35. doi: 10.1086/589868.
365. **Bouvresse S, Del Giudice P, Franck N, Buffet M, Avril MF, Mondain V, Rolain JM, Raoult D, Dupin N.** 2008. Two cases of cellulitis in the course of African tick bite fever: a fortuitous association? Dermatology **217:**140–142.
366. **Hochedez P, Canestri A, Guihot A, Brichler S, Bricaire F, Caumes E.** 2008. Management of travelers with fever and exanthema, notably dengue and chikungunya infections. Am. J. Trop. Med. Hyg. **78:**710–713.
367. **Consigny PH, Rolain JM, Mizzi D, Raoult D.** 2005. African tick-bite fever in French travelers. Emerg. Infect. Dis. **11:**1804–1806.
368. **Schleenvoigt BT, Keller P, Stallmach A, Pletz MW.** 2012. African tick bite fever—rickettsiosis after holiday in South Africa. Dtsch. Med. Wochenschr. **137:**891–893. (In German.)
369. **Tappe D, Dobler G, Stich A.** 2009. Tache noire in African tick bite fever. Am. J. Trop. Med. Hyg. **81:**733–734.
370. **Schuster J, Tantcheva-Poor I, Wickenhauser C, Chemnitz JM, Hunzelmann N, Krieg T, Hartmann K.** 2008. African tick bite fever—papulovesicular exanthem with fever after staying in South Africa. J. Dtsch. Dermatol. Ges. **6:**379–381.
371. **Reshef R, Levo Y, Giladi M.** 2007. African tick bite fever in a returned traveler. Isr. Med. Assoc. J. **9:**680–681.
372. **Atias D, Meltzer E, Leshem E, Schwartz E.** 2010. *Rickettsia africae* infection among participants in a women's safari to South Africa. Harefuah **149:**572–575, 620. (In Hebrew.)
373. **Beltrame A, Angheben A, Casolari S, Castelli F, Magnani G, Gaiera G, Brillo F, Cattani G, Anselmi M, Tomasoni L, Prati F, Norberto C, Socolovschi C, Bisoffi Z, Raoult D, Parola P.** 2012. Imported rickettsioses in Italy. Travel Med. Infect. Dis. **10:**201–204.
374. **Fujisawa T, Kadosaka T, Fujita H, Ando S, Takano A, Ogasawara Y, Kawabata H, Seishima M.** 2012. *Rickettsia africae* infection in a Japanese traveller with many tick bites. Acta Derm. Venereol. **92:**443–444.
375. **Rolain JM, Gouriet F, Brouqui P, Larrey D, Janbon F, Vene S, Jarnestrom V, Raoult D.** 2005. Concomitant or consecutive infection with *Coxiella burnetii* and tickborne diseases. Clin. Infect. Dis. **40:**82–88.
376. **Bellini C, Monti M, Potin M, Dalle Ave A, Bille J, Greub G.** 2005. Cardiac involvement in a patient with clinical and serological evidence of African tick-bite fever. BMC Infect. Dis. **5:**90. doi:10.1186 /1471-2334-5-90.
377. **Althaus F, Greub G, Raoult D, Genton B.** 2010. African tick-bite fever: a new entity in the differential diagnosis of multiple eschars in travelers. Description of five cases imported from South Africa to Switzerland. Int. J. Infect. Dis. **14**(Suppl 3):e274–e276. doi:10.1016/j.ijid.2009.11.021.
378. **Tsai KH, Lu HY, Tsai JJ, Yu SK, Huang JH, Shu PY.** 2008. Human case of *Rickettsia felis* infection, Taiwan. Emerg. Infect. Dis. **14:**1970–1972.
379. **Oostvogel PM, van Doornum GJ, Ferreira R, Vink J, Fenollar F, Raoult D.** 2007. African tickbite fever in travelers, Swaziland. Emerg. Infect. Dis. **13:**353–355.
380. **Wieten RW, Hovius JW, Groen EJ, van der Wal AC, de Vries PJ, Beersma MF, Tijsse-Klasen E, Sprong H, Grobusch MP.** 2011. Molecular diagnostics of *Rickettsia africae* infection in travelers returning from South Africa to the Netherlands. Vector Borne Zoonotic Dis. **11:**1541–1547.
381. **Auce P, Rajakulendran S, Nesbitt A, Chinn R, Kennedy A.** 2011. Neurological picture. Internuclear ophthalmoplegia following African tick bite fever. J. Neurol. Neurosurg. Psychiatry **82:**681. doi:10.1136/jnnp .2010.236216.
382. **Snape MD, Pollard AJ.** 2006. African tick bite fever. Lancet Infect. Dis. **6:**750. doi:10.1016/S1473-3099(06)70633-8.
383. **Bottieau E, Clerinx J, Van den Enden E, Van Esbroeck M, Colebunders R, Van Gompel A, Van den Ende J.** 2007. Fever after a stay in the tropics: diagnostic predictors of the leading tropical conditions. Medicine (Baltimore) **86:**18–25.
384. **Daneman N, Slinger R.** 2008. Tache noire. CMAJ **178:**841. doi:10.1503 /cmaj.070102.

385. **Jensenius M, Davis X, von Sonnenburg F, Schwartz E, Keystone JS, Leder K, Lopez-Velez R, Caumes E, Cramer JP, Chen L, Parola P.** 2009. Multicenter GeoSentinel analysis of rickettsial diseases in international travelers, 1996-2008. Emerg. Infect. Dis. **15:**1791–1798.
386. **Mendelson M, Davis XM, Jensenius M, Keystone JS, von Sonnenburg F, Hale DC, Burchard GD, Field V, Vincent P, Freedman DO.** 2010. Health risks in travelers to South Africa: the GeoSentinel experience and implications for the 2010 FIFA World Cup. Am. J. Trop. Med. Hyg. **82:**991–995.
387. **Schlagenhauf P, Chen LH, Wilson ME, Freedman DO, Tcheng D, Schwartz E, Pandey P, Weber R, Nadal D, Berger C, von Sonnenburg F, Keystone J, Leder K.** 2010. Sex and gender differences in travel-associated disease. Clin. Infect. Dis. **50:**826–832.
388. **Jensenius M, Fournier PE, Fladby T, Hellum KB, Hagen T, Prio T, Christiansen MS, Vene S, Raoult D, Myrvang B.** 2006. Sub-acute neuropathy in patients with African tick bite fever. Scand. J. Infect. Dis. **38:**114–118.
389. **Schwartz RA, Kapila R, McElligott SC, Atkin SH, Lambert WC.** 2012. Cutaneous leishmaniasis and rickettsial African tick-bite fever: a combination of exotic traveler's diseases in the same patient. Int. J. Dermatol. **51:**960–963.
390. **de Almeida DN, Favacho AR, Rozental T, Barcaui H, Guterres A, Gomes R, Levis S, Coelho J, Chebabo A, Costa LC, Andrea S, Barroso PF, de Lemos ER.** 2010. Fatal spotted fever group rickettsiosis due to *Rickettsia conorii conorii* mimicking a hemorrhagic viral fever in a South African traveler in Brazil. Ticks Tick Borne Dis. **1:**149–150.
391. **Prabhu M, Nicholson WL, Roche AJ, Kersh GJ, Fitzpatrick KA, Oliver LD, Massung RF, Morrissey AB, Bartlett JA, Onyango JJ, Maro VP, Kinabo GD, Saganda W, Crump JA.** 2011. Q fever, spotted fever group, and typhus group rickettsioses among hospitalized febrile patients in northern Tanzania. Clin. Infect. Dis. **53:**e8–e15. doi:10.1093/cid/cir411.
392. **Buchau AS, Wurthner JU, Bylaite M, Kukova G, Ruzicka T, Reifenberger J.** 2006. Rickettsiosis subsequent to vacation in Swaziland. Hautarzt **57:**328–330. (In German.)
393. **Yoshikawa H, Kimura M, Ogawa M, Rolain JM, Raoult D.** 2005. Laboratory-confirmed Mediterranean spotted fever in a Japanese traveler to Kenya. Am. J. Trop. Med. Hyg. **73:**1086–1089.
394. **Pader V, Nikitorowicz BJ, Abdissa A, Adamu H, Tolosa T, Gashaw A, Cutler RR, Cutler SJ.** 2012. *Candidatus Rickettsia hoogstraalii* in Ethiopian *Argas persicus* ticks. Ticks Tick Borne Dis. **3:**338–345.
395. **Matsumoto K, Parola P, Rolain JM, Jeffery K, Raoult D.** 2007. Detection of "*Rickettsia* sp. strain Uilenbergi" and "*Rickettsia* sp. strain Davousti" in *Amblyomma tholloni* ticks from elephants in Africa. BMC Microbiol. **7:**74. doi:10.1186/1471-2180-7-74.
396. **Cutler SJ, Browning P, Scott JC.** 2006. *Ornithodoros moubata*, a soft tick vector for *Rickettsia* in east Africa? Ann. N. Y. Acad. Sci. **1078:**373–377.
397. **Byambaa B.** 2008. Nature-focal rickettsioses in Mongolia. Two decades of Russian-Mongolian scientific collaboration. Vestn. Ross. Akad. Med. Nauk **2008**(7)**:**44–45. (In Russian.)
398. **Jang WJ, Choi YJ, Kim JH, Jung KD, Ryu JS, Lee SH, Yoo CK, Paik HS, Choi MS, Park KH, Kim IS.** 2005. Seroepidemiology of spotted fever group and typhus group rickettsioses in humans, South Korea. Microbiol. Immunol. **49:**17–24.
399. **Mediannikov OI, Makarova VA.** 2008. Far-Eastern spotted fever: description of new infectious disease. Vestn. Ross. Akad. Med. Nauk **2008**(7)**:**41–44. (In Russian.)
400. **Tarasevich IV, Mediannikov OY.** 2006. Rickettsial diseases in Russia. Ann. N. Y. Acad. Sci. **1078:**48–59.
401. **Shpynov S, Fournier PE, Rudakov N, Arsen'eva I, Granitov M, Tarasevich I, Raoult D.** 2009. Tick-borne rickettsiosis in the Altay region of Russia. Clin. Microbiol. Infect. **15**(Suppl 2)**:**313–314.
402. **Shpynov SN, Fournier PE, Rudakov NV, Samoilenko IE, Reshetnikova TA, Yastrebov VK, Schaiman MS, Tarasevich IV, Raoult D.** 2006. Molecular identification of a collection of spotted fever group rickettsiae obtained from patients and ticks from Russia. Am. J. Trop. Med. Hyg. **74:**440–443.
403. **Cao WC, Zhan L, De Vlas SJ, Wen BH, Yang H, Richardus JH, Habbema JD.** 2008. Molecular detection of spotted fever group *Rickettsia* in *Dermacentor silvarum* from a forest area of northeastern China. J. Med. Entomol. **45:**741–744.
404. **Speck S, Derschum H, Damdindorj T, Dashdavaa O, Jiang J, Kaysser P, Jigjav B, Nyamdorj E, Baatar U, Munkhbat E, Choijilsuren O, Gerelchuluun O, Romer A, Richards AL, Kiefer D, Scholz H, Wolfel R, Zoller L, Dobler G, Essbauer S.** 2012. *Rickettsia raoultii*, the predominant *Rickettsia* found in Mongolian *Dermacentor nuttalli*. Ticks Tick Borne Dis. **3:**227–231.
405. **Ando S, Kurosawa M, Sakata A, Fujita H, Sakai K, Sekine M, Katsumi M, Saitou W, Yano Y, Takada N, Takano A, Kawabata H, Hanaoka N, Watanabe H, Kurane I, Kishimoto T.** 2010. Human *Rickettsia heilongjiangensis* infection, Japan. Emerg. Infect. Dis. **16:**1306–1308.
406. **Mediannikov O, Sidelnikov Y, Ivanov L, Fournier PE, Tarasevich I, Raoult D.** 2006. Far eastern tick-borne rickettsiosis: identification of two new cases and tick vector. Ann. N. Y. Acad. Sci. **1078:**80–88.
407. **Li W, Liu L, Jiang X, Guo X, Garnier M, Raoult D, Parola P.** 2009. Molecular identification of spotted fever group rickettsiae in ticks collected in central China. Clin. Microbiol. Infect. **15**(Suppl 2)**:**279–280.
408. **Zhang LJ, Han J, Xu JG, Turchetto J, Mediannikov O, Rolain JM, Raoult D, Fournier PE.** 2009. Identification of a new serotype of *Rickettsia heilongjiangensis* in wild rats from Guangdong Province, China. Clin. Microbiol. Infect. **15**(Suppl 2)**:**338–339.
409. **Liang CW, Zhao JB, Li J, Chang LT, Yu HL, Zhang LX, Zhang LJ, Yu XJ.** 2012. Spotted fever group *Rickettsia* in Yunnan Province, China. Vector Borne Zoonotic Dis. **12:**281–286.
410. **Duan C, Meng Y, Wang X, Xiong X, Wen B.** 2011. Exploratory study on pathogenesis of far-eastern spotted fever. Am. J. Trop. Med. Hyg. **85:**504–509.
411. **Gaywee J, Sunyakumthorn P, Rodkvamtook W, Ruang-areerate T, Mason CJ, Sirisopana N.** 2007. Human infection with *Rickettsia* sp. related to *R. japonica*, Thailand. Emerg. Infect. Dis. **13:**671–673.
412. **Takada N, Fujita H, Kawabata H, Ando S, Sakata A, Takano A, Chaithong U.** 2009. Spotted fever group *Rickettsia* sp. closely related to *Rickettsia japonica*, Thailand. Emerg. Infect. Dis. **15:**610–611.
413. **Mahara F.** 2006. Rickettsioses in Japan and the Far East. Ann. N. Y. Acad. Sci. **1078:**60–73.
414. **Tabara K, Kawabata H, Arai S, Itagaki A, Yamauchi T, Katayama T, Fujita H, Takada N.** 2011. High incidence of rickettsiosis correlated to prevalence of *Rickettsia japonica* among *Haemaphysalis longicornis* tick. J. Vet. Med. Sci. **73:**507–510.
415. **Sashika M, Abe G, Matsumoto K, Inokuma H.** 2010. Molecular survey of rickettsial agents in feral raccoons (*Procyon lotor*) in Hokkaido, Japan. Jpn. J. Infect. Dis. **63:**353–354.
416. **Chung MH, Lee SH, Kim MJ, Lee JH, Kim ES, Kim MK, Park MY, Kang JS.** 2006. Japanese spotted fever, South Korea. Emerg. Infect. Dis. **12:**1122–1124.
417. **Dong X, El Karkouri K, Robert C, Raoult D, Fournier PE.** 2012. Genomic analysis of *Rickettsia japonica* strain YHT. J. Bacteriol. **194:**6992. doi:10.1128/JB.01928-12.
418. **Sentausa E, El Karkouri K, Robert C, Raoult D, Fournier PE.** 2012. Genome sequence of "*Rickettsia sibirica* subsp. *mongolitimonae*." J. Bacteriol. **194:**2389–2390.
419. **Harrus S, Perlman-Avrahami A, Mumcuoglu KY, Morick D, Baneth G.** 2011. Molecular detection of *Rickettsia massiliae*, *Rickettsia sibirica mongolitimonae* and *Rickettsia conorii israelensis* in ticks from Israel. Clin. Microbiol. Infect. **17:**176–180.
420. **Chaudhry D, Garg A, Singh I, Tandon C, Saini R.** 2009. Rickettsial diseases in Haryana: not an uncommon entity. J. Assoc. Physicians India **57:**334–337.
421. **Miah MT, Rahman S, Sarker CN, Khan GK, Barman TK.** 2007. Study on 40 cases of rickettsia. Mymensingh Med. J. **16:**85–88.
422. **Phongmany S, Rolain JM, Phetsouvanh R, Blacksell SD, Soukkhaseum V, Rasachack B, Phiasakha K, Soukkhaseum S, Frichithavong K, Chu V, Keolouangkhot V, Martinez-Aussel B, Chang K, Darasavath C, Rattanavong O, Sisouphone S, Mayxay M, Vidamaly S, Parola P, Thammavong C, Heuangvongsy M, Syhavong B, Raoult D, White NJ, Newton PN.** 2006. Rickettsial infections and fever, Vientiane, Laos. Emerg. Infect. Dis. **12:**256–262.
423. **Stokes PH, Walters BJ.** 2009. Spotted fever rickettsiosis infection in a traveler from Sri Lanka. J. Travel Med. **16:**436–438.
424. **Joshi HS, Thomas M, Warrier A, Kumar S.** 2012. Gangrene in cases of spotted fever: a report of three cases. BMJ Case Rep. **2012:** bcr2012007295. doi:10.1136/bcr-2012-007295.
425. **Sentausa E, El Karkouri K, Robert C, Raoult D, Fournier PE.** 2012. Genome sequence of *Rickettsia conorii* subsp. *indica*, the agent of Indian tick typhus. J. Bacteriol. **194:**3288–3289.
426. **Sentausa E, El Karkouri K, Robert C, Raoult D, Fournier PE.** 2012.

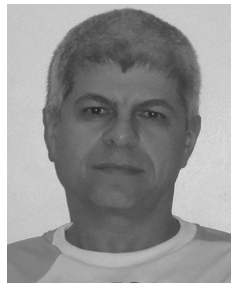
Genome sequence of *Rickettsia conorii* subsp. *israelensis*, the agent of Israeli spotted fever. J. Bacteriol. **194:**5130–5131.
427. **Graves S, Stenos J.** 2009. Rickettsioses in Australia. Ann. N. Y. Acad. Sci. **1166:**151–155.
428. **Jiang J, Sangkasuwan V, Lerdthusnee K, Sukwit S, Chuenchitra T, Rozmajzl PJ, Eamsila C, Jones JW, Richards AL.** 2005. Human infection with *Rickettsia honei*, Thailand. Emerg. Infect. Dis. **11:**1473–1475.
429. **Sangkasuwan V, Chatyingmongkol T, Sukwit S, Eamsila C, Chuenchitra T, Rodkvamtook W, Jiang J, Richards AL, Lerdthusnee K, Jones JW.** 2007. Description of the first reported human case of spotted fever group rickettsiosis in urban Bangkok. Am. J. Trop. Med. Hyg. **77:**891–892.
430. **Murphy H, Renvoise A, Pandey P, Parola P, Raoult D.** 2011. *Rickettsia honei* infection in human, Nepal, 2009. Emerg. Infect. Dis. **17:**1865–1867.
431. **Xin D, El Karkouri K, Robert C, Raoult D, Fournier PE.** 2012. Genomic comparison of *Rickettsia honei* strain RBT and other *Rickettsia* species. J. Bacteriol. **194:**4145. doi:10.1128/JB.00802-12.
432. **Motoi Y, Asano M, Inokuma H, Ando S, Kawabata H, Takano A, Suzuki M.** 2013. Detection of *Rickettsia tamurae* DNA in ticks and wild boar (*Sus scrofa leucomystax*) skins in Shimane Prefecture, Japan. J. Vet. Med. Sci. **75:**263–267.
433. **Imaoka K, Kaneko S, Tabara K, Kusatake K, Morita E.** 2011. The first human case of *Rickettsia tamurae* infection in Japan. Case Rep. Dermatol. **3:**68–73.
434. **Rolain JM, Mathai E, Lepidi H, Somashekar HR, Mathew LG, Prakash JA, Raoult D.** 2006. "*Candidatus Rickettsia kellyi*," India. Emerg. Infect. Dis. **12:**483–485.
435. **Keysary A, Eremeeva ME, Leitner M, Din AB, Wikswo ME, Mumcuoglu KY, Inbar M, Wallach AD, Shanas U, King R, Waner T.** 2011. Spotted fever group rickettsiae in ticks collected from wild animals in Israel. Am. J. Trop. Med. Hyg. **85:**919–923.
436. **Tian ZC, Liu GY, Shen H, Xie JR, Luo J, Tian MY.** 2012. First report on the occurrence of *Rickettsia slovaca* and *Rickettsia raoultii* in *Dermacentor silvarum* in China. Parasit. Vectors **5:**19. doi:10.1186/1756-3305-5-19.
437. **Ahantarig A, Malaisri P, Hirunkanokpun S, Sumrandee C, Trinachartvanit W, Baimai V.** 2011. Detection of *Rickettsia* and a novel *Haemaphysalis shimoga* symbiont bacterium in ticks in Thailand. Curr. Microbiol. **62:**1496–1502.
438. **Inokuma H, Ohashi M, Jilintai, Tanabe S, Miyahara K.** 2007. Prevalence of tick-borne *Rickettsia* and *Ehrlichia* in *Ixodes persulcatus* and *Ixodes ovatus* in Tokachi district, Eastern Hokkaido, Japan. J. Vet. Med. Sci. **69:**661–664.
439. **Filippova NA.** 1997. Ixodid ticks from subfamily Ambliomminae, p 436. *In* Tsalolikhin SY (ed), Fauna of Russia and neighboring countries. Arachnidae. Nauka, St Petersburg, Russia.
440. **Jilintai, Seino N, Matsumoto K, Hayakawa D, Suzuki M, Hata H, Kondo S, Yokoyama N, Inokuma H.** 2008. Serological and molecular survey of rickettsial infection in cattle and sika deer in a pastureland in Hidaka District, Hokkaido, Japan. Jpn. J. Infect. Dis. **61:**315–317.
441. **Tsui PY, Tsai KH, Weng MH, Hung YW, Liu YT, Hu KY, Lien JC, Lin PR, Shaio MF, Wang HC, Ji DD.** 2007. Molecular detection and characterization of spotted fever group rickettsiae in Taiwan. Am. J. Trop. Med. Hyg. **77:**883–890.
442. **Tsai KH, Wang HC, Chen CH, Huang JH, Lu HY, Su CL, Shu PY.** 2008. Isolation and identification of a novel spotted fever group rickettsia, strain IG-1, from *Ixodes granulatus* ticks collected on Orchid Island (Lanyu), Taiwan. Am. J. Trop. Med. Hyg. **79:**256–261.
443. **Fujita H, Kadosaka T, Nitta Y, Ando S, Takano A, Watanabe H, Kawabata H.** 2008. *Rickettsia* sp. in *Ixodes granulatus* ticks, Japan. Emerg. Infect. Dis. **14:**1963–1965.
444. **Kawabata H, Ando S, Kishimoto T, Kurane I, Takano A, Nogami S, Fujita H, Tsurumi M, Nakamura N, Sato F, Takahashi M, Ushijima Y, Fukunaga M, Watanabe H.** 2006. First detection of Rickettsia in softbodied ticks associated with seabirds, Japan. Microbiol. Immunol. **50:**403–406.
445. **Chahan B, Jian Z, Jilintai, Miyahara K, Tanabe S, Xuan X, Sato Y, Moritomo T, Nogami S, Mikami T, Maruyama S, Inokuma H.** 2007. Detection of DNA closely related to '*Candidatus Rickettsia* principis' in *Haemaphysalis danieli* recovered from cattle in Xinjiang Uygur Autonomous Region Area, China. Vet. Parasitol. **144:**184–187.
446. **Pinn TG, Sowden D.** 1998. Queensland tick typhus. Aust. N. Z. J. Med. **28:**824–826.
447. **Unsworth NB, Stenos J, Faa AG, Graves SR.** 2007. Three rickettsioses, Darnley Island, Australia. Emerg. Infect. Dis. **13:**1105–1107.
448. **Birch TF, Muller M.** 2009. Severe Queensland tick typhus complicated by diabetes in south-eastern Queensland. Med. J. Aust. **191**(5)**:**290–291.
449. **McBride WJ, Hanson JP, Miller R, Wenck D.** 2007. Severe spotted fever group rickettsiosis, Australia. Emerg. Infect. Dis. **13:**1742–1744.
450. **Sexton DJ, King G, Dwyer B.** 1990. Fatal Queensland tick typhus. J. Infect. Dis. **162:**779–780.
451. **Barker SC, Murrell A.** 2004. Systematics and evolution of ticks with a list of valid genus and species names. Parasitology **129**(Suppl)**:**S15–S36.
452. **Roberts FHS.** 1970. Australian ticks, Melbourne. Commonwealth Scientific and Industrial Research Organization, Clayton South, Victoria, Australia.
453. **Stenos J, Graves S, Popov VL, Walker DH.** 2003. *Aponomma hydrosauri*, the reptile-associated tick reservoir of *Rickettsia honei* on Flinders Island, Australia. Am. J. Trop. Med. Hyg. **69:**314–317.
454. **Unsworth NB, Stenos J, McGregor AR, Dyer JR, Graves SR.** 2005. Not only 'Flinders Island' spotted fever. Pathology **37:**242–245.
455. **Lane AM, Shaw MD, McGraw EA, O'Neill SL.** 2005. Evidence of a spotted fever-like rickettsia and a potential new vector from northeastern Australia. J. Med. Entomol. **42:**918–921.
456. **Unsworth NB, Stenos J, Graves SR, Faa AG, Cox GE, Dyer JR, Boutlis CS, Lane AM, Shaw MD, Robson J, Nissen MD.** 2007. Flinders Island spotted fever rickettsioses caused by "marmionii" strain of *Rickettsia honei*, Eastern Australia. Emerg. Infect. Dis. **13:**566–573.
457. **Unsworth N, Graves S, Nguyen C, Kemp G, Graham J, Stenos J.** 2008. Markers of exposure to spotted fever rickettsiae in patients with chronic illness, including fatigue, in two Australian populations. QJM **101:**269–274.
458. **Kelly PJ, Beati L, Mason PR, Matthewman LA, Roux V, Raoult D.** 1996. *Rickettsia africae* sp. nov., the etiological agent of African tick bite fever. Int. J. Syst. Bacteriol. **46:**611–614.
459. **Eldin C, Mediannikov O, Davoust B, Cabre O, Barre N, Raoult D, Parola P.** 2011. Emergence of *Rickettsia africae*, Oceania. Emerg. Infect. Dis. **17:**100–102.
460. **Owen H, Unsworth N, Stenos J, Robertson I, Clark P, Fenwick S.** 2006. Detection and identification of a novel spotted fever group rickettsia in Western Australia. Ann. N. Y. Acad. Sci. **1078:**197–199.
461. **Owen H, Clark P, Stenos J, Robertson I, Fenwick S.** 2006. Potentially pathogenic spotted fever group rickettsiae present in Western Australia. Aust. J. Rural Health **14:**284–285.
462. **Li AY, Adams PJ, Abdad MY, Fenwick SG.** 2010. High prevalence of *Rickettsia gravesii* sp. nov. in *Amblyomma triguttatum* collected from feral pigs. Vet. Microbiol. **146:**59–62.
463. **Pearce RL, Grove DI.** 1987. Tick infestation in soldiers who were bivouacked in the Perth region. Med. J. Aust. **146:**238–240.
464. **Izzard L, Graves S, Cox E, Fenwick S, Unsworth N, Stenos J.** 2009. Novel rickettsia in ticks, Tasmania, Australia. Emerg. Infect. Dis. **15:**1654–1656.
465. **Vilcins IM, Old JM, Deane EM.** 2008. Detection of a spotted fever group *Rickettsia* in the tick *Ixodes tasmani* collected from koalas in Port Macquarie, Australia. J. Med. Entomol. **45:**745–750.
466. **Angelakis E, Richet H, Rolain JM, La Scola B, Raoult D.** 2012. Comparison of real-time quantitative PCR and culture for the diagnosis of emerging rickettsioses. PLoS Negl. Trop. Dis. **6:**e1540. doi:10.1371/journal.pntd.0001540.
467. **Stenos J, Graves SR, Unsworth NB.** 2005. A highly sensitive and specific real-time PCR assay for the detection of spotted fever and typhus group rickettsiae. Am. J. Trop. Med. Hyg. **73:**1083–1085.
468. **Kidd L, Maggi R, Diniz PP, Hegarty B, Tucker M, Breitschwerdt E.** 2008. Evaluation of conventional and real-time PCR assays for detection and differentiation of spotted fever group *Rickettsia* in dog blood. Vet. Microbiol. **129:**294–303.
469. **Renvoise A, Rolain JM, Socolovschi C, Raoult D.** 2012. Widespread use of real-time PCR for rickettsial diagnosis. FEMS Immunol. Med. Microbiol. **64:**126–129.
470. **Fournier PE, Drancourt M, Raoult D.** 2007. Bacterial genome sequencing and its use in infectious diseases. Lancet Infect. Dis. **7:**711–723.
471. **Mouffok N, Socolovschi C, Benabdellah A, Renvoise A, Parola P, Raoult D.** 2011. Diagnosis of rickettsioses from eschar swab samples, Algeria. Emerg. Infect. Dis. **17:**1968–1969.

472. **Socolovschi C, Renvoise A, Brouqui P, Parola P, Raoult D.** 2012. The use of eschar swabs for the diagnosis of African tick-bite fever. Ticks Tick Borne Dis. **3:**361–363.
473. **Myers T, Lalani T, Dent M, Jiang J, Daly PL, Maguire JD, Richards AL.** 2013. Detecting *Rickettsia parkeri* infection from eschar swab specimens. Emerg. Infect. Dis. **19:**778–780.
474. **Parola P, Raoult D.** 2001. Ticks and tickborne bacterial diseases in humans: an emerging infectious threat. Clin. Infect. Dis. **32:**897–928.
475. **Seng P, Rolain JM, Fournier PE, La Scola B, Drancourt M, Raoult D.** 2010. MALDI-TOF-mass spectrometry applications in clinical microbiology. Future Microbiol. **5:**1733–1754.
476. **Karger A, Kampen H, Bettin B, Dautel H, Ziller M, Hoffmann B, Suss J, Klaus C.** 2012. Species determination and characterization of developmental stages of ticks by whole-animal matrix-assisted laser desorption/ionization mass spectrometry. Ticks Tick Borne Dis. **3:**78–89.
477. **Yssouf A, Flaudrops C, Drali R, Kernif T, Socolovschi C, Berenger JM, Raoult D, Parola P.** 2013. Matrix-assisted laser desorption ionization-time of flight mass spectrometry for rapid identification of tick vectors. J. Clin. Microbiol. **51:**522–528.
478. **Botelho-Nevers E, Socolovschi C, Raoult D, Parola P.** 2012. Treatment of *Rickettsia* spp. infections: a review. Expert Rev. Anti Infect. Ther. **10:**1425–1437.
479. **Audoly G, Vincentelli R, Edouard S, Georgiades K, Mediannikov O, Gimenez G, Socolovschi C, Mege JL, Cambillau C, Raoult D.** 2011. Effect of rickettsial toxin VapC on its eukaryotic host. PLoS One **6:**e26528. doi:10.1371/journal.pone.0026528.
480. **Botelho-Nevers E, Edouard S, Leroy Q, Raoult D.** 2012. Deleterious effect of ciprofloxacin on Rickettsia conorii-infected cells is linked to toxin-antitoxin module up-regulation. J. Antimicrob. Chemother. **67:**1677–1682.
481. **Jensenius M, Parola P, Raoult D.** 2006. Threats to international travellers posed by tick-borne diseases. Travel. Med. Infect. Dis. **4:**4–13.
482. **Holland CA, Kiechle FL.** 2005. Point-of-care molecular diagnostic systems—past, present and future. Curr. Opin. Microbiol. **8:**504–509.

Philippe Parola, M.D., Ph.D., is a French clinician and Professor of Infectious Diseases and Tropical Medicine (IDTM) at the Faculty of Medicine of Marseille, Aix-Marseille University, France. There, he is director in charge of the IDTM Residency program. His clinical medical activities take place in the University Hospital Institute for IDTM of Marseille, where he is particularly involved in management of ill returned travelers. His research interests include vector-borne rickettsioses and emerging infectious diseases. By January 2013, Dr. Parola had coauthored more than 270 publications in the international literature. He is Director of the WHO Collaborative Center for Rickettsial and Other Arthropod Borne Bacterial Diseases and a worldwide-recognized expert on tick-borne rickettsioses. In the field of travel medicine, he is Director of EuroTravNet, the European CDC Collaborative Network for Travel and Tropical Medicine; and he has been appointed as GeoSentinel, Global Surveillance Network, Project Director—Europe.

Christopher D. Paddock is a rickettsiologist and pathologist at the Centers for Disease Control and Prevention (CDC) in Atlanta, GA. Dr. Paddock received his B.S. and M.S. degrees in Entomology at the University of California, Davis, in 1981 and 1986, respectively, and his M.D. and M.P.H.T.M. degrees at Tulane University in New Orleans, LA, in 1990. He completed his residency in Anatomic Pathology and Laboratory Medicine at the University of California, San Francisco, in 1995. His employment with the CDC began in 1996, as medical officer in the Viral and Rickettsial Zoonoses Branch, where he worked until taking a position as staff pathologist with the Infectious Disease Pathology Branch in 2003. He has authored or coauthored approximately 150 scientific publications and 20 book chapters. His research interests include clinical, diagnostic, and epidemiologic aspects of rickettsial diseases, primarily newly recognized spotted fever group rickettsioses.

Cristina Socolovschi is an infectious diseases clinician who obtained her M.D. degree at the faculty of Chisinau, Moldova. In 2002, she joined the University Hospital of Marseille and started her research activity at the Unité des Rickettsies. Working on the relationship between spotted fever group rickettsiae and ixodid ticks, she obtained her Ph.D. degree in 2009. She is now in charge of diagnosis and management of vector-borne diseases, especially rickettsiosis, in the infectious diseases department of the University Hospital of Marseille and continues her research activity with the team of Philippe Parola. Her research interests include tropical diseases and medical entomology, focused on relationships of hosts and pathogens in rickettsial diseases. She has published more than 50 research articles in the field of vector-borne diseases.



Marcelo B. Labruna is a veterinarian with a Ph.D. in epidemiology and a member of the Sociedade de Investigadores de Antricola (SIA). He is an Associate Professor of Animal Parasitic Diseases of the Faculty of Veterinary Medicine of the University of São Paulo, Brazil. His research interest has been systematic biology and ecology of neotropical ticks and tick-borne diseases, with emphasis on rickettsioses. He is the curator of the Coleção Nacional de Carrapatos (CNC), one of the largest tick collections of Latin America. In the past years, he has provided major contributions in the field of vector-associated rickettsiae.

Oleg Mediannikov graduated from medical university in Khabarovsk, Russia, in 1998 and specialized in infectious diseases. With a research interest focusing on vector-borne diseases, including anaplasmosis, spotted fever, and borrelioses, he obtained his Ph.D. degree in 2004. Particularly, he identified the role of *Rickettsia heilongjiangensis* as a cause of tick-borne spotted fever in the Russian Far East. He then joined Didier Raoult's team in France, and since 2011, he has led a research group within the IRD component in Senegal. There, he continues his studies of the origins of acute febrile diseases in Africa, particularly emerging vector-borne diseases (relapsing fever, spotted fevers, and bartonelloses). He is an expert on the isolation of fastidious bacteria. He isolated and described such bacteria, including new species such as *Rickettsia raoultii*, *Diplorickettsia massiliensis*, *Orientia massiliensis*, *Bartonella senegalensis*, *Bartonella florenciae*, and *Bartonella massiliensis.*

Tahar Kernif has obtained the title of veterinary doctor and parasitologist at the Veterinary School of Algiers, Algeria. Subsequently, he obtained his Ph.D. degree at the Faculty of Medicine of Marseille, Aix-Marseille University, France. He is now a research fellow on vector diseases and arthropods at the Pasteur Institute of Algiers, Algeria. He is also working within the MABAVECT team created by Idir Bitam. His research interests focus on vector-borne infectious diseases and medical entomology because these diseases are underestimated and misdiagnosed in North Africa.

Mohammad Yazid Abdad received his Ph.D. from Murdoch University, Western Australia, investigating the epidemiology and prevalence of a novel rickettsia in humans, feral pigs, and potential invertebrate reservoirs. He then proceeded to complete a 3-year postdoctoral fellowship with the Australian Rickettsial Reference Laboratory in Geelong, Australia, studying rickettsial organisms in Australia and the region. He is currently employed by the Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea, as a Senior Research Fellow. His current research focus encompasses zoonotic and emerging diseases, and he spends much of his time in the jungles and rural parts of Papua New Guinea. He leads a team of scientists investigating zoonotic transmission, emerging disease outbreaks, and prevalences of various neglected diseases in local communities and animal populations (both wild and domestic).

John Stenos completed a science degree with majors in microbiology and biochemistry at the University of Melbourne in Australia in 1989. This was followed immediately with an Honors project assessing various assays in quantifying *Rickettsia australis*. He continued in the same field with a Ph.D. project looking at the characterization of Australian rickettsial agents. His love of rickettsiology was cemented further with a postdoctoral fellow position in the United States. His research in rickettsial genomics was undertaken in the world-renowned rickettsial laboratory, with direction from Dr. David Walker, at the University of Texas Medical Branch, USA. He was then invited back to Australia by a pioneer in Australian rickettsiologist, Dr. Stephen Graves, to help run the Australian Rickettsial Reference Laboratory in 1998. In the following years, the laboratory established a world-renowned reputation in its diagnostics and research activities supporting both scientists and students in this emerging field.

Idir Bitam is Associate Professor at the University of Boumerdes, Algeria. After having obtained a master's degree in Entomology in Algiers, Algeria, he completed a Ph.D. degree at the Faculty of Medicine of Marseille, Aix-Marseille University, France, under the direction of Didier Raoult. He published most of the current available data about tick- and flea-associated rickettsiae from Algeria. Back in Algeria, he has created the Young Investigators research team "Malbavect," in partnership with the IRD. His research interests include vector-borne bacterial diseases, particularly flea- and tick-borne diseases.

Pierre-Edouard Fournier, M.D., Ph.D., is a clinical microbiologist and Professor of Microbiology at the Faculty of Medicine of Marseille, Aix-Marseille University, France. There, within the Research Unit in Infectious and Tropical Emergent Diseases, he is Director of the French reference center for the diagnosis of rickettsioses, bartonelloses, and Q fever. He specializes in the diagnosis of infectious diseases, notably infections caused by intracellular bacteria. Dr. Fournier authored or coauthored more than 250 internationally published articles.

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Didier Raoult holds M.D. and Ph.D. degrees, specializes in infectious diseases, and is Professor of Microbiology at the Faculty of Medicine of Marseille, Aix-Marseille University. There, in 1984, he created, *ex nihilo*, his research laboratory, the Rickettsia Unit. It has now become the Research Unit in Infectious and Tropical Emergent Diseases, collaborating with the CNRS (National Center for the Scientific Research), IRD (Research for the Development Institute), and INSERM (National Institute of Health and Medical Research). Since 2011, he has been the director of the University Hospital Institute Mediterranée Infection, a 600-person medical institute working on infectious diseases. It includes the largest diagnostic and research microbiology laboratory in France. Providing one of the largest genomic, transcriptomic, and proteomic platforms, it is a leader within the fields of microbiology, infectious diseases, and emerging infections. As of 2013, Dr. Raoult has published around 1,700 indexed publications and remains the world expert in the field of rickettsioses.

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Update on Tick-Borne Rickettsioses around the World: a Geographic Approach

Philippe Parola, Christopher D. Paddock, Cristina Socolovschi, Marcelo B. Labruna, Oleg Mediannikov, Tahar Kernif, Mohammad Yazid Abdad, John Stenos, Idir Bitam, Pierre-Edouard Fournier, Didier Raoult

Aix Marseille Université, Unité de Recherche en Maladies Infectieuses et Tropicales Emergentes (URMITE), UM63, CNRS 7278, IRD 198, Inserm 1095, WHO Collaborative Center for Rickettsioses and Other Arthropod-Borne Bacterial Diseases, Faculté de Médecine, Marseille, France; Centers for Disease Control and Prevention, Atlanta, Georgia, USA; Departamento de Medicina Veterinária Preventiva e Saúde Animal, Faculdade de Medicina Veterinária e Zootecnia Universidade de São Paulo, Cidade Universitária, São Paulo, SP, Brazil; Service d'Ecologie des Systèmes Vectoriels, Institut Pasteur d'Algérie, Algiers, Algeria; Division of Veterinary and Biomedical Science, Murdoch University, Australian Rickettsial Reference Laboratory, Barwon Health, Geelong, Victoria, Australia; University of Boumerdes, Boumerdes, Algeria

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