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Rickettsiosis as Threat for the Traveller

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1. Introduction

Over the past six decades, tourism has experienced continued expansion and diversification becoming one of the largest and fastest growing economic sectors in the world. Many new destinations have emerged alongside the traditional ones of Europe and North America. In the next years an increase of travelling is expected, and the number of related infections will also be higher (http://www.unwto.org/facts/menu.html). Rickettsioses are an important chapter in the field of travel medicine.

Rickettsiae are small gram-negative intracellular bacteria (belonging to the alpha-1 proteobacteria) mainly transmitted by arthropods (lice, fleas, ticks and other acari) with two genera: *Orientia* with a unique specie (*Orientia tsutsugamushi*) and *Rickettsia* with several species. The clinical pictures that they cause are named rickettsioses (Raoult, 2010a).

Rickettsioses have been a threat all along the History and nowadays they are an important cause of morbi-mortality in some areas of the world. To know the distribution of the different diseases caused by these bacteria and how the clinical pictures are recognized may be essential for a quick diagnoses and starting the correct treatment. Some of these infections can be also easily prevented with basic rules. Main rickettsioses with their distribution area are showed in the table 1.

In the 21st Century in most parts of the world hygienic conditions have improved and epidemic typhus is absent. To acquire this condition it is necessary to be in contact with body lice. Furthermore, if people have personal hygiene and change their clothing, body lice are removed. Nevertheless it is possible that if we travel for cooperation to catastrophic areas or other places with poverty, we may take body lice (refugees' camps) and may develop exanthematic typhus.

There are a lot of references of rickettsioses acquired by travellers and considered imported diseases (McDonald et al., 1988; Bottieau et al. 2006; Freedman et al., 2006; Askling et al. 2009; Chen & Wilson, 2009; Jensenius et al., 2009; Stokes & Walters, 2009).

Nowadays ticks cause most travel-associated rickettsioses. Ticks are considered to be one of the most important vectors of infectious diseases in the world, preceded only by mosquitoes. Therefore, tick-borne rickettsioses are endemic all over the world (Hechemy et al., 2006). The majority of travel-associated rickettsioses refer to Sub-Saharan Africa tourists who develop African tick-bite fever (ATBF), mainly transmitted by *Amblyomma hebraeum* (Figure 1). In addition to malaria, ATBF is an important cause of fever in people returning from the tropic (Field et al., 2010). Other reports describe Mediterranean spotted fever (MSF) acquired by tourists bitten by *Rhipicephalus* spp. ticks (Figure 2) when visiting Europe, being

more scarce references about other rickettsioses. Flea-borne rickettsioses and chigger-transmitted rickettsioses are less frequent in travellers and tourists, and some of them as murine typhus are associated with poor hygienic conditions. Most travel-acquired rickettsioses are related to outdoors leisure activities, like camping, trekking, hunting, safaris, etc.

It will be impossible to describe all rickettsioses in few pages. Since rickettsioses have very similar clinical pictures and they can be grouped in different syndromes, we will describe these syndromes emphasizing the typical features (i.e.: Presence of eschar or type of rash). Afterwards, distribution can be observed in the table 1. We will also write a specific paragraph for some infections (i.e.: Diseases caused by *Rickettsia akari* and *Orientia tsutsugamushi*).

Fig. 1. *Amblyomma hebraeum*, the principal vector of African-tick bite fever (ATBF) in southern Africa.

Fig. 2. *Rhipicephalus* spp., the main vector of Mediterranean spotted fever (MSF).

DISEASE	CAUSATIVE AGENT	VECTOR	DISTRIBUTION
Epidemic typhus	*R. prowazekii*	Body lice (*Pediculus humanus corporis*)	Peru, northern Africa, Senegal, Burundi, Rwanda, Russia, sporadic cases in USA associated with flying squirrels. Potentially, all over the world associated to poverty and dirt.
Murine typhus	*R. typhi*	Fleas (*Xenopsylla cheopis* and *Ctenocephalides felis*)	All over the world (more prevalent in tropical and subtropical areas)
Flea-borne spotted fever	*R. felis*	Cat fleas (*Ctenocephalides felis*)	All over the world

DISEASE	CAUSATIVE AGENT	VECTOR	DISTRIBUTION
Scrub typhus	*Orientia tsutsugamushi*	Trombiculid mite larvae (chiggers)	Thailand, Laos, India, Pakistan, Kashmir, Sri-Lanka, Afghanistan, Nepal, China, Japan, Korea, Indonesia. Philippines, Papua-New Guinea, Australia
Rickettsialpox	*R. akari*	Mouse mites (*Liponyssoides sanguineus*)	Eastern Europe, Korea, South Africa, USA
RMSF[1]	*R. rickettsii*	*Dermacentor variabilis* and other American ticks	USA, Mexico, Colombia, Brazil, Argentina, Panama, Costa Rica
RMSF-like	*R. parkeri*	*Amblyomma* spp. ticks	USA, Uruguay, Brazil, Argentina
MSF[2]	*R. conorii conorii, R. conorii israelensis, R. conorii caspia, R. conorii indica*	*Rhipicephalus* spp. ticks	Mediterranean area, Central Europe, Russia, India and Africa
MSF-like	*R. monacensis*	*Ixodes ricinus* ticks	Europe
MSF-like	*R. massiliae*	*Rhipicephalus sanguineus* ticks	Mediterranean area, Argentina, USA?
MSF-like	*R. aeschlimannii*	*Hyalomma marginatum* ticks	Africa, Europe?
DEBONEL / TIBOLA[2]	*R. slovaca R. rioja R. raoultii*	*Dermacentor marginatus* ticks	Europe
LAR[4]	*R. sibirica mongolitimonae*	*Hyalomma* spp. and *Rhipicephalus pusillus* ticks	Europe, Africa.
ATBF[5]	*R. africae*	*Amblyomma* spp. ticks	Sub-Saharan Africa and West Indies
Siberian tick typhus	*R. sibirica sibirica*	*Dermacentor* spp. ticks	Russia, Pakistan, China
R. helvetica infection	*R. helvetica*	*Ixodes ricinus* ticks	Central and northern Europe, Asia
Japanese spotted fever	*R. japonica*	Ticks	Japan
Queensland tick typhus	*R. australis*	*Ixodes* spp. ticks	Eastern Australia
Flinder's Island spotted fever	*R. honei*	Ticks	Australia, Southeast Asia
Far Eastern spotted fever	*R. heilonjgiangensis*	*Dermacentor* spp. ticks	Eastern Asia

[1]RMSF: Rocky Mountain spotted fever; [2]MSF: Mediterranean spotted fever; [3]DEBONEL/TIBOLA: *Dermacentor*-borne, necrosis, erythema, lymphadenopathy/Tick-borne lymphadenopathy; [4]LAR: Lymphangitis-associated rickettsiosis; [5]ATBF: African tick-bite fever.

Table 1. *Rickettsia* spp. causing medical diseases, vectors and distribution

2. Typhus syndrome

Typhus syndrome refers to a febrile syndrome with mental status impairment and rash. It is caused by *Rickettsia prowazekii* (epidemic typhus) and *Rickettsia typhi* (formerly, *R. mooseri*). *Rickettsia felis* may also produce a typhus syndrome named flea-borne spotted fever, which is similar to *R. typhi* infection (perhaps less severe) (Walker & Raoult, 2010; Dumler & Walker 2010; Oteo et al., 2006).

Nowadays epidemic typhus is only present in some regions of Africa, Russia and in Peru. It is associated with bad hygienic conditions that are necessary for body lice parasitization. Sporadic cases associated with contact with flying squirrels and their parasite arthropods, which have been involved as new reservoirs of the infection, have also been reported in USA. A possible source of *R. prowazekii* infection may be a recrudescent case (Brill-Zinsser disease) of *R. prowazekii* infection. If hygienic conditions are altered and an epidemic of body lice appears may be an epidemic of typhus, as occurred in Burundi with hundreds of affected people (Raoult et al., 1998). Some cases of louse-borne typhus in travellers have been published (Zanetti et al., 1998; Kelly et al., 2002).

Endemic typhus or murine typhus is associated with the presence of fleas. The main vector is the rat flea (*Xenopsylla cheopis*) associated with dirt and poor hygienic conditions. Flea-borne spotted fever is associated with the cat flea, and in this case bad hygienic conditions are not necessary. Murine typhus and flea-borne spotted fever are distributed all over the world. Although they are more frequent in tropical and subtropical areas, cases have also been reported in the Mediterranean area (Greece, Italy, Spain, France and Portugal) (Bernabeu-Wittel et al., 1999; Angel-Moreno et al., 2006; Gikas et al,. 2009; Pérez-Arellano et al., 2005; Oteo et al., 2006).

The clinical pictures of murine typhus and flea-borne spotted fever are less severe than the one of epidemic typhus. Thus, 1-2 weeks after the flea exposure, patients begin with fever, headache, myalgia, nausea and vomiting. Rash can be difficult to see in some cases, but is present until 80%. For *R. typhi* infection, rash is macular or maculo-papular and typically affects trunk and less frequently extremities. In epidemic typhus, petechial rash is more frequent than in endemic typhus, and cough, nausea and vomiting are frequent features. On the contrary of tick-borne rickettsioses or scrub typhus, an inoculation eschar (*tache noire*) is not observed. In most cases, fever and rash disappear in a few weeks but complications can be developed (central nervous, kidney involvement with renal insufficiency, respiratory failure, etc.). These complications are more frequent for epidemic typhus and in older people or patients suffering chronic diseases (Walker & Raoult, 2010; Dumler & Walker 2010). In all these conditions a raise in hepatic enzymes, C reactive protein as well as in leucocytes and platelets counts can be observed. We can also observe hepatosplenomegaly. In severe cases mainly associated with epidemic typhus, evolution to a multiple-organ dysfunction syndrome and coagulation disorders may appear.

Some references related to travellers are: Zanetti et al., 1998; Niang et al., 1999; Kelly et al., 2002; Jensenius et al., 2004; Azuma et al., 2006; Angelakis et al., 2010; Walter et al., 2011.

3. Tick-borne spotted fever

Tick-borne spotted fever are worldwide distributed and the clinical picture is very similar, although the severity is different related with the *Rickettsia* species involved.

ATBF and MSF are the most frequent tick-borne spotted fever rickettsioses in travellers (Smoak et al., 1996; Fournier et al., 1998; Oteo et al., 2004a; Raoult et al., 2001; Caruso et al., 2002; Jensenius et al., 2003; Roch et al., 2008; Tsai et al., 2008; Consigny et al., 2009; Stephany et al., 2009; Althaus et al., 2010; Jensenius et al., 2004; Boillat et al., 2008; Laurent et al., 2009). For this reason, we will refer to these conditions taking into account that few differences in the incubation period and severity may exist. For Rocky Mountain spotted fever (RMSF) and MSF caused by *R. conorii israelensis*, higher mortality than with the rest of spotted fever rickettsioses has been communicated (de Sousa et al., 2003). Some features of the main spotted fever rickettsioses are shown in table 2.

From 4 to 21 days after the tick bite, fever suddenly starts in 100% cases (less severe in ATBF). A characteristic inoculation lesion (eschar) (figure 3) is typically found until 72% of MSF cases and until 95% for ATBF. Multiple eschars are observed in some cases. This is more frequent in ATBF. Fever is accompanied of chills, headache, etc. (table 2). From 3 to 5 days after the onset of fever, the rash appears. This is a maculo-papular rash with purpuric elements in some cases (figure 4). It is more frequent in extremities and typically affects palms and soles. In ATBF the rash can be vesicular (figure 5), as occurs in *R. akari* and *R. australis* infections. For *R. sibirica mongolitimonae* infection, known as lymphangitis-associated rickettsiosis (LAR), lymphangitis from the eschar may appear in approximately

Fig. 3. Eschar (*tache noire*) and maculo-papular rash in a patient with Mediterranean spotted fever.

50% cases. It also can be observed in ATBF (Figure 6). There are few reported cases of tick-borne spotted fever caused by other of *Rickettsia* species (*R. monacensis, R. aeschlimannii, R. massiliae, R. helvetica, R. sibirica mongolitimonae, R. parkeri, R. japonica* and *R. honei*, among others) but it seems that the clinical pictures are very similar to the one of MSF cases. Data about the incidence of these infections among travellers to endemic areas are very scarce (Jensenius et al., 2004; Socolovschi et al., 2010).

For *R. helvetica* infections rash can be absent and fever is often the unique clinical manifestation. All these diseases are more frequent in spring and summer, when the vectors are more active. In all these conditions a raise in hepatic enzymes, C reactive protein and in leucocytes and platelets counts can be observed. We can also observe hepatosplenomegaly. In severe cases mainly associated to RMSF or MSF, evolution to a multiple-organ dysfunction syndrome and coagulation disorders may appear.

Distribution of human cases of tick-borne rickettsioses in Europe, Africa and Americas are showed in figures 7-10. Human cases of tick-borne rickettsioses and scrub typhus in Asia and Oceania are showed in figure 11.

DISEASE	RASH	SPECIFITIES	ESCHAR	FEVER
MSF[1]	>95%	10% purpuric rash	72%. Multiple in 32% (children)	100%
RMSF[2]	90%	45% purpuric rash	<1%	100%
ATBF[3]	30%	Vesicular rash	100%. Frequently multiple	100%
DEBONEL/TIBOLA[4]	Possible	Lymph nodes	100%. Larger than in other rickettsioses	30%
LAR[5]	>90%	50% lymphangitis	Frequent	100%
R. aeschlimannii infection	Possible	-	Possible	100%
R. helvetica infection	Possible	-	Absent	Not always
R. massilliae infection	Possible	Rash can be purpuric	Possible	100%
R. monacensis infection	Possible	-	?	100%
Queensland tick typhus	100%	Vesicular rash	65%	100%
Flinder's Island spotted fever	85%	8% purpuric rash	28%	100%
Siberian tick typhus	100%	-	77%	100%
Japanese spotted fever	100%	-	90%	100%
Far eastern spotted fever	Possible	-	Possible	100%

[1]MSF: Mediterranean spotted fever; [2]RMSF: Rocky Mountain spotted fever; [3]ATBF: African tick-bite fever; [4]DEBONEL/TIBOLA: *Dermacentor*-borne, necrosis, erythema, lymphadenopathy/Tick-borne lymphadenopathy; [5]LAR: Lymphangitis-associated rickettsiosis.

Table 2. Main clinical characteristics of tick-borne rickettsioses

Fig. 4. Vasculitic rash affecting soles in a patient with Mediterranean spotted fever.

Fig. 5. Vesicular rash in a patient with African-tick bite fever.

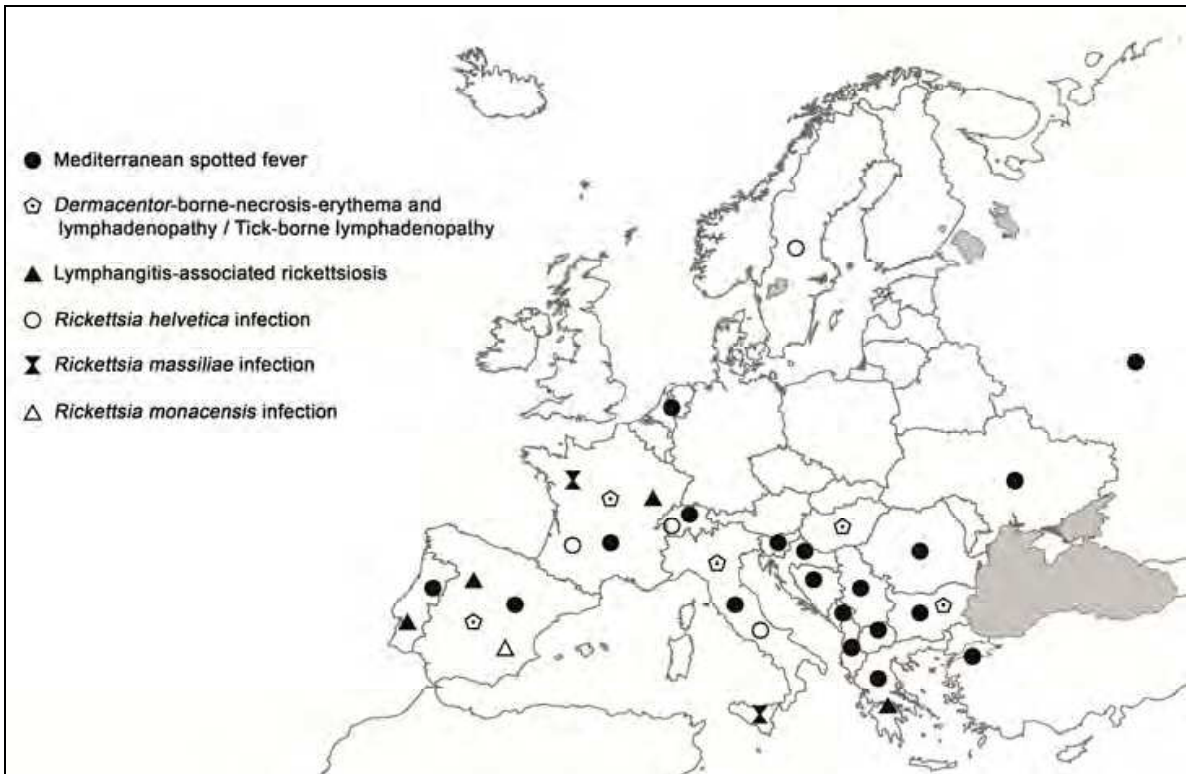Fig. 6. Eschar and lymphangitis in a patient with African tick-bite fever.

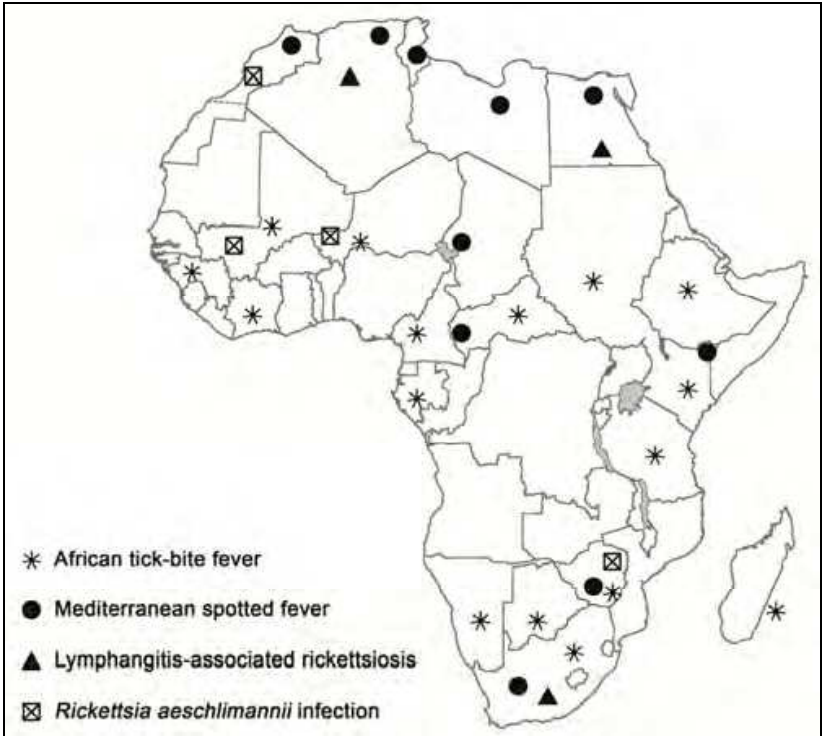Fig. 7. Map showing distribution of human cases of tick-borne rickettsioses in Europe.

Fig. 8. Map showing distribution of human cases of tick-borne rickettsioses in Africa.
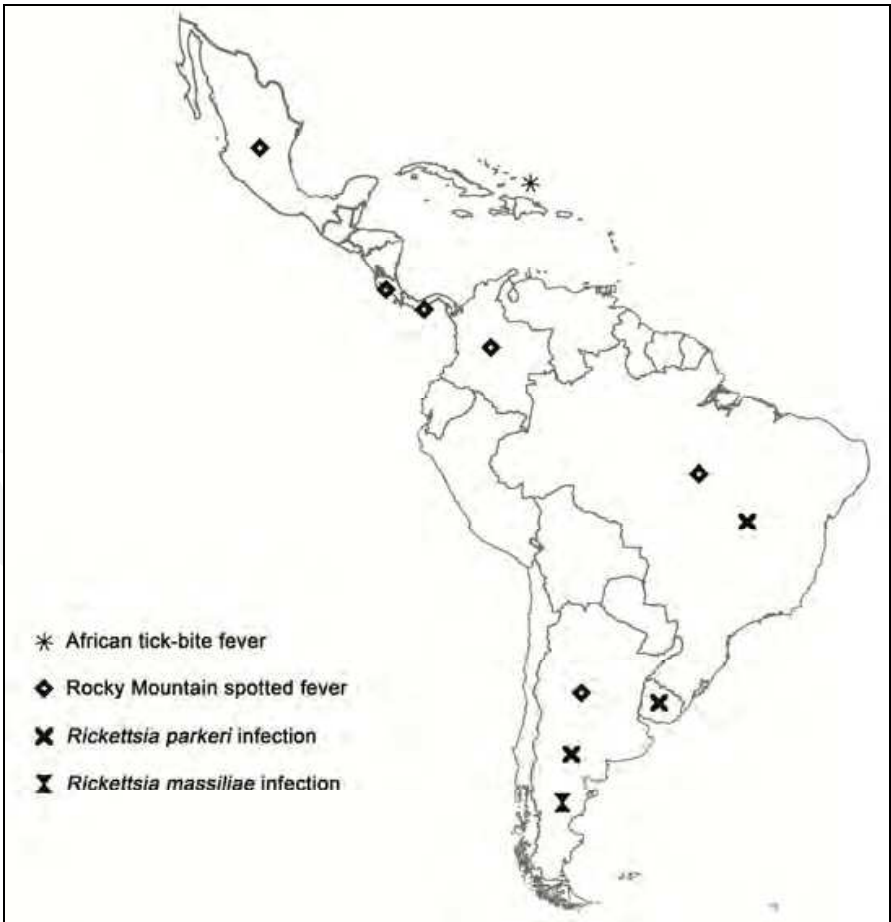

Fig. 9. Map showing distribution of human cases of tick-borne rickettsioses in Latin America.
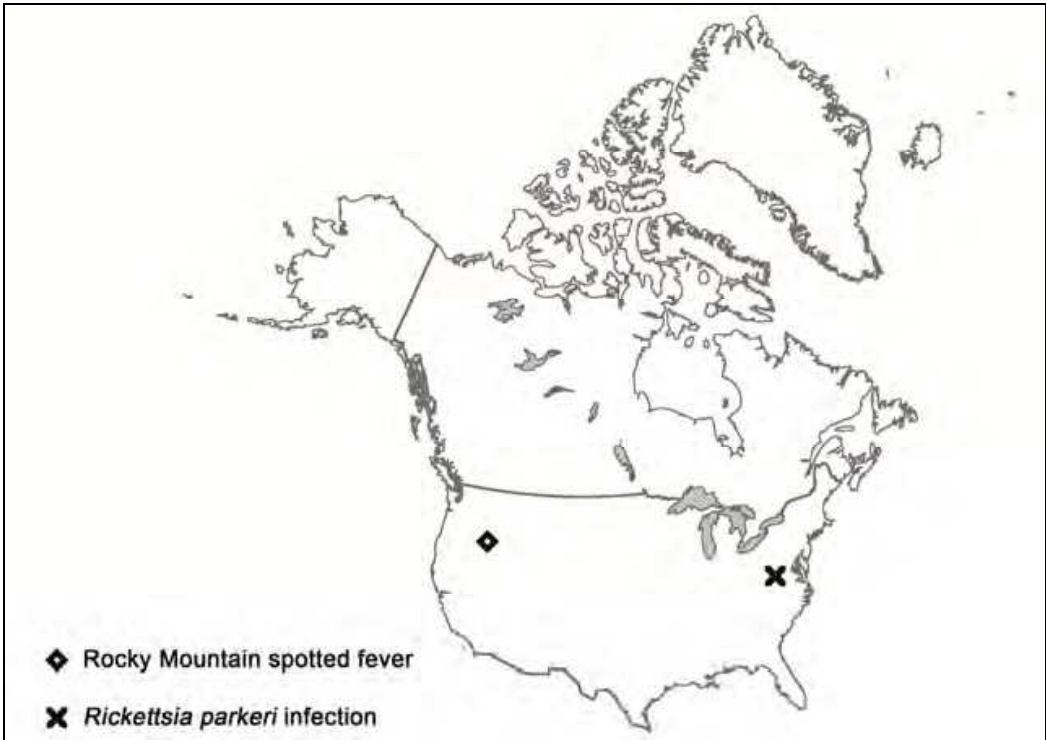
Fig. 10. Map showing distribution of human cases of tick-borne rickettsioses in North America.
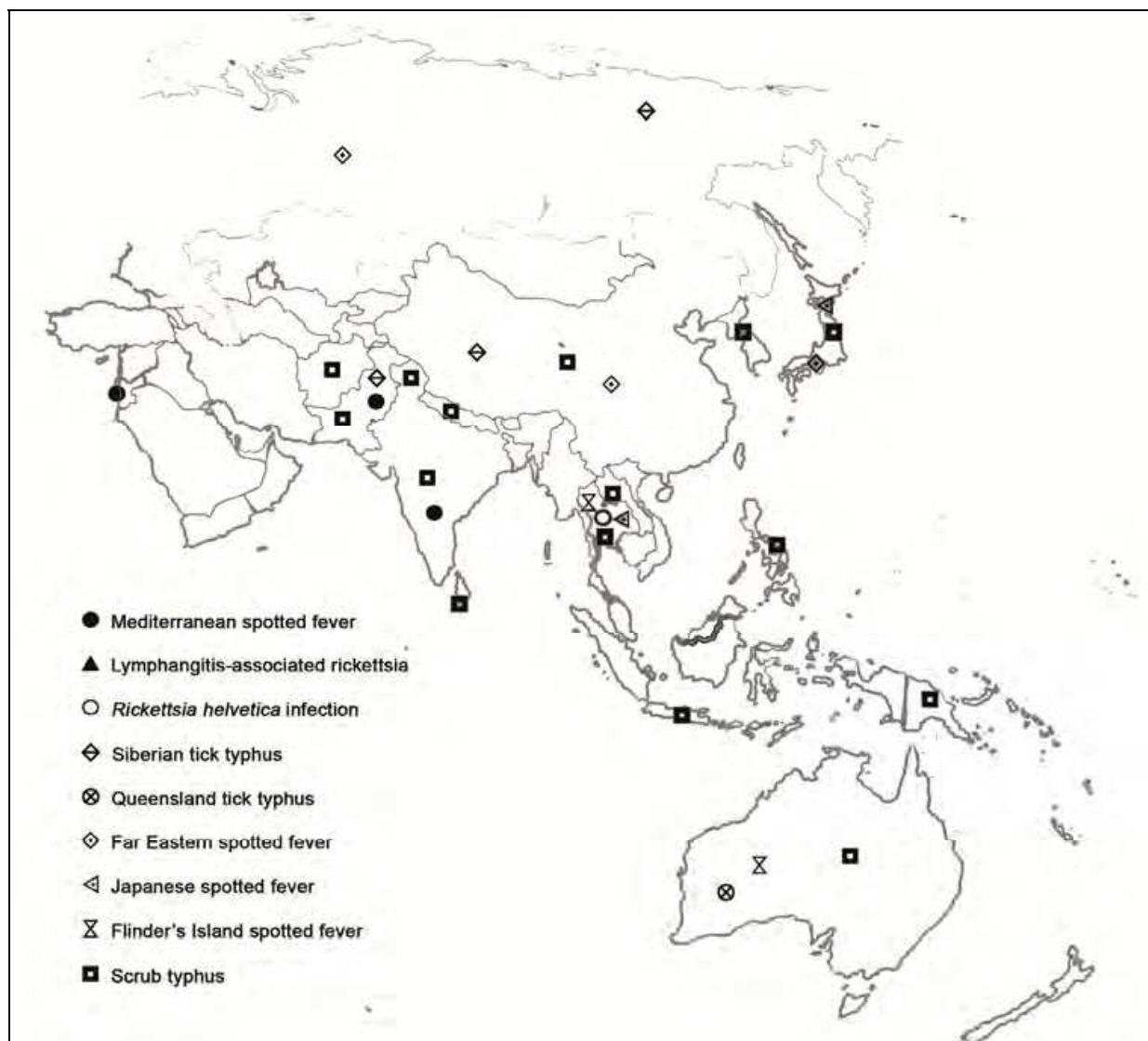
- ● Mediterranean spotted fever
- ▲ Lymphangitis-associated rickettsia
- ○ *Rickettsia helvetica* infection
- ◈ Siberian tick typhus
- ⊗ Queensland tick typhus
- ◇ Far Eastern spotted fever
- ◁ Japanese spotted fever
- ⅀ Flinder's Island spotted fever
- ▣ Scrub typhus

Fig. 11. Map showing distribution of human cases of tick-borne rickettsioses and srub typhus in Asia and Oceania.

4. Eschar and lymphadenopathy

This clinical syndrome has been recently reported in Europe, where it is named TIBOLA (TIck-BOrne LimphAdenopaty) or DEBONEL (*DErmacentor*-BOrne Necrosis-Erythema-Lymphadenopathy). *R. slovaca, R. rioja* and *R. raoultii* are the etiological agents, and *Dermacentor marginatus* is the main vector. This tick species is distributed all over Europe as well as in the North of Africa. Since this rickettsiosis appears in the coldest months of the year, the risk of acquisition for the travellers is lower than for the rickettsioses that are prevalent in spring and summer. In most cases (>90%) the tick-bite is located on the scalp (head) and always in the upper site of the body. After 1-15 days (mean: 4.8 days) of incubation period, the characteristic skin lesion starts as a crusted lesion at the site of the tick-bite (frequently on the scalp). A honey-like discharge from the lesion is observed in some cases. Few days later, a necrotic eschar appears (figure 12). This eschar is usually bigger than the one observed in MSF cases, and it is surrounded by an erythema. When the

tick-bite is out of the head, the skin lesion resembles the erythema migrans of Lyme disease. Other typical manifestation, which is always present when the bite is on the head, is the presence of regional and very painful lymphadenopathies.

On the contrary of other rickettsioses, in DEBONEL/TIBOLA there are not systemic clinical signs (or they are rare), such as fever or maculo-papular rash (Oteo et al., 2004b). The clinical course is sub-acute and no severe complications have been described.

Fig. 12. DEBONEL/TIBOLA patient with the typical crusted lesion on the scalp.

5. Scrub typhus

The etiological agent of scrub typhus is *Orientia tsutsugamushi*, which is transmitted by chigger bites (trombiculid mite larvae). It is mainly distributed in Afghanistan, India, Pakistan, Sri-Lanka, Kashmir, China, Nepal, Japan, Korea, Vietnam, Indonesia, Laos, Philippines, Papua New Guinea and Australia (Figure 11). Cases are mainly observed in autumn and spring, in temperate zones where the bite of this arthropod, which is on vegetation, is frequent. The incubation period is about 10 or more days and the clinical signs and symptoms are similar to typhus syndrome, including the rash which is transient and easily missed. A difference with typhus syndrome is the presence of eschar that is frequently multiple. The presence of regional lymphadenopathy is also more frequent. The mortality can be high despite the correct antimicrobial treatment. Outbreaks related to military operations have been reported (Pages et al., 2010). Most travel acquired cases of scrub typhus occur in patients returning from Southeast Asia (Jensenius et al., 2004, 2006).

6. Rickettsialpox

Rickettsialpox is a worldwide (North America, Eastern Europe, Korea and southern Africa) rickettsiosis caused by *Rickettsia akari* and transmitted by the bite of the mouse mite *Lyponyssoides sanguineus*. We can consider it a remerging infection since several cases have been detected in New York City after September 11 attacks (Paddock et al., 2003). Patients have fever, a prominent eschar -which is the best sign of the disease- and rash that, as occurs in ATBF and Queensland tick typhus, may be vesicular. Palms and soles are not involved. The presence of regional lymphadenopathy is common. Patients recover without treatment in most cases (Raoult, 2010b).

7. Laboratory diagnostic tools

As occurs for all infectious diseases, the most definitive diagnostic method is the rickettsial isolation in culture. The main problem is that *Rickettsia* spp. are strictly intracellular bacteria, conventional growth media cannot be used, and a laboratory with P3 safety level (not generally available in clinical microbiology labs) is necessary. Furthermore, culture is not very sensitive and the yield decreases when clinical samples are taken after antibiotic treatment or when samples are not processed within 24 hours. It is a slow technique that is used for research purposes but not for the routine clinical practice. Centrifugation shell-vial technique is a commercially available adaptation of cell cultures that is easier to handle, faster and less hazardous. Isolation attempts on cell cultures may be performed using buffy coat or tissue samples (eschar biopsies when possible). If not processed within 24 h, samples must be frozen at -70ºC or in liquid nitrogen.

Detection of rickettsiae by Giménez or Giemsa staining from blood and tissue samples would allow the confirmation of the diagnosis, but these techniques are non-specific and their sensitivity is very low.

In some laboratories molecular biology tools, such as polymerase chain reaction (PCR) and sequencing, are also available. PCR-based assays from anticoagulated blood, biopsies and arthropod tissue samples targeting *Rickettsia* spp. genes are quite sensitive and useful for a quick diagnosis of these infections. The evaluation of several primer sets for the molecular diagnosis of rickettsioses demonstrated that the performance of three sequential PCRs (nested or semi-nested ones) allowed the detection and identification of *Rickettsia* species in a high percentage of the samples with previous clinical diagnosis or microbiological confirmation (serological analysis) of rickettsiosis (Santibáñez et al., 2011). Blood and tissue samples should be stored at -20ºC or lower if PCR-based diagnosis is delayed for more than 24 hours. The European guidelines for the diagnosis of tick-borne bacterial diseases contain useful information for clinicians and microbiologists (Brouqui et al., 2004).

Indirect diagnostic tests and specifically, immunofluorescence assays (IFA) are considered the standard tests. Besides, since most traveller patients are investigated after returning, IFA are the most available tools for diagnosis. Acute and convalescent sera (collected 4-6 weeks after the onset of the illness) should be taken. In many cases we cannot observe seroconversion but a high titre of antibodies. Cross-reactions among *Rickettsia* spp. make very difficult to definitively identify the causative agent by means of IFA. This can only be achieved in reference centres in which different antigens and other serological assays, such as western-blot, are available. Serum samples can be preserved at -20ºC or lower for several months without significant degradation of antibodies.

Ticks removed from patients can be used as tools for the diagnosis of tick-borne rickettsioses. The strategy includes the identification of the tick to the species level, and the detection or isolation of rickettsias (Table 3).

1.	Identification of the ticks to the species level
2.	Detection of bacteria in ticks with the use of staining tests (haemolymph for viable ticks; salivary glands if ticks were frozen), or PCR-based methods (using one-half of the tick, the other half being kept frozen). PCR may also be done using only ticks that stain positive.
3.	Sequencing of the amplified PCR fragment and comparison with available sequences in sequence databases.
4.	If there is 100% similarity between the tested sequence and the corresponding sequence of a known organism, the presumptive identification is confirmed
5.	If the tested sequence appears to be different from all corresponding sequences available, the organism is probably a new strain and should be isolated and characterized from the stored frozen part of the tick

Table 3. Strategy for detecting and/or isolating rickettsias from ticks

Diagnostic scores with epidemiological, clinical and laboratory tests for some tick-borne rickettsioses (ATBF and MSF) have been proposed (Tables 4 and 5).

a.	Direct evidence of *R. africae* infection by culture and/or PCR *or*
b.	Clinical and epidemiological features highly suggestive of ATBF, such as multiple inoculation eschars and / or regional lymphadenitis and / or a vesicular rash and / or similar symptoms among other members of the same group of travellers coming back from an endemic area (sub-Saharan Africa or French West Indies) *and* Positive serology against spotted fever group rickettsiae *or*
c.	Clinical and epidemiological features consistent with a spotted fever group rickettsiosis such as fever and / or any cutaneous rash and / or single inoculation eschar after travel to sub-Saharan Africa or French West Indies *and* Serology specific for a recent *R. africae* infection (seroconversion or presence of IgM ‡ 1:32), with antibodies to *R. africae* greater than those to *R. conorii* by at least two dilutions, and / or a Western blot or cross-absorption showing antibodies specific for *R. africae*

Table 4. Diagnostic criteria for African-tick bite fever (ATBF). A patient is considered to have ATBF when criteria A, B or C are met

CRITERIA	SCORE[a]
Epidemiological criteria	
Stay in endemic area	2
Occurrence in May–October	2
Contact (certain or possible) with dog ticks	2
Clinical criteria	
Fever > 39ºC	5
Eschar	5
Maculopapular or purpuric rash	5
Two of the above criteria	3
All three of the above criteria	5
Non-specific laboratory findings	
Platelets < 150 G/L	1
SGOT or SGPT > 50 U/L	1
Bacteriological criteria	
Blood culture positive for *Rickettsia conorii*	25
Detection of *Rickettsia conorii* in a skin biopsy	25
Serological criteria	
Single serum and IgG > 1/128	5
Single serum and IgG > 1/128 and IgM > 1/64	10
Four-fold increase in two sera obtained within a 2-week interval	10

SGOT, serum glutamate–oxaloacetate transaminase; SGPT, serum glutamate–pyruvate transaminase.
[a]A positive diagnosis is made when the overall score is ≥ 25.

Table 5. Diagnostic criteria for Mediterranean spotted fever caused by *Rickettsia conorii*

8. Prophylaxis

An important chapter in the field of rickettsioses is related to prophylaxis. Since the majority of rickettsioses associated to travels are transmitted by ticks, the main preventive measure is to avoid tick-bites. Measures to avoid chiggers' attacks are the same as the ones used against ticks. Only fleas can be more difficult to avoid when cats and other pets are abundant. If there is risk of getting lice, hygiene measures such as changing clothing (they live in the seams of clothing) may be sufficient.

How can we avoid tick-bites? There are some rules that can be useful to avoid arthropod-bites:

1. You must not wear dark clothes to see the ticks and remove them before attaching. Curiously, dark clothes attract less arthropods than clear ones. But, in our opinion, to look for the arthropods and remove them as soon as possible is more effective.
2. For outdoor activities (grass areas or mountains) you do not have to exposure your body to ticks. Thus, it is very useful to wear clothing that covers the majority of your body. The trousers must be tucked in your shocks with boots. Long sleeves shirt must be tucked into trousers. You must also wear a cap (especially children).
3. Permethrin-based repellents can be used on clothing, although their effect is short in time and the application should be repeated every few hours.
4. A careful inspection of clothing and body looking for ticks after returning from outdoors activities in endemic areas as well as removing them correctly has been

effective for the prevention of Lyme disease. The tick needs at least 24-48 hours for the transmission of *Borrelia burgdorferi.* This measure can be less efficient for *Rickettsia* spp. because these microorganisms can be transmitted since the first hours. But, anyway, the removal of the tick has to be done.

5. The contact with parasitized pets and wild animals must be avoided.

There are two questions that physicians have linked up with tick-bites: How must I remove the tick? Must I take prophylactic drugs after a tick-bite?

The first question is easy to answer. The most useful method to remove an attached tick is using forceps. Smooth forceps (without teeth) must be introduced between the tick's head and the skin in a 90º angle and then pull (Oteo et al., 1996). Other traditional methods as using oil, burning or freezing must be forgotten.

The other question is the use of prophylactic drugs after arthropod bites. There are no studies to answer this question. The transmission of rickettsias may be very quick, so we cannot extrapolate the recommendations for Lyme disease. Anyway, when people have been bitten by several ticks in an endemic area for a determinate disease (i.e.: Kruger National Park in South Africa and ATBF) and if the patient is anxious, we can offer doxycycline. It has been demonstrated that 3 doses of 100 mg. every 12 hours is safety and sufficient as treatment for the majority of rickettsioses. We must be cautious with the sun to avoid photo-sensibility. Children can take doxycycline for a short period of time. It is only contraindicated for pregnant women and in this case we can use macrolides (i.e. azythromycin).

Vaccine approaches for prevention of rickettsial diseases have been developed since the past century, but currently no vaccine is available. Major surface protein antigens (OmpA and OmpB) of *R. rickettsii* and *R. conorii* are candidate vaccine antigens. Molecular biology techniques such as selection, cloning and expression of genes encoding *R. prowazekii* virulence-associated proteins, offer the opportunity to develop new rickettsial vaccines against typhus group rickettsiae. Further research is needed to develop effective vaccines without undesirable toxic reactions (Azad & Radulovic, 2003; Walker, 2009).

9. Treatment

The treatment of rickettsiosis should be initiated as soon as possible. Antibiotics are very effective and may avoid severe complications and death. In all cases if rickettsiosis is suspected, samples should be sent for laboratory confirmation. In DEBONEL/TIBOLA, in which the clinical signs and symptoms are less severe, recovery without antimicrobials occurs but the use of antibiotics shortens the clinical course and improves the clinical picture (Ibarra et al., 2005).

Doxycycline is the most useful drug in children and adults. Doxycycline can be administered in short course (100 mg. every 12 hours for one day) for the treatment of typhus and scrub typhus. In the case of MSF, 2 doses of 200 mg./12 hous are also very effective (in children, 5 mg./kg./12hours); although most physicians use 100 mg. every 12 hours for 3-7 days after fever disappears. The same can be recommended for ATBF. This antibiotic regimen could probably be followed in other tick-borne rickettsioses but there are not good evidences (clinical assays) to support a recommendation. In RMSF the administration of doxycycline for 7 days is recommended. Other drugs that can be prescribed when not using doxycycline (allergy or pregnancy) are chloramphenicol (50-75 mg./kg./day given in 4 doses for 7-10 days) and azythromycin (500 mg./day for 5 days). Doxycycline for 7 days is the treatment of choice for rickettsialpox. Although there is *in vitro*

susceptibility to quinolones, the use of these drugs has been associated with worse clinical course (Botelho-Nevers et al., 2011).

10. Conclusion

In conclusion, rickettsioses are a worldwide threat that must be suspected in travellers returning from endemic areas. Most cases are caused by tick-bites, although in some areas of the world old diseases as typhus are present, and the risk exists. Rickettsiosis must be suspected in all patients with fever, exanthema with or without rash. Starting treatment with doxycycline when possible may be essential to rapidly recover and avoid complications. ATBF along with malaria is the leading cause of fever after returning from Sub-Saharan Africa.

11. Acknowledgment

12. References

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. *International Journal of Infectious Diseases*, Vol.14, Suppl.3 (September 2010), pp. e274-276, ISSN 1201-9712

Angelakis, E., Botelho, E., Socolovschi, C., Sobas, C.R., Piketty, C., Parola, P. & Raoult, D. (2010). Murine typhus as a cause of fever in travelers from Tunisia and Mediterranean areas. *Journal of Travel Medicine*, Vol.17, No.5, (September 2010), pp. 310-315, ISSN 1195-1982

Angel-Moreno, A., Bolaños, M., Santana, E., Pérez-Arellano, J.L. (2006). Murine typhus imported from Senegal in a travelling immigrant. *Enfermedades Infecciosas y Microbiología Clínica*, Vol.24, No.6, (June-July 2006), pp. 406-407, ISSN 0213-005X

Askling, H.H., Lesko, B., Vene, S., Berndtson, A., Björkman, P., Bläckberg, J., Bronner, U., Follin, P., Hellgren, U., Palmerus, M., Ekdahl, K., Tegnell, A. & Struwe J. (2009). Serologic analysis of returned travelers with fever, Sweden. *Emerging Infectious Diseases*, Vol.15, No.11, (November 2009), pp. 1805-1808, ISSN 1080-6059

Azad, A.F. & Radulovic, S. (2003). Pathogenic rickettsiae as bioterrorism agents. *Annals of the New York Academy of Sciences*, Vol.990 (June 2003), pp. 734-8, ISSN 0077-8923

Azuma, M., Nishioka, Y., Ogawa, M., Takasaki, T., Sone, S. & Uchiyama, T. (2006). Murine typhus from Vietnam, imported into Japan. *Emerging Infectious Diseases*, Vol.12, No.9, (September 2006), pp. 1466-1468, ISSN 1080-6059

Bernabeu-Wittel, M., Pachón, J., Alarcón, A., López-Cortés, L.F., Viciana, P., Jiménez-Mejías, M.E., Villanueva, J.L., Torronteras, R. & Caballero-Granado, F.J. (1999). Murine typhus as a common cause of fever of intermediate duration: a 17-year study in the south of Spain. *Archives of Internal Medicine*, Vol.159, No.8, (April 1999), pp. 872-876, ISSN 0003-9926

Boillat, N., Genton, B., D'Acremont, V., Raoult, D. & Greub, G. (2008). Fatal case of Israeli spotted fever after Mediterranean cruise. *Emerging Infectious Diseases,* Vol.14, No.12, (December 2008), pp. 1944-1946, ISSN 1080-6059

Botelho-Nevers, E., Rovery, C., Richet, H. & Raoult, D. (2011). Analysis of risk factors for malignant Mediterranean spotted fever indicates that fluoroquinolone treatment has a deleterious effect. *Journal of Antimicrobial Chemotherapy,* Vol.66, (June 2011), pp. 1821-1830, ISSN 0305-7453

Bottieau, E., Clerinx, J., Schrooten, W., Van den Enden, E., Wouters, R., Van Esbroeck, M., Vervoort, T., Demey, H., Colebunders, R., Van Gompel, A. & Van Den Ende, J. (2006). Etiology and outcome of fever after a stay in the tropics. *Archives of Internal Medicine*, Vol.166, No.15, (August 2006), pp. 1642-1648, ISSN 0003-9926

Brouqui, P., Bacellar, F., Baranton, G., Birtles, R.J., Bjoërsdorff, A., Blanco, J.R., Caruso, G., Cinco, M., Fournier, P.E., Francavilla, E., Jensenius, M., Kazar, J., Laferl, H., Lakos, A., Lotric-Furlan, S., Maurin, M., Oteo, J.A., Parola, P., Perez-Eid, C., Peter, O., Postic, D., Raoult, D., Tellez, A., Tselentis, Y. & Wilske, B.; ESCMID Study Group on *Coxiella, Anaplasma, Rickettsia* and *Bartonella*; European Network for Surveillance of Tick-Borne Diseases. (2004). Guidelines for the diagnosis of tick-borne bacterial diseases in Europe. *Clinical Microbiology and Infection,* Vol.10, (December 2004), pp. 1108-1132, ISSN 1198-743X

Caruso, G., Zasio, C., Guzzo, F., Granata, C., Mondardini, V., Guerra, E., Macrì, E. & Benedetti, P. (2002). Outbreak of African tick-bite fever in six Italian tourists returning from South Africa. *European Journal of Clinical Microbiology & Infectious Diseases*, Vol.21, No.2, (February 2002), pp. 133-136, ISSN 0934-9723

Chen LH, Wilson ME. (2009). Tick-borne rickettsiosis in traveler returning from Honduras. *Emerging Infectious Diseases*, Vol.15, No.8, (August 2009), pp. 1321-3, ISSN 1080-6059

Consigny, P.H., Schuett, I., Fraitag, S., Rolain, J.M., Buffet, P. (2009). Unusual location of an inoculation lesion in a traveler with African tick-bite fever returning from South Africa. *Journal of Travel Medicine*, Vol.16, No.6, (November-December 2009), pp. 439-440, ISSN 1195-1982

de Sousa, R., Nóbrega, S.D., Bacellar, F., Torgal, J. (2003). Mediterranean spotted fever in Portugal: risk factors for fatal outcome in 105 hospitalized patients. *Annals of the New York Academy of Sciences*, Vol.990 (June 2003), pp. 285-294, ISSN 1749-6632

Dumler J.S. & Walker, D.H. (2010). *Rickettsia tyhi* (Murine typhus), In: *Mandell, Douglas, and Bennett´s Principles and Practice of Infectious Diseases*, Mandell G.L., Bennett J.E., Dolin R. (Eds.), pp. 2525-2528, Churchill Livingstone Elsevier, ISBN 978-0-4430-6839-3, Philadelphia-USA.

Field, V., Gautret, P., Schlagenhauf, P., Burchard, G.D., Caumes, E., Jensenius, M., Castelli, F., Gkrania-Klotsas, E., Weld, L., Lopez-Velez, R., de Vries, P., von Sonnenburg, F., Loutan, L. & Parola, P.; EuroTravNet network. (2010). Travel and migration associated infectious diseases morbidity in Europe, 2008. *BMC Infectious Diseases*, Vol.10, (November 2010), 330, ISSN 1471-2334

Fournier, P.E., Roux, V., Caumes, E., Donzel, M. & Raoult, D. (1998). Outbreak of *Rickettsia africae* infections in participants of an adventure race in South Africa. *Clinical Infectious Diseases*, Vol.27, No.2, (August 1998), pp. 316-323, ISSN 1058-4838

Freedman, D.O., Weld, L.H., Kozarsky, P.E., Fisk, T., Robins, R., von Sonnenburg, F., Keystone, J.S., Pandey, P. & Cetron, M.S.; GeoSentinel Surveillance Network.

(2006). Spectrum of disease and relation to place of exposure among ill returned travelers. *The New England Journal of Medicine*, Vol.354, No.2, (January 2006), pp. 119-130, ISSN 0028-4793

Gikas, A., Kokkini, S., Tsioutis, C., Athenessopoulos, D., Balomenaki, E., Blasak, S., Matheou, C., Tselentis, Y. & Psaroulaki, A. (2009). Murine typhus in children: clinical and laboratory features from 41 cases in Crete, Greece. *Clinical Microbiology and Infection*, Vol.15, Suppl. 2 (December 2009), pp. 211-212, ISSN 1198-743X

Hechemy, K.E., Oteo, J.A., Raoult, D., Silverman, D.J. & Blanco, J.R. (2006). A century of rickettsiology: emerging, reemerging rickettsioses, clinical, epidemiologic, and molecular diagnostic aspects and emerging veterinary rickettsioses: an overview. *Annals of the New York Academy of Sciences*, Vol.1078 (October 2006), pp. 1-14, ISSN 0077-8923

Ibarra, V., Blanco, J.R., Portillo, A., Santibáñez, S., Metola, L., Oteo, J.A. (2005). Effect of antibiotic treatment in patients with DEBONEL/TIBOLA. *Annals of the New York Academy of Sciences*, Vol.1063 (December 2005), pp. 257-258, ISSN 0077-8923

Jensenius, M., Davis, X., von Sonnenburg, F., Schwartz, E., Keystone, J.S., Leder, K., Lopéz-Véléz, R., Caumes, E., Cramer, J.P., Chen, L. & Parola, P.; GeoSentinel Surveillance Network. (2009). Multicenter GeoSentinel analysis of rickettsial diseases in international travelers, 1996-2008. *Emerging Infectious Diseases*, Vol.15, No.11, (November 2009), pp. 1791-1798, ISSN 1080-6059

Jensenius, M., Fournier, P.E. & Raoult, D. (2004). Rickettsioses and the international traveler. *Clinical Infectious Diseases*, Vol.39, No.10, (November 2004), pp. 1493-1499, ISSN 1058-4838

Jensenius, M., Fournier, P.E., Vene, S., Hoel, T., Hasle, G., Henriksen, A.Z., Hellum, K.B., Raoult, D. & Myrvang, B.; Norwegian African Tick Bite Fever Study Group. (2003). African tick bite fever in travelers to rural sub-Equatorial Africa. *Clinical Infectious Diseases*, Vol.36, No.11, (June 2003), pp. 1411-1417, ISSN 1058-4838

Jensenius, M., Montelius, R., Berild, D. & Vene, S. (2006). Scrub typhus imported to Scandinavia. *Scandinavian Journal of Infectious Diseases*, Vol.38, No.3, pp. 200-202, ISSN 0036-5548

Kelly, D.J., Richards, A.L., Temenak, J., Strickman, D., Dasch, G.A. (2002). The past and present threat of rickettsial diseases to military medicine and international public health. *Clinical Infectious Diseases*, Vol.34, Suppl.4, (June 2002), pp. S145-169, ISSN 1058-4838

Laurent, M., Voet, A., Libeer, C., Lambrechts, M., Van Wijngaerden, E. (2009). Mediterranean spotted fever, a diagnostic challenge in travellers. *Acta Clinica Belgica*, Vol.64, No.6, (November-December 2009), pp. 513-516, ISSN 0001-5512

McDonald, J.C., MacLean, J.D. & McDade, J.E. (1988). Imported rickettsial disease: clinical and epidemiologic features. *American Journal of Medicine*, Vol.85, No.6, (December 1988), pp. 799-805, ISSN 0002-9343

Niang, M., Brouqui, P., Raoult, D. (1999). Epidemic typhus imported from Algeria. *Emerging Infectious Diseases*, Vol.5, No.5, (September-October 1999), pp. 716-718, ISSN 1080-6059

Oteo, J.A., Ibarra, V., Blanco, J.R., Martínez de Artola, V., Márquez, F.J., Portillo, A., Raoult, D., Anda, P (2004b). *Dermacentor*-borne Necrosis Erythema and Lymphadenopathy:

Clinical and epidemiological features of a new tick-borne disease. *Clinical Microbiology and Infection,* Vol.10, pp. 327-331, ISSN 1198-743X

Oteo, J.A., Martínez de Artola, V., Gómez-Cadiñanos, R., Casas, J.M., Blanco, J.R. & Rosel, L. (1996). Evaluation of methods of tick removal in human ixodidiasis. *Revista Clínica Española* Vol.196, No.9, (September 1996), pp. 584-587, ISSN 0014-2565

Oteo, J.A., Portillo, A., Blanco, J.R., Ibarra, V. & Santibáñez, S. (2004a). Medicina Clínica, Vol.122, No.20, (May 2004), pp. 786-788, ISSN 0025-7753

Oteo, J.A., Portillo, A., Santibáñez, S., Blanco, J.R., Pérez-Martínez, L. & Ibarra, V. (2006). Cluster of cases of human *Rickettsia felis* infection from southern Europe (Spain) diagnosed by PCR. *Journal of Clinical Microbiology*, Vol.44, No.7, (July 2006), pp. 2669-2671, ISSN 0095- 1137

Paddock, C.D., Zaki, S.R., Koss, T., Singleton, J. Jr., Sumner, J.W., Comer, J.A., Eremeeva, M.E., Dasch, G.A., Cherry, B. & Childs, J.E. Rickettsialpox in New York City: a persistent urban zoonosis. *Annals of the New York Academy of Sciences*, Vol.990, (June 2003), pp. 36-44, ISSN 1749-6632

Pages F., Faulde M., Orlandi-Pradines E. & Parola P. (2010). The past and present threat of vector-borne diseases in deployed troops. *Clinical Microbiology and Infection*, Vol.16, No.3, (March 2010), pp. 209-224, ISSN 1198-743X

Pérez-Arellano, J.L., Fenollar, F., Angel-Moreno, A., Bolaños, M., Hernández, M., Santana, E., Hemmersbach-Miller, M., Martín, A.M. & Raoult, D. (2005). Human *Rickettsia felis* infection, Canary Islands, Spain. *Emerging Infectious Diseases*, Vol.11, No.12, (December 2005), pp. 1961-1964, ISSN 1080-6059

Raoult D. (2010b). *Rickettsia akari* (Rickettsialpox), In: *Mandell, Douglas, and Bennett´s Principles and Practice of Infectious Diseases*, Mandell G.L., Bennett J.E., Dolin R. (Eds.), pp. 2509-2510, Churchill Livingstone Elsevier, ISBN 978-0-4430-6839-3, Philadelphia-USA.

Raoult, D. (2010a). Introduction to Rickettsioses, Ehrlichioses, and Anaplasmosis, In: *Mandell, Douglas, and Bennett´s Principles and Practice of Infectious Diseases*, Mandell G.L., Bennett J.E., Dolin R. (Eds.), pp. 2495-2498, Churchill Livingstone Elsevier, ISBN 978-0-4430-6839-3, Philadelphia-USA.

Raoult, D., Fournier, P.E., Fenollar, F., Jensenius, M., Prioe, T., de Pina, J.J., Caruso, G., Jones, N., Laferl, H., Rosenblatt, J.E. & Marrie, T.J. (2001). *Rickettsia africae*, a tick-borne pathogen in travelers to sub-Saharan Africa. *The New England Journal of Medicine*, Vol.344, No.20, (May 2001), pp. 1504-1510, ISSN 0028-4793

Raoult, D., Ndihokubwayo, J.B., Tissot-Dupont, H., Roux, V., Faugere, B., Abegbinni, R. & Birtles, R.J. (1998). Outbreak of epidemic typhus associated with trench fever in Burundi. *Lancet*, Vol.352, No.9125, (August 1998), pp. 353-358, ISSN 0140-6736

Roch, N., Epaulard, O., Pelloux, I., Pavese, P., Brion, J.P., Raoult, D. & Maurin M. (2008). African tick bite fever in elderly patients: 8 cases in French tourists returning from South Africa. *Clinical Infectious Diseases*, Vol.47, No.3, (August 2008), pp. e28-35, ISSN 1058-4838

Santibáñez, S., Portillo, A., Santibáñez, P., Ibarra, V., Palomar, A., Oteo, J.A. (2011). Utility of five PCR targets for molecular diagnosis of human rickettsioses, *Proceedings of the 6th International Meeting on Rickettsiae and Rickettsial Diseases*, Heraklion, Crete, Greece, June 2011.

Smoak, B.L., McClain, J.B., Brundage, J.F., Broadhurst, L., Kelly, D.J., Dasch, G.A. & Miller, R.N. (1996). An outbreak of spotted fever rickettsiosis in U.S. Army troops deployed to Botswana. *Emerging Infectious Diseases*, Vol.2, No.3, (July-September 1996), pp. 217-221, ISSN 1080-6059

Socolovschi, C., Barbarot, S., Lefebvre, M., Parola, P. & Raoult, D. (2010). *Rickettsia sibirica mongolitimonae* in traveler from Egypt. *Emerging Infectious Diseases*, Vol.16, No.9, (September 2010), pp.1495-1496, ISSN 1080-6059

Stephany, D., Buffet, P., Rolain, J.M., Raoult, D. & Consigny, P.H. (2009). *Rickettsia africae* infection in man after travel to Ethiopia. *Emerging Infectious Diseases*, Vol.15, No.11, (November 2009), pp. 1867-1870, ISSN 1080-6059

Stokes, P.H. & Walters, B.J. (2009). Spotted fever rickettsiosis infection in a traveler from Sri Lanka. *Journal of Travel Medicine*, Vol.16, No.6, (November-December 2009), pp. 436-438, ISSN 1195-1982

Tsai, Y.S., Wu, Y.H., Kao, P.T., Lin, Y.C. (2008). African tick bite fever. *Journal Formosan Medical Association*, Vol.107, No.1, (January 2008), pp. 73-76, ISSN 0929-6646

Walker, D.H. & Raoult, D. (2010). *Rickettsia prowazekii* (Epidemic or louse-borne typhus), In: *Mandell, Douglas, and Bennett´s Principles and Practice of Infectious Diseases*, Mandell G.L., Bennett J.E., Dolin R. (Eds.), pp. 2521-2524, Churchill Livingstone Elsevier, ISBN 978-0-4430-6839-3, Philadelphia-USA.

Walker, D.H. (2009). The realities of biodefense vaccines against Rickettsia. *Vaccine*, Vol. 27, Suppl. 4 (November 2009), pp. D52-5, ISSN 0264-410X

Walter, G., Botelho-Nevers, E., Socolovschi, C., Raoult, D. & Parola, P. (2011). Murine typhus in returned travelers: a report of thirty-two cases, *Proceedings of the 6th International Meeting on Rickettsiae and Rickettsial Diseases*, Heraklion, Crete, Greece, June 2011.

Zanetti, G., Francioli, P., Tagan, D., Paddock, C.D. & Zaki, S.R. (1998). Imported epidemic typhus. *Lancet*, Vol.352, No.9141, (November 1998), pp. 1709, ISSN 0140-6736

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