



## Bacterial arthropod-borne diseases in West Africa



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### ABSTRACT

Arthropods such as ticks, lice, fleas and mites are excellent vectors for many pathogenic agents including bacteria, protozoa and viruses to animals. Moreover, many of these pathogens can also be accidentally transmitted to humans throughout the world. Bacterial vector-borne diseases seem to be numerous and very important in human pathology, however, they are often ignored and are not well known. Yet they are in a phase of geographic expansion and play an important role in the etiology of febrile episodes in regions of Africa. Since the introduction of molecular techniques, the presence of these pathogens has been confirmed in various samples from arthropods and animals, and more rarely from human samples in West Africa. In this review, the aim is to summarize the latest information about vector-borne bacteria, focusing on West Africa from 2000 until today in order to better understand the epidemiological risks associated with these arthropods. This will allow health and veterinary authorities to develop a strategy for surveillance of arthropods and bacterial disease in order to protect people and animals.

### 1. Introduction

Bacterial arthropod-borne diseases are still often ignored. They are numerous and unevenly distributed within countries, depending on the presence of specific arthropod vectors. Among the most important, we may cite Lyme disease, different spotted fevers, tick-borne and louse-borne relapsing fevers, human anaplasmoses and ehrlichioses.

The impact of these diseases on public health is significant. Considering only Lyme disease, 26,000 cases and 300,000 cases per year have been reported respectively in France and United States (over a period of 14 years) (Khatchikian et al., 2015; Vourc'h et al., 2015). Spotted fevers are another example: Brazilian spotted fever was found in 1245 people over 4 years, causing the death of 417 people in Brazil (de Oliveira et al., 2016). Most of these diseases correspond to neglected zoonoses. We may therefore estimate their incidence to be 10–100 times higher than the published data (WHO, 2006). In practice, these diseases are often difficult to distinguish because of the lack of specific signs or symptoms – one disease can mimic or coexist with another (Nogueras et al., 2015). They can cause further severe complications when they are not easily recognized (Halperin, 2016).

In Africa, bacterial vector-borne diseases are rarely reported. However, the real incidence may be high: for instance, up to 13% of cases of febrile exanthemas were reported to be due to arthropod-borne diseases (Mokrani et al., 2012). It appears that Rickettsiose due to *Rickettsia felis* represents one of the main causes of non-malarial fever in

sub-Saharan Africa, particularly in Senegal and Kenya. It was present in up to 15% of febrile patients in malaria-endemic regions of these countries (Mediannikov et al., 2013; Richards et al., 2010). It may be even higher in patients living in rural areas in Gabon (39.7%) (Mourembou et al., 2015). This proportion is considerably higher than that observed in Europe and Asia (up to 6.5%) (Angelakis et al., 2016).

Another deadly disease, epidemic typhus, was observed in Burundi during the civil war and affected more 100,000 people (Raoult et al., 1997). Its mortality rate has been estimated to be more than 10–15% in persons who live in environments where hygiene is precarious (Raoult et al., 2004). Flea-borne murine typhus has also been reported in sub-Saharan Africa as a cause of febrile illness (Jensenius et al., 2013; Portillo et al., 2015). Mediterranean spotted fever caused by *Rickettsia conorii conorii* causes a disease in humans characterized by high fever, maculopapular rash and eschar. Several cases have also been reported. The mortality rate of this disease is similar in Africa (3.6% in 2009) and Europe (3.6% in 2015) (Crespo et al., 2015; Mouffok et al., 2009), although some outbreaks may be much more severe, with mortality up to 32% (de Sousa et al., 2003). Tick-borne spotted fevers, mostly African tick bite fever (ATBF), represent a major health problem for tourists (Jensenius et al., 2009). They were responsible for the febrile illnesses in 1.5% of travelers returning from tropical countries, associated with a 40% hospitalization rate (Jensenius et al., 2013). Other arthropod-borne bacterial diseases such borrelioses are also present in Africa. Louse-borne relapsing fever (LBRF), a forgotten epidemic

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disease, caused 20,000 cases with a death rate ranging 10–14% in Sudan in 1999 (Cutler, 2006). It was responsible for 27% of hospital admissions and 6% of deaths in Ethiopia (Cutler et al., 2010; Tewdros et al., 2002). Tick-borne relapsing fever (TBRF) is widespread in Africa (Parola et al., 2011; Sarih et al., 2009) and can even be fatal (Rustenhoven-Spaan et al., 2013). Its incidence has been estimated to be 384/1000 and 163/1000 in children under 1 year and under 5 years of age, respectively, in Tanzania. A high perinatal mortality (436/1000) was also registered in this country (McConnell, 2003). The lack of consolidated information on arthropod-borne bacterial infections in Africa led us to present this information in the form of the present manuscript.

## 2. Rickettsioses and rickettsiae

Rickettsioses are infectious diseases caused by the obligatory intracellular Gram-negative bacteria of the genus *Rickettsia* and *Orientia* (Parola et al., 2013). These infections are transmitted by arthropod vectors such as ticks, but also fleas, mites or body lice (Chikeka and Dumler, 2016), which explains their presence in certain regions. In Africa, although serological evidence of human infection by *Orientia* has been reported (Ghorbani et al., 1997; Maina et al., 2016), only *Rickettsia* species are the causative agents of rickettsioses (Horton et al., 2016; Parola et al., 2005). These are traditionally divided into the spotted fever group (SFG) rickettsiae, associated mainly with ticks, and also fleas or mites, and typhus group (TG) rickettsiae, associated with body lice or fleas (Chikeka and Dumler, 2016). In practice, disease diagnosis can be achieved by molecular methods, although serological tests reveal the presence of antibodies against the bacteria. The high seropositivity rates against *Rickettsia* in Africans have been known for a long time, but very few acute cases have been identified. Epidemiological studies have shown that in different countries, the proportion of the population with elevated rickettsiae antibody titers varies from 10–48% (Mediannikov et al., 2010b; Niang et al., 1998). We have attempted to summarize here the knowledge of rickettsial diseases described in West Africa based on definitive diagnoses, such as molecular identification.

### 2.1. Flea-borne spotted fever (*R. felis* infection)

It appears that this disease, which was still considered rare 10 years ago, is the most widespread in Africa. The agent responsible, *R. felis*, was described in 1990 and isolated for the first time in 2001 in infected cells of cat fleas (Adams et al., 1990; Raoult et al., 2001). Since the recognition of *R. felis* as a human pathogen in 1994 in United States America (Schriefer et al., 1994), it has also been reported on other continents. The seroprevalence of *R. felis* was less than 7% in febrile patients in Europe, Asia and North Africa (Angelakis et al., 2016). Currently, little is known about the real incidence of this disease in sub-Saharan Africa. However, it seems that *R. felis*-associated fever may be extremely frequent, at least in some regions. *R. felis* has been independently reported to be associated with 4–5% of febrile diseases in Senegal and Kenya (Richards et al., 2010; Socolovschi et al., 2010). Moreover, its incidence may be even higher, affecting up to 15% of people with fever in some regions (Mediannikov et al., 2013; Mourembou et al., 2015). To date, *R. felis* is considered as a common cause of fever in Africa, and thus an emerging pathogen (Brown and Macaluso, 2016). Although it has been shown that *R. felis* is maintained by transstadial and transovarial transmission in *Ctenocephalides felis*, it has also been horizontally transmitted between infected and uninfected cat fleas during co-feeding (Hirunkanokpun et al., 2011). These capabilities make the cat flea the potential vector and reservoir of *R. felis* (Bitam et al., 2006; Reif and Macaluso, 2009). These findings led us to think that *R. felis* was transmitted only by fleas. Recently, *R. felis* has been reported in mosquitoes for the first time in West Africa (Socolovschi et al., 2012b) and more recently, it has been demonstrated

that *Anopheles gambiae* mosquitoes may be an effective vector of the bacterium (Dieme et al., 2015). *R. felis* was also identified in another species of fleas (*Ctenocephalides canis*) from Côte d'Ivoire (Berrelha et al., 2009). It has also been shown to be harbored by a common household insect pest, *Liposcelis* booklice (Behar et al., 2010).

In domestic animals, *R. felis* has been found in blood from dogs and cats. Thus, they are also considered to be potential reservoirs of *R. felis* (Ahmed et al., 2016; Hii et al., 2011a; Hii et al., 2011b). Other mammals, including rodents, hedgehogs and monkeys, as well as humans, are also hosts (Ahmed et al., 2016; Rolain et al., 2005), but no animal infection has been reported in West Africa.

For the first time in West Africa, *R. felis* in humans was reported as a cause of fever of unknown origin in febrile patients in Senegal in 2010. The signs associated with this fever were weakness, headache with sleep disorders, and digestive and respiratory signs (Socolovschi et al., 2010). At the same time, Richards et al. discovered in 6 (3.7%) febrile Kenyan patients that *R. felis* was responsible for their fever (Richards et al., 2010). In West Africa, 3% and 15% of febrile patients residing respectively in Mali and Senegal were also infected by *R. felis*, according to Mediannikov et al. (2013). One may suppose that if two independent teams working in two different countries find the same result, it indicates that the disease is presumably neglected and exists everywhere in Africa, and its real prevalence may be underestimated due to the lack of information and diagnostic tools.

### 2.2. Flea-borne murine typhus

Flea-borne murine typhus is also distributed worldwide in diverse regions, including Europe, Africa, Southeast Asia and the United States (Azuma et al., 2006; Dumler et al., 1991; Parola et al., 1998). Murine typhus is also reported as a major cause of fever in unhealthy areas (Duffy et al., 1990; Mayxay et al., 2015; Mcgreedy et al., 2010). It is a health problem frequently encountered by international travelers (Jensenius et al., 2013). This disease is caused by *Rickettsia typhi* (Peniche-Lara et al., 2015; Znazen et al., 2013), and the rat flea *Xenopsylla cheopis* is the major vector (Bitam et al., 2006). Other flea vectors, mostly rodent-associated, enabling transmission of the bacterium are *Xenopsylla brasiliensis*, *Ctenocephalides felis*, *Leptopsylla segnis*, *Ctenophthalmus congeneroides* and *Rhadinopsylla insolita* (Christou et al., 2010; Ko et al., 2010; Leulmi et al., 2014; Nogueras et al., 2013). Recently, *R. typhi* has been found in *Xenopsylla cheopis* fleas collected from Benin in West Africa (Leulmi et al., 2014). In addition to flea vectors, *Ixodes ricinus* ticks, *Pediculus humanus humanus*, polyplax lice and bloodsucking mites of rats may transmit *R. typhi* (Gillespie et al., 2009; Sprong et al., 2009).

Ubiquitous *Rattus rattus* and *Rattus norvegicus* rats are the potential reservoirs of this bacterium (Laudisoit et al., 2014). In animals, *R. typhi* has been reported by molecular methods in other rodents as well as in wild and domestic animals, such as cats and opossums, that may possibly be its hosts (Blanton et al., 2016; Kuo et al., 2015; Leulmi et al., 2014; Nogueras et al., 2013).

In addition, human cases of murine typhus in febrile patients in Africa have been identified recently in Algeria, and more recently in Tunisia (Gastellier et al., 2015; Mokrani et al., 2012; Znazen et al., 2015). In West Africa, this infection is suspected, because it has been reported in a traveling immigrant in Senegal (Angel-Moreno et al., 2006). As this disease is a *priori* distributed throughout the world (because the reservoirs are rodents and vectors are fleas), the lack of information in West Africa may be due to underestimation and not the absence of disease.

### 2.3. Tick-borne rickettsioses and rickettsiae

Different pathogenic spotted fever group rickettsiae are transmitted by ticks of the genera *Amblyomma*, *Rhipicephalus* and *Hyalomma* (Mediannikov et al., 2010b; Parola et al., 2013; Stachurski, 2006).

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