2

Human Ehrlichioses and Rickettsioses in Cameroon

Lucy Ndip[1], Roland Ndip[1], David Walker[2] and Jere McBride[2]
[1]*University of Buea*
[2]*University of Texas Medical Branch, Galveston*
[1]*Cameroon*
[2]*USA*

1. Introduction

Human ehrlichioses and rickettsioses are important arthropod borne infectious diseases which are transmitted by ticks, mites, lice and fleas. Infections result in mild to fatal outcomes, with clinical presentations that resemble other tropical infectious diseases such as malaria making clinical diagnosis difficult. Despite recognition as important causes of life-threatening diseases in the United States, the geographic distribution of these diseases worldwide remains undefined due to their recent emergence, challenges in diagnosis and lack of comprehensive epidemiological studies needed to determine incidence in developing countries. Recently, the transfer of technological developments to other parts of the world especially developing countries has encouraged basic epidemiological inquiry and generated scientific interest in understanding the epidemiology of these tick borne diseases and their role as causes of undifferentiated febrile illnesses. In this chapter, we review the current knowledge of human monocytotropic ehrlichiosis (HME) and spotted fever rickettsiosis (African tick bite fever) in Cameroon.

2. Ehrlichiosis

2.1 Etiologic agents

Ehrlichioses are diseases caused by small (approximately 0.4–1.5 µm diameter) Gram negative, obligately intracellular bacteria belonging to the genus *Ehrlichia* of the family Anaplasmataceae, Order Rickettsiales and the alpha sub-division Proteobacteria (Dumler et al., 2001). Although they have a characteristic Gram negative cell wall structure, they lack the necessary enzymes to synthesize cell membrane components such as lipopolysaccharide and peptidoglycan (Lin & Rikihisa, 2003). As intracellular pathogens, *Ehrlichia* reside in cytoplasmic membrane-bound vacuoles inside host cells (granulocytes or monocytes) forming microcolonies called morulae, derived from the Latin word "morus" for mulberry (Popov et al., 1995; Paddock et al., 1997; Ismail et al., 2010). These morulae (ranging in size from 1.0 to 6.0 µm in diameter) may contain 1 to >40 organisms of uniform or mixed cell types (Popov et al., 1995; Rikihisa, 1999).

Organisms in the family *Anaplasmataceae* were first described in 1910 when Theiler described *Anaplasma marginale*, the etiologic agent of an economically important and severe disease of

cattle (Mahan, 1995). This discovery was followed shortly thereafter by the description of *E. ruminantium* (formerly *Cowdria ruminantium)* by Cowdry in 1925; *E. canis* by Donatien and Lestoquard in 1935; and *A. phagocytophilum* (formerly *E. phagocytophila*) by Gordon in 1940. Hence, the genus *Ehrlichia* was established in 1945 in honour of the German microbiologist Paul Ehrlich (Uilenberg, 1983).

Ehrlichia species cause significant diseases in their natural hosts (livestock and companion animals) and emerging zoonoses in humans (McBride & Walker, 2010). The first human ehrlichial infection (sennetsu fever) was reported in 1953 (Rapmund, 1984; Dumler et al., 2007). Sennetsu fever, caused by *Neorickettsia sennetsu,* was identified in Japan and Malaysia (Dumler et al., 2001; Dumler et al., 2007). However, recent phylogenetic reclassifications based on molecular analysis revealed that *E. sennetsu* is not a member of the *Ehrlichia* genus (Dumler et al., 2001). Presently, the genus *Ehrlichia* consists of five recognized species including *E. canis, E. chaffeensis*, *E. ewingii, E. muris,* and *E. ruminantium,* all of which are at least 97.7% similar in 16S rRNA gene sequence (Perez et al., 1996; Paddock et al., 1997; Dumler et al., 2001; Perez et al., 2006).

Ehrlichiae have relatively small genomes (0.8–1.5 Mb) with low G+C content and a high proportion of non-coding sequences but can synthesize all nucleotides, vitamins and cofactors (Dunning et al., 2006). They also have small subsets of genes associated with host-pathogen interactions (Ismail et al., 2010). *E. chaffeensis* have immunodominant outer membrane proteins (OMP-1/MSP2/P28) (Ohashi et al., 1998; Yu et al., 2000; Huang et al., 2008), and in infected macrophages ehrlichiae express the p28-Omp 19 and 20 genes as dominant protein products (Ganta et al., 2009; Peddireddi et al., 2009). Ehrlichiae also express several targets of the humoral immune response including tandem repeat and ankyrin repeat containing proteins (Yu et al., 1997; Sumner et al., 1999; McBride et al., 2003; McBride et al., 2007). *E. chaffeensis*, a human pathogen that was first recognised in the United States in 1986 and isolated in 1991 (Maeda et al., 1987; Dawson et al., 1991) is the cause of human monocytotropic ehrlichiosis (HME) (Anderson et al., 1992), a moderate to severe disease with a case fatality rate of 3% (Fishbein et al., 1994; McBride & Walker, 2010). *E. chaffeensis* is an obligately intracellular bacterium that primarily infects mononuclear leukocytes and replicates by binary fission. *E. chaffeensis* morulae can be detected in peripheral blood smears obtained from infected patients when observed with a light microscope (Rikihisa, 1991). When tissues (including clinical samples), mononuclear leucocytes or cell lines of mammalian origin infected with *E. chaffeensis* are viewed by electron microscopy, two distinct morphologic cell types are identified: a predominantly coccoid form which has a centrally condensed nucleoid DNA and ribosomes (dense-cored cells) measuring between 0.4 and 0.6 μm in diameter and reticulate or the coccobacillary form, which measures about 0.4 to 0.6 μm by 0.7 to 1.9 μm (Paddock et al., 1995; Popov et al., 1997).

2.2 Vectors and reservoirs

Investigative studies following the discovery of *E. chaffeensis* in the late 1980s revealed that the agent is transmitted to humans by the tick *Amblyomma americanum*, commonly referred to as the lone star tick which has a limited geographic distribution to the United States (Anderson et al., 1993). Molecular analysis (PCR) has demonstrated *E. chaffeensis* DNA in adult *A. americanum* ticks collected from different states. The increased recognition of *E. chaffeensis* as an emerging problem has evoked renewed interest in this and other tick borne diseases, and this has stimulated epidemiologic investigations of this pathogen and its vector in other regions where the tick *A. americanum* is not found. Results not only indicate

that *E. chaffeensis* has a wider distribution than the United States (Ndip et al., 2010), but also indicates that the pathogen exists outside of the known range of *A. americanum* and is harbored by other tick species. These tick species include *Ixodes pacificus* in California (Kramer et al., 1999), *Dermacentor variabilis* in Missouri (Roland et al., 1998), *Ixodes ricinus* in Russia (Alekseev et al., 2001), *Amblyomma testudinarium* in China, (Cao et al., 2000), *Haemaphysalis longicornis* (Lee et al., 2003), and *Ixodes persulcatus* (Kim et al., 2003) in Korea.

(a) (b)

Fig. 1. a) *Rhipicephalus sanguineus* (brown dog tick) and b) Male *Amblyomma variegatum* tick (courtesy Laboratory for Emerging Infectious Diseases, University of Buea)

Studies carried out by Ndip and colleagues in Cameroon identified *Ehrlichia chaffeensis* in *Rhipicephalus sanguineus* ticks. *R. sanguineus*, commonly known as the brown dog tick (Figure 1a) is a species that infests canids worldwide. In one study in Limbe, Cameroon, a very high prevalence of *E. chaffeensis* was detected in *R. sanguineus* ticks infesting dogs inhabiting one kennel (Ndip et al., 2010). *E. chaffeensis* DNA was detected in 33 (56%) of 63 *R. sanguineus* ticks collected from five dogs as opposed to 4 (6%) ticks infected with *E. canis*. Furthermore, co-infection with more than one pathogen was not uncommon. The *E. chaffeensis* strain circulating in Cameroon is similar to the North American strain AF403710 based on the analysis of the 378 bp fragment of the disulphide bond formation (Dsb) protein gene (Ndip et al., 2010). Earlier reports revealed *E. canis*, *E. chaffeensis*, and *E. ewingii* in *R. sanguineus* ticks collected from 51 dogs from different localities in Cameroon (Figure 2), suggesting that dogs could be a reservoir for *E. chaffeensis* and that *R. sanguineus* is the probable vector (Ndip et al., 2007).

In the United States, the white-tailed deer (*Odocoileus virginianus*) has been recognised as the primary natural reservoir of *E. chaffeensis* (Dugan et al., 2000). However, animals such as goats, dogs, and coyotes have also been identified as reservoirs which could play a limited role in the transmission of the pathogen to humans (Breitschwerdt et al., 1998; Dugan et al., 2000; Kocan et al., 2000). Unlike rickettsial species, ehrlichial species are not transmitted trans-ovarially (ie., larvae are uninfected) suggesting that the pathogen is maintained trans-stadially after the infection is acquired (Ismail et al., 2010). Although the reservoirs for *E. chaffeensis* in Cameroon have not yet been conclusively identified, preliminary studies detected antibodies reactive to *E. chaffeensis* in 56% of goats analysed suggesting a probable role of goats in maintaining the pathogen in nature. Moreover, *E. chaffeensis* DNA was detected in 17% of ticks collected from these animals (Ndip, unpubished data).

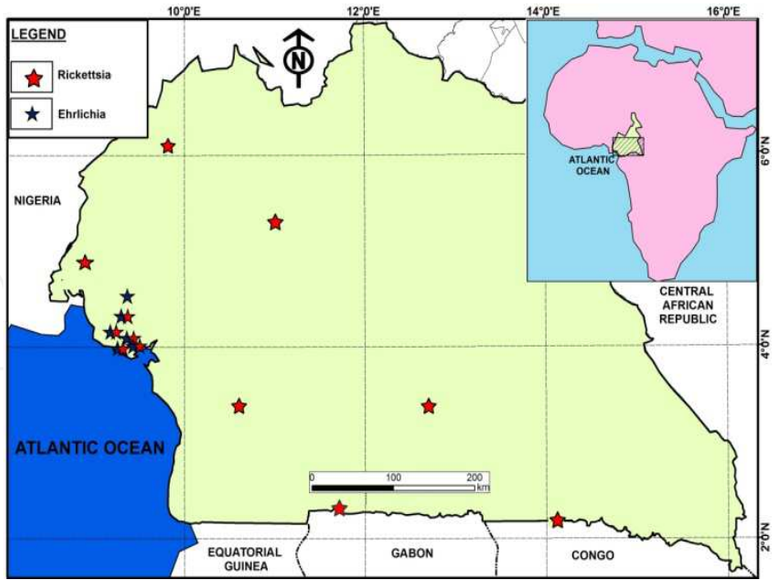


Fig. 2. Known distribution of ehrlichiae and rickettsiae in Cameroon

2.3 Clinical manifestations

The comprehensive data available in literature today on symptoms observed in HME infection is based on cases reported to the United States' Centers for Disease Control and Prevention in addition to a series of patients studied since the disease was described. After exposure to an infecting tick, an incubation period of 1 to 2 weeks (median, 9 days) ensues after which patients develop a febrile illness (often >39°C) characterized by general malaise, low-back pain, or gastrointestinal symptoms (Paddock & Childs, 2003). These signs and symptoms most often resemble manifestations caused by other infectious and non-infectious causes. After 3 to 4 days, symptoms progress and patients may seek medical attention presenting with fever (>95%), headache (60 to 75%), myalgias (40 to 60%), nausea (40 to 50%), arthralgias (30 to 35%), and malaise (30 to 80%) (Fishbein et al., 1994).

Some patients (10-40%) may present with cough, pharyngitis, diarrhea, or abdominal pain and may even progress to changes in mental status (Fishbein et al., 1994; Olano et al., 2003). Some populations especially HIV-infected patients (Paddock et al., 2001) and children (Jacobs & Schutze, 1997) may develop a rash on the extremities, trunk and face (Edwards, 1991). Hematological changes include leukopenia in approximately 60 to 70% of patients and thrombocytopenia (Fishbein et al., 1994; Olano & Walker, 2002). Liver enzymes (hepatic transaminases) may become slightly elevated (Nutt & Raufman, 1999). About 60 to 70% of patients require hospitalization and untreated cases last for 2-3 weeks or progress to a fatal outcome during the second week (Fishbein et al., 1994; Standaert et al., 2000). About 20% of patients develop neurologic signs, cough or other respiratory symptoms (Fishbein et al., 1994; Olano et al., 2003). Case-fatality ratio is approximately 3% (McQuiston et al., 2003) with risk factors for severe or fatal disease including older age (Paddock et al., 2001), underlying debilitating diseases such as HIV infection, immunosuppressive therapies (Olano & Walker, 2002) and sickle cell disease (Paddock & Childs, 2003).

These reported symptoms are quite similar to those manifested by Cameroonian HME patients. In one series of 206 acutely ill patients studied, 30 (14.6%) demonstrated anti-

ehrlichial IgM antibodies, and these probable HME patients presented with headache (83%), fatigue (37%), abdominal pain (47%), joint pain (60%), anorexia (37%) and diarrhoea (13%) in addition to fever (>38^{o}C). Their mean hematocrit, AST and ALT values were 48±21%, 46±23% and 36± 21%, respectively. Five (17%) of the patients were anaemic while 10 (33%) and 5 (17%) had abnormal AST and ALT values, respectively (Ndip, unpublished data). In another series of 118 acutely ill febrile patients studied with HME diagnosed by detection of *E. chaffeensis* DNA in patient's blood (n=12), these patients presented with fever (100%), headache (seen in 72% of the patients), arthralgia (58%), myalgia (42%), cough (17%) and a diffuse maculopapular rash (17%). The rash was present on the trunk of one patient and the arms of another. One patient of the 12 with detectable *E. chaffeensis* DNA required hospitalization (see Table 1) (Ndip et al., 2009).

2.4 Epidemiology

The epidemiology and ecology of HME worldwide is not well documented. Since its description in 1986 more than 1000 cases of HME from at least 30 U.S. states have been reported to the Centers for Disease Control and Prevention in Atlanta, Georgia with nearly all occurring in the southeastern and south-central United States where the vector, *A. americanum* is common (Paddock & Childs, 2003; Dumler et al., 2007). However, the evidence of the disease and/or the pathogen is increasingly being reported in other parts of the world. This includes Africa (Uhaa et al., 1992; Brouqui et al., 1994; Ndip et al., 2009; Ndip et al., 2010), Israel (Dawson et al., 1991; Keysary et al., 1999; Brouqui & Dumler, 2000), Latin America (Gongora-Biachi et al., 1999; Calic et al., 2004;) and Asia (Heppner et al., 1997; Cao et al., 2000; Heo et al., 2002; Kim et al., 2003; Park et al., 2003, Lee & Chae, 2010).

In Cameroon, HME has been identified in patients along the coast of Cameroon, in Buea (4^{o}10'0''N9^{o}14'0''E), Limbe (4^{o}01'N 9^{o}13'13''E), Muyuka (4^{o}43'18''N 9^{o}38'27''E), Tiko (4^{o}4'0''N 9^{o}22'60''E), and Kumba (4^{o}38'38'' N9^{o}26'19''E) and the agent, *E. chaffeensis,* in ticks collected from Limbe (Figure 2). HME was observed in both males and females as well as in children and adults although results suggested that older age was a risk factor for the disease (Ndip et al., 2009). The majority of the patients were adults which suggests that exposure to infected ticks may have occurred during outdoor activities such as farming. Another risk factor is that of owning a companion or domestic animal since most Cameroonian HME patients indicated they had tick-infested pets and domestic animals.

2.5 Microbiological diagnosis

The diagnosis of HME requires specialized microscopy equipment and skills which are not readily available in many diagnostic laboratories. Several methods have been proposed for the diagnosis of HME (Paddock & Childs, 2003; Ismail et al., 2010), including serologic tests such as immunofluorescent assay (IFA), western immunoblot employing specific proteins or ehrlichial whole cell antigens or the recently developed *Ehrlichia* recombinant protein or peptide ELISA for detection of the antibody (Cardenas et al., 2007; Luo et al., 2010; O'Connor et al., 2010). Though these tests can be used to confirm diagnosis retrospectively, some patients may not sero-convert during the early days of the disease and cannot be diagnosed with serologic tests. However, collecting paired sera (at acute and convalescent phases of illness) is confirmatory as a four-fold rise in titer indicates current infection. However, this

always presents a problem because patients who recover may not return to the hospital for follow up. Moreover, another issue with the interpretation of serological tests such as IFA is cross-reactive antibodies against other organisms, including *Anaplasma* species. PCR has also been employed to identify ehrlichial DNA in acutely ill patients when antibodies have not reached detectable levels. Several genes have been proposed and used including the VLPT gene (TRP32), TRP36, 16S rRNA, the TRP120, the Dsb, 28-kDa outer membrane protein gene have been used as genus or species specific targets (Yu et al., 1999; Doyle et al., 2005). IFA, western blot and PCR have been used to study the prevalence of ehrlichiae in blood of acutely ill patients, reservoirs, or in suspected tick vectors and anti-ehrlichial antibody in sera (Ndip et al., 2005; Ndip et al., 2007; Ndip et al., 2009; Ndip et al., 2010). Figure 3 shows IFA photomicrographs of whole cell of *E. chaffeensis* reacting with antibodies in an HME patient serum. A rapid method to detect *E. chaffeensis* is the observation of morulae in smears of peripheral blood buffy coat using the Diff Quik or Giemsa stain. However, this technique is very insensitive, and morulae are detected in leukocytes in only 10% of HME patients.

Patients	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Gender	F	F	M	F	M	M	F	M	F	F	M	M
Age (yr)	63	40	5	23	22	20	21	1	16	26	35	25
Location	A	B	C	D	C	D	A	C	A	A	B	A
Clinical Manifestations												
Fever >38^{o}C	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
*Day(s)	6	8	4	7	4	3	1	1	2	7	2	2
Headache	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	No
Myalgia	Yes	Yes	No	No	No	Yes	No	No	Yes	No	Yes	No
Arthralgia	Yes	Yes	No	No	No	Yes	Yes	No	Yes	Yes	Yes	No
Rash	No	No	No	Yes	No	No	No	Yes	No	No	No	No

*Days after onset (i.e., before collection of sample).
Locations: A - Buea , B – Limbe, C – Tiko, D - Muyuka

Table 1. Epidemiologic and clinical characteristics of twelve Cameroonian patients with HME

2.6 Treatment

The drug of choice for the treatment of *E. chaffeensis* infection is the tetracyclines (particularly doxycycline) and their derivatives. Generally, between 1 and 3 days after a patient with HME commences treatment with doxycycline, the patient becomes afebrile (Olano & Walker, 2002). However, treatment may continue for up to 10 days or at least 3 days after the patient becomes afebrile (Chapman et al., 2006). Clinical experience and *in-vitro* susceptibility testing of *E. chaffeensis* to some classes of antibiotics have revealed that fluoroquinolones, penicillins, aminoglycosides, macrolides and cotrimoxazole are not effective therapeutics (Dumler et al., 1993; Brouqui et al., 1994; Brouqui & Raoult, 1994; McBride & Walker, 2010).

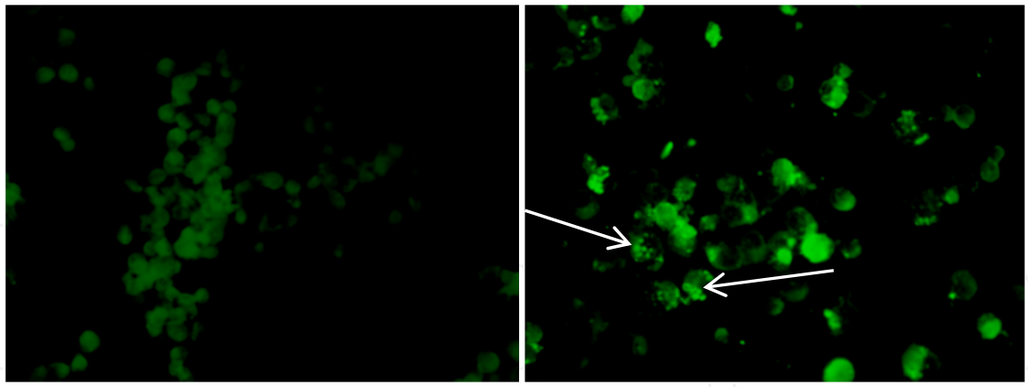


Fig. 3. Reactions of patient serum with *Ehrlichia chaffeensis* antigen and staining with Fluorescein isothiocynate (FITC)-labelled goat, IgG anti-human antibody (X40 magnification). **A**: Negative IFA slide, no inclusion bodies in cells. **B**: Positive IFA slide with morulae in monocytes (arrows) (Courtesy Laboratory for Emerging Infectious Diseases, University of Buea).

3. Rickettsiosis

3.1 The Genus *Rickettsia*

Rickettsial organisms are Gram-negative bacteria belonging to the order Rickettsiales, Family Rickettsiaceae and the Genus *Rickettsia*. They are strict intracellular parasites that are transmitted by arthropods including fleas, lice, mites and ticks (Kelly et al., 1992). These organisms are typically short rods (coccobacilli) measuring about 0.8-2.0µm in length and 0.3-0.5µm in diameter. They exhibit most of the biochemical and morphological characteristics of the Gram-negative cell (Gimenez, 1964; La Scola & Raoult, 1997). Based on antigenic characteristics, species of the genus *Rickettsia* have been divided into three groups; namely the typhus group (TG), the spotted fever group (SFG) and the transitional group (TRG). The TG has two members (*R. prowazekii* and *R. typhi*), which are mainly transmitted by lice and fleas, respectively (Raoult & Roux, 1997). The largest of the antigenic groups is the SFG that is made up of the tick-transmitted pathogens (except *R. bellii* and *R. canadensis*) (Parola et al., 2005). It has been grouped into several genogroups based on the *16S rRNA*, the *gltA*, *ompA*, *ompB* and *sca2* sequences. These groups include the *R. rickettsii* group, the *R. massiliae* group and *R. helvetica* group. The transitional group includes *R. akari, R. australis, and R. felis.* There are many ancestral organisms including *R. canadensis* and *R. bellii* (Parola et al., 2005), as well as numerous rickettsiae in herbivorous insects, and other hosts (leaches and amoeba). Also in the family Rickettsiaceae is *Orientia tsutsugamushi*, which is transmitted by *Leptotrombidium deliense (*Tamura et al., 1995).

Rickettsial organisms are of worldwide occurrence, although species/vector differences may exist along various geographical lines. In Africa, several species have been reported. These include *R. conorii* Malish strain, the cause of Mediterranean spotted fever or "boutonneuse fever". It was first documented in Tunis (Conor & Bruch, 1910), and today the disease continues to be reported in Tunisia (Romdhane et al., 2009; Sfar et al., 2009) and South Africa. The infection has the characteristic of a papular rash, in addition to an eschar at the site of the tick bite (Anton et al., 2003). The pathogen is transmitted by *R. sanguineus* ticks,

and is considered an urban disease (Font & Segura, 1983). Human infections with another strain of *R. conorii* (Israeli spotted fever strain) have been recently documented in Tunisia (Znazen et al., 2011). *R. conorii* Astrakhan strain is the cause of Astrakhan fever first detected in Astrakhan, Russia in the 1970s and transmitted by *R. sanguineus* and *R. pumilio* ticks (Parola et al., 2005). The Astrakhan strain has also been isolated from a patient in Chad (Fournier et al., 2003). *R. sibirica* mongolitimonae strain was identified in *Hyalomma truncatum* ticks in Niger in 2001 (Parola et al., 2001) and the first human case in Africa was documented in South Africa (Pretorius & Birtles, 2004). Other cases have been reported to have been acquired in Algeria (Fournier et al., 2005) and Egypt (Socolovschi et al., 2010). Another species, *R. aeschlimannii,* which was first isolated in *H. marginatum* ticks in Morocco (Beati et al., 1997) and later detected in *H. marginatum rufipes* in Mali and Niger, have been known to cause infections in tourists returning from Morocco and South Africa (Parola et al., 2001). *R. massiliae*, first isolated from *R. sanguineus* ticks in Marseille, France (Parola et al., 2005) was detected in *R. muhsame*, *R. lunalatus* and *R. sulcatus* from Central African Republic (Dupont et al., 1994) and in *R. muhsame* ticks collected from cattle in Mali 2001) and Ivory Coast (Berrelha et al., 2009). *Rickettsia felis* is a recently identified pathogen which was first detected in *Ctenocephalides felis* fleas (Bouyer et al., 2001). In Africa, the agent has been reported in Ivory Coast (Berrelha et al., 2009) and Senegal (Socolovsch et al., 2010), and human infections have been reported in Kenya (Richards et al., 2010). *Rickettsia africae,* the etiologic agent of African tick bite fever appears to be the most prevalent rickettsiosis in Africa. The disease was first reported in Mozambique and South Africa (McQuiston et al., 2004). The first isolate (*R. africae* strain ESF-5), was recovered from *A. variegatum* ticks in Ethiopia although it was only characterized as *R. africae* later (Roux et al., 1996). The agent was later isolated in *A. hebraeum* ticks in Zimbabwe in 1990, and in 1992, the first isolate from a patient was obtained (Kelly et al., 1991; Kelly et al., 1994). The pathogen has been detected in many other African countries including Senegal (Mediannikov et al., 2010), Ethiopia (Stephany et al., 2009) and Cameroon (Ndip et al., 2004a; Ndip et al., 2004b). In the following, we give a synopsis of our current knowledge of African tick bite fever in Cameroon.

3.2 Causative organism

R. africae, a member of the SFG is the only species that has been detected in Cameroon. The organism which measures about 0.4 μm by 1.0 μm, has an outer slime layer and a trilaminar cell wall which contains immunogenic lipopolysaccharide antigens responsible for cross-reactivity with the other SFG rickettsiae (Hechemy et al., 1989; Kelly et al., 1996). Like other Gram-negative organisms, rickettsiae have outer membrane proteins (dubbed OmpA and OmpB) present as species-specific antigens (Fournier et al., 1998; Roux & Raoult, 2000). The organism lives freely in the cytoplasm and usually infects endothelial cells. According to phylogenetic studies, this rickettsial species, which belongs to the *R. rickettsii* group is closely related to *R. parkeri* in North America and *R. sibirica* in northeast Asia (Parola et al., 2005).

3.3 Tick vectors and reservoirs

R. africae is a tick-borne pathogen, and ticks serve both as vectors and reservoirs. The pathogen is maintained in the tick through trans-stadial and trans-ovarial transmission, and this situation indicates the potential for transmission to humans by all stages (larvae, nymphs, and adults) of the feeding ticks. Ixodid ticks (hard ticks) of the genus *Amblyomma* have been recognized as the vectors (Kelly, 2001). In Cameroon, *A. variegatum* (Figure 1b)

has been identified as the potential vector with about 75% of ticks (male and female) collected from cattle found to be infected with *R. africae* (Ndip et al., 2004b). Reports from other studies have indicated that *R. africae* infection in *Amblyomma* ticks frequently has a high prevalence (up to 100%) reported in ticks collected in some disease-endemic countries (Dupont et al., 1994; Parola et al., 2001). Like any other tick borne disease, the ecological characteristics of the vector influence the epidemiology of the disease. The ticks are usually found all year round, but they peak during and after the rainy season when humidity is very high (Walker et al., 2003). *Ambylomma* are predominantly cattle ticks, and infestation of cattle can be very high (Kelly & Mason, 1991). *A. variegatum,* commonly found in central and west Africa typically enjoys a wide variety of different habitats although they have a preference for semi-arid and humid areas with tall grass, trees, and/or bush cover. These ticks usually quest on vegetation and would usually attack legs although they may crawl to other areas such as groin and perineum where they attach (Jensenius et al., 2003).

3.4 Clinical presentation

Since the description of ATBF in 1992, most of the knowledge available regarding the disease has been documented in travelers who become infected with *R. africae* during travel in Africa. After inoculation from a tick bite, the bacteria invade the vascular endothelial system causing a focal or disseminated vasculitis. Endothelial cells of small blood vessels become infected leading to the destruction of the endothelial cells (Toutous-Trellu et al., 2003) of the host where they have multiplied and eventually injured the host cells, leading to the disease symptoms. Multiple eschars typical of ATBF develop at the sites of tick bite, and following an incubation period between 5 and 7 days (up to two weeks in some cases), after the tick bite a febrile illness develops (Raoult et al., 2001). In most cases, symptoms of ATBF are usually mild and include headaches, nausea, chills, myalgia, lymphadenopathy and prominent neck ache (Jensenius et al., 2003; Raoult et al., 2001). Although there have been some controversies over the differences in the clinical presentations of African tick bite fever, our study of acutely ill patients in Cameroon revealed that the some individuals may manifest severe symptoms while in others the symptoms are mild. However, symptoms reported include fever >38°C (100%), headache (71%), myalgia (71%), arthralgia (57%), rash (15%) and pulmonary signs (28%).

3.5 Epidemiology

ATBF has been recognized as an emerging problem in sub-Saharan Africa, especially for international travelers to rural areas (Jensenius et al., 2003). Most of the victims reported are tourists who visit game reserves or participate in outdoor activities such as running, trekking and hiking in forested areas, usually inhabited by *Amblyomma* ticks. The patients acquire the disease in rural Africa, but most often symptoms manifest only after they have returned to their various countries in Europe and America. The first report suggesting that rickettsiosis could be prevalent in Cameroon was published in 1968 (Maurice et al., 1968). The report based on a serologic survey that used an unreliable technique demonstrated rickettsial antibodies in cattle and humans in the northern region of Cameroon and in other animals in the south of the country (Maurice et al., 1968; Le et al., 1977). Efforts to determine the epidemiology and ecology later re-emerged in 2004 when anti-rickettsial IgM antibodies were detected in some Cameroonian patients along the coastal region of Cameroon (Ndip et

al., 2004a). These results were further confirmed by detection of *R. africae* DNA in about 6% of acutely ill febrile patients (Ndip et al., 2004b). Human infections or the agent has been detected in all regions of southern Cameroon where epidemiologic investigations have been made (Figure 3). According to these studies, age appeared to be a risk factor of acquiring the disease, and it is suggested that activities such as game hunting usually constitutes a risk factor (Ndip et al., 2011). Other activities which could predispose to infection include cattle rearing and exposure to tick habitats.

Cameroon is a sub-saharan tropical country with a vast equatorial forest providing a good habitat for ticks (especially *A. variegatum* ticks). Individuals residing in lowland rainforest habitats have a higher risk of acquiring ATBF probably because these habitats are ideal for *A. variegatum* ticks because of their moderate canopy cover, providing microclimates favoring tick survival (Ndip et al., 2011). Although ATBF has been shown to be prevalent in the southern part of Cameroon (Figure 2), the actual epidemiology of the disease through wider disease surveillance needs to be documented.

3.6 Diagnosis

Diagnosis of ATBF can be achieved by either serological analysis of acute and convalescent serum samples or molecular detection of the DNA of the bacterium by real-time or conventional PCR. Target genes that have been utilized include the rickettsial *gltA* and *ompA* genes. For serological diagnosis, the indirect immunofluorescent test has been used in conjunction with western blot assay to detect antibodies reactive with whole cells or specific proteins of cell lysates of *R. africae*. However, these tests are not very reliable in distinguishing species because cross-reactivity may be observed among the SFG rickettsiae. However, some authors have proposed that a fourfold or greater titer for *R. africae* compared to other species is confirmatory (Raoult et al., 2001; Ndip et al., 2004a). The western immunoblot assay can also be used to detect antibodies against species-specific OmpA and OmpB proteins.

3.7 Treatment

The drug of choice for the treatment of ATBF is doxycycline (100 mg twice daily) for 3-7 days. *In-vitro* studies also indicate that *R. africae* is susceptible to tetracyclines, fluoroquinolones, some macrolides and chloramphenicol (Rolain et al., 1998). Mild cases of ATBF have also been shown to recover naturally (Jensenius et al., 1999).

4. Prevention of ehrlichiosis and rickettsiosis

Studies in Cameroon indicate that one risk factor for contracting *E. chaffeensis* infection and ATBF appears to be exposure to potential tick vectors. Many reports involving acquisition of rickettsial diseases have also indicated that exposure to ticks during safari tours and visit to parks constitute an important risk factor. Therefore, an important method of preventing ehrlichiosis and rickettsiosis is by reducing contact with infected ticks. Personal protective measures are quite important, including wearing light colored clothes when walking in tick infested areas, using insect repellents and examination of clothing after a visit to a tick infested area, and prompt removal of attached tick can all reduce the risk of infection. Companion animals and other domesticated animals should be taken care of and tick infestation controlled.

4.1 Conclusions

These data emphasize the importance of ehrlichiosis and ATBF as prevalent diseases in an indigenous Cameroonian population. Although these diseases present as febrile illnesses, they are rarely considered when evaluating patients with acute, undifferentiated febrile illnesses. This situation can be attributed in part to lack of adequate knowledge of the epidemiology and ecology of the disease to prompt diagnosis; unavailability of specific laboratory tests, equipment, and expertise and also the limited economic resources. Sharing new knowledge on these diseases and techniques to facilitate diagnosis are important factors that can change the types and frequencies of diseases diagnosed in febrile patients and necessitate surveillance for these diseases. Future efforts will attempt to address other issues requiring investigations such as the full description of the clinical spectrum of these diseases in African patients and risk factors for severe illness.

5. References

Alekseev, A.N., Dubinina, H.V., Semenov, A.V. & Bolshakov, C.V. (2001). Evidence of ehrlichiosis agents found in ticks (Acari: Ixodidae) collected from migratory birds. *Journal of Medical Entomolology.* 38 : 471-474.

Anderson, B.E., Sims, K.G., Olson, J.G., Childs, J.E., Piesman, J.F., Happ, C.M., Maupin, G.O. & Johnson, B.J. (1993). *Amblyomma americanum*: a potential vector of human ehrlichiosis. *American Journal of Tropical Medicine & Hygiene.* 49:239-244.

Anderson, B.E., Sumner, J.W., Dawson, J.E., Tzianabos, T., Greene, C.R., Olson, J.G., Fishbein, D.B., Olsen-Rasmussen, M., Holloway, B.P., George, E.H., et al. (1992). Detection of the etiologic agent of human ehrlichiosis by polymerase chain reaction. *Journal of Clinical Microbiology.* 30: 775-780.

Anton, E., Font, B., Munoz, T., Sanfeliu, I. & Segura, F. (2003). Clinical and laboratory characteristics of 144 patients with Mediterranean spotted fever. *European Journal of Clinical Microbiology & Infectious Diseases.* 22:126-128.

Beati, L., Meskini, M., Thiers, B. & Raoult, D. (1997). *Rickettsia aeschlimannii* sp. nov., a new spotted fever group rickettsia associated with *Hyalomma marginatum* ticks. *International Journal of Systematic Bacteriology.* 47:548-554.

Berrelha, J., Briolant, S., Muller, F., Rolain, J.M., Marie, J.L., Pages, F., Raoult, D. & Parola, P. (2009). *Rickettsia felis* and *Rickettsia massiliae* in Ivory Coast, Africa. *Clinical Microbiology & Infection.* 15: 251-252.

Bouyer, D.H., Stenos, J., Crocquet-Valdes, P., Moron, C.G., Popov, V.L., Zavala-Velazquez, J.E., Foil, L.D., Stothard, D.R., Azad, A.F. & Walker, D.H. (2001). *Rickettsia felis*: molecular characterization of a new member of the spotted fever group. *International Journal of Systematic Bacteriology.* 51: 339-347.

Breitschwerdt, E.B., Hegarty, B.C. & Hancock, S.I. (1998). Sequential evaluation of dogs naturally infected with *Ehrlichia canis, Ehrlichia chaffeensis, Ehrlichia equi, Ehrlichia ewingii,* or *Bartonella vinsonii. Journal of Clinical Microbiology.* 36:2645-2651.

Brouqui, P. & Dumler, J.S. (2000). Serologic evidence of human monocytic and granulocytic ehrlichiosis in Israel. *Emerging Infectious Diseases*. 6:314-315.

Brouqui, P., Le, C.C., Kelly, P.J., Laurens, R., Tounkara, A., Sawadogo, S., Velo, M., Gondao, L., Faugere, B., Delmont, J., et al. (1994). Serologic evidence for human ehrlichiosis in Africa. *European Journal of Epidemiology.* 10:695-698.

Brouqui, P. & Raoult, D. (1994). Human ehrlichiosis. *New England Journal of Medicine.* 330:1760-1761.

Calic, S.B., Galvao, M.A., Bacellar, F., Rocha, C.M., Mafra, C.L., Leite, R.C. & Walker, D.H. (2004). Human ehrlichioses in Brazil: first suspect cases. *Brazilian Journal of Infectious Diseases.* 8: 259-262.

Cao, W.C., Gao, Y.M., Zhang, P.H., Zhang, X.T., Dai, Q.H., Dumler, J.S., Fang, L.Q. & Yang, H. (2000). Identification of *Ehrlichia chaffeensis* by nested PCR in ticks from Southern China. *Journal of Clinical Microbiology.* 38: 2778-2780.

Cardenas, A.M., Doyle, C.K., Zhang, X., Nethery, K., Corstvet, R.E., Walker, D.H. & McBride, J.W. (2007). Enzyme-linked immunosorbent assay with conserved immunoreactive glycoproteins gp36 and gp19 has enhanced sensitivity and provides species-specific immunodiagnosis of *Ehrlichia canis* infection. *Clinical &Vaccine Immunology.* 14:123-128.

Chapman, A.S., Bakken, J.S., Folk, S.M., Paddock, C.D., Bloch, K.C., Krusell, A., Sexton, D.J., Buckingham, S.C., Marshall, G.S., Storch, G.A., Dasch, G.A., McQuiston, J.H., Swerdlow, D.L., Dumler, S.J., Nicholson, W.L., Walker, D.H., Eremeeva, M.E. & Ohl, C.A. (2006). Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis--United States: a practical guide for physicians and other health-care and public health professionals. *MMWR Recommended Report.* 55: (RR-4) 1-27.

Dawson, J.E., Anderson, B.E., Fishbein, D.B., Sanchez, J.L., Goldsmith, C.S., Wilson, K.H. & Duntley, C.W. (1991). Isolation and characterization of an *Ehrlichia* sp. from a patient diagnosed with human ehrlichiosis. *Journal of Clinical Microbiology.* 29:2741-2745.

Doyle, C.K., Labruna, M.B., Breitschwerdt, E.B., Tang, Y.W., Corstvet, R.E., Hegarty, B.C., Bloch, K.C., Li, P., Walker, D.H. & McBride, J.W. (2005). Detection of medically important *Ehrlichia* by quantitative multicolor TaqMan real-time polymerase chain reaction of the *dsb* gene. *Journal of Molecular Diagnostics.* 7: 504-510.

Dugan, V.G., Little, S.E., Stallknecht, D.E., & Beall, A.D. (2000). Natural infection of domestic goats with *Ehrlichia chaffeensis*. *Journal of Clinical Microbiology.* 38: 448-449.

Dumler, J.S., Barbet, A.F., Bekker, C.P., Dasch, G.A., Palmer, G.H., Ray, S.C., Rikihisa, Y. & Rurangirwa, F.R. (2001). Reorganization of genera in the families Rickettsiaceae and Anaplasmataceae in the order Rickettsiales: unification of some species of *Ehrlichia* with *Anaplasma*, *Cowdria* with *Ehrlichia* and *Ehrlichia* with Neorickettsia, descriptions of six new species combinations and designation of *Ehrlichia equi* and 'HGE agent' as subjective synonyms of *Ehrlichia phagocytophila*. *International Journal of Systematic Bacteriology.* 51:2145-2165.

Dumler, J.S., Madigan, J.E., Pusterla, N. & Bakken, J.S. (2007). Ehrlichioses in humans: epidemiology, clinical presentation, diagnosis, and treatment. *Clinical InfectiousDiseases.* 45:S45-S51.

Dumler, J.S., Sutker, W.L. & Walker, D.H. (1993). Persistent infection with *Ehrlichia chaffeensis*. *Clinical Infectious Diseases.* 17:903-905.

Dunning Hotopp, J.C., Lin, M., Madupu, R., Crabtree, J., Angiuoli, S.V., Eisen, J.A., Seshadri, R., Ren, Q., Wu, M., Utterback, T.R., Smith, S., Lewis, M., Khouri, H., Zhang, C., Niu, H., Lin, Q., Ohashi, N., Zhi, N., Nelson, W., Brinkac, L.M., Dodson, R.J., Rosovitz, M.J., Sundaram, J., Daugherty, S.C., Davidsen, T., Durkin, A.S., Gwinn,

M., Haft, D.H., Selengut, J.D., Sullivan, S.A., Zafar, N., Zhou, L., Benahmed, F., Forberger, H., Halpin, R., Mulligan, S., Robinson, J., White, O., Rikihisa, Y. & Tettelin, H. (2006). Comparative genomics of emerging human ehrlichiosis agents. *PLoS.Genetics.* 2 (2): e21.

Dupont, H.T., Cornet, J.P. & Raoult, D. (1994). Identification of rickettsiae from ticks collected in the Central African Republic using the polymerase chain reaction. *American Journal of Tropical Medicine &Hygiene.* 50:373-380.

Edwards, M.S. (1991). Human ehrlichiosis. *Advances in Pediatric Infectious Diseases.* 6:163-178.

Fishbein, D.B., Dawson, J.E. & Robinson, L.E. (1994). Human ehrlichiosis in the United States, 1985 to 1990. *Annals of Internal Medicine.* 120:736-743.

Font, C.B. & Segura, P.F. (1983). Mediterranean boutonneuse fever. *Medicina Clinica (Barcelona).* 80:182-186.

Fournier, P.E., 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. *Clinical Infectious Diseases.* 40:1435-1444.

Fournier, P.E., Roux, V. & Raoult, D. (1998). Phylogenetic analysis of spotted fever group rickettsiae by study of the outer surface protein rOmpA. *International Journal of Systematic Bacteriology.* 48:839-849.

Fournier, P.E., Xeridat, B. & Raoult, D. (2003). Isolation of a rickettsia related to Astrakhan fever rickettsia from a patient in Chad. *Annals of the New York Academy of Sciences.* 990: 152-157.

Ganta, R.R., Peddireddi, L., Seo, G.M., Dedonder, S.E., Cheng, C. & Chapes, S.K. (2009). Molecular characterization of *Ehrlichia* interactions with tick cells and macrophages. *Frontiers in Bioscience.* 14: 3259-3273.

Gongora-Biachi, R.A., Zavala-Velazquez, J., Castro-Sansores, C.J. & Gonzalez-Martinez, P. (1999). First case of human ehrlichiosis in Mexico. *Emerging Infectious Diseases.* 5:481.

Hechemy, K.E., Raoult, D., Fox, J., Han, Y., Elliott, L.B. & Rawlings, J. (1989). Cross-reaction of immune sera from patients with rickettsial diseases. *Journal of Medical Microbiology.* 29:199-202.

Heo, E.J., Park, J.H., Koo, J.R., Park, M.S., Park, M.Y., Dumler, J.S. & Chae, J.S. (2002). Serologic and molecular detection of *Ehrlichia chaffeensis* and *Anaplasma phagocytophila* (human granulocytic ehrlichiosis agent) in Korean patients. *Journal of Clinical Microbiology.* 40:3082-3085.

Heppner, D.G., Wongsrichanalai, C., Walsh, D.S., McDaniel, P., Eamsila, C., Hanson, B. & Paxton, H. (1997). Human ehrlichiosis in Thailand. *The Lancet.* 350:785-786.

Huang, H., Lin, M., Wang, X., Kikuchi, T., Mottaz, H., Norbeck, A. & Rikihisa, Y. (2008). Proteomic analysis of and immune responses to *Ehrlichia chaffeensis* lipoproteins. *Infection & Immunity.* 76:3405-3414.

Ismail, N., Bloch, K.C. & McBride, J.W. (2010). Human ehrlichiosis and anaplasmosis. *Clinical Laboratory Medicine.* 30:261-292.

Jacobs, R.F. & Schutze, G.E. (1997). Ehrlichiosis in children. *Journal of Pediatrics.* 131:184-192.

Jensenius, M., Fournier, P.E., Vene, S., Hoel, T., Hasle, G., Henriksen, A.Z., Hellum, K.B., Raoult, D. & Myrvang, B. (2003). African tick bite fever in travelers to rural sub-Equatorial Africa. *Clinical Infectious Diseases.* 36:1411-1417.

Jensenius, M., Hasle, G., Henriksen, A.Z., Vene, S., Raoult, D., Bruu, A.L. & Myrvang, B. (1999). African tick-bite fever imported into Norway: presentation of 8 cases. *Scandinavian Journal of Infectious Diseases.* 31:131-133.

Kelly, P., Matthewman, L., Beati, L., Raoult, D., Mason, P., Dreary, M. & Makombe, R. (1992). African tick-bite fever: a new spotted fever group rickettsiosis under an old name. *The Lancet*. 340: 982-983.

Kelly, P.J. (2001). *Amblyomma hebraeum* is a vector of *Rickettsia africae* and not *R. conorii*. *Journal of South African Veterinary Association.* 72:182.

Kelly, P.J., Beati, L., Mason, P.R., Matthewman, L.A., Roux, V. & Raoult, D. (1996). *Rickettsia africae* sp. *nov*., the etiological agent of African tick bite fever. *International Journal Systematic Bacteriology.* 46:611-614.

Kelly, P.J., Beati, L., Matthewman, L.A., Mason, P.R., Dasch, G.A. & Raoult, D. (1994). A new pathogenic spotted fever group rickettsia from Africa. *Journal of Tropical Medicine & Hygiene. 97*:129-137.

Kelly, P.J. & Mason, P.R. (1991). Transmission of a spotted fever group rickettsia by *Amblyomma hebraeum* (Acari: Ixodidae). *Journal of Medical Entomology.* 28:598-600.

Kelly, P.J., Raoult, D. & Mason, P.R. (1991). Isolation of spotted fever group rickettsias from triturated ticks using a modification of the centrifugation-shell vial technique. *Transactions of the Royal Society of Tropical Medicine & Hygiene.* 85:397-398.

Keysary, A., Amram, L., Keren, G., Sthoeger, Z., Potasman, I., Jacob, A., Strenger, C., Dawson, J.E. & Waner, T. (1999). Serologic evidence of human monocytic and granulocytic ehrlichiosis in Israel. *Emerging Infectious Diseases.* 5:775-778.

Kim, C.M., Kim, M.S., Park, M.S., Park, J.H. & Chae, J.S. (2003). Identification of *Ehrlichia chaffeensis*, *Anaplasma phagocytophilum*, and *A. bovis* in *Haemaphysalis longicornis* and *Ixodes persulcatus* ticks from Korea. *Vector Borne & Zoonotic Diseases.* 3:17-26.

Kocan, A.A., Levesque, G.C., Whitworth, L.C., Murphy, G.L., Ewing, S.A. & Barker, R.W. (2000). Naturally occurring *Ehrlichia chaffeensis* infection in coyotes from Oklahoma. *Emerging Infectious Diseases.* 6: 477-480.

Kramer, V.L., Randolph, M.P., Hui, L.T., Irwin, W.E., Gutierrez, A.G., & Vugia, D.J. (1999). Detection of the agents of human ehrlichioses in ixodid ticks from California. *American Journal of Tropical Medicine & Hygiene.* 60:62-65.

Le, N.P., Rickenbach, A., Ravisse, P. & Le, N.D. (1977). Serological survey of animal rickettsioses in Cameroon. II. Results of the survey. *Bulletin de la Societe de Pathologie Exotique et de ses Filiales.* 70: 410-421.

Lee, J.H., Park, H.S., Jung, K.D., Jang, W.J., Koh, S.E., Kang, S.S., Lee, I.Y., Lee, W.J., Kim, B.J., Kook, Y.H., Park, K.H. & Lee, S.H. (2003). Identification of the spotted fever group rickettsiae detected from *Haemaphysalis longicornis* in Korea. *Microbiology & Immunology.* 47:301-304.

Lee, M.J. & Chae, J.S. (2010). Molecular detection of *Ehrlichia chaffeensis* and *Anaplasma bovis* in the salivary glands from *Haemaphysalis longicornis* ticks. *Vector Borne Zoonotic Diseases.* 10:411-413.

Lin, M. & Rikihisa, Y. (2003). *Ehrlichia chaffeensis* and *Anaplasma phagocytophilum* lack genes for lipid A biosynthesis and incorporate cholesterol for their survival. *Infection & Immunity.* 71: 5324-5331.

Luo, T., Zhang, X., Nicholson, W.L., Zhu, B. & McBride, J.W. (2010). Molecular characterization of antibody epitopes of *Ehrlichia chaffeensis* ankyrin protein 200 and

tandem repeat protein 47 and evaluation of synthetic immunodeterminants for serodiagnosis of human monocytotropic ehrlichiosis. *Clinical & Vaccine Immunology*. 17: 87-97 .

Maeda, K., Markowitz, N., Hawley, R.C., Ristic, M., Cox, D., & McDade, J.E. (1987). Human infection with *Ehrlichia canis*, a leukocytic rickettsia. *New England Journal of Medicine*. 316:853-856.

Mahan, S.M. (1995). Review of the molecular biology of *Cowdria ruminantium*. *Veterinary Parasitology*. 57:51-56.

Maurice, Y., Fernagut, R., & Gerome, R. (1968). Rickettsial diseases of North Cameroon; epidemiological study. *Revue d Elevage et de Medecine Veterinaire des Pays Tropicaux.* 21:341-349.

McBride, J.W., Comer, J.E. & Walker, D.H. (2003). Novel immunoreactive glycoprotein orthologs of *Ehrlichia spp*. *Annals of the New York Academy of Sciences*. 990:678-684.

McBride, J.W., Doyle, C.K., Zhang, X., Cardenas, A.M., Popov, V.L., Nethery, K.A. & Woods, M.E. (2007). Identification of a glycosylated *Ehrlichia canis* 19-kilodalton major immunoreactive protein with a species-specific serine-rich glycopeptide epitope. *Infection & Immunity*. 75:74-82.

McBride, J.W. & Walker, D.H. (2010). Progress and obstacles in vaccine development for the ehrlichioses. *Expert Review onVaccines.* 9:1071-1082 .

McQuiston, J.H., McCall, C.L. & Nicholson, W.L. (2003). Ehrlichiosis and related infections. *Journal of the American Veterinary Medical Association*. 223:1750-1756.

McQuiston, J.H., Paddock, C.D., Singleton, J., Jr., Wheeling, J.T., Zaki, S.R. & Childs, J.E. (2004). Imported spotted fever rickettsioses in United States travelers returning from Africa: a summary of cases confirmed by laboratory testing at the Centers for Disease Control and Prevention, 1999-2002. *American Journal of Tropical Medicine & Hygiene*. 70:98-101.

Mediannikov, O., Trape, J.F., Diatta, G., Parola, P., Fournier, P.E. & Raoult, D. (2010). *Rickettsia africae,* Western Africa. *Emerging Infectious Diseases.* 16:571-573.

Ndip, L.M., Bouyer, D.H., Travassos Da Rosa, A.P., Titanji, V.P., Tesh, R.B. & Walker, D.H. (2004a). Acute spotted fever rickettsiosis among febrile patients, Cameroon. *Emerging Infectious Diseases.* 10:432-437.

Ndip, L.M., Fokam, E.B., Bouyer, D.H., Ndip, R.N., Titanji, V.P., Walker, D.H. & McBride, J.W. (2004b). Detection of *Rickettsia africae* in patients and ticks along the coastal region of Cameroon. *American Journal of Tropical Medicine & Hygiene*. 71:363-366.

Ndip, L.M., Ndip, R.N., Esemu, S.N., Dickmu, V.L., Fokam, E.B., Walker, D.H. & McBride, J.W. (2005). Ehrlichial infection in Cameroonian canines by *Ehrlichia canis* and *Ehrlichia ewingii*. *Veterinary Microbiology*. 111:59-66.

Ndip, L.M., Ndip, R.N., Ndive, V.E., Awuh, J.A., Walker, D.H. & McBride, J.W. (2007). *Ehrlichia* species in *Rhipicephalus sanguineus* ticks in Cameroon. *Vector Borne & Zoonotic Diseases*. 7:221-227.

Ndip, L.M., Labruna, M., Ndip, R.N., Walker, D.H. & McBride, J.W. (2009). Molecular and clinical evidence of *Ehrlichia chaffeensis* infection in Cameroonian patients with undifferentiated febrile illness. *Annals of Tropical Medicine & Parasitology*. 103:19-725.

Ndip, L.M., Ndip, R.N., Esemu, S.N., Walker, D.H. & McBride, J.W. (2010). Predominance of *Ehrlichia chaffeensis* in *Rhipicephalus sanguineus* ticks from kennel-confined dogs in Limbe, Cameroon. *Experimental & Applied Acarology.* 50:163-168.

Ndip, L.M., Biswas, H.H., Nfonsam, L.E., LeBreton, M., Ndip, R.N., Bissong, M.A., Mpoudi-Ngole, E., Djoko, C., Tamoufe, U., Prosser, A.T., Burke, D.S. & Wolfe, N.D. (2011). Risk factors for African tick-bite fever in rural central Africa. *American Journal of Tropical Medicine &Hygiene.* 84:608-613.

Nutt, A.K. & Raufman, J. (1999). Gastrointestinal and hepatic manifestations of human ehrlichiosis: 8 cases and a review of the literature. *Digestive Diseases.* 17:37-43.

O'Connor, T.P., Saucier, J.M., Daniluk, D., Stillman, B.A., Krah, R., Rikihisa, Y., Xiong, Q., Yabsley, M.J., Adams, D.S., Diniz, P.P., Breitschwerdt, E.B., Gaunt, S.D. & Chandrashekar, R. (2010). Evaluation of peptide- and recombinant protein-based assays for detection of anti-*Ehrlichia ewingii* antibodies in experimentally and naturally infected dogs. *American Journal Veterinary Research.* 71: 1195-1200.

Ohashi, N., Zhi, N., Zhang, Y. & Rikihisa, Y. (1998). Immunodominant major outer membrane proteins of *Ehrlichia chaffeensis* are encoded by a polymorphic multigene family. *Infection & Immunity.* 66:132-139.

Olano, J.P. & Walker, D.H. (2002). Human ehrlichioses. *Medical Clinics of North America.* 86: 375-392.

Olano, J.P., Hogrefe, W., Seaton, B. & Walker, D.H. (2003). Clinical manifestations, epidemiology, and laboratory diagnosis of human monocytotropic ehrlichiosis in a commercial laboratory setting. *Clinical Diagnostic & Laboratory Immunology.* 10: 891-896.

Paddock, C.D., Sumner, J.W., Shore, G.M., Bartley, D.C., Elie, R.C., McQuade, J.G., Martin, C.R., Goldsmith, C.S. & Childs, J.E. (1997). Isolation and characterization of *Ehrlichia chaffeensis* strains from patients with fatal ehrlichiosis. *Journal of Clinical Microbiology.* 35:2496-2502.

Paddock, C.D., Folk, S.M., Shore, G.M., Machado, L.J., Huycke, M.M., Slater, L.N., Liddell, A.M., Buller, R.S., Storch, G.A., Monson, T.P., Rimland, D., Sumner, J.W., Singleton, J., Bloch, K.C., Tang, Y.W., Standaert, S.M. & Childs, J.E. (2001). Infections with *Ehrlichia chaffeensis* and *Ehrlichia ewingii* in persons coinfected with human immunodeficiency virus. *Clinical Infectious Diseases.* 33:1586-1594.

Paddock, C.D. & Childs, J.E. (2003). *Ehrlichia chaffeensis*: a prototypical emerging pathogen. *Clinical Microbiology Reviews.* 16: 37-64.

Park, J.H., Heo, E.J., Choi, K.S., Dumler, J.S. & Chae, J.S. (2003). Detection of antibodies to *Anaplasma phagocytophilum* and *Ehrlichia chaffeensis* antigens in sera of Korean patients by western immunoblotting and indirect immunofluorescence assays. *Clinical & Diagnostic Laboratory Immunology.* 10:1059-1064.

Parola, P., Inokuma, H., Camicas, J.L., Brouqui, P. & Raoult, D. (2001). Detection and identification of spotted fever group Rickettsiae and Ehrlichiae in African ticks. *Emerging Infectious Diseases.* 7:1014-1017.

Parola, P., Paddock, C.D. & Raoult, D. (2005). Tick-borne rickettsioses around the world: emerging diseases challenging old concepts. *Clinical Microbiology Reviews.* 18:719-756.

Peddireddi, L., Cheng, C. & Ganta, R.R. (2009). Promoter analysis of macrophage- and tick cell-specific differentially expressed *Ehrlichia chaffeensis p28-Omp* genes. *BMC Microbiology.* 9:99.

Perez, M., Bodor, M., Zhang, C., Xiong, Q. & Rikihisa, Y. (2006). Human infection with *Ehrlichia canis* accompanied by clinical signs in Venezuela. *Annals of the New York Academy of Sciences.* 1078:110-117.

Perez, M., Rikihisa, Y. & Wen, B. (1996). *Ehrlichia canis*-like agent isolated from a man in Venezuela: antigenic and genetic characterization. *Journal of Clinical Microbiology.* 34:2133-2139.

Popov, V.L., Chen, S.M., Feng, H.M. & Walker, D.H. (1995). Ultrastructural variation of cultured *Ehrlichia chaffeensis. Journal of Medical Microbiology.* 43:411-421.

Pretorius, A.M. & Birtles, R.J. (2004). *Rickettsia mongolotimonae* infection in South Africa. *Emerging Infectious Diseases.* 10:125-126.

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. *New England Journal of Medicine.* 344: 504-1510.

Raoult, D. & Roux, V. (1997). Rickettsioses as paradigms of new or emerging infectious diseases. *Clinical Microbiology Reviews.* 10:694-719.

Rapmund, G. (1984). Rickettsial diseases of the Far East: new perspectives. *Journal of Infectious Diseases.* 149:330-338.

Richards, A.L., Jiang, J., Omulo, S., Dare, R., Abdirahman, K., Ali, A., Sharif, S.K., Feikin, D.R., Breiman, R.F. & Njenga, M.K. (2010). Human infection with *Rickettsia felis*, Kenya. *Emerging Infectious Diseases.* 16:1081-1086.

Rikihisa, Y. (1991). The tribe Ehrlichieae and ehrlichial diseases. *Clinical Microbiology Reviews.* 4:286-308.

Rikihisa, Y. (1999). Clinical and biological aspects of infection caused by *Ehrlichia chaffeensis*. *Microbes & Infection.* 1:367-376.

Rolain, J.M., Maurin, M., Vestris, G. & Raoult, D. (1998). *In vitro* susceptibilities of 27 rickettsiae to 13 antimicrobials. *Antimicrobial Agents & Chemotherapy.* 42:1537-1541.

Roland, W.E., Everett, E.D., Cyr, T.L., Hasan, S.Z., Dommaraju, C.B. & McDonald, G.A. (1998). *Ehrlichia chaffeensis* in Missouri ticks. *American Journal of Tropical Medicine & Hygiene.* 59:641-643.

Romdhane, F.B., Loussaief, C., Toumi, A., Yahia, S.B., Khaiyrallah, M., Bouzouaia, N. & Chakroun, M. (2009). Mediterranean spotted fever: a report of 200 cases in Tunisia. *Clinical Microbiology & Infection.* 15(S2):209-210.

Roux, V., Fournier, P.E. & Raoult, D. (1996). Differentiation of spotted fever group rickettsiae by sequencing and analysis of restriction fragment length polymorphism of PCR-amplified DNA of the gene encoding the protein rOmpA. *Journal of Clinical Microbiology.* 34:2058-2065.

Roux, V. & Raoult, D. (2000). Phylogenetic analysis of members of the genus Rickettsia using the gene encoding the outer-membrane protein rOmpB (*ompB*). *International Journal of Systematic and Evolutionary Microbiology.* 50:1449-1455.

Sfar, N., Kaabia, N., Letaief, A., Rolain, J.M., 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. *Clinical Microbiology & Infection.* 15(S2):309-310 .

Socolovschi, C., Barbarot, S., Lefebvre, M., Parola, P. & Raoult, D. (2010). *Rickettsia sibirica mongolitimonae* in traveler from Egypt. *Emerging Infectious Diseases.* 16:1495-1496.

Socolovschi, C., Mediannikov, O., Sokhna, C., Tall, A., Diatta, G., Bassene, H., Trape, J.F. & Raoult, D. (2010). *Rickettsia felis*-associated uneruptive fever, Senegal. *Emerging Infectious Diseases.* 16:1140-1142 .

Standaert, S.M., Yu, T., Scott, M.A., Childs, J.E., Paddock, C.D., Nicholson, W.L., Singleton, J., Jr. & Blaser, M.J. (2000). Primary isolation of *Ehrlichia chaffeensis* from patients with febrile illnesses: clinical and molecular characteristics. *Journal of Infectious Diseases.* 181:1082-1088.

Stephany, D., Buffet, P., Rolain, J.M., Raoult, D. & Consigny, P.H. (2009). R*ickettsia africae* infection in man after travel to Ethiopia. *Emerging Infectious Diseases.* 15:1867-1870.

Sumner, J.W., Childs, J.E. & Paddock, C.D. (1999). Molecular cloning and characterization of the *Ehrlichia chaffeensis* variable-length PCR target: an antigen-expressing gene that exhibits interstrain variation. *Journal of Clinical Microbiology.* 37:1447-1453.

Toutous-Trellu, L., Peter, O., Chavaz, P. & Saurat, J.H. (2003). African tick bite fever: not a spotless rickettsiosis! *Journal of the American Academy of Dermatology.* 48(2S):S18-S19.

Uhaa, I.J., MacLean, J.D., Greene, C.R. & Fishbein, D.B. (1992). A case of human ehrlichiosis acquired in Mali: clinical and laboratory findings. *American Journal of Tropical Medicine & Hygiene.* 46:161-164.

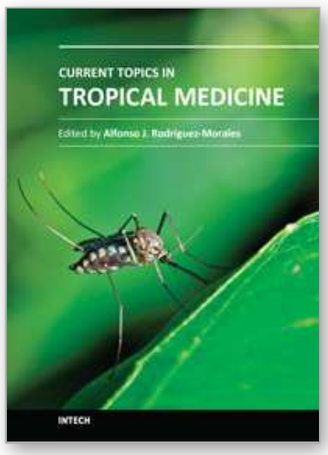
Uilenberg, G. (1983). Heartwater (*Cowdria ruminantium* infection): current status. *Advances inVeterinary Science & Comparative Medicine.* 27:427-480.

Yu, X.J., Crocquet-Valdes, P. & Walker, D.H. (1997). Cloning and sequencing of the gene for a 120-kDa immunodominant protein of *Ehrlichia chaffeensis*. *Gene*. 184:149-154.

Yu, X.J., McBride, J.W. & Walker, D.H. (1999). Genetic diversity of the 28-kilodalton outer membrane protein gene in human isolates of *Ehrlichia chaffeensis*. *Journal of Clinical Microbiology.* 37:1137-1143.

Yu, X., McBride, J.W., Zhang, X. & Walker, D.H. (2000). Characterization of the complete transcriptionally active *Ehrlichia chaffeensis* 28 kDa outer membrane protein multigene family. *Gene*. 2481-2):59-68.

Znazen, A., Hammami, B., Lahiani, D., Ben, J.M. & Hammami, A. (2011). Israeli spotted Fever, Tunisia. *Emerging Infectious Diseases.* 17:1328-1330.



Current Topics in Tropical Medicine
Edited by Dr. Alfonso Rodriguez-Morales

ISBN 978-953-51-0274-8
Hard cover, 564 pages
Publisher InTech
Published online 16, March, 2012
Published in print edition March, 2012

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

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Lucy Ndip, Roland Ndip, David Walker and Jere McBride (2012). Human Ehrlichioses and Rickettsioses in Cameroon, Current Topics in Tropical Medicine, Dr. Alfonso Rodriguez-Morales (Ed.), ISBN: 978-953-51-0274-8, InTech, Available from: http://www.intechopen.com/books/current-topics-in-tropical-medicine/human-ehrlichiosis-and-rickettsiosis-in-cameroon

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen