Common Epidemiology of 
*Rickettsia felis* Infection 
and Malaria, Africa


This study aimed to compare the epidemiology of *Rickettsia felis* infection and malaria in France, North Africa, and sub-Saharan Africa and to identify a common vector. Blood specimens from 3,122 febrile patients and from 500 nonfebrile persons were analyzed for *R. felis* and *Plasmodium* spp. We observed a significant linear trend (p<0.0001) of increasing risk for *R. felis* infection. The risks were lowest in France, Tunisia, and Algeria (1%), and highest in rural Senegal (15%). Co-infections with *R. felis* and *Plasmodium* spp. and occurrences of *R. felis* relapses or reinfections were identified. This study demonstrates a correlation between malaria and *R. felis* infection regarding geographic distribution, seasonality, asymptomatic infections, and a potential vector. *R. felis* infection should be suspected in these geographical areas where malaria is endemic. Doxycycline chemoprophylaxis against malaria in travelers to sub-Saharan Africa also protects against rickettsioses; thus, empirical treatment strategies for febrile illness for travelers and residents in sub-Saharan Africa may require reevaluation.

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Investigations examining the etiologic spectrum of fever of unknown origin in Africa rapidly progressed during 2008–2011 (1–3), providing increased knowledge about bacterial infections. Bacterial agents that have been most frequently identified in North and sub-Saharan Africa by culture are non-typhoidal *Salmonella*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, and *Mycobacterium tuberculosis* (2). Several studies have assessed the effect of fastidious bacterial infections in systemic febrile illness, including *Rickettsia felis* (4–6), *Coxiella burnetii* (7), *Tropheryma whippelii* (3), and *Borrelia* spp. (1,8). Tourism, immigration, international business travel, international aid work, and the deployment of troops overseas were documented as contributors to a tremendous increase in international travel during 1996–2004 (9). International tourist arrivals reached 940 million worldwide during 2010, an increase of 6.6% over 2009, and the current total number of international migrants has increased to an estimated 214 million persons in 2012 (10). Consequently, physicians in the Western hemisphere increasingly encounter febrile patients returning from international travel who were exposed to tropical infections that the physicians are unfamiliar with (9,10). Among international travelers, malaria, dengue, and rickettsiosis are among the most identified etiologies of febrile illness, and exposure to mosquitoes is reported as the most common source of fever (11).

*Rickettsia felis*, an obligate intracellular Gram-negative bacterium belonging to the spotted fever group of *Rickettsia*, has been shown to be a common agent of bloodstream infections in among humans Senegal and Kenya, identified in 7% of the population evaluated (4–6). However, the epidemiology (including vectors and reservoirs)
and clinical picture of this emerging infection in the rest of Africa is largely unknown (12,13). During 2011, a possibly primary infection with *R. felis*, named “yaaf,” was hypothesized in the case of an 8-month-old girl in Senegal with polymorphous skin lesions (12).

The considerable frequency of *R. felis* infections observed in febrile patients in malaria-endemic regions and the many relapses previously reported (4,5) led us to investigate the possible correlation of *R. felis* and that of the parasite, *Plasmodium falciparum*, a known vector of malaria. The reservoirs for malaria and many rickettsial species are mammals, including humans; humans have long been known to be a reservoir for malaria, and were documented as the reservoir for *R. prowazekii*, the agent of epidemic typhus (14). Vectors for both organisms are arthropods: for rickettsial diseases vectors are typically ticks, lice or mites, and infected humans are susceptible to relapse (such as epidemic and scrub typhus) (14).

The vectors for malaria are mosquitoes of the genus *Anopheles* that breed in warm and humid areas (15). Malaria is particularly common among young patients, because progressive immunity develops following multiple infections as the child grows older. Great apes in Cameroon were recently identified as targets or possibly the origin of malaria (16). *R. felis* has recently been detected in *Anopheles gambiae* mosquitoes in molecular form S, in *Aedes albopictus* mosquitoes, and in gorilla fecal samples (17–19). These elements suggest comparable features within the epidemiologic cycles of malaria and *R. felis* infection. In addition, co-infections by *R. felis* and *P. falciparum* have been reported in Kenya (5). To prove the hypothesis of the similar epidemiology of malaria and *R. felis* infection, target populations, clinical phenomena (relapses and bacteremia in apparently asymptomatic patients), and geographic and seasonal distribution should be compared. The objective of this work is to clarify the epidemiology of *R. felis* infection and to compare it with malarial epidemiology.

**Materials and Methods**

**Study Areas and Participants**

**Febrile Patients**

During June 2010–March 2012, a cohort of 2,075 patients (67% <15 years of age; sex ratio, 1:1) from 14 health centers distributed throughout rural Senegal (Senegal study sites S1–S6) were enrolled in this study. The study sites spanned various ecosystems, from dry regions in the north (Dieilmo, Senegal study region 1,–S1, Ndiop–S2, Keur Momar Sarr–S3, and Niakhar–S4) to humid regions in the south (Basse-Casamance–S5 and Kedougou–S6) that had a rainy season during June through October (online Technical Appendix Table, wwwnc.cdc.gov/EID/article/19/11/13-0361-Techapp1.pdf; Table). In addition, patients from various medical facilities were included: 100 from rural Mali dispensaries: Diankabou-Mali study site M1 and Kole-Mali study site M2; 50 from Franceville, in urban Gabon (pediatric consultation); 183 from Sfax, Tunisia (infectious diseases and pediatric departments); 266 from Oran, Algeria (department of infectious diseases); 48 from the Kenitra region, rural Morocco (dispensaries); and 400 from Marseille, France (hospital emergency units) (Figure 1). Questionnaires and informed consent forms were completed upon enrollment in the study. For each febrile patient (axillary temperature >37.5°C), an interview was conducted, a blood sample (200 µl blood containing EDTA) was collected, and a medical examination was performed. The national ethics committees of Senegal, Gabon, and France approved this project (No. 0–00.87MSP/DS/CNERS and No. 001380MSP/DS/CNERS).

**Control Group**

Samples were obtained from 400 afebrile persons (62% >15 years of age) from S1,2 who participated in a longitudinal study of malaria (20) and 100 persons from France who were under the medical care of 1 of the authors (D.R.) for conditions other than malaria.

**Arthropod Collection in Senegal**

Arthropod specimens collected in Senegal consisted of 949 adult mosquitoes from 3 locations (Table 1, 154 mosquito larvae from Mariste, Dakar, 370 ticks from 2 locations, 160 adult bed bugs from 6 locations, and 384 midges from 2 locations. The *Anopheles arabiensis* mosquito larvae were collected from breeding sites in Mariste, Dakar. The pooled larvae were maintained under laboratory conditions until they grew to the adult stage. In sites S1,2, 144 adult ticks (2 *Rhipicephalus* spp., 4 *Argas persicus*, and 138 *Ornithodoros sonrai*) from 55 burrows inside of 16 human dwellings were collected. A total of 226 *Ornithodoros capensis* ticks were manually collected from the nests of great cormorants (*Phalacrocorax carbo*) in Sarpan Island (îles de la Madeleine) near Dakar. Bed bugs were manually captured from the beds of ill persons. The collection of *Culicoides* spp. was performed in S1,2 by using overnight posed CDC light traps with 0.7-mm mesh size. The arthropods were identified at the species level by using morphological characteristics according to identification keys.

**Molecular Analysis**

DNA was extracted by using the 2-stage protocol for a QIAamp kit (QIAGEN, Hilden, Germany) for the S1,6 groups (3,4,7), and a Biorobot EZ1 Workstation (QIAGEN, Courtaboeuf, France) was used to extract DNA from.
samples from S1–2, Algeria, Tunisia, Morocco, and France. In Gabon, the DNA Blood Omega Bio-tek-E.Z.N.A method (Omega Bio-tek, Norcross, GA, USA) was used according to the manufacturer’s protocol. For all locations, DNA was eluted in 100 µL of elution buffer, and 5 µL was used per reaction.

Quantitative real-time reverse transcription PCR (qRT-PCR) was performed by using a 7900HT-thermocycler (Applied Biosystems) with the QuantiTect-Probe PCR Kit (QIAGEN, Courtabeuf, France). Only samples positive for the β-actin gene product were considered reliable (3); thus, 51 and 9 samples from Senegal and Algeria, respectively, were excluded. All samples were screened by using a Rickettsia genus-specific qRT-PCR targeting the gltA gene and an R. felis-specific qRT-PCR targeting the bioB gene (4). The positive samples were tested by a second R. felis-specific qRT-PCR targeting the orfB gene (18). A sample was considered positive when the qRT-PCRs were positive for the 2 different specific genes. Positive samples from arthropods were further tested for plasmid pRFδ (21) and by a newly designed R. felis-specific qRT-PCR targeting the vapB1 gene with the primers VapB1.R (5′-AGGCGAAAGCTTTTGCAC-3′) and VapB1.F (5′-TGTCTTTCTATGAATTCGTAGCAGA-3′) and the probe VapB1.P (6-FAM-5′-AAGGCTTGGTTCTGCGAG-3′TAMRA).

Blood smears stained with Giemsa were examined for the samples collected in Gabon. All other samples were tested by using a Plasmodium-genus specific qRT-PCR targeting the Cox-1 gene found in all Plasmodium species; the primers Psp_15.F (5′-AGGAAACTCGACTGCTAC-3′) and Psp_16.R (5′-CCACGCGACGCGTTTATGACT-3′) and the (6FAM-5′-CGAACGCTTTTAACGCCTGACATGG-3′TAMRA) probe were used. The positive samples were subsequently tested by Plasmodium-genus specific qRT-PCR targeting 18S rRNA with the primers Plasmo_18S_2_MBFR (5′-AGGCAACACAGCTCTGTGAC-3′) and Plasmo_18S_2_MBR (5′-GCAATAATCTATCCCACGTG-3′) and the (6FAM-5′-GAACTAGGCTGCACGCTG-3′TAMRA) probe.

**Statistical Analysis**

Statistical analyses were performed by using the Statcalc module of Epi Info 3.5.3 (Centers for Disease Control and Prevention, Atlanta, GA, USA) to calculate the χ² values for the incidence rate trends calculated for each country. PASW Statistics software 17.0 (IBM, SPSS Inc., Armonk, NY, USA) was used to perform Pearson correlation analyses. The relative risk (RR) and the 95% CI of the risk were calculated by using either the Mantel-Haenszel χ² test or Fisher’s exact test. The statistical significance of the χ² values was evaluated at α = 0.05. The attack rates of R. felis infection and malaria were calculated for each country, site, sex, and age range. In contrast, the incidence rates of R. felis infection and malaria for S1–2 were calculated monthly and yearly from June 13, 2010 through October 13, 2011. The data from a study performed in 2009 (4) were combined with those of this study to determine the frequency of relapses or re-infections of R. felis infections in S1–2.
The risk of developing R. felis infection was 15% (312/2,024); those infections occurred primarily during the rainy season rather than the dry season (207/1,105 vs. 105/916, respectively; p<0.0001). The attack rate of R. felis infection was 145M/162F (1:1.1). When calculated by site, substantial differences in the rates of R. felis infection were observed (Table 2). The highest attack rates were observed in S5–6, reaching 40% (92/231) during the rainy period (95% CI 1.3–2) than during the dry period. When calculated by site, substantial differences in the rates of R. felis infection were observed (Table 2). The highest attack rates were observed in S5–6, reaching 40% (92/231) during the rainy period (95% CI 1.3–2) than during the dry period.

### Results

#### Rickettsia felis Detection

**Senegal**

The attack rate of R. felis infections in febrile patients was 15% (312/2,024); those infections occurred primarily during the rainy season rather than the dry season (207/1,105 vs. 105/916, respectively; p<0.0001). The risk of developing R. felis infection was 1.6× higher during the rainy period (95% CI 1.3–2) than during the dry period. When calculated by site, substantial differences in the rates of R. felis infection were observed (Table 2). The highest attack rates were observed in S5–6, reaching 40% (92/231) from August–October 2011. The lowest attack rate was observed in S1–2 (7%–8%) and was significantly lower than that observed at the 4 other sites S3–6 (p>0.001) (Table 2).

Incidence rates were obtained from 2 health centers in S1–2. A second R. felis infection was diagnosed in 5 patients after 44 to 911 days, and 1 patient was positive for R. felis infection a second and third time at days 378 and 441, respectively. The 6 patients (4 male, 2 female) who had relapses in S1 were from S1, and 5 were <6 years of age.

When the incidence rates by age group were calculated according to sex, a significant difference was observed only in the male group, in which the incidence rate was significantly higher in the patients <15 years of age than in the patients >15 years of age (0.29 vs. 0.07 per 100 person-months, RR 5.97, 95% CI 2.28–17.15, p = 0.001).

### Other Countries

Samples from 3 patients (3%, 3/100) in rural Mali (M1, 1/50; M2, 2/50), 5 patients (10%, 5/50) in urban...
R. felis Infection and Malaria, Africa

Table 2. Attack rate of Rickettsia felis infection and malaria by country and geographic site, Africa, 2010–2012

<table>
<thead>
<tr>
<th>Participant status, country, and study site (site abbreviation)</th>
<th>Collection period</th>
<th>No. samples*</th>
<th>R. felis</th>
<th>Plasmodium spp.</th>
<th>R. felis/Plasmodium spp. co-infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Febrile patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senegal</td>
<td>Jun 2010–Mar 2012</td>
<td>2,024</td>
<td>312/2,024 (15)</td>
<td>400/1,867† (21)</td>
<td>66/285 (23)*</td>
</tr>
<tr>
<td>Dielmo (S1)</td>
<td>Jun 2010–Feb 2012</td>
<td>540</td>
<td>39/540 (7)</td>
<td>118/509 (23)</td>
<td>8/36 (22)</td>
</tr>
<tr>
<td>Ndop (S2)</td>
<td>Jun 2010–Feb 2012</td>
<td>246</td>
<td>20/246 (8)</td>
<td>33/237 (14)</td>
<td>3/18 (17)</td>
</tr>
<tr>
<td>Keur-Momar Sarr (S3)</td>
<td>Mar–Nov 2011</td>
<td>223</td>
<td>36/223 (16)</td>
<td>44/196 (22)</td>
<td>9/33 (27)</td>
</tr>
<tr>
<td>Niakhar (S4)</td>
<td>Oct 2010–Mar 2012</td>
<td>316</td>
<td>76/316 (24)</td>
<td>74/303 (24)</td>
<td>18/74 (24)</td>
</tr>
<tr>
<td>Basse-Casamance (S5)</td>
<td>Jan 2011–Mar 2012</td>
<td>411</td>
<td>84/411 (20)</td>
<td>37/350 (11)</td>
<td>7/69 (10)</td>
</tr>
<tr>
<td>Kedougou (S6)</td>
<td>2011</td>
<td>288</td>
<td>57/288 (20)</td>
<td>94/272 (34)</td>
<td>21/55 (38)</td>
</tr>
<tr>
<td>Gabon</td>
<td></td>
<td></td>
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<tr>
<td>Franceville</td>
<td>2011</td>
<td>50</td>
<td>5/50 (10)</td>
<td>19/50 (38)†‡</td>
<td>2/5 (40)**</td>
</tr>
<tr>
<td>Mali</td>
<td>2011</td>
<td>100</td>
<td>3/100 (3)</td>
<td>90% (90/100)</td>
<td>3/3 (100)</td>
</tr>
<tr>
<td>Diakambou (M1)</td>
<td>Oct</td>
<td>50</td>
<td>1/50 (2)</td>
<td>82% (41/50)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>Kole (M2)</td>
<td>Nov</td>
<td>50</td>
<td>2/50 (4)</td>
<td>98% (49/50)</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td>Algeria</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Oran</td>
<td>Jul–Sep 2012</td>
<td>257</td>
<td>2/257 (1)</td>
<td>1/257 (0.4%)</td>
<td>0/1</td>
</tr>
<tr>
<td>Morocco</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Casablanca</td>
<td>May–Jun 2006</td>
<td>48</td>
<td>1/48 (2)</td>
<td>0/38†‡</td>
<td>0</td>
</tr>
<tr>
<td>Tunisia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sfax</td>
<td>2012</td>
<td>183</td>
<td>0/183</td>
<td>0/183</td>
<td>0</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marseille</td>
<td>2012</td>
<td>400</td>
<td>0/400</td>
<td>0/400</td>
<td>0</td>
</tr>
<tr>
<td><strong>Afebrile persons</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senegal (S1–S2)</td>
<td>Dec 2011–Apr 2012</td>
<td>391</td>
<td>17/391 (4)</td>
<td>5/391 (1)</td>
<td>0/5</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td>100</td>
<td>0/100</td>
<td>0/100</td>
<td>0</td>
</tr>
</tbody>
</table>

*Reliable samples.
†There were insufficient DNA samples for the analysis of Plasmodium spp., as decided a posteriori.
‡Positive by blood smear.

Gabon, 1 patient (2%, 1/48) in rural Morocco, and 2 patients (1%, 2/257) in Algeria were positive for R. felis (Table 2). Conversely, R. felis DNA was not detected among the samples from febrile persons in France and Tunisia.

When the R. felis infection rates of the different countries were compared, R. felis was detected more often in countries with high malaria rates compared with countries with low malaria rates (Senegal, Gabon, and Mali vs. Algeria, Tunisia, Morocco, and France; p<0.001) (Figure 1). The trend analysis showed a significant linear trend of increasing risk for R. felis infection; a lower risk was shown in northern countries (France, Tunisia, Morocco, and Algeria) and a higher risk in southern countries (Mali, Gabon, and Senegal) (p < 0.0001). The probability of R. felis infection was 1.00 for Algeria (baseline), 2.8 for Morocco, 4 for Mali, 14.5 for Gabon, and 24 for Senegal.

Malaria

Senegal

The attack rate of Plasmodium spp. in febrile persons from Senegal was 21% (400/1868, 206 females); those infections occurred significantly more often during the rainy season compared with the dry season (256/1042 vs. 144/822, respectively; p = 0.0002). The risk for malaria was 1.4× higher during the rainy period than during the dry period (95% CI 1.2–1.7, p<0.0001). The highest rate was in southeastern S6, whereas the lowest rate, 11% (37/350), was in southwestern S5 (Table 2). During the same time period, the incidence rate of malaria was 17.6 per 100 person-years or 0.42 per 100 person-months for S5, and 5.1 per 100 person-years or 0.18 per 100 person-months, RR 3.38, 95% CI 1.15–3.18, p = 0.01; and boys (0.62 (0.47–0.81) versus 0.22 (0.16–0.30) per 100 person-months, RR 2.51, 95% CI 1.73–3.65, p<0.0001).

When the incidence rate by age group was calculated according to sex, the highest incidence was found among patients <15 years of age in S6 (0.55 (0.44–0.67) versus 0.22 (0.16–0.30) per 100 person-months, RR 2.51, 95% CI 1.73–3.65, p<0.0001).

When the incidence rate by age group was calculated according to sex, the highest incidence was found among girls <15 years of age: 0.47 (0.37–0.65) versus 0.25 (0.16–0.37) per 100 person-months, RR 1.92, 95% CI 1.15–3.18, p = 0.01; and boys (0.62 (0.47–0.81) versus 0.18 (0.10–0.30) per 100 person-months, RR 3.38, 95% CI 1.90–5.99, p<0.0001) groups. Table 3 shows the age distribution of malaria. Patients 7–15 years of age (33%) were infected with Plasmodium spp. significantly more often than those in other age groups (15% for patients 1–3 years of age, p<0.0001 to 23% for patients 4–6 years of age, p = 0.004). Co-infection of Plasmodium spp. and R. felis was found in 66 case-patients (23%, 66/285), mostly in women (61%) and in children 7–15 years of age (43%).
Other Countries

Plasmodium DNA was detected in 90% of the blood samples collected in Mali; 3 patients with malaria from Mali were co-infected with R. felis (Table 2). In Gabon, samples from 38% (19/50) of the patients tested positive for malaria by using blood smears; 2 of those patients were co-infected with R. felis. We most likely misdiagnosed malaria among the patients in Gabon, as based on the lower sensitivity and high specificity of microscopy versus PCR as the standard (22). Plasmodium DNA was not detected in the samples from Tunisia, Morocco, or France. However, 1 Plasmodium spp.-positive sample was collected in Algeria from a 21-year-old woman who was hospitalized for high fever, chills, and sweats after having spent >2 months visiting her family in Niger without malaria chemoprophylaxis. Correlation of R. felis with Malaria

Using the Pearson correlation test, we found a significant correlation between the number of patients infected with R. felis and those infected with Plasmodium spp. (p<0.002): a higher number of R. felis infections correlated with a higher number of malaria cases. A significant correlation was also found for seasonality for infection by both pathogens: most cases occurred during the rainy period (p<0.0001). In addition, children <3 years of age were infected with both organisms less often than persons >4 years of age, and the Pearson test showed a significant correlation between R. felis and malaria (p = 0.001) for this age group.

Control Group

R. felis DNA was detected in 4% of the afebrile persons (17/391) from Senegal, 12 of whom were children (<15 years of age); malaria was detected in 5 afebrile persons, 3 of whom were children. Both pathogens were detected significantly less often in afebrile patients than in febrile patients (p<0.001). DNA from R. felis and Plasmodium were not detected among persons in the control group in France.

Arthropod Study

Samples from 9 mosquitoes (≈1%, 9/1,103) and 1 bed bug (≈1%, 1/160) tested positive in 2 R. felis-specific qRT-PCRs (Tables 1,4). The pRFδ plasmid was detected in 8 mosquito samples (21). In Dakar, 1% (2/154) of the An. arabiensis mosquitoes collected were positive for R. felis, including 1 male, suggesting transovarian transmission. One Aedes luteocephalus from Ferlo 0.5% (1/203) was positive for R. felis. In S1, 15% (6/40) mosquitoes collected in September 2012 were positive for R. felis, including 1 An. ziemanni, 1 An. pharoensis, 2 Mansonia uniformis, and 2 An. funestus. None of the 24 mosquito samples collected from this region in July tested positive. In addition, 1 Cimex hemipterus bed bug (3%) (1/39), collected from a household in S1 in February 2012, tested positive. No R. felis DNA was detected in soft or hard ticks or in Culicoides species.

Discussion

This study shows that Rickettsia felis is an emerging pathogen commonly detected in sub-Saharan rural

Table 3. Age distribution of infections with Rickettsia felis and Plasmodium spp. among patients in Senegal, by age group, 2010–2012^*^

<table>
<thead>
<tr>
<th>Species</th>
<th>&lt;1 y</th>
<th>1–3 y</th>
<th>4–6 y</th>
<th>7–15 y</th>
<th>16–29 y</th>
<th>&gt;30 y</th>
<th>ND</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmodium spp.</td>
<td>20/169 (12)</td>
<td>60/327 (16)</td>
<td>57/251 (23)</td>
<td>134/401 (33)</td>
<td>56/271 (21)</td>
<td>58/310 (19)</td>
<td>15/78 (19)</td>
<td>400/1,867 (21)</td>
</tr>
<tr>
<td>R. felis</td>
<td>27/184 (15)</td>
<td>40/422 (10)</td>
<td>40/270 (15)</td>
<td>69/425 (16)</td>
<td>49/298 (16)</td>
<td>57/336 (17)</td>
<td>30/89 (34)</td>
<td>312/2,024 (15)</td>
</tr>
</tbody>
</table>

ND, no age data available.
Leptospira \textit{robi} (49). Mixed infections for rickettsioses, including co-
ranged from 6% in rural Mozambique (49), but higher than the rate of simultaneous bacterial
infections and malaria parasitemia, which (49) was lower in Senegal (23%) than in Kenya (79%)
ture, but 26). This result should be confirmed by cul-
without a fever (49–76). Plasmodium
not previously been reported in afebrile persons, low-grade
reported results in Kenya (49). 25 have been described (49).

26 years of age (Figure 2), but no coincidental relationship
was found; the highest risk for \textit{R. felis} infection was in rural Senegal (24 times than in Algeria). In Senegal, DNA from
\textit{Plasmodium} spp. and \textit{R. felis} were detected at high levels, mostly during the rainy season and among children <15
years of age (Figure 2), but no coincidental relationship
was found. The incidence of co-infection of \textit{R. felis} and malaria was lower in Senegal (23%) than in Kenya (79%)
(5), but higher than the rate of simultaneous bacterial
bloodstream infections and malaria parasitemia, which ranged from 6% in rural Mozambique (23) to 11% in Nairobi (24). Mixed infections for rickettsioses, including co-
infections with malaria or with other bacteria (\textit{Leptospira}
sp., \textit{Coxiella burnetii}, and \textit{Burkholderia pseudomallei})
have been described (25).

\textit{R. felis} was detected in afebrile persons, most of whom
were children <15 years of age, confirming the previously
reported results in Kenya (5). Although rickettsioses have not previously been reported in afebrile persons, low-grade
\textit{Plasmodium} parasitemia has been reported among persons
without a fever (26). This result should be confirmed by cul-
ture, but \textit{R. felis} has never been isolated, even from acutely
ill patients. Nonetheless, the absence of positive tests in the
control group located in France confirmed the specificity
of our tests. The \text{S₁₂₅} population was screened serologically
for \textit{R. felis}, and low titters were identified in 1 of 479 se-
rum samples tested (27), which is substantially lower than the
seroprevalence of other spotted fever group rickettsiae.
The mechanism of absence of a serologic response and the
occurrence of multiple re-infections or relapses of \textit{R. felis}
should be investigated further.

Africa. We are confident that our molecular results are
reliable and that the negative results in samples from
France illustrate a correlation between \textit{R. felis} infection and malaria with regard to the geographic distribution and seasonality. A trend of higher risk for \textit{R. felis} infection in southern countries than in northern countries was revealed; the highest risk for \textit{R. felis} infection was in rural Senegal (24 times than in Algeria). In Senegal, DNA from
\textit{Plasmodium} spp. and \textit{R. felis} were detected at high levels, mostly during the rainy season and among children <15
years of age (Figure 2), but no coincidental relationship
was found. The incidence of co-infection of \textit{R. felis} and malaria was lower in Senegal (23%) than in Kenya (79%)
(5), but higher than the rate of simultaneous bacterial
bloodstream infections and malaria parasitemia, which ranged from 6% in rural Mozambique (23) to 11% in Nairobi (24). Mixed infections for rickettsioses, including co-
infections with malaria or with other bacteria (\textit{Leptospira}
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The mechanism of absence of a serologic response and the
occurrence of multiple re-infections or relapses of \textit{R. felis}
should be investigated further.

In this work, we demonstrated a greater frequency of
\textit{R. felis} during the rainy season among children in the sub-
tropical zones, a period coinciding with circulation of \textit{P. falciparum}. There are other seasonal diseases, including in-
fluenza, which are most common during the rainy season in subtropical Africa, particularly in Senegal (28). Influenza is a disease found throughout the year, with seasonal peaks,
in Africa; none of the tested patients had influenza symp-
toms. Furthermore, leptospirosis, for which rickettsial dis-
ease could be mistaken, has not been documented in Sen-
egal. Last, the most common seasonal disease in the most
northern part of the intertropical area is malaria; a disease,
however, which is common in all seasons in equatorial wet-
lands. These data, for which confirmation is needed, show
a seasonal correlation between \textit{R. felis} and malaria; the cor-
relation is related to the presence and activity of \textit{Anopheles}
mosquitoes. Although the cat flea, \textit{Ctenocephalides felis}, is
currently the only known vector of \textit{R. felis}, a variety of oth-
er arthropods have been suspected, including different flea
species, ticks, mites, and lice (13). In Senegal, the source of
\textit{R. felis} is yet to be determined. We did not detect \textit{R. felis} in
fleas that were screened during 1 year in \textit{S₁} and \textit{S₂} (13).
In other studies, \textit{R. felis} was not detected in soft or hard ticks
(27,29), tsetse flies (30), or midges. These findings support
the hypothesis of the role of \textit{Anopheles} in the transmission
of \textit{R. felis}; this hypothesis should be confirmed or refuted
by future studies.

The clinical findings for \textit{R. felis} infection are often un-
clear and are typically misdiagnosed as other febrile illnesses
(12,31). Recently, the primary infection was described in a
patient with polymorphous skin lesions, including papules,
vesicles, erosions, and ulcers (12), similar to patients from
Mexico (32). In the current study, a high incidence of \textit{R. felis}
infection was identified in children <15 years of age, as de-
scribed (4). Fortunately, such patients improve rapidly with
doxycycline treatment (12). For travelers to sub-Saharan

<table>
<thead>
<tr>
<th>Group</th>
<th>Species</th>
<th>No. samples tested</th>
<th>Type of rickettsia (%) positive samples</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fleas</td>
<td>\textit{Ctenocephalides felis}</td>
<td>48</td>
<td>None</td>
<td>(13)</td>
</tr>
<tr>
<td></td>
<td>\textit{Echidnophaga gallinacea}</td>
<td>150</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td>\textit{Synosternus pallidus}</td>
<td>41</td>
<td>\textit{Rickettsia sp., group R. felis} (93)</td>
<td></td>
</tr>
<tr>
<td>Tsetse flies</td>
<td>\textit{Glossina morsitans}</td>
<td>78</td>
<td>\textit{Rickettsia sp., group R. felis} (100)</td>
<td>(30)</td>
</tr>
<tr>
<td>Hard ticks</td>
<td>\textit{Amblyomma variegatum}</td>
<td>492</td>
<td>\textit{Rickettsia africana} (87)</td>
<td>(29)</td>
</tr>
<tr>
<td></td>
<td>\textit{Rhipicephalus decoloratus}</td>
<td>40</td>
<td>\textit{Rickettsiae spotted fever group} (0–51)</td>
<td>(27)</td>
</tr>
<tr>
<td></td>
<td>\textit{Hyalomma marginatum}</td>
<td>173</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>\textit{H. truncatum}</td>
<td>141</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>\textit{R. evertsi evertsi}</td>
<td>2358</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>\textit{R. guilhoni}</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>\textit{Rhipicephalus sp.}</td>
<td>2</td>
<td>None</td>
<td>This study</td>
</tr>
<tr>
<td>Soft ticks</td>
<td>\textit{Ornithodoros sonrai}</td>
<td>138</td>
<td>None</td>
<td>This study</td>
</tr>
<tr>
<td></td>
<td>\textit{O. capensis}</td>
<td>40</td>
<td>\textit{Rickettsia sp., group R. felis} (20)</td>
<td>This study</td>
</tr>
<tr>
<td></td>
<td>\textit{Argas persicus}</td>
<td>4</td>
<td>None</td>
<td>This study</td>
</tr>
<tr>
<td>Midge</td>
<td>\textit{Culicoides spp.}</td>
<td>384</td>
<td>None</td>
<td>This study</td>
</tr>
<tr>
<td>Bed bugs</td>
<td>\textit{Cimex hemipterus}</td>
<td>160</td>
<td>1/160, (0.6)</td>
<td>This study</td>
</tr>
</tbody>
</table>
Africa, the medications recommended for the chemoprophylaxis of malaria include doxycycline, which has the added advantage of being effective against rickettsioses (33).

This study showed the wide distribution and high incidence of R. felis infection; therefore, rickettsiosis should be considered one of the major causes of febrile diseases in sub-Saharan Africa. The demonstrated geographic distribution, seasonality, target population, incidence of relapses or re-infections, and asymptomatic infections of R. felis infection are similar to malaria. Further studies are needed to investigate the hypotheses that humans, as for epidemic typhus, another vector-borne relapsing rickettsiosis, or apes could be reservoirs and mosquitoes could be a vector for R. felis infection.

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Dr Socolovschi is a physician of infectious diseases and tropical medicine at the Medical School of Marseille, France. Her research interests focus on vector-borne infectious tropical diseases and medical entomology.

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Common Epidemiology of *Rickettsia felis* Infection and Malaria, Africa

Technical Appendix

Technical Appendix Table. Rural health centers and laboratories that participated in study of epidemiology of *Rickettsia felis* infection and malaria, featuring the demography, geography, and climate of the study regions*

<table>
<thead>
<tr>
<th>Country and study site (site abbreviation)</th>
<th>Region/department/district</th>
<th>Population size</th>
<th>Climate, vegetation</th>
<th>Annual precipitation, mm</th>
<th>Village</th>
<th>Coordinates</th>
<th>Other activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senegal Dielmo-Ndiop (S₁-S₂)</td>
<td>Toubacouta/Foundiougne/Fatick</td>
<td>120,554</td>
<td>Sudanian†, wooded savannah</td>
<td>939</td>
<td>Dielmo</td>
<td>13°43′N, 16°24′W</td>
<td>Point-of-care laboratory</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ndiop</td>
<td>13°41′N, 16°23′W</td>
<td>None</td>
</tr>
<tr>
<td>Keur Momar Sarr (S₃)</td>
<td>Keur Momar Sarr/Louga/Louga</td>
<td>70,743</td>
<td>Sahelian‡, steppe-type</td>
<td>400</td>
<td>Keur Momar Sarr</td>
<td>15°55′N, 15°58′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Loboudou</td>
<td>15°57′N, 15°55′W</td>
<td>None</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ganket Balla</td>
<td>15°58′N, 15°55′W</td>
<td>None</td>
</tr>
<tr>
<td>Niakhar (S₄)</td>
<td>Niakhar/Fatick/Fatick</td>
<td>69,446</td>
<td>Sahelo-Sudanian§, wooded steppe</td>
<td>757</td>
<td>Toucar</td>
<td>14°32′N, 16°28′W</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Diohine</td>
<td>14°30′N, 16°30′W</td>
<td>None</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ngayokheme</td>
<td>14°32′N, 16°26′W</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Niakhar</td>
<td>14°28′N, 16°23′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td>Basse Casamance (S₅)</td>
<td>Loudia-Oulof/Oussouye/Ziguinchor</td>
<td>57,505</td>
<td>Sub-Guinean¶, primary and secondary gallery forests</td>
<td>1,432</td>
<td>Mlomp</td>
<td>12°33′N, 16°34′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kagnout</td>
<td>12°33′N, 16°37′W</td>
<td>None</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>Elinkine</td>
<td>12°30′N, 16°39′W</td>
<td>None</td>
</tr>
<tr>
<td>Kedougou (S₆)</td>
<td>Bandafassi/Kedougou/Kedougou</td>
<td>20,021</td>
<td>Sudano-Guinean#, woodland, wooded savannah</td>
<td>1,189</td>
<td>Bandafassi</td>
<td>12°32′N, 12°18′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ibel</td>
<td>12°30′N, 12°22′W</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tiabeji</td>
<td>12°38′N, 12°25′W</td>
<td>None</td>
</tr>
<tr>
<td>Country and study site (site abbreviation)</td>
<td>Region/department/district</td>
<td>Population size</td>
<td>Climate, vegetation</td>
<td>Annual precipitation, mm</td>
<td>Village</td>
<td>Coordinates</td>
<td>Other activities</td>
</tr>
<tr>
<td>----------------------------------------</td>
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<td>---------</td>
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<td>------------------</td>
</tr>
<tr>
<td>Mali</td>
<td>Diankambou (M), Mopti</td>
<td>11,333</td>
<td>Sahelian, savannah</td>
<td>580</td>
<td>–</td>
<td>14°35′N; 3°05′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td>Kole–M₂</td>
<td>Sikasso</td>
<td>3,508</td>
<td>Sudano-Guinean, savannahs, forest</td>
<td>700–1,500</td>
<td>–</td>
<td>10°5′N; 7°20′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td>Gabon</td>
<td>Mpasa/Haut-Ogooué</td>
<td>56,000</td>
<td>Equatorial**, savannah and tropical forest</td>
<td>1,862</td>
<td>–</td>
<td>1°37′S; 13°34′E</td>
<td>DNA extraction</td>
</tr>
<tr>
<td>Algeria</td>
<td>Oran Province</td>
<td>18,682,000</td>
<td>Semi-arid climate, halophytic vegetation</td>
<td>326</td>
<td>–</td>
<td>35°41′N; 0°37′W</td>
<td>DNA extraction</td>
</tr>
<tr>
<td>Morocco</td>
<td>Gharb-Chrarda-Béni Hssen</td>
<td>1,859,540</td>
<td>Mild Mediterranean climate, woody flora</td>
<td>750</td>
<td>Sidi Mohamed Lahmar</td>
<td>34°15′N; 6°35′W</td>
<td>None</td>
</tr>
<tr>
<td>Tunisia</td>
<td>Sfax Governorate</td>
<td>2,256,320</td>
<td>Mediterranean climate, wild grasses</td>
<td>465</td>
<td>–</td>
<td>36°48′N; 10°11′E</td>
<td>None</td>
</tr>
<tr>
<td>France</td>
<td>Provence-Alpes-Côte d'Azur</td>
<td>1,582,000</td>
<td>Mediterranean climate, Mediterranean maquis shrubland† †</td>
<td>515</td>
<td>–</td>
<td>43°17′N; 5°22′E</td>
<td>DNA extraction</td>
</tr>
</tbody>
</table>

*– no participants at village level; NA, not applicable.

†Sudanian, tropical semi-arid climate with a mean annual precipitation between around 600 and 800 mm.

‡Sahelian, tropical semi-arid climate with a dry season mainly during the coldest 6 months of the year and a mean annual precipitation =200–400 mm.

§Sahelo-Sudanian tropical semi-arid climate with a mean annual precipitation =400–600 mm.

¶Sub-Guinean, tropical monsoon maritime climate characterized by the changing of dry and wet seasons; mean annual precipitation rate =1200–1500 mm.

#Sudano-Guinean, transitional climate between Sudanian and sub-Guinean climates; annual precipitation = 800–1200 mm.

††Maquis, a shrubland biome in the Mediterranean region, typically consisting of densely growing evergreen shrubs such as holm oak, Kermes Oak, tree heath, strawberry tree, sage, juniper, buckthorn, spurge olive, and myrtle.