Systemic bacterial infections have been found to contribute substantially to the causes of febrile illnesses in sub-Saharan Africa (SSA). In blood cultures, Salmonella enterica, Streptococcus pneumoniae, Staphylococcus aureus, and Escherichia coli are the most common pathogens.1 Bacteria are the most common pathogens.1 Bacteria such as Rickettsia are still underdiagnosed despite their public health importance.2 Besides typhus group and spotted fever group rickettsiae, Rickettsia felis has been recently found to be a potential widespread in SSA, where R. felis-specific circulating DNA has been detected in the blood of up to 15% of febrile patients from Mali, Senegal, Gabon, and Kenya.3–5 However, its role as a pathogen is still unclear and data on the geographical distribution, epidemiology, and clinical features of R. felis are limited. In West Africa, R. felis has been only reported in patients from the Sahel-zone countries of Mali and Senegal.4–6 Since appropriate diagnostic methods are largely unavailable and standard antibiotic regimens usually do not cover Rickettsia spp., further data are critical to aid physicians in the empirical management of febrile illness.

We screened blood samples from febrile children to evaluate the epidemiology and clinical features of rickettsial disease in Ghana. Recruitment took place at St. Michael's Hospital, Pramso, located in the suburban belt of Kumasi, the capital of Ghana's Ashanti Region, where malaria is endemic with high transmission intensity throughout the year.8 Venous blood was taken from all children below 15 years of age visiting the outpatient department with fever ≥ 38°C (tympanic) between January and December 2010. Blood cultures and malaria microscopy (thick and thin films) were done at each presentation and a blood sample (ethylene-diaminetetraacetic acid [EDTA]) was stored for further diagnostics. Rickettsia polymerase chain reaction (PCR) was performed on 470 randomly selected blood samples, from patients with negative blood cultures and reporting regular contact with domestic animals.

For molecular diagnosis of Rickettsia spp., total DNA was extracted from EDTA-blood and tested by real-time PCR targeting the rickettsial gltA gene, using previously reported oligonucleotides.8 The amplicons were bidirectionally sequenced (Seqlab, Göttingen, Germany) and were 100% identical with R. felis upon BLAST analysis (https://blast.ncbi.nlm.nih.gov/Blast.cgi). Species identification was confirmed using a second real-time PCR specific for theompB sequence of R. felis (see Supplemental Material for details on molecular methods).10 No other Rickettsia species were found. In total, 470 blood samples from 431 individuals were tested. Of the 431 individuals, 216 (50.1%) were females and median age at presentation was 38 months (interquartile range [IQR]: 12–71). 204 (43%) samples were malaria positive. R. felis was found in seven (1.5%) samples from six (1.4%) individuals (three males and three females) out of whom one tested positive twice during the study period. The median age of positive patients was 35 months (IQR: 12–59), with the youngest positive patient 1 month and the oldest 87 months of age (Table 1).

Apart from fever, R. felis-positive patients complained of cough (six out of seven visits) and vomiting (four out of seven visits); however, there were no reports of rash. Malaria coinfection was found in the three oldest positive patients and was absent in patients younger than 36 months. None of the R. felis-positive patients had started antibiotic or antimalarial treatment before presentation and one patient was admitted for treatment. No patient received empirical antimicrobial therapy covering Rickettsia spp. (Table 1).

One patient tested positive for Rickettsia at two out of three visits: Plasmodium falciparum alone was detected on January 25, 2012; R. felis was detected on June 12, 2012 with no concurrent malaria infection identified; at the third presentation on August 17, 2012, a clinical diagnosis of severe malaria was made and tests were positive for both P. falciparum and R. felis. The patient was hospitalized, treated for severe malaria, and discharged 5 days later.
R. felis has been associated with febrile infections and symptoms similar to murine typhus, and was implicated as the causative agent of vesicular fever (‘yaaf’). It occurs worldwide, but data on its distribution in Africa are limited. Here, we report the first detection of R. felis in Ghana with 1.5% of febrile pediatric patients being infected. No other rickettsial pathogen was detected. Although infections with the primarily tick-borne spotted fever group rickettsiae appear to be common in West Africa, as suggested by high seroprevalences in Côte d’Ivoire (35%) and Burkina Faso (36%), R. felis as a member of the transitional group rickettsiae has only been detected in West Africans from the Sahel-zone countries of Senegal and Mali, where up to 24% of febrile patients were PCR positive.

Malaria coinfection was present in three out of seven R. felis-positive patients, and all coinfected patients were older than 36 months. Although these observations need to be interpreted with care, they are consistent with similar findings from Senegal, where coinfection was commonly observed and mostly occurred in older children. Similar age and seasonality patterns of infection, along with the recently reported potential of Anopheles gambiae mosquitoes to transmit R. felis, have given rise to a new hypothesis on possible common transmission routes of R. felis and malaria.

The clinical significance of R. felis infection and malaria–R. felis coinfection has been controversially discussed. In our study, all patients were febrile, but additional symptoms were nonspecific. No rash was found, which is consistent with other reports from Africa. Remarkably, some authors have detected R. felis DNA in blood samples of afebrile individuals, albeit at lower percentages than in febrile patients, thus challenging its role as an obligate pathogen. None of our R. felis-positive patients received empirical antimicrobial treatment covering Rickettsia spp. and the course of disease could not be monitored as patients were treated on an outpatient basis. Our study design did not allow the definitive determination of R. felis as the disease-causing agent. It also remains unclear whether a coinfection with malaria alleviated or aggravated the course of disease.

The significance of repeated detection of R. felis, as seen in one of our patients and also observed in other studies, is subject to ongoing discussion and may be explained either by persistence or reinfection. The detection of R. felis in afebrile individuals has furthermore led to the hypothesis that humans could be a natural reservoir of R. felis. However, as R. felis DNA has also been detected on the skin of healthy Senegalese villagers and in the feces of several arthropod vectors such as Ctenocephalides felis or Liposcelis bostrychophila, it is still unclear to which extent these findings may be influenced by skin contamination.

In conclusion, our study is the first report on the detection of R. felis in febrile children in Ghana, and thus adds to the growing evidence for a widespread occurrence of R. felis in SSA. To better understand the pathogenesis of R. felis infections, future studies should longitudinally monitor the presence of R. felis DNA and specific antibodies following infection, and use control groups to determine the clinical significance of R. felis, both in the absence and presence of malaria coinfection as well as in asymptomatic patients.

Received September 16, 2016. Accepted for publication December 7, 2016.

Published online January 23, 2017.

Note: Supplemental information appears at www.ajtmh.org.

Financial support: This work was supported by grants from the German Center for Infection Research (Deutsches Zentrum für Infektionsforschung, DZIF, www.dzif.de) to Ralf Krumkamp (grant number: 80 00 201-3, TI 03.001) and Benno Kreuels (grant number: TI 07.001).

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors’ addresses: Peter Sothmann, Division of Tropical Medicine, 1st Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, and Infectious Disease Epidemiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, E-mail: p.sothmann@uke.de. Christian Keller, Institute of Virology, University Hospital Giessen and Marburg, Marburg, Germany, E-mail: christian.keller@staff.uni-marburg.de. Ralf Krumkamp and Juergen May, Infectious Disease Epidemiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, and German Center for Infection Research (DZIF), Partner Site Hamburg-Borstel-Lübeck, Hamburg, Germany, E-mails: krumkamp@bnitm.de and may@bnitm.de. Benno Kreuels, Division of Tropical Medicine, 1st Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, Infectious Disease Epidemiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, and German Center for Infection Research (DZIF), Partner Site Hamburg-Borstel-Lübeck, Hamburg, Germany, E-mail: kreuels@bnitm.de; Cassandra Aldrich, Stefanie Steierberg, Doris Winter, and Daniel Eibach, Infectious Disease Epidemiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, E-mails: aldrich@bnitm.de, stefanie@steierberg.de, winter@bnitm.de, and eibach@bnitm.de; Nimako Sarpong, Kennedy Gyau Boahen, and Ellis Owusu-Dabo, Kumasi Centre for Collaborative Research in Tropical Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, E-mails: nimakosarpong@yahoo.com, gyauken@kccr.de, and owusudabo@kkcr.de.

REFERENCES


