

***Rickettsia felis* Infection in Man, France**

To the Editor: In August 2008, a 64-year-old man was admitted to the Salon-de-Provence Hospital, France. He had fever (39°C) and a maculopapular rash. No eschars or adenopathy were noted. The patient had a relatively mild illness; the only abnormal laboratory values were elevated aminotransferase levels (aspartate aminotransferase 85 U/L and alanine aminotransferase 135 U/L). The man was an agricultural worker who had originated from Algeria but at this time lived in a shelter in southern France. His potential for contact with dogs in his environment was noted, but no history of flea exposure was elicited. This disease was postulated to be rickettsiosis because no other cause for his fever and rash was evident. Doxycycline was then administered, and the patient rapidly improved.

Serum testing at the Unité des Rickettsies (Marseilles, France), using a multiple-antigen immunofluorescent assay (1), showed the following titers: spotted fever group (SFG) (e.g., *Rickettsia felis*, *R. conorii*, *R. aeschlimannii*, *R. massiliae*) 1,024 and 512 for immunoglobulin (Ig) G and IgM, respectively, and typhus group 512 and 256 for IgG and IgM, respectively. Serum was tested by real-time PCR by using a probe that enabled screening for spotted fever and a probe specific for *R. felis*; results were negative. A Western blot with cross-adsorption (2) showed *R. felis* as the causative agent (Figure). At a follow-up visit 3 months later, the patient had no signs or symptoms.

Rickettsiae were first described in the cat flea (*Ctenocephalides felis*) in 1918 and tentatively named *R. ctenocephali*. However, this work was overlooked until 1990, when an ELB agent was found in *C. felis* fleas by electron microscopy (3); the agent was

demonstrated to be a *Rickettsia*-like organism. Results of subsequent studies were controversial because of suspected contamination of cultures. The species *R. felis* was formally validated by molecular criteria in 2001, and the reference strain was isolated in 2002 (4). *R. felis* has been demonstrated to belong to the SFG (5).

R. felis is distributed worldwide (online Technical Appendix, available from www.cdc.gov/EID/content/15/7/1126-Techapp.pdf), although it has not been found in the northern, coldest regions. The vectors described include fleas, ticks, and mites; however, the only currently recognized vector is the *C. felis* flea (6). The reported hosts for these vectors are mainly cats, dogs, and rodents. *R. felis* is the only SFG species that is transmitted by fleas. Studies have confirmed that *R. felis* in *C. felis* flea populations is mostly maintained by transstadial and transovarial transmission (7). Levels of *R. felis* infestation in *C. felis* fleas are variable, and the specific mechanisms of maintenance within each flea remain unknown. Prevalence is increased by fleas feeding on mammalian hosts infected with *R. felis*. Nevertheless, the precise relationship between the vector and the host remains unknown, and the mechanisms of rickettsial replication have not yet been examined (7).

We searched PubMed and found reports (case reports and seroprevalence studies) of 68 *R. felis* infections. Cases have been reported in the Americas, Asia, Tunisia, and Europe (online Technical Appendix). Such clinical cases rarely occur in warm countries, unlike the worldwide distribution of the bacteria, mentioned above. Reports of human infection with *R. felis* are rare, but the organism is frequently isolated from fleas.

We summarized the available clinical findings for 34 persons infected with *R. felis*: 32 had fever; 24, cutaneous rash (mostly maculopapular); 4, cutaneous eschar; 5, neurologic signs; 7, digestive symptoms; 3, cough without pneumonia; and 2, pneumonia. Clinical findings for *R. felis* are often confused with those found for patients with murine typhus or other febrile illnesses, and they appear to be more complex and more severe than initially thought.

R. felis infections can be diagnosed by serologic testing (1), molecular analysis, or a combination of each. Several molecular methods for detection of *R. felis* have focused on the presence of several genes, but real-time PCR assays are becoming increasingly useful (8). Serologic profiles for *R. felis* infections differ; cross-reactions with SFG rickettsiae as well as with

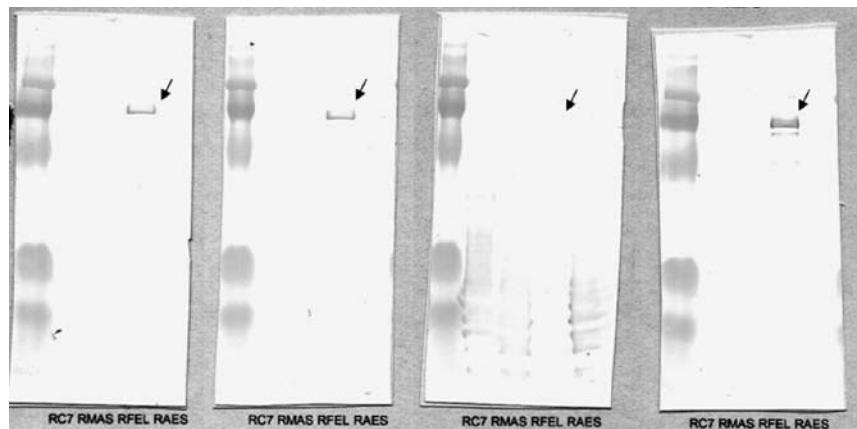


Figure. Western blot after cross-adsorption with (left to right) *Rickettsia conorii*, *R. massiliae*, *R. felis*, and *R. aeschlimannii*. When cross-adsorption is performed with *R. felis*, the specific antigen-corresponding line disappears, which indicates *R. felis* as the causative microorganism.

SFG rickettsiae and *R. typhi* have been observed, but a lack of cross-reactions has also been observed (9). It has been noted (10) that when cross-reactions were observed between *R. felis* and both *R. conorii* and *R. typhi*, the infection was probably related to *R. felis*. When cross-reactions were observed between *R. felis* and only *R. typhi*, the causative agent was most probably of the typhus group.

R. felis infections occur globally and are linked to the worldwide distribution of vectors, but the occurrence is relatively rare when compared with the high frequency of *R. felis* infections related to flea infestation. Human infections remain poorly characterized and are apparently underappreciated, possibly because of the lack of specific signs and symptoms. Further characterization of the interactions between *R. felis* and fleas could elucidate the particular epidemiology and pathology of flea-borne spotted fever.

This work was supported by the French Centre National de la Recherche Scientifique.

**Aurélie Renvoisé,
Antoine-Yves Joliot,
and Didier Raoult**

Author affiliations: Université de la Méditerranée, Marseille, France (A. Renvoisé, D. Raoult); and Centre Hospitalier de Salon de Provence, Salon-de-Provence, France (A.-Y. Joliot)

DOI: 10.3201/eid1507.090029

References

1. Rolain JM, Gouriet F, Brouqui P, Larrey D, Janbon F, Vene S, et al. Concomitant or consecutive infection with *Coxiella burnetii* and tickborne diseases. *Clin Infect Dis*. 2005;40:82–8. DOI: 10.1086/426440
2. La Scola B, Raoult D. Laboratory diagnosis of rickettsioses: current approaches to diagnosis of old and new rickettsial diseases. *J Clin Microbiol*. 1997;35:2715–27.
3. Schriefer ME, Sacci JB Jr, Dumler JS, Bullen MG, Azad AF. Identification of a novel rickettsial infection in a patient diagnosed with murine typhus. *J Clin Microbiol*. 1994;32:949–54.
4. La Scola B, Meconi S, Fenollar F, Rolain JM, Roux V, Raoult D. Emended description of *Rickettsia felis* (Bouyer et al. 2001), a temperature-dependent cultured bacterium. *Int J Syst Evol Microbiol*. 2002;52:2035–41. DOI: 10.1099/ijs.0.02070-0
5. Mehrej V, El Karkouri K, Raoult D. Whole genome-based phylogenetic analysis of rickettsiae. *Clin Microbiol Infect*. 2009. In press.
6. Pérez-Osorio CE, Zavala-Velázquez JE, Arias León JJ, Zavala-Castro JE. *Rickettsia felis* as emergent global threat for humans. *Emerg Infect Dis*. 2008;14:1019–23. DOI: 10.3201/eid1407.071656
7. Reif KE, Stout RW, Henry GC, Foil LD, Macaluso KR. Prevalence and infection load dynamics of *Rickettsia felis* in actively feeding cat fleas. *PLoS One*. 2008;3:e2805. DOI: 10.1371/journal.pone.0002805
8. Henry KM, Jiang J, Rozmajzl PJ, Azad AF, Macaluso KR, Richards AL. Development of quantitative real-time PCR assays to detect *Rickettsia typhi* and *Rickettsia felis*, the causative agents of murine typhus and flea-borne spotted fever. *Mol Cell Probes*. 2007;21:17–23. DOI: 10.1016/j.mcp.2006.06.002
9. Pérez-Arellano JL, Fenollar F, Angel-Moreno A, Bolaños M, Hernández M, Santana E, et al. Human *Rickettsia felis* infection, Canary Islands, Spain. *Emerg Infect Dis*. 2005;11:1961–4.
10. Znazen A, Rolain JM, Hammami A, Jemaa MB, Raoult D. *Rickettsia felis* infection, Tunisia. *Emerg Infect Dis*. 2006;12:138–40.

Address for correspondence: Didier Raoult, Unité des Rickettsies, CNRS-IRD UMR 6236-198, Université de la Méditerranée, Faculté de Médecine, 27 blvd Jean Moulin, 13385 Marseille CEDEX 5, France; email: didier.raoult@gmail.com

Rapid Increase of Scrub Typhus, South Korea, 2001–2006

To the Editor: Scrub typhus, or tsutsugamushi disease, is a febrile illness caused by the rickettsial bacteria *Orientia tsutsugamushi*. Scrub typhus is endemic to a geographically distinct region, the so-called tsutsugamushi triangle, which includes Japan, Taiwan, China, and South Korea (1,2). Scrub typhus is a public health issue in Asia, where 1 billion persons may be at risk for the disease (3). In South Korea, scrub typhus is the most common rickettsial disease, and public health authorities are concerned about its increased incidence.

Scrub typhus has been a reportable disease in South Korea since 1994. Physicians who diagnose suspected or confirmed cases must report these cases to their local health bureau and the Korea Centers for Disease Control and Prevention (KCDC) through the National Notifiable Disease Surveillance System (NNDSS). For a patient's illness to meet the case definition for scrub typhus, the clinical signs (acute febrile illness and skin eschar) must be present or there must be laboratory confirmation (4-fold rise in antibody titer, antigen detected in blood, or genetic material detected by PCR).

We analyzed NNDSS data confirmed by KCDC and classified all reported cases into 2 groups according to residential area. Cases with rural administrative address codes “eup” or “myun” were defined as rural cases, whereas cases with a city administrative address code of “dong” were defined as urban cases. All case-patients were classified by occupation as farmer or nonfarmer; all agricultural, fishery, and forest workers from rural areas were defined as farmers.

In total, 23,929 cases, including 16,199 (67.7%) serologically con-



Rickettsia felis Infection in Man, France

Technical Appendix

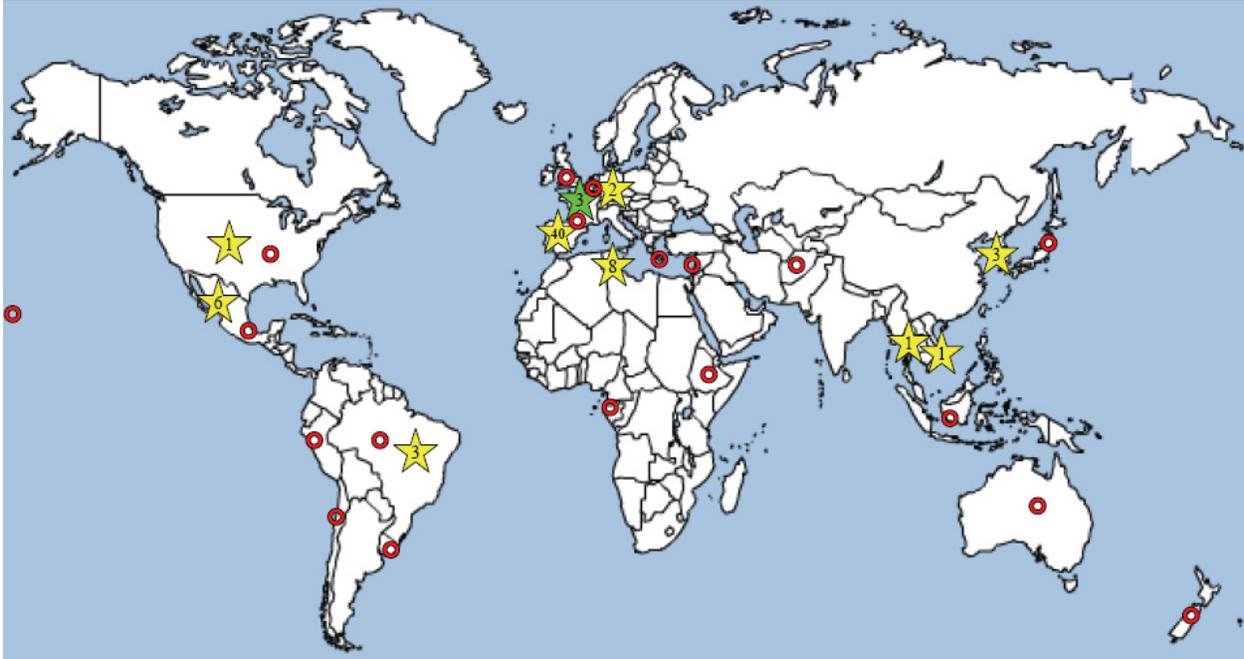


Figure. Distribution of clinical findings of *Rickettsia felis* infections and of reported potential vectors infected with *R. felis*. The numbers in the stars indicate the number of clinical cases (green star indicates case reported in this article), and the circles indicate locations of potential infected vectors per country. References are as follows: Texas (1), Mexico (2–4), Brazil (3,5), South Korea (6), Laos (7), Thailand (8), Tunisia (9), Germany (10), Spain (11–14), and France (5).

References

1. La Scola B, Meconi S, Fenollar F, Rolain JM, Roux V, Raoult D. Emended description of *Rickettsia felis* (Bouyer et al. 2001), a temperature-dependent cultured bacterium. *Int J Syst Evol Microbiol*. 2002;52:2035–41. [Medline DOI: 10.1099/ijss.0.02070-0](https://doi.org/10.1099/ijss.0.02070-0)
2. Zavala-Velázquez JE, Ruiz-Sosa JA, Sánchez-Elias RA, Becerra-Carmona G, Walker DH. *Rickettsia felis* rickettsiosis in Yucatán. *Lancet*. 2000;356:1079–80. [Medline DOI: 10.1016/S0140-6736\(00\)02735-5](https://doi.org/10.1016/S0140-6736(00)02735-5)
3. Galvão MA, Zavala-Velazquez JE, Zavala-Castro JE, Mafra CL, Calic SB, Walker DH. *Rickettsia felis* in the Americas. *Ann N Y Acad Sci*. 2006;1078:156–8. [Medline DOI: 10.1196/annals.1374.027](https://doi.org/10.1196/annals.1374.027)

4. Zavala-Velazquez J, Laviada-Molina H, Zavala-Castro J, Pérez-Osorio C, Becerra-Carmona G, Ruiz-Sosa JA, et al. *Rickettsia felis*, the agent of an emerging infectious disease: report of a new case in Mexico. Arch Med Res. 2006;37:419–22. [Medline DOI: 10.1016/j.arcmed.2005.08.003](#)
5. Raoult D, La Scola B, Enea M, Fournier PE, Roux V, Fenollar F, et al. A flea-associated *Rickettsia* pathogenic for humans. Emerg Infect Dis. 2001;7:73–81. [Medline](#)
6. Choi YJ, Jang WJ, Ryu JS, Lee SH, Park KH, Paik HS, et al. Spotted fever group and typhus group rickettsioses in humans, South Korea. Emerg Infect Dis. 2005;11:237–44. [Medline](#)
7. Phongmany S, Rolain JM, Phetsouvanh R, Blacksell SD, Soukkhaseum V, Rasachack B, et al. Rickettsial infections and fever, Vientiane, Laos. Emerg Infect Dis. 2006;12:256–62. [Medline](#)
8. Parola P, Miller RS, McDaniel P, Telford SR III, Rolain JM, Wongsrichanalai C, et al. Emerging rickettsioses of the Thai-Myanmar border. Emerg Infect Dis. 2003;9:592–5. [Medline](#)
9. Znazen A, Rolain JM, Hammami A, Jemaa MB, Raoult D. *Rickettsia felis* infection, Tunisia. Emerg Infect Dis. 2006;12:138–40. [Medline](#)
10. Richter J, Fournier PE, Petridou J, Häussinger D, Raoult D. *Rickettsia felis* infection acquired in Europe and documented by polymerase chain reaction. Emerg Infect Dis. 2002;8:207–8. [Medline](#)
11. Bernabeu-Wittel M, del Toro MD, Nogueras MM, Muniain MA, Cardeñosa N, Márquez FJ, et al. Seroepidemiological study of *Rickettsia felis*, *Rickettsia typhi*, and *Rickettsia conorii* infection among the population of southern Spain. Eur J Clin Microbiol Infect Dis. 2006;25:375–81. [Medline DOI: 10.1007/s10096-006-0147-6](#)
12. Nogueras MM, Cardeñosa N, Sanfeliu I, Muñoz T, Font B, Segura F. Serological evidence of infection with *Rickettsia typhi* and *Rickettsia felis* among the human population of Catalonia, in the northeast of Spain. Am J Trop Med Hyg. 2006;74:123–6. [Medline](#)
13. Oteo JA, Portillo A, Santibáñez S, Blanco JR, Pérez-Martínez L, Ibarra V. Cluster of cases of human *Rickettsia felis* infection from southern Europe (Spain) diagnosed by PCR. J Clin Microbiol. 2006;44:2669–71. [Medline DOI: 10.1128/JCM.00366-06](#)
14. Pérez-Arellano JL, Fenollar F, Angel-Moreno A, Bolaños M, Hernández M, Santana E, et al. Human *Rickettsia felis* infection, Canary Islands, Spain. Emerg Infect Dis. 2005;11:1961–4. [Medline](#)