Rickettsia felis and Changing Paradigms about Pathogenic Rickettsiae

To the Editor: Mediannikov et al. recently reported several features common to the epidemiology of Rickettsia felis infection and malaria in Africa (1). Similar to the findings of several other recent studies in Africa (2,3), the authors diagnosed R. felis infection in febrile—and to a lesser extent in afebrile—persons by detecting R. felis DNA in human blood samples processed by highly sensitive real-time PCR. These results challenge some paradigms in rickettsiology that need to be more critically evaluated.

Because R. felis DNA was detected in circulating blood of asymptomatic persons (albeit more frequently in patients with mild febrile illness), Mediannikov et al. proposed that humans could be a natural reservoir of R. felis, as they are for malaria parasites. R. felis antibodies failed to develop in nearly all patients in whom R. felis DNA was detected, even after repeated detection of R. felis DNA. In 2 other studies, the same researchers proposed that patients might have several episodes of R. felis infection (relapse or reinfection) to explain why DNA of the agent was detected in the blood at multiple times (2,3). They also proposed that the absence of an antibody response would explain why the disease relapses in some persons (3).

These changing paradigms in rickettsiology require thorough evaluation. Once inside a vertebrate host, pathogenic rickettsiae have been believed to multiply primarily within endothelial cells in the patient’s organs. As far as we know, rickettsiae do not multiply within circulating blood cells (4). In contrast, the agents of malaria (Plasmodium spp.) are typically parasites of erythrocytes. Therefore, a blood sample from a person with malaria is an excellent source for PCR diagnostic testing. The sensitivity of PCR for rickettsiae in human blood samples is very low because the sensitivity depends on the magnitude of the vasculitic lesions, i.e., the number of endothelial cells destroyed or detached by rickettsial growth, resulting in circulating rickettsiae. R. conorii (5) and R. rickettsii (6) were detected by highly sensitive PCR in 100% of fatal cases and in only very few nonfatal cases.

In addition to never having been isolated from humans, R. felis has many characteristics of a symbiotic organism. It possesses a mosaic structure genome (size 1.48 Mb) with a high coding capacity (83%) that is typical of symbiotic bacteria (7). Merhej et al. have proposed that within a given bacterial genus (including Rickettsia), pathogenic species have smaller genomes than nonpathogenic species (8). In the genus Rickettsia, the pathogens R. rickettsii, R. prowazekii, R. sibiriaca, R. typhi, R. parkeri, and R. conorii have genomes of ≈1.2–1.3 Mb, whereas the apparently nonpathogenic R. bellii has a 1.5-Mb genome, similar to that of R. felis. In contrast to the well-known pathogenic Rickettsia species, R. felis has been reported in a variety of invertebrate hosts, including hematophagous (fleas, ticks, flies, mosquitoes) and non-hematophagous (book lice) arthropods (9). Behar et al. have suggested that R. felis is responsible for inducing parthenogenesis in book lice, similar to the manner of Wolbachia organisms in various invertebrate hosts (9). Furthermore, R. felis forms mycetomes in book lice, a growth feature typical of bacterial endosymbionts (10).

The current view in rickettsiology has a strong anthropocentric bias because the studies have concentrated on parasitic arthropods that feed on humans rather than on free-living arthropods. In fact, the number of Rickettsia species associated with nonhematophagous hosts might be much greater than the ones of medical importance (9). Thus, considering R. felis as an important pathogen in Africa (and in the world) might be premature. Several questions need to be answered before such a conclusion. In asymptomatic persons in whom endothelial cells are likely to be intact, where does R. felis grow to be released at detectable levels in the circulating blood? Considering that all classical spotted fever agents induce an antibody response (4), why do R. felis antibodies fail to develop in humans after a clinical illness attributed to R. felis? In addition, repeated reports that the main vector of R. felis is the cat flea, Ctenocephalides felis, need to be proven by experimental demonstration of its vector capacity.

Given the numerous questions about R. felis, we would add another: could R. felis be a symbiont of a human parasite, such as a protozoan or a helminth? Obviously, the answer is unknown. However, had we not known that Wolbachia organisms are typically endosymbiotic bacteria of both human and animal filarial nematodes, what would we conclude if we detected Wolbachia DNA in blood of either asymptomatic or ill patients?

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References
1. Mediannikov O, Socolovschi C, Eduoard S, Fenollar F, Mouffok N, Bassene H, et al. Common epidemiology of Rickettsia felis infection and malaria, Africa. Emerg Infect Dis. 2013;19:1775–83. http://dx.doi.org/10.3201/eid1911.130361
2. Mediannikov O, Fenollar F, Bassene H, Tall A, Sokhna C, Trape JF, et al. Description of “vaill”, the vesicular fever caused by acute Rickettsia felis infection in Senegal. J Infect. 2013;66:536–40. http://dx.doi.org/10.1016/j.jinf.2012.10.005
Pulmonary Disease Caused by Mycobacterium marseillense, Italy

To the Editor: Mycobacterium marseillense was recently described as a new species belonging to the Mycobacterium avium complex (MAC) (1). We describe a case of pulmonary disease caused by M. marseillense in an immunocompetent patient. All strains isolated from the patient were preliminarily identified as M. intracellulare; however, a retrospective molecular analysis corrected the identification to M. marseillense.

In December 2005, a 65-year-old man was admitted to the University Hospital, Modena, Italy, with a 2-week history of fever, cough, and hemoptysis. Physical examination detected diffuse rales, and chest radiographs showed a diffuse nodular opacity and bronchial thickening, confirmed by high-resolution computed tomography (CT) of the chest (Figure, panel A). The patient had experienced several previous episodes of hemoptysis and persistent productive cough since 1998, and tubular bronchiectasis had been detected on previous high-resolution CT images. The patient had a history of thalassemia minor, was HIV negative, and was formerly a mild smoker (10 cigarettes/day for 4 years during his youth). He had no chronic disorders and no history of immunosuppressive-drug or alcohol use.

Bacterial and fungal cultures and a smear for acid-fast bacilli performed on a bronchoalveolar lavage (BAL) sample were all negative. A nontuberculous mycobacterium strain was isolated by culture and preliminarily identified as M. intracellulare by using the GenoType Mycobacterium CM/AS Kit (Hain Lifesciences, Nehren, Germany). At that time, a drug susceptibility test for isoniazid, rifampin, streptomycin, and ethambutol was improperly performed (i.e., was not applicable for MAC) by using the agar proportion method; sensitivity information for macrolides was unavailable. The strain was resistant to ethambutol and susceptible to the other drugs. The physician prescribed rifampin, isoniazid, and amikacin. After remission of fever and hemoptysis and improvement of chronic cough, the patient was discharged from the hospital.

In March 2006, he was readmitted to the hospital for worsening of his condition and onset of side effects associated with rifampin and isoniazid use. The treatment was discontinued and replaced by levofloxacin, terizidone, and azithromycin, which resulted in remission of symptoms. This therapy was continued after hospital discharge.

In 2007, the patient was twice admitted for follow-up and microbiological testing to determine bacteriologic status. All 3 separate sputum samples were negative for mycobacteria, other bacteria, and fungi. However, BAL sample culture results were positive for the same mycobacterium despite continued therapy with levofloxacin, terizidone, and azithromycin.

During 2008, as an investigation of the possibility of persistent excretion of organisms, additional samples were collected 5 times. The sputum cultures were intermittently positive, while the BAL sample cultures were persistently positive.

In May 2009, after the patient had been persistently stable and had negative culture results for 14 months, the antimicrobial drug therapy was stopped. In December 2010, the patient’s only symptom was persistent productive cough; however, the sputum culture was again positive, and high-resolution CT revealed a worsening condition of his lungs (Figure, panel B). A new antimycobacterial drug regimen of ethambutol, rifampin, and azithromycin was started, in accordance with the international