Vector-Borne Rickettsioses in North Africa

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KEYWORD

• Fleas • Ticks • Lice • Rickettsioses • North Africa

KEY POINTS

- Rickettsioses are an important causes of fever in North Africa and in travellers returned from this area.
- Fever, rash and eschar are typical signs for rickettsioses. When typical signs are lacking, rickettsioses can be misdiagnosed with many other infectious diseases.
- An history of exposure to ticks, lice, or fleas has to be investigate in patients with fever, including the returned travelers.
- Prevention of rickettsioses is based on appropriate mesure to avoid tick, flea, and lice bites.
- Doxycycline remains the treatment of choice for rickettsioses.

INTRODUCTION

Rickettsiae are obligate intracellular bacteria within the family *Rickettsiaceae* of the order *Rickettsiales*. They are associated with both vertebrate and invertebrate hosts, but rickettsial species differ in terms of their associations with arthropods, behavior of the vector to infection, pathophysiology, and outcome of the disease. The rickettsial field has undergone a significant evolution due to technological advances in molecular genetics and genomics. The taxonomy of rickettsiae has been reorganized and continues to be modified as new data become available.[1] Currently, 25 species are recognized in the *Rickettsia* genus, which is divided into 2 main groups: the spotted fever group (SFG) and the typhus group (TG) rickettsia.[2]

Rickettsioses represent some of the oldest known vector-borne diseases, which cause mild to fatal diseases in people. In North Africa, which the United Nations defines

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as the northernmost region of the African continent, including 8 countries or territories: Algeria, Egypt, Libya, Morocco, South Sudan, Sudan, Tunisia, and western Sahara (http://millenniumindicators.un.org/unsd/methods/m49/m49regi), SFG and TG rickettsiosis have been described since the beginning of the 20th century.[3] The first clinical cases of Mediterranean spotted fever (MSF), which were caused by *Rickettsia conorii*, were described in 1910 by Conor and Brush of the Pasteur Institute in Tunis, Tunisia.[3] Subsequently, Conor and Hayat described the clinical features (an abrupt onset, high fever, headache, chills, arthromyalgias, and conjunctivitis) of another 4 clinical cases in Tunisia.[4] The exanthema was papular rather than macular, which they termed bouton, often turned red–purple in color, and involved the palms and soles. The duration of the illness was 12 to 15 days with no fatal cases.[4] In 1928, Burnet and Olmer conducted the first experimental infection of a chimpanzee in Tunisia. After 10 days with a fever, the chimpanzee died.[5] After the discovery of tache noire, an eschar at the point of inoculation of the infectious agent in Marseille, France, all researchers believed in the existence of the disease's vector. At that time, Olmer believed that the vector of the disease was the brown dog tick. In 1930, in Tunisia, this hypothesis was confirmed by Durand and Conseil, who inoculated patients with crushed infected *Rhipicephalus sanguineus* ticks and noted that the patients subsequently contracted MSF.[6] These results were confirmed later by Blanc and Caminopetros in Greece.[7]

The first observations of the role of lice in epidemic typhus transmission (caused by *Rickettsia prowazekii*) were observed in Tunisia by Nicolle,[8] a discovery for which he received the Nobel Prize in 1928. In 1903, Tunis was heavily populated by typhus patients, and Charles Nicolle, director of the Pasteur Institute in Tunis, observed that patients could infect others out on the street and that their clothing was also infectious. After the patients had a hot bath and were dressed in hospital clothing, they ceased to be infectious. Later, he fed uninfected lice to experimentally infected bonnet monkeys (*Macacus sinicus*) and then transferred the lice to uninfected monkeys that later developed typhus.[8] Moreover, Plazy, Marcandier, and Pirot observed the first Mediterranean cases of murine typhus, which was caused by *Rickettsia typhi*, in sailors on warships from Toulon, France. From 1926 to 1932, 135 cases of murine typhus were observed on warships from Toulon. Observations were even made by Lépine in Greece and Liban, by Blanc in Morocco, and by Nicolle in Tunis that indicated the presence of the microorganism in the brains of rats.[9]

After the 1930s, there was an absence of rickettsiosis investigations in North Africa for about 60 years. However, in the early 1970s, *R prowazekii* itself was isolated from the blood of Egyptian donkeys.[10] In contrast, other investigators had previously failed to isolate *R prowazekii* from many species of wild animals and ticks in Egypt and Sudan.[11] Since 1990, there have been a few fragmentary reports on the ecology and epidemiology of rickettsioses in North Africa, including a sero-survey of MSF infections, indicating that the seroprevalence of *R conorii* antibodies among blood donors was 1% in Egypt[12] and 5% to 9% in Tunisia, Algeria, and Morocco.[13,14] Subsequently, an important increase in the number of MSF cases was recorded in northern African countries.[15–17] Moreover, murine typhus is often unrecognized in Africa. However, 43 patient cases from southern Sudan were linked to *R typhi* in 1988 by a sero-survey,[18] and in northern Africa (ie, Tunisia and Algeria), several sporadic cases of typhus were reported in the last decade.[19] Furthermore, *R typhi* antibodies were present in healthy individuals and in patients with acute fevers of an undetermined origin in Tunisia.[16,20]

Several SFG rickettsiae have been detected in arthropods, and among these rickettsiae, some are recognized as emerging pathogens or as potential pathogens. The use of polymerase chain reaction (PCR) and sequencing methods for the identification of SFG and TG rickettsiae in ticks and fleas has led to new questions regarding the