



Review

Syndromic classification of rickettsioses: an approach for clinical practice



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SUMMARY

Rickettsioses share common clinical manifestations, such as fever, malaise, exanthema, the presence or absence of an inoculation eschar, and lymphadenopathy. Some of these manifestations can be suggestive of certain species of *Rickettsia* infection. Nevertheless none of these manifestations are pathognomonic, and direct diagnostic methods to confirm the involved species are always required. A syndrome is a set of signs and symptoms that characterizes a disease with many etiologies or causes. This situation is applicable to rickettsioses, where different species can cause similar clinical presentations. We propose a syndromic classification for these diseases: exanthematic rickettsiosis syndrome with a low probability of inoculation eschar and rickettsiosis syndrome with a probability of inoculation eschar and their variants. In doing so, we take into account the clinical manifestations, the geographic origin, and the possible vector involved, in order to provide a guide for physicians of the most probable etiological agent.

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1. Introduction

Rickettsioses are zoonotic infections caused by obligate intracellular bacteria of the genera *Rickettsia* and *Orientia*, belonging to the family Rickettsiaceae.^{1–3} The lifecycle of these microorganisms is determined by their survival in small mammals (which can act as reservoirs or as amplifiers) and in arthropods, such as ticks, fleas, lice, and mites, which can also act as vectors. In this regard, and with the exception of *Rickettsia prowazekii*, the human is usually an accidental host.⁴

From the first description of *R. prowazekii* as an etiological agent of epidemic typhus in 1916 up to the late 1980s, eight further species were described as causes of rickettsioses around the world: *Rickettsia rickettsii*, *Rickettsia typhi*, *Rickettsia conorii* subsp. *conorii*, *Rickettsia akari*, *Rickettsia sibirica*, *Rickettsia australis*, *Rickettsia conorii* subsp. *israelensis*, and *Orientia tsutsugamushi*.⁵ However, with the development and implementation of molecular biology in the 1990s, this list has since grown and more than 30 species and subspecies are recognized. Most of them have been implicated as human pathogens.⁶

Rickettsioses have no pathognomonic signs, although there are signs and symptoms that are highly suggestive, such as the presence of fever, rash, lymphadenopathy, and an eschar (tache noire). Unfortunately not always and not all rickettsioses present typical signs and symptoms. In most cases clinical suspicion together with a positive serology is sufficient to make the diagnosis of rickettsiosis, although in order to reach an accurate diagnosis and confirm the etiological agent, isolation or molecular biology assays are needed.

By definition, a syndrome is a set of signs and symptoms that characterizes a disease with several causes or etiologies.⁷ This definition is applicable to rickettsioses because different species can cause similar clinical presentations. Therefore, we propose a syndromic classification for these infections (exanthematic rickettsiosis syndrome with a low probability of inoculation eschar and rickettsiosis syndrome with a probability of inoculation eschar and their variants) in order to provide clinicians with a guide to the suspected etiological agent and thus direct the diagnosis taking the clinical manifestations, geographic area, and the possible vector involved into account. We provide only a brief description of the recommended treatment, since the antibiotic management of rickettsioses is simple (doxycycline, except where there are contraindications) and remains the same regardless of the species

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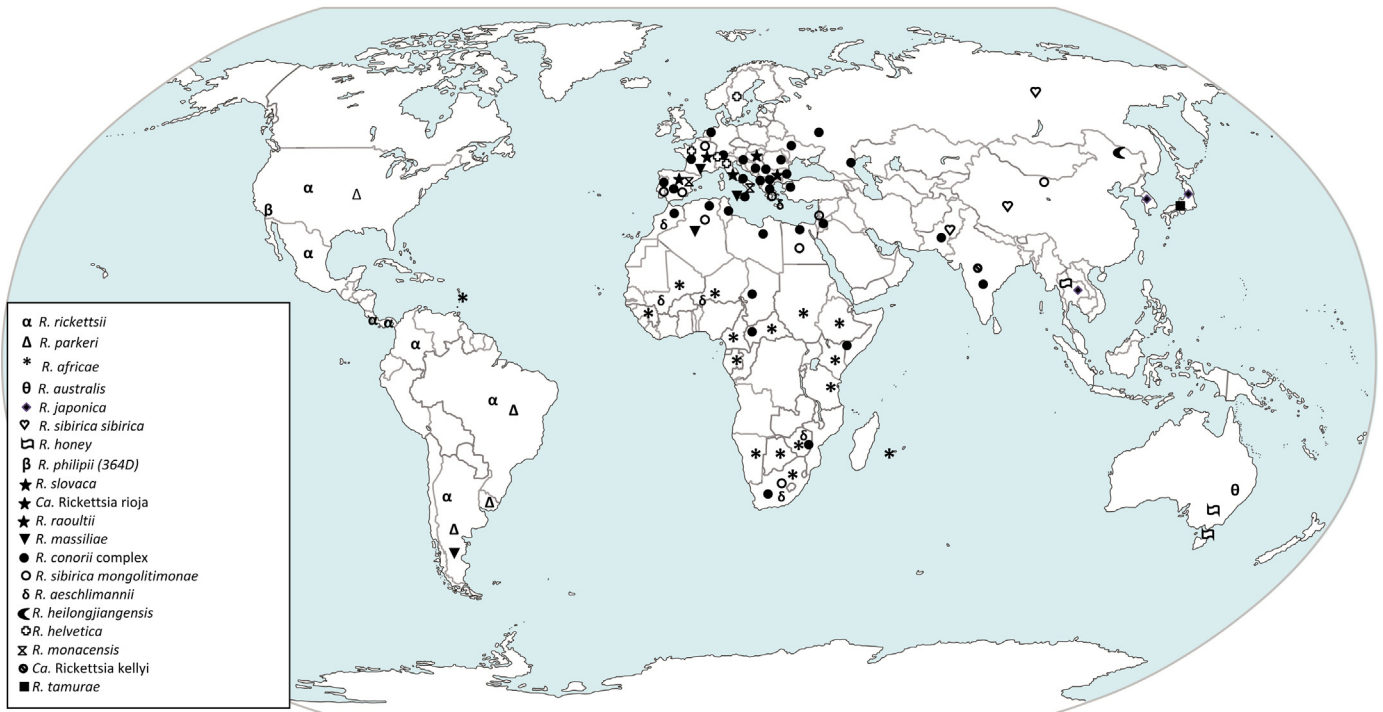


Figure 1. Map showing the distribution of the main human tick-borne rickettsioses.

involved. Figure 1 is a map showing the distribution of the main human tick-borne rickettsioses.

2. Exanthematic rickettsioses syndrome with a low probability of inoculation eschar

This is characterized by an acute febrile illness where a rash is the predominant clinical manifestation and the presence of an inoculation eschar cannot be seen or its presence is exceptional. Two variants are proposed taking into account the distribution of the rash (Figure 2).

2.1. With centripetal rash distribution

This type of rash is characteristic of the rickettsioses caused by *R. rickettsii*. It occurs only in 3–5% in the first 3 days, increasing to 60–70% between days 7 and 10 of the disease.⁸ It usually starts on the wrists and ankles as small not itchy red macular lesions, with subsequent extension to the extremities and palmoplantar and

trunk involvement. Maculopapular, petechial, or purpuric lesions can be observed (Figure 3).⁹ In 10% of cases we do not observe rash, generally in dark skin people and elderly people.¹⁰ In *R. rickettsii* infection, the presence of an inoculation eschar is an unusual finding (only five cases reported in the literature from 1981 to 2012).^{11–14}

The geographical distribution of *R. rickettsii*, the most pathogenic species of the tick-borne rickettsiae, is limited to the Western Hemisphere where its primary vectors are ticks of the genera *Dermacentor*, *Rhipicephalus*, and *Amblyomma* (Table 1).¹⁵

2.2. With centrifugal rash distribution

This is typical of *R. typhi* and *R. prowazekii* infections. The rash usually starts on the trunk and spreads to the extremities without palmoplantar involvement. In both rickettsioses, the exanthema is characterized by macular, maculopapular, or petechial lesions.²⁷ The latter lesions and compromise of the axillary area are more frequent in *R. prowazekii* infection.²⁸ Characteristically, an

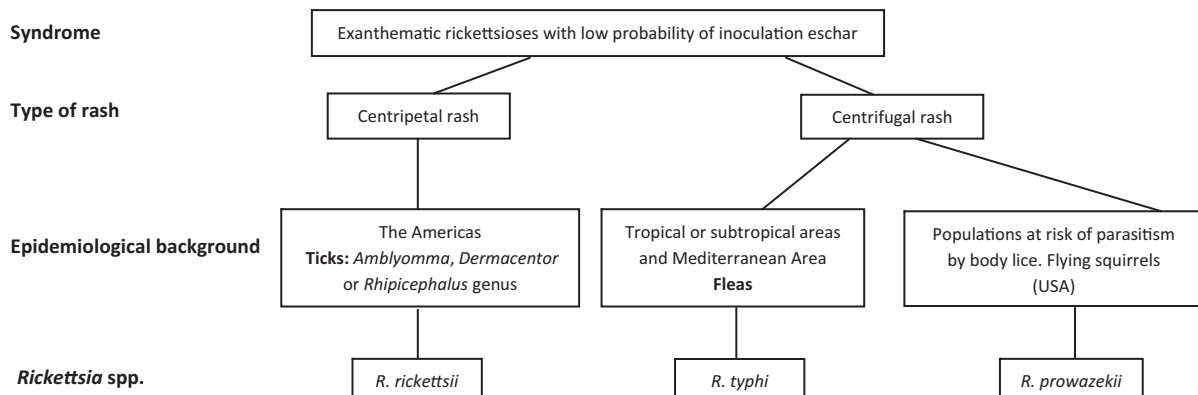


Figure 2. Algorithm for exanthematic rickettsioses and a low probability of inoculation eschar.

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