**Acquisition and Transmission of Spotted Fever Group *Rickettsia* in Tick Vector (*Amblyomma maculatum*)**

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Spotted fever group (SFG) *Rickettsia* species, like Rocky Mountain Spotted Fever, are pathogens commonly associated with insect vectors. Ticks in particular are more commonly associated with SFG *Rickettsia* transmission. Because of their anthropomorphic feeding and broad habitation, ticks are the most effective insect transmitter of the *Rickettsia* species to humans. However, the dynamics of *Rickettsia* species transmission between the ticks and the host are still unclear. Suwanbongkot *et al.* (2019) found higher amounts of *Rickettsia* *parkeri* in the tick salivary glands, saliva, and in the vertebrate host tick feeding sites than *Candidatus* Rickettsia andeanae. They also identified a discernable lesion pattern in vertebrate hosts fed on by *R. parkeri* – infected ticks. These findings suggest patterns of pathogen acquisition and transmission specific to differing species of SFG *Rickettsia* in *Amblyomma maculatum,* as well as identification of pathogens from feeding sites on vertebrate hosts. However, they were unable to fully discern the transmission dynamics of *Rickettsia* species in ticks from their results, due to the conditions of multiple pathogen inoculations of a tick in a natural environment. Further investigations should test characterized rickettsial isolates, utilize bioassays that control for tick variables, and research other tick vectors of major SFG diseases.

**Introduction**

The spotted fever group (SFG) *Rickettsia*, a Gram-negative, obligate intracellular bacteria, is distinctly recognized from other species of *Rickettsia* by their life cycles involving ectoparasitic arthropods such as fleas, mites, and ticks (Socolovschi *et al.*, 2009). Of the arthropod vectors, ticks are the most commonly associated transmitters of SFG *Rickettsia*. According to the Center for Disease Control (CDC), tickborne spotted fever rickettsioses are the most frequently reported travel-associated rickettsial infections (CDC, 2017). The diseases caused by tickborne SFG *Rickettsia* are found worldwide, and include: Rickettsiosis (*R. aeschlimannii*), African tick-bite fever (*R. africae*), Mediterranean spotted fever (or Boutonneuse fever; *R. conorii*), Mediterranean spotted fever-like disease (*R. massiliae*), Mediterranean spotted fever-like illness (*R. monacensis*), Maculatum infection (or Tidewater spotted fever, or American boutonneuse fever; *R. parkeri*), Rocky Mountain spotted fever (or Brazilian spotted fever; *R. rickettsia*), and North Asian tick typhus (or Siberian tick typhus; *R. sibirica mongolotimonae*).

Rickettsial diseases are considered difficult to diagnose, and are most often discernable due to recent travel, animal reservoir interactions, or outdoor activities conducted by the patient. Most rickettsial diseases cause moderately severe illness, with symptoms such as fever, headache, malaise, rash, nausea, and vomiting, as well as a rash or eschar at the site of the tick bite. For more severe diseases such as Rocky Mountain spotted fever and Mediterranean spotted fever, 20-60% of untreated cases may be fatal (CDC, 2017). No vaccine is currently available for preventing rickettsial infections, and treatment is restricted to use of tetracycline, most commonly doxycycline. Therefore, the most effective mode of prevention for spotted fever diseases is to take precautionary measures against tick attachment in endemic areas, such as using insect repellents and protective clothing.

Ticks and other arthropod vectors of SFG *Rickettsia* are optimal vectors of disease due to their wide spread in outdoor environments and variable host feeding. Ticks take a bloodmeal in order to develop and reproduce, and so can feed on as many as 3-4 different hosts in a single life cycle (Socolovschi *et al.*, 2009). The ecology of SFG *Rickettsia* is still unclear, as researchers are unsure whether ticks are the main reservoir. The transmission of *Rickettsia* species in ticks has been observed to move vertically, and horizontally. For vertical movement, the tick spreads the disease to its offspring, therefore the young are already infected prior to host feeding. This is especially problematic because ticks feed in multiple stages during development, so there is an increased likelihood of pathogen transmission to the hosts. In horizontal transmission, the tick acquires the pathogen only after feeding on an infected host. This is a lower likelihood for host infection. Because *Rickettsia* species can be transmitted in both ways, the transmission of the pathogen is optimized. A single infected female can produce thousands of infected young, and an uninfected tick can acquire the pathogen from an infected host after just one feed, after which the pathogen spreads to its own species. Due to the effective pathogen transmission of this system, understanding the dynamics of *Rickettsia* acquisition and transmission is important in discerning potential modes of prevention in the future.

**Recent Progress**

Suwanbongkot *et al.* (2019) investigated the infection and transmission dynamics of *Rickettsia parkeri* and *Candidatus* Rickettsia andeanae in the tick species *Amblyomma americanum*, a vector of multiple *Rickettsia* species. Most often, pathogen acquisition and transmission is observed via the tick saliva, salivary glands, and the host lesion site. In this study,*R. parkeri*-infected *A. maculatum* and *Ca*. R. andeanae-infected *A. maculatum* fed on rats for 2, 6, and 10 days post-attachment (dpa).  Rat tissues, rat blood, tick saliva, and tick salivary glands were collected from the hosts at each time interval and analyzed for concentrations of infection.

From prior knowledge on the transmission of *Rickettsia* species, Suwanbongkot *et al.* (2019) discovered two main pieces of data in the study. One of the major results of the study was a significantly higher bacterial load of *R. parkeri* in both tick saliva and salivary glands when compared to *Ca.* R. andeanae. *Ca.* R. andeanae from tick saliva was found to increase in concentration in relation to the increased feeding activity time. In contrast, *R. parkeri* was 100% positive in all saliva samples across all time points of post-attachment. When the total number of rickettsiae were enumerated, it was also found that the rickettsial load for both *Rickettsia* species was found to reach a 6-day peak in the saliva before decreasing by 10 days. However, the rickettsial load was significantly more for *R. parkeri* in tick saliva than *Ca.* R. andeanae. For the tick salivary glands, both species increased in number over tick feeding. *R. parkeri-*infected salivary glands were again observed to contain higher rickettsial loads. Finally, the salivary glands tended to have a higher density of rickettsial species than the tick saliva.

Another major result of the study was the larger transmission of *R. parkeri* to the vertebrate host skin, as well as more severe lesions. One of the most surprising findings was the detection of *Ca.* R. andeanae on the skin around the tick infestation site only at 10 days of tick feeding. *R. parkeri* detection on the lesion site skin samples were detected at 2, 6, and 10 days of tick feeding. Like the saliva, the highest density of *R. parkeri* on the skin of hosts was at 6 days of feeding. No rickettsial DNA was found from host blood, or skin, away from tick attachment site. The lesion sites had observable differences in characteristics as well, making differentiation between the feeding sites of the two tick species distinguishable. One point was that no immunostaining was observed for any of the rats exposed to *Ca.* R. andeanae-infected tick feeding. Variation in the level of inflammation, stromal pallor, superficial coagulative necrosis, and atrophied hair follicles were the drastic lesion patterns unique of *R. parkeri* that helped to distinguish the pathogen infection in the host.

**Discussion**

The greatest benefits from the results of this study were the characterization of *R. parkeri* in ticks and their hosts in comparison to that of *Ca.* R. andeanae. From these results, it was identified that *R. parkeri*-infected ticks secreted more rickettsiae, and that they secreted more rickettsia in their saliva over the period of bloodmeal acquisition. It was determined that the severity of host lesions coincided with the molecular detection of rickettsia at the tick feeding site of the host. A tick-derived infectious dose and distinct lesion pattern in hosts exposed to *R. parkeri* infected ticks was also identified. This study also suggests the rickettsial load in tick salivary glands and saliva may influence lesion patterns, although there were no observable lesions associated with *Ca.* R. andeanae infection in the host from tick feeding. While lesion patterning helped to distinguish between the two rickettsial species used in this study, it is important to point out that it was established that gross analysis cannot differentiate the infections of rickettsiae species, and it requires microscopic analysis, IHC and PCR assays. It was also suggested that tick saliva influences a hosts response, facilitates rickettsial dissemination, and alters lesions in the vertebrate host.

As Suwanbongkot *et al.* (2019) suggested, the fault of this study is that these ticks are only infected with one species of *Rickettsia.* In reality, a single tick is often infected with multiple pathogens that, when combined, could alter some of the observed characteristics of this study. Therefore, future studies need to identify potentially synergistic interactions between vector saliva and *Rickettsia* species to better understand the transmission kinetics that result in a disease within a natural environment. Another issue is that factors contributing to a feeding threshold prior to rickettsiae being secreted in the saliva and transmitted to the host needs to be identified. This can be assumed from the variable counts of positive rickettsia observed in the tick saliva and salivary glands, as well as the host lesion sites. There is also no prior exploration of the strain variation for *A. maculatum*, since it is most known for infection of *R. parkeri*, another strain of spotted fever. Relatively, there is no demonstration of tick strain dependent differences in transmission efficiency for any known rickettsial pathogen, including the ones used in this study.

With an increase in tick-borne diseases throughout the United States recently, investigations into the transmission dynamics of tick vectors is highly important. In regard to SFG *Rickettsia,* the biggest step would be for the characterization of rickettsial isolates and a suitable infection/acquisition bioassay to control for tick variables. Further study of the transmission dynamics of a tick with multiple pathogen infections is also important due to the natural acquisition of ticks. Multiple infections in a tick could potentially be changing the transmission dynamics of a single pathogen, or causing a chain reaction for all the pathogens within the tick and eventually the host. Another point of interest to further study is the acquisition and transmission of SFG *Rickettsia* in other tick species. Considering the severity of Rocky Mountain Spotted Fever in comparison to that of other SFG diseases, including those of this particular study, it is especially encouraged to further investigate the common tick vectors of this disease.

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