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Capybaras, ticks, and spotted fever

Capibaras, garrapatas y fiebre manchada

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Brazilian spotted fever (BSF) is a tick-borne disease, caused by the intracellular bacterium *Rickettsia rickettsii*, which has been reported in southeastern Brazil since the end of the 1920s (Angerami *et al.*). Indeed, BSF is the deadliest spotted fever of the world, with fatality rates around 50% during this new century. The most important vector of *R. rickettsii* to humans in Brazil is the tick species *Amblyomma sculptum*, which is also the most important human-biting tick in the country (Krawczak *et al.,* 2014; Labruna *et al.,* 2017).

While *A. sculptum* is a competent vector of *R. rickettsii,* only <1% of the ticks are found infected by *R. rickettsii* under natural conditions (Krawczak *et al.,* 2014; Labruna *et al.,* 2017). These low infection rates are indeed related to three factors inherent to *A. sculptum*: (i) Larvae, nymphs and adults of *A. sculptum* are partially refractory to *R. rickettsii* infection (Labruna *et al.,* 2008; Soares e*t al.,* 2012), (ii) Among the *R. rickettsii*-infected females of *A. sculptum,* vertical transmission of *R. rickettsii* usually occurs in <50% of them, and when it occurs, filial infection rate is commonly <50% (Soares e*t al.,* 2012), (iii) *R. rickettsii*-infected females have lower reproductive performance than uninfected females (Soares e*t al.,* 2012). Due to these reasons, it is generally accepted the tick population is not able to maintain the *R. rickettsii* infection over subsequent generations, since in each generation the uninfected ticks would have better fitness than infected ticks, besides the continuous low number of ticks that would get the infection through vertical transmission (trans-ovarial transmission). Under these conditions, vertebrate amplifier hosts are required to maintain the bacterium active in the tick population. These amplifier hosts maintain the bacterium in their bloodstream for some days or weeks, at sufficient levels to infect new tick cohorts, amplifying the rickettsial infection among the tick population (Labruna *et al.,* 2013).

Within most of the BSF-endemic areas in southeastern Brazil, the *A. sculptum* populations are sustained chiefly by capybaras (*Hydrochoerus hydrochaeris*; Krawczak *et al.,* 2014; Labruna *et al.,* 2017), which are known as the largest extant rodents of the world (Moreira *et al.,* 2013). Besides being a preferential host for all parasitic stages of *A. sculptum* in BSF-endemic areas, capybaras also act as amplifier hosts for *R. rickettsii* infection in the tick population (Labruna *et al.,* 2013).

Experimental studies have shown that once infested by a *R. rickettsii*-infected *A. sculptum* tick for the first time, capybaras develop a rickettsemia of nearly 10 d, when 20-40% of the uninfected ticks acquire *R. rickettsii* infection. After this primary infection, capybaras become immune and do not develop a second rickettsemia (Souza *et al.,* 2009; Ramírez-Hernández and Labruna, unpublished data). Therefore, the number of capybaras developing rickettsemia (susceptible animals) in a capybara population depends chiefly on the magnitude of births (Labruna *et al.,* 2013).

Recent studies indicate that the maintenance of *R. rickettsii* in an *A. sculptum* population depends on the high reproduction rate of the capybaras; the more

capybara pups are generated in an area, the greater the rate of ticks infected by *R. rickettsii* (Labruna *et al.,* 2013; Polo *et al.,* 2017). One of these studies (Polo *et al.,* 2017) has shown, through mathematical models, that an 80% reduction in capybaral birth rate promotes the elimination of *R. rickettsii* from the tick population in up to 4 years; if this reduction in the birth rate is 90%, elimination can occur in 2 years. Thus, the control of the capybara natality becomes a promising tool for the control and prevention of BSF in humans. Obviously, in conjunction with this, it is essential to use other measures of tick control at the site (vegetation clearance, environmental application of acaracides) and the installation of physical barriers to limit the access of capybaras to some areas of greater human exposure to ticks. In Southeastern Brazil, two tick species, *A. sculptum* and *Amblyomma dubitatum,* are commonly seen parasitizing capybaras nearly everywhere this vertebrate is sampled (Pacheco *et al.,* 2009; Pinter *et al.,* 2011). Among these two tick species, only *A. sculptum* is recognized as a vector of *R. rickettsii* to humans. While many studies have reported rickettsial infection in field-collected *A. dubitatum* ticks, all these infections referred to rickettsial agents of possibly non-pathogenicty to humans, such as *Rickettsia bellii, Rickettsia* sp strain Cooperi, and *Rickettsia* sp strain Pampulha (Labruna *et al.,* 2004; Pacheco *et al.,* 2009; Almeida *et al.,* 2011). An ongoing study in the state of São Paulo has evaluated tick populations sustained by capybaras in multiple areas endemic or non-endemic for BSF.

While the overall number of ticks was similar between BSF-endemic and non-endemic areas, a notable difference has been observed in the tick species composition. In the BSF-endemic areas, nearly 100% of the ticks belong to the species *A. sculptum*; only <10% were of the species *A.dubitatum.* In contrast, in the non-endemic areas, only about 50% of the ticks were *A. sculptum,* and the other 50% were *A. dubitatum* (unpublished data). Observations of these studies have led to the hypothesis that in order to become a BSF-endemic area in southeastern Brazil, there must be a shift in the tick population composition sustained by capybaras, towards the predominance of *A. sculptum.* However, the reasons for this shift are not known, although it could be an important target to prevent new areas of BSF transmission in the future.

Finally, our statements are valid only for those areas in southeastern Brazil, where *R. rickettsii* is transmitted to humans by *A. sculptum,* and where this tick species is sustained chiefly by capybaras. While this scenario is indeed the most common among all BSF-endemic areas in Brazil, there are other areas in Brazil and other American countries where *R. rickettsii* is transmitted by other tick species, with no role of capybaras; therefore, their epidemiological inferences would be completely different from the ones here presented.

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