Chapter 23
Brazilian Spotted Fever: The Role of Capybaras

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23.1 Introduction

Capybaras (*Hydrochoerus hydrochaeris*) are hosts for the tick species *Amblyomma dubitatum* and *Amblyomma cajennense*. The latter, popularly known in Brazil as "carrapato-estrela", is the main vector of the bacterium *Rickettsia rickettsii*, the etiological agent of Brazilian spotted fever, the most deadly rickettsiosis in the world. Current public opinion associates human cases of Brazilian spotted fever with capybaras and their ticks, and this has led to capybaras being blamed for the increasing occurrence of the disease over the last few decades in southeastern Brazil. In fact, the ecology of Brazilian spotted fever is more complex, involving many agents, including, but not restricted to, capybaras. This chapter discusses the role of capybaras in the occurrence of Brazilian spotted fever, especially in the state of São Paulo, southeastern Brazil, where this issue has been well studied. There may be a causal relationship between the rising capybara population and the re-emergence of the disease in the state of São Paulo, since both capybara populations and the number of Brazilian spotted fever cases have increased significantly in this state over the last three decades (Labruna 2009; Del Fiol et al. 2010). However, capybaras are not the sole vertebrate species associated with the reemergence of the disease. We present what is known of the current epidemiology of Brazilian spotted fever, in order to target control and prevention of the disease in areas where capybaras have been shown to play a primary role.

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23.2 Spotted Fever Group Rickettsiae

The genus *Rickettsia* encompasses bacteria of the alpha (α) subdivision of the class Proteobacteria, which are cocco-bacillar gram-negative organisms, with an obligate association with eukaryote cells. The *Rickettsia* species have been classified into three general groups based on antigenic, molecular, and ecological characteristics: the typhus group (TG), composed of the species *Rickettsia prowazekii* and *Rickettsia typhi,* primarily associated with lice and fleas, respectively; the spotted fever group (SFG), composed of more than 20 species, the majority primarily associated with ticks (the only exceptions within this group are *Rickettsia felis* and *Rickettsia akari,* which are associated with fleas and Gamasida mites, respectively); and finally, the ancestral group (AG) and other related basal groups, which include the tick-associated species *Rickettsia bellii* and *Rickettsia canadensis,* and other agents associated with annelids, and various insects (Roux et al. 1997; Kikuchi and Fukatsu 2005; Perlman et al. 2006).

Some *Rickettsia* species are transmitted by their invertebrate host (e.g., tick) to animals including humans, which may then become infected, sometimes severely ill, with a disease known, generically, as spotted fever. On the American continent, several SFG agents have been reported to cause disease in humans, including *R. rickettsii, R. parkeri, R. africae, R. massiliae, R. akari*, and *R. felis* (Parola et al. 2009). Various other SFG species are known to infect ticks, and sometimes cause infections in nonhuman animals, but their role as human pathogens is unknown (Blair et al. 2004; Labruna et al. 2004b, 2005a, 2007; Labruna 2009).

23.2.1 Rickettsia rickettsii

Rickettsia rickettsii is the etiological agent of the most severe form of rickettsiosis, referred to as Brazilian spotted fever in Brazil, or as Rocky Mountain spotted fever in the USA. The disease also occurs in Mexico, Costa Rica, Panama, Colombia, and Argentina. When infecting vertebrate hosts, *R. rickettsii* multiplies almost exclusively within endothelial cells. In ticks, the bacterium causes generalized infection, multiplying within the cells of the guts, ovaries, salivary glands, malpighian tubules, and in the hemolymph (Weiss and Moulder 1984). Known tick vectors of *R. rickettsii* to humans are *Dermacentor andersoni*, *Dermacentor variabilis*, and *Rhipicephalus sanguineus* in the USA (Demma et al. 2005); *R. sanguineus* and *Amblyomma cajennense* in Mexico (Bustamante and Varela 1947); *A. cajennense* in Panama (Rodaniche 1953), Colombia (Patino-Camargo 1941), and Argentina (Paddock et al. 2008); and *A. cajennense* and *Amblyomma aureolatum* in Brazil (Guedes et al. 2005; Pinter and Labruna 2006; Labruna 2009).

Transmission of *R. rickettsii* to a human through the parasitism of an infected tick results in classical symptoms that generally occur after an incubation period of 5–10 days: these include high fever, headache, and myalgia. A typical cutaneous rash also develops in most patients during this febrile period. Fatality rates of untreated cases can be as high as 80%. However, if treated with specific antibiotics (tetracyclines, chloramphenicol) started in the first days of fever, fatality rates are usually less than 10% (Galvão 1996).

Brazilian spotted fever has been known since the 1920s, but mostly restricted to the southeastern states of Brazil, namely, São Paulo, Minas Gerais, Rio de Janeiro, and Espírito Santo (Silva and Galvão 2004). There have been confirmed cases in the state of Bahia, in northeastern Brazil (Plank et al. 1979). More recently, during the last 10 years, the disease was first confirmed in southern Brazil (states of Paraná, Santa Catarina, and Rio Grande do Sul), as well as in central and northern Brazil (Del Fiol et al. 2010). However, the *Rickettsia* species responsible for the infection in these states has not been identified. It is suspected that at least some of these human cases were caused by a *Rickettsia* species other than *R. rickettsii,* since there were peculiar clinical and epidemiological characteristics observed that appeared to be distinct from the classical Brazilian spotted fever encountered in southeastern Brazil (Labruna 2009).

23.3 Ecology of Brazilian Spotted Fever

In the USA, *R. rickettsii* is maintained in nature between its tick vectors (*D. andersoni* and *D. variabilis*) and several small rodent species (*Microtus pennsylvanicus, Microtus pinetorum, Peromyscus leucopus* and *Sigmodon hispidus*; McDade and Newhouse 1986; Burgdorfer 1988). *R. rickettsii* is partially pathogenic to ticks so, although the bacterium undergoes transovarial transmission (hereditary transmission) between successive tick generations, the infection rate drops in the tick population with each tick generation because mortality rates are higher among infected than among uninfected ticks (Burgdorfer 1988; Niebylski et al. 1999; Labruna et al. 2011). Under these conditions, an amplifier host is required to maintain the bacterium active in nature. The amplifier hosts (in this case, rodents) 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 (Burgdorfer 1988).

In general, a vertebrate host species has to fulfill the following requirements to function as an efficient amplifier host in this system (Labruna 2009): (1) It has to be abundant in the *R. rickettsii*-endemic area; (2) it has to be a major host for the tick vector; (3) it has to be susceptible to *R. rickettsii* infection; (4) once infected by *R. rickettsii,* the host has to develop a rickettsemia of sufficient length and degree to infect ticks that feed on this host; and (5) it has to be a prolific species, to continuously produce nonimmune animals into the host population.

In Brazil the situation differs from that in the USA, because *A. cajennense* (Fig. 23.1), the main tick vector of *R. rickettsii* in Brazil, does not feed on small rodents at any stage in its life cycle. The larvae and nymphs of *A. cajennense* feed preferentially on medium and large-sized mammals, while adults parasitize chiefly large mammals (Labruna et al. 2005b).

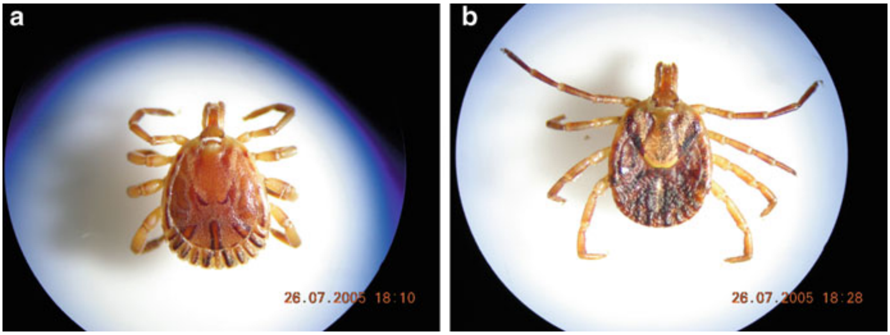
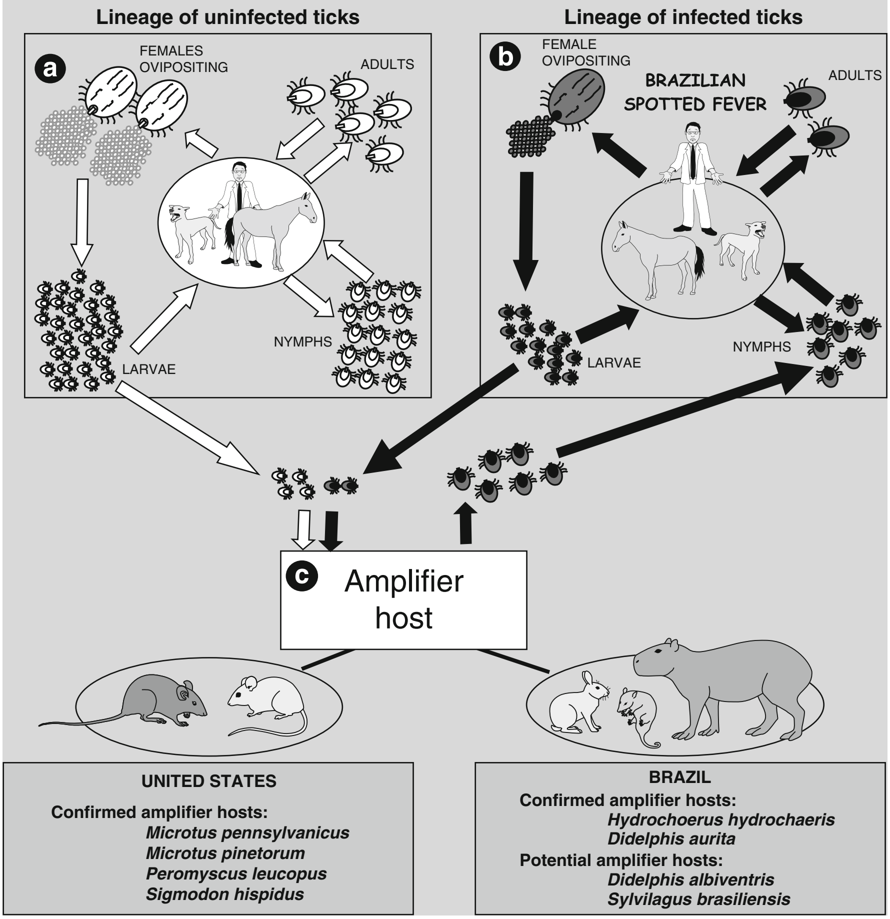


Fig. 23.1 The tick *Amblyomma cajennense*. (**a**) Male (**b**) Female

Box 23.1 Ecological Aspects of the Cycle of *Rickettsia rickettsii*



(continued)

Box 23.1 (continued)

(**a**) Larvae, nymphs, and adults of an uninfected tick lineage are maintained free of infection while feeding on uninfected hosts; hence, when they feed on humans, they do not transmit Brazilian spotted fever. (**b**) A lineage of *R. rickettsii*-infected ticks maintain the agent in the tick population, through transovarial and transstadial transmissions. Due to the lethal effect of *R. rickettsii* on some ticks, the infected lineage tend to have lower reproductive performance and survivorship throughout the generations. Thus, it is necessary the participation of amplifier hosts (**c**), which are vertebrate hosts that once primo-infected with *R. rickettsii* via an infected tick, they keep the bacterium circulating in their blood (rickettsemia) for a few days or weeks, when new uninfected ticks become infected while feeding on the host, starting new lineages of infected ticks.

Both transstadial (transmission between developmental stages) and transovarial transmission of *R. rickettsii* occurs in *A. cajennense* (Monteiro et al. 1932; Monteiro and Fonseca 1932; Brumpt 1933), and recent studies have demonstrated that both capybaras and opossums (*Didelphis aurita*) can act as amplifier hosts in Brazil (Horta et al. 2009; Souza et al. 2009). This latter finding corroborates earlier suspicions, dating back to the 1930s, when capybaras, opossums, and wild rabbits were incriminated as possible amplifier hosts (Box 23.1).

23.3.1 The Role of Capybaras in the Ecology of Spotted Fever

It is expected that capybaras play a major role in the maintenance and transmission of Brazilian spotted fever because this animal can act as the main host for the tick *A. cajennense*. On this basis, it could be predicted that the higher the population density of capybaras, the larger the tick population and, consequently, the higher the risk of human infection.

Capybaras fulfill very well the five requirements described above for an amplifier host for *R. rickettsii*. Indeed, capybaras are abundant in many Brazilian spotted fever-endemic areas, where they act as primary hosts for all parasitic stages of *A. cajennense*. Their susceptibility to *R. rickettsii* has been known since the 1940s (Travassos and Vallejo 1942; Souza et al. 2004), and it was recently shown that after being experimentally infected with *R. rickettsii*, capybaras maintained viable rickettsiae circulating in their blood (rickettsemia) for 1–2 weeks, when they infected 20–25% of the *A. cajennense* nymphs that fed on them. Capybaras are prolific, producing a mean of six pups per female per year (Ojasti 1973), generating a constant introduction of susceptible animals, not previously infected by *R. rickettsii*. For these reasons, capybaras have an important role in the ecology of Brazilian spotted fever in many endemic areas of Brazil. However, the capybara clearly cannot be the only vertebrate host involved because there are areas of Brazil where *R. rickettsii* is endemic but where capybaras are absent. Further, it is perhaps noteworthy that when experimentally infected with *R. rickettsii,* capybaras showed no clinical signs of infection (Souza et al. 2009).

23.3.2 Other Animals Involved or Possibly Involved in the Ecology of Brazilian Spotted Fever

Like capybaras, opossums (*Didelphis aurita*, and possibly *Didelphis albiventris*) also fulfill the five requirements for a suitable amplifier host of *R. rickettsii* for *A. cajennense* ticks. Opossums are very abundant in nearly all endemic areas, where they are frequently infested by the larvae and nymphs of *A. cajennense* (Horta 2006). The susceptibility of opossums to *R. rickettsii* infection has been documented since the 1930s (Moreira and Magalhães 1935; Horta 2006). A recent study in Brazil showed that *R. rickettsii*-experimentally infected opossums (*D. aurita*) developed rickettsemia lasting up to 3–4 weeks, when ≈ 5–20% of the *A. cajennnense* immature ticks that fed on them became infected by *R. rickettsii* (Horta et al. 2009). Opossums are also relatively prolific.

In the past, wild rabbits (*Sylvilagus* spp.) were considered an important amplifier host of *R. rickettsii* in the USA. Rabbits and their ticks (namely, the rabbit tick, *Haemaphysalis leporispalustris*) can be infected by *R. rickettsii*. Rabbits are abundant in *R. rickettsii*-endemic areas and they present rickettsemia of sufficient magnitude to infect ticks that feed on them (Parker et al. 1951; Shirai et al. 1961; Bozeman et al. 1967). However, in the USA, small rodents are much more frequently parasitized by tick vectors (*D. variabilis* and *D. andersoni*) than are rabbits, and they present rickettsemia of much higher magnitude, resulting in a larger proportion of infected ticks (Burgdorfer et al. 1980; Burgdorfer 1988). In Brazil, the wild rabbit *Sylvilagus brasiliensis* is abundant in many endemic areas, especially in the states of Minas Gerais and Rio de Janeiro. However, there is a lack of studies focusing on the role of these animals in the ecology of Brazilian spotted fever.

The role of the domestic dog (*Canis familiaris*) as amplifier host for *R. rickettsii* has been controversial, especially in the USA (Weiss and Moulder 1984; McDade and Newhouse 1986). Although Norment and Burdorfer (1984) reported that dogs, experimentally infected with *R. rickettsii*, did not develop rickettsemia of sufficient magnitude to infect more than 1% of *R. sanguineus* ticks that fed on them, earlier studies reported that rickettsemic dogs infected the majority of the *D. variabilis* ticks that fed on them (Price 1954; Keenan et al. 1977). More recently, human cases of Rocky Mountain spotted fever (*R. rickettsii*) vectored by *R. sanguineus* in Arizona, USA, resurrected the hypothesis that dogs might play a role as an amplifier host of *R. rickettsii.* All parasitic stages (larvae, nymphs, and adults) of *R. sanguineus* feed primarily on the domestic dog (Demma et al. 2005) and it is a primary host for the adult stage of *A. aureolatum,* one of the vectors of Brazilian spotted fever in the state of São Paulo (Pinter et al. 2004; Pinter and Labruna 2006).

The tick *R. sanguineus,* a confirmed vector of *R. rickettsii* in Mexico and USA, is the principal tick species that parasitizes dogs in Brazil, especially in urban areas (Labruna 2004). A recent study in Brazil showed that dogs could act as amplifier hosts for *R. sanguineus* ticks, after being experimentally infected with a Brazilian strain of *R. rickettsii* (Piranda et al. 2011). However, the role of *R. sanguineus* as a vector of *R. rickettsii* to humans in Brazil is unknown because, in Brazil, this tick very rarely bites humans.

Horses (*Equus caballus*), primary hosts for *A. cajennense,* are abundant in many Brazilian spotted fever-endemic areas in Brazil. Horta et al. (2004) demonstrated by serum cross-absorption techniques that horses became naturally infected by *R. rickettsii,* showing high antibody homologous titers. In some endemic areas of the states of São Paulo and Minas Gerais, where *A. cajennense* is a natural vector, 57–90% of the horses are serologically positive for *R. rickettsii* (Lemos et al. 1996; Horta et al. 2004). However, both the clinical symptoms (if any) induced by *R. rickettsii* in horses, or the role of horses as amplifier hosts, have yet to be investigated.

Tapirs (*Tapirus terrestris*) and possibly peccaries (*Tayassu pecari* and *Pecari tajacu*), despite being primary hosts for *A. cajennense*, are not present in any known Brazilian spotted fever-endemic area. Thus, there is no evidence that they play any direct role in the ecology of the disease.

It can be seen from the preceding discussion that any human interference that raises the reproduction rate of the amplifier host population would also increase the number of susceptible animals (that would develop rickettsemia) and, consequently, the *R. rickettsii*-infection rate in the tick population would be higher, increasing the risk of human disease.

23.4 Prevention of the Disease

As for any vector-borne disease, the occurrence of spotted fever is directly related to the size of the vector population (ticks). Human infestation by *Amblyomma* ticks is an accidental event, resulting from the large number of free-living ticks in the environment. Therefore, the most efficient method to minimize human infections, and prevent Brazilian spotted fever, is to reduce the size of the tick population.

Once a *R. rickettsii*-infected tick attaches itself to a host, it takes a minimum of 4–6 h to inoculate the bacterium into the host. Therefore, the faster a person removes a recently attached tick, the lower the chance of acquiring spotted fever. Since there are no commercial vaccines to prevent spotted fever in humans, the most efficient method to prevent the disease is to keep the tick population controlled at low levels and to reduce the chance of a tick coming into contact with a human, thus minimizing human infestations.

The establishment and growth of an *A. cajennense* population in a given area is dependent on the presence of at least one of its primary host species (horses, capybaras, tapirs, or peccaries) and the existence of suitable environmental conditions for its free-living developmental stages. The control of ticks, therefore, can be achieved directly by targeting either the parasitic population or the free-living population of ticks, or indirectly by reducing (or eliminating) the population of its primary host from the area. Educational programs for the human population inhabiting *R. rickettsii*-endemic areas are also important, and control efforts must be continuous to minimize the risk of transmission of spotted fever between nontreated and treated areas.

23.4.1 Control of *A. cajennense* by Targeting the Parasitic Population

The traditional method to control ticks is by treatment of parasitized animals with acaricides (pesticides that kill ticks and mites). A suitable method for continuous application of acaricides on free-living wild hosts, such as capybaras, however, is yet to be developed, so this approach is only suitable for domestic animals, such as horses. Details of treatment protocols for *A. cajennense* on horses can be found elsewhere (Leite et al. 1997; Labruna et al. 2004a; Cunha et al. 2007).

Any tick control program must be continuous, and results should only be expected in the medium or long-term, namely, after 1–3 years of control. There is a natural human desire for treatment to produce a rapid effect. However, immediate results, following a single acaricide application, will only be seen in a single infestation on a severely infested animal. The main aim of the control program is to reduce the environmental burden of ticks, through continuous treatments on animals. Occasional curative treatments have no effect on the free-living tick population; i.e., they do not control ticks.

23.4.2 Control of *A. cajennense* by Targeting the Free-Living Population

One study of 40 horse farms in the state of São Paulo showed that both the presence and the abundance of *A. cajennense* infestations on horses was associated with the presence of at least one overgrown mixed pasture on the farm (Fig. 23.2; Labruna et al. 2001). It is likely that the vegetation composition of a mixed pasture, composed of bushes and shrubs as well as grass, provides the ideal microclimate for the free-living developmental stages of the tick.

For isolated pastures, where there are no forests or preservation areas in the vicinity, the environmental tick burden can be reduced by destroying the microclimate conditions required for tick survival and development by mechanical mowing. The whole pasture should be mowed, close to the soil, at least once a year in the second half of the rainy season (January to March). After mowing, all cut grass must be immediately removed from the pasture and discarded. Annual mowing during

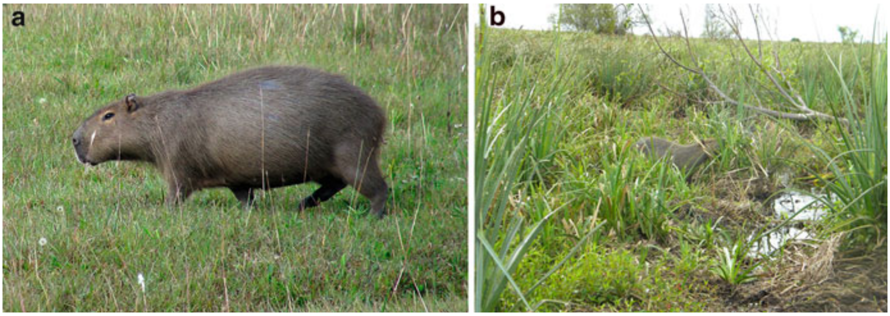


Fig. 23.2 Distinct situations with the presence of capybaras. (**a**) A pasture in good condition (without bushes and shrubs interspersed with grasses) inhabited by capybaras, but without *Amblyomma cajennense,* since that environment is not suitable for this tick species (Photo by J.R. Moreira). (**b**) A mixed overgrowth pasture inhabited by capybaras, with abundance of *A. cajennense,* since this denser vegetation favors the free-living stages of the tick (Photo by M.B. Labruna)

the rainy season prevents the formation of mixed overgrowth pasture, since it favors the regrowth of grasses over bushes and shrubs (which themselves are undesired invaders). Ideally, mowing should be carried out during the second half of the rainy season, when the vast majority of free-living ticks exist as eggs or unfed larvae in diapause prior to the larval infestation peak at the end of the rainy season and first half of the dry season (April to June; Labruna et al. 2003). Eggs and larvae are particularly sensitive to desiccation, so reducing the vegetation cover available should be extremely harmful to these tick stages.

For horses reared in forest or preservation areas, where mechanical destruction of the vegetation is not possible, the only feasible alternative is direct treatment of the horses with acaricides (above). However, restricting the horses' access to these forest areas will also give satisfactory results, since in the absence of primary hosts, most ticks will not be able to feed efficiently and will die of starvation. Nevertheless, the impacts of such an approach will not be seen for a year or two, because ticks can remain viable without feeding for up to a year or more in a suitable environment (Rohr 1909).

The worst situation arises when a forest area harbors high populations of *A. cajennense* that are sustained by wildlife (e.g., capybaras). In this case, neither direct treatment of horses nor mechanical removal of the vegetation will be effective. Local inhabitants can be advised not to enter forest areas harboring infected ticks, but educational activities (below) are crucial. Scientific research into methods to control populations of both ticks and capybaras in these areas is urgently needed.

23.4.3 Control of A. cajennense Through Exclusion of Primary Hosts

In places where there are no capybaras, and horses are the sole primary host for *A. cajennense*, the tick population can be successfully controlled by simply removing all horses from this area. However, it must be borne in mind that the free-living stages of *A. cajennense* (especially the adult stage) can remain viable without feeding in the environment for about 1 year (Rohr 1909). Therefore, results should only be expected 1 or 2 years after removing the primary host.

If capybaras are the primary host for *A. cajennense*, exclusion will only be efficient for tick control if *all* animals are removed, and if there are no means by which capybaras can recolonize the area. Partial exclusion of capybaras, without decreasing the food resources in a given area, will increase their reproductive rate (see Chap. 18), giving rise to a larger number of capybaras susceptible to infection by *R. rickettsii* (see requirement five for a species to be considered a good amplifier host). Although such a scenario has not been demonstrated under field conditions, it is quite feasible that an increased reproductive rate in capybaras could result in an increase in the *R. rickettsii*-infection rate in the tick population, since a greater number of capybaras would be acting as amplifier hosts. Consequently, the risk of humans contracting Brazilian spotted fever would also be likely to increase in the area. For this reason, partial removal of capybaras in a Brazilian spotted fever-endemic area, without decreasing food resources, is banned by law.

23.4.4 Educating the Population to Decrease Risks of Spotted Fever

In *R. rickettsii* endemic areas, only a small portion of the tick population is actually infected with *R. rickettsii.* For *A. cajennense,* this portion is usually below 1% (Sangioni et al. 2005). Thus, in these endemic areas, the more ticks on a person, the higher the chances are of that person harboring an infected tick. For this reason, it is mandatory to inform the human population of appropriate methods of tick control as described above.

In parallel with appropriate tick control, public health services need to inform local human populations about the risks of acquiring spotted fever. In areas where the disease is known to occur, people should search for and remove ticks from their bodies every 2–3 h while in the tick-infested area. When entering such areas, clothes that provide physical barriers against ticks should be worn (arms and legs should be covered and long boots should be worn with trousers tucked inside them). Light-colored clothes are best, because ticks can be more easily seen on them, before they can reach the skin.

Finally, it is important to remember that Brazilian spotted fever is a bacterial disease easily treated with antibiotics (tetracyclins or chloramphenicol), provided these drugs are prescribed in the very first days of the febrile period. For this reason, it is mandatory to inform local medical services of the risks, symptoms and treatment. They should therefore be aware that any case of acute febrile disease may be a clinical sign of spotted fever, and to ensure that an appropriate antibiotic therapy is given as early as possible in all suspected or probable cases.

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