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A wolf at the door: the ecology, epidemiology, and emergence of community- and urban-level Rocky Mountain spotted fever in the Americas

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Abstract
RMSF, a tickborne infection caused by *Rickettsia rickettsii*, produces severe and fatal disease in humans and dogs. Since the beginning of the 21st century, cases have risen dramatically, most notably in Mexico and Brazil, where outbreaks occur in urban centers including cities with populations of > 1,000,000 persons. Reported case fatality rates can exceed 50%. Factors consistent with high case fatality include lack of awareness of disease ecology, limited capacity for diagnosis, and delay in appropriate antimicrobial treatment. The emergence of urban hyperendemic foci has been leveraged by 2 distinct but similar anthropogenic events that create disproportionately high numbers of vertebrate amplifiers of *R rickettsii*, as well as the tick species that transmit this pathogen in proximity with dense human populations. This often occurs in neighborhoods with a highly marginalized at-risk population that includes persons in poverty and particularly children, and health management systems that are under-resourced. We discuss strategies to reduce host dog populations, particularly in Mexico, and capybaras in Brazil. We review challenges to the control of tick populations in these settings. Robust systems are required to enhance awareness of RMSF among medical practitioners and people at risk of RMSF. Public health campaigns should incorporate innovative behavioral science (eg, diverse learning models, motivational interviews, and gamification) to increase prevention and understanding within communities. While anti-*Rickettsia* or anti-tick vaccines will be necessary to resolve this One Health crisis, impactful implementation will require data-driven and multiple-target innovations to address challenges with hosts, ticks, medical systems, and public welfare. The companion Currents in One Health by Foley, Backus, and López-Pérez, JAVMA, March 2025, addresses helpful information for the practicing veterinarian.

Keywords: tick-borne disease, emerging infectious disease, binational One Health, rickettsial disease, tick control

Rocky Mountain spotted fever (RMSF), caused by the bacterium *Rickettsia rickettsii*, is among the deadliest infectious diseases on Earth. *Rickettsia rickettsii* infects mammalian endothelial cells of capillaries, arterioles, and venules of all major tissues and organ systems. Damage to the endothelium of the dermis, skeletal muscle, brain, heart, lungs, kidneys, and gastrointestinal tract results in progressively systemic and life-threatening manifestations.[1] Cell injury leads to microvascular damage and fluid leakage into extravascular spaces. In the skin, diffuse small-vessel injury causes maculopapular and petechial rashes that evolve into confluent ecchymoses **(Figure 1)**, and edema is often evident on the dorsum of the hands during advanced disease. Advanced disease can include pneumonitis, myocarditis, interstitial nephritis, meningoencephalitis,

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and hepatitis, characterized clinically as acute respiratory distress syndrome, pulmonary edema acute kidney injury, cardiac conduction abnormalities, obtundation, coma, jaundice, and disseminated intravascular coagulopathy. Peripheral gangrene can necessitate amputation. While contemporary RMSF case fatality rates (CFRs) in the Americas range from 5% to 67%, Latin American CFRs approximate those described for outbreaks of Ebola hemorrhagic fever **(Table 1)**.[14] Half of all RMSF deaths occur in the first 8 days of illness.

Rickettsia rickettsii can be transmitted by > 9 species representing 4 genera of ticks. Cases are confirmed from Canada, the US, Mexico, Costa Rica, Panama, Colombia, Brazil, and Argentina. Initially rare and sporadic, community outbreaks became common in the late 20th century, and beginning in the early 21st century, a particularly sinister epidemiology of RMSF

Figure 1—Clinical characteristics of Rocky Mountain spotted fever (RMSF) in humans. A— Maculopapular rash on the shoulder of an adult patient with RMSF in São Paulo State, Brazil. B—Maculopapular rash on the arm of a child in Sonora, Mexico, on day 3 of RMSF. C—Rash involving palm of a Brazilian patient with RMSF. D— Edema and rash on the dorsum of the hand of a child from Sonora, Mexico, on day 4 of RMSF that culminated in death. E and F—Petechial rash involving the dorsum of the hand of a 4-year-old Mexican child (E) and on the abdomen of an adult Brazilian patient (F). G—Confluent ecchymoses on the lower extremity of a severely ill 5-year-old child in Sonora, Mexico. H—Epistaxis and scleral icterus in a Brazilian patient with fatal RMSF. I—Gangrene involving the pinna of a child from Sonora, Mexico. J—Gangrene involving the digits of an adult Brazilian patient with advanced RMSF. K—Bilateral amputation of the feet of a 2-year-old child in Sonora, Mexico, following severe RMSF. Images in A, C, F, H, and J are courtesy of Rodrigo Angerami, University of Campinas, Campinas, SP, Brazil.

Table 1—Ecological and epidemiological spectrum of Rocky Mountain spotted fever for selected locations in the Americas, 1885–2024.

Location	Period	Predominant setting	Predominant tick vector(s)	Predominant amplifying hosts	No. deaths/ No. cases (CFR)	Representative references
Bitterroot Valley in Montana, US	1885–1911	Sylvatic	*Dermacentor andersoni*	Multiple wildlife species	137/215 (63.7%)	2
Sinaloa and Sonora, Mexico	1918–1943	Community	*Rhipicephalus sanguineus*	*Canis lupus familiaris*	172/215 (80%)	3, 4
Tribal lands in Arizona, US	2002–2023	Community	*Rhipicephalus sanguineus*	*C lupus familiaris*	28/554 (5.1%)	5
Northern states,[a] Mexico	2009–2023	Community and urban	*Rhipicephalus sanguineus*	*C lupus familiaris*	1,345/4,373 (30.8%)	1
Southern Brazil	1929–1949	Sylvatic and community	*Amblyomma sculptum*	N/A	791 (86%)	6
São Paulo, Brazil	1985–2002	Sylvatic and community	*A sculptum*, *Amblyomma aureolatum*	*Hydrochoerus hydrochaeris*, *C lupus familiaris*	36/76 (47.6%)	7
	2013–2024	Sylvatic, community, and urban	*A sculptum*, *A aureolatum*	*H hydrochaeris*, *C lupus familiaris*	457/846 (54%)	7–11
Panama	1950–2024	Sylvatic, community, and urban	*A mixtum*, *Rhipicephalus sanguineus* (?)	Multiple wildlife species, *C lupus familiaris?*	18/27 (66.7%)	12, 13

[a]Cumulative data for Baja California, Coahuila, Chihuahua, Nuevo León, and Sonora.

emerged in large metropolitan centers in Mexico and Brazil. Mexican urban epidemics are maintained by large populations of dogs (*Canis lupus familiaris*) that perpetuate enormous numbers of brown dog ticks (*Rhipicephalus sanguineus* sensu lato [sl]). Clinical manifestations of naturally acquired RMSF in dogs can include fever; depression and lethargy; vomiting; anorexia; lameness; hyperemia and petechiae of oral, ocular, and genital mucous membranes; limb edema; neurologic abnormalities; orchitis; and peripheral gangrene **(Figure 2)**. Severe cases of disease can progress to death.[15] In Brazil, a similar ecological scenario occurs with free-roaming and stray dogs and *Amblyomma aureolatum* ticks. Proliferation of capybara (*Hydrochoerus hydrochaeris*) populations and incursion into urban centers support *R rickettsii*–infected *Amblyomma sculptum* ticks in and around city parks and waterways, resulting in unprecedented numbers of RMSF cases in Brazil, particularly in the state of São Paulo.

Herein, we apply a One Health focus to characterize the varied ecologies and epidemiologic presentations of RMSF in the Americas. We focus principally on *Rhipicephalus sanguineus* sl–, *A aureolatum*–, and *A sculptum*–associated RMSF; discuss how anthropogenic behaviors create imbalances in the numbers and distributions of host species, particularly dogs and capybaras; and offer data-driven and innovative solutions to protect public health from the devastating impact of this zoonosis, particularly at community and urban levels.

The Ecological and Epidemiological Spectrum of RMSF

Sylvatic RMSF

For more than 100 years after its first description,[16] cases of RMSF were rare. The ecology in the US and Canada was a predominantly sylvatic transmission cycle involving *Dermacentor andersoni* in the west and *Dermacentor variabilis* in the east.[17] Transient natural infections of multiple vertebrate species, including golden-mantled ground squirrels (*Citellus lateralis*), chipmunks (*Eutamias amoenus*), snowshoe hares (*Lepus americanus*), cottontail rabbits (*Sylvilagus floridanus*), opossums (*Didelphis virginiana*), white footed mice (*Peromyscus leucopus*), cotton rats (*Sigmodon hispidus*), meadow voles (*Microtus pennsylvanicus*), and pine voles (*Microtus pinetorum*) maintain an infected population of *Dermacentor* spp ticks.[18,19] In several of these mammals, rickettsemia persists for 1 to 2 weeks[20]; in this context, the vertebrate animals serve as amplifying hosts for *R rickettsii* and the ticks as reservoirs. Nonetheless, the frequency of infection with *R rickettsii* in *Dermacentor* spp in sylvatic settings is typically quite low: historically even in relatively high incidence regions such as the Bitterroot Valley, estimates of infection of *D andersoni* ranged from 0.3% to 1.9%.[21,22]

Sylvatic ecologies for RMSF also exist in regions of Latin America where *R rickettsii* is endemic. From 2005 to 2007 among rural families in the state of Yucatan, Mexico, there were at least 10 cases, mostly in children.[23] People reportedly "living in poor conditions" were exposed to family gardens and orchids, which suggests harborage for certain ticks and hosts, particularly the *Amblyomma parvum* vector.[24] Cases in Veracruz in the 1940s may have been sylvatic, with the "*Amblyomma cajennense*" complex (likely *Amblyomma mixtum*) as the implicated vector.[25] Across rural Colombia and Panama, *R rickettsii* has also been detected in *Dermacentor nitens*, a synanthropic species that mainly parasitizes horses,[26] and *A mixtum* and *Amblyomma patinoi*, which have broad host tropisms to include wildlife and humans.[12,27] In

Figure 2—Clinical characteristics of RMSF in dogs can include lethargy and depression (A), arthralgia and lameness (B), conjunctival edema and episcleral injection (C), petechial exanthem of oral mucosae (D), orchitis and scrotal edema (E), and peripheral gangrene (F). Images are courtesy of Edward Breitschwerdt, DVM, North Carolina State University College of Veterinary Medicine, Raleigh, NC.

rural Colombia, *A patinoi* and RMSF cases were more likely in homes with palm roofs and other risk factors favoring access by wildlife.[28]

Community-level RMSF

Peridomestic circulation of *R rickettsii* occurs when the pathogen and vector are introduced by synanthropic and domesticated host species. This ecology can culminate in endemic and epidemic RMSF at a community level, exemplified by the *A aureolatum*–dog ecology in the state of São Paulo, Brazil, and the *Rhipicephalus sanguineus*–dog ecology in the southwestern US, Mexico, Colombia, Panama, and Costa Rica (Table 1).

Community-level RMSF emerged in tribal lands of Arizona in 2003 and was leveraged by large populations of free-roaming and stray dogs that supported enormous peridomestic populations of *Rhipicephalus sanguineus* sl. Many residents in these communities live in poverty and have minimal or nonexistent access to animal wellness and vector control services.[29] These communities are typically remote, with low human population density, but nonetheless maintain hyperendemic levels of RMSF. Here, the risk of disease is greatest among children, with 33% of cases in people < 18 years old. Dogs are keystone hosts for all feeding stages of *Rhipicephalus sanguineus* sl, although a small percentage can feed on other hosts, including humans, particularly at elevated ambient temperatures.[30] Experimental infections of dogs suggest that once infected, they remain rickettsemic and can transmit *R rickettsii* to feeding ticks for as long as 7 days.[31] Dogs therefore serve both as amplifying hosts for the pathogen and principal hosts for the vector, creating enormous numbers of ticks, including infected ticks at the community level.[32]

In Brazil, Rocky Mountain spotted fever was first identified in 1929 in the state of São Paulo,[33] but it now occurs in multiple distinct ecologies.[7] Community-level RMSF is transmitted by *A aureolatum*, a tick normally maintained by crab-eating foxes (*Cerdocyon thous*). However, the disturbed Atlantic rainforest patches, interspersed with the urban matrix, no longer support wild carnivores. The poorest people are at greatest risk for RMSF, living near large numbers of free-roaming or stray dogs that maintain and amplify *A aureolatum.*[34–36] *Amblyomma aureolatum* is not typically aggressively human-feeding; however, ticks that have pre-fed on dogs activate *R rickettsii* in their salivary glands, and can then rapidly transmit to human hosts.[37] Most cases in the *A aureolatum* ecology occur in children due to close, frequent contact with dogs.[38] There are anecdotal reports of cases in children associated with contact with domestic cats, which also frequent the surrounding forests and can become infested with *A aureolatum*. Relevant socioeconomic factors are that these poorer populations do not have the resources for tick preventive products on dogs. There also is a constant renewal of the dog population in these areas, both due to deficiencies in population control and high rates of abandonment of dogs in the area.[35,36]

Most of the earliest Costa Rican cases occurred in rural areas and involved boys and men employed as agricultural workers.[39] Four outbreaks reported from 2003 to 2008 had CFRs of 30%.[40] Reservoir hosts for RMSF transmitted by *A mixtum* in Central America have not been confirmed. There are well-documented outbreaks of RMSF in Costa Rica, totaling 18 cases from 1975 to 2011 with a CFR of 83.3% (Table 1).[41] There has been little recent literature on RMSF in Costa Rica, with the exception of a case report published in 2019.[42] In Panama the CFR of RMSF approaches 90%,[43,44] and cases are both rural and urban. The potential vectors *A mixtum* and *Rhipicephalus sanguineus* sl are widely distributed in Panama, which suggests the risk of additional unrecognized cases.[12] Distributions of both tick species may expand with ongoing alteration of native forests and decline of biodiversity, while cases may continue to emerge with increased ecotourism, hunting, logging, expansion of human settlements into adjacent wilderness areas, and roaming animals in cities.[12] Of particular concern is a case series in Panama of 7 people including 4 fatalities in a remote indigenous community, which may reflect underlying health disparities.[43]

Many Mexican villages suffer community-level RMSF associated with *Rhipicephalus sanguineus* sl. Sinaloa and Sonora states had more than 200 sporadic and rural cases from as early as 1918 and then a reemergence in the latter 20th century[1,3,23] (and many others). The earliest CFRs ranged from 27 to 80%[45] and occurred in homes where dogs were typically infested with *Rhipicephalus sanguineus* sl.[46] During the late 20th century and early 2000s, there were small case clusters in Yucatan associated with *Rhipicephalus sanguineus* sl.[47] Cases and outbreaks continue to occur in towns across Baja California (Mexicali Valley and San Quintin), a small community of 35,000 people west of Hermosillo in Sonora, and many other villages and towns as well.[48–50]

Urban RMSF

There is recent and ominous hyperendemic RMSF in large urban centers, including San Jose in Costa Rica, São Paulo in Brazil, and Mexicali, Tijuana, Ensenada, Hermosillo, and Ciudad Juarez in Mexico (Table 1).[7,8,32,48,51–54] Cases in Costa Rica in 2003, 2010, and 2011 were within cities,[41,55] while cases in 1987 were reported from an urbanized area near forest in the north[56]; these urban cases are likely to have been acquired from *Rhipicephalus sanguineus* sl. The presence of this highly fatal disease in large cities is of enormous concern, as underlying social and ecological factors allow infected ticks to spread rapidly among homes in these densely populated areas.

Urban epidemic Brazilian RMSF is associated with *A sculptum* populations sustained by capybaras,[54,57] exemplified in **Figure 3**. In southeastern Brazil, a total of 1471 RMSF cases were laboratory confirmed from 2013 to 2023, of which 667 (45%) were fatal (Table 1). More than half of the cases are in the state of São Paulo, followed by Minas Gerais, Rio de Janeiro, and Espírito Santo.[9,54] Urban and peridomiciliary exposure accounts for 35% of all Brazilian RMSF.[9]

Amblyomma sculptum is an aggressive host generalist that readily bites humans[59] and feeds extensively on horses (*Equus caballus*), capybaras, and tapirs (*Tapirus terrestris*).[60] Horses serve to spread ticks but are not amplifying hosts for *R rickettsii.*[61] In contrast, capybaras sustain huge populations of *A sculptum* in RMSF-endemic areas and are amplifying hosts for *R rickettsii*,[58] which contributes to high RMSF burdens in regions where capybaras are abundant.[62]

Amblyomma sculptum is partially refractory to *R rickettsii* infection with transovarial transmission rates < 50%, resulting in overall infection rates < 1% among *A sculptum* populations in the RMSF-endemic areas.[63] This situation means that the establishment of *R rickettsii* in *A sculptum* populations is directly dependent on large tick populations and a constant source of amplifying hosts. Because capybaras are semiaquatic grazing rodents that live close to water, persons at greatest risk for RMSF in urban settings are those who frequent areas close to lakes, rivers, and other watercourses for work or leisure activities. Most cases of RMSF have been reported in adult men (who in this area are more likely to access areas with infected ticks, regardless of economic status).[9,10]

Capybaras are tolerant of human presence and have expanded in range and numbers with deforestation and encroaching agriculture, including into urban and suburban parks, golf courses, university campuses, and large swaths of cattle ranches and cropland, especially in sugar cane, corn, and rice fields and where predators have been eliminated.[64] Their abundant supply of food in RMSF-endemic areas (eg, sugar cane and corn crops, irrigated grasses), ability to thrive even on marginal-quality diets, and social structure of large groups of 40 or more individuals support a high reproduction rate, high population renewal, and capacity for population size increase.[65]

In Mexico, urban epidemics are maintained by free-roaming stray dogs and *Rhipicephalus sanguineus* sl ticks **(Figure 4)**. Sonora reports the greatest number of cases and deaths with 2,160 cases confirmed from 2004 to 2023 and 596 deaths, half of

Figure 3—Tick vectors and ecological characteristics of endemic settings for RMSF in São Paulo State, Brazil. A—Community of Santo André in the São Paulo Metropolitan area that exemplifies habitat. In this community, *Amblyomma aureolatum* (B [male] and C [female]) serve as the principal vector of RMSF (Scinachi et al[35]) and *Amblyomma sculptum* (D [male] and E [female]) predominates as the principal vector for RMSF in other regions of São Paulo State, where it occurs in peridomestic settings (F) and urban settings such as the city of Campinas, where lakes (G) and streams (H) within the city provide ideal habitat for capybara (*Hydrochoerus hydrochaeris*; I). Capybara are amplifying hosts for *Rickettsia rickettsii* (Ramírez-Hernández et al[58]) and important vertebrate hosts for all feeding stages of *A sculptum*. Images in (F) to (H) are courtesy of Zoonoses Surveillance Unit, Health Surveillance Department, Campinas, SP, Brazil.

which occurred in children and adolescents, most of whom live in poverty.[1,66] Hyperendemic foci concentrate 80% of the burden of cases and deaths in urban centers such as Hermosillo, Ciudad Obregon, and Nogales on the US border. Multiple foci of cases in Coahuila extend from the north to the city of Saltillo in the south with a CFR as high as 76%.[67] Chihuahua had documented 484 cases from 2020 to 2023, mostly in Ciudad Juárez and the city of Chihuahua.[1] In Baja California, cases were first seen in 2009 in the city of Mexicali near the border with Sonora; they have exceeded 854 through 2022.[51] The epidemic spread to the city of Tijuana which (together with near-border cities) had 33 cases and 11 deaths in 2022 and early 2023 and to the more southerly coastal city of Ensenada (21 cases/5 deaths). Epidemiological studies in urban Mexican epidemics highlight the abundance of stray and roaming dogs as a risk for human cases.[32,48,51,52,68] Cases tend to occur in parts of cities where people are impoverished, community sanitary infrastructure is precarious, and there are barriers to access to medical care.[48,52,68,69] The greatest risk factors for severe disease are in children who may play near the ground and with dogs and among elders, pregnant people, and migrant laborers.[1] In recent literature, 50% to 70% of dogs in Baja Californian cities have been seropositive, although finding PCR-positive dogs is quite rare; likewise, ticks are rarely

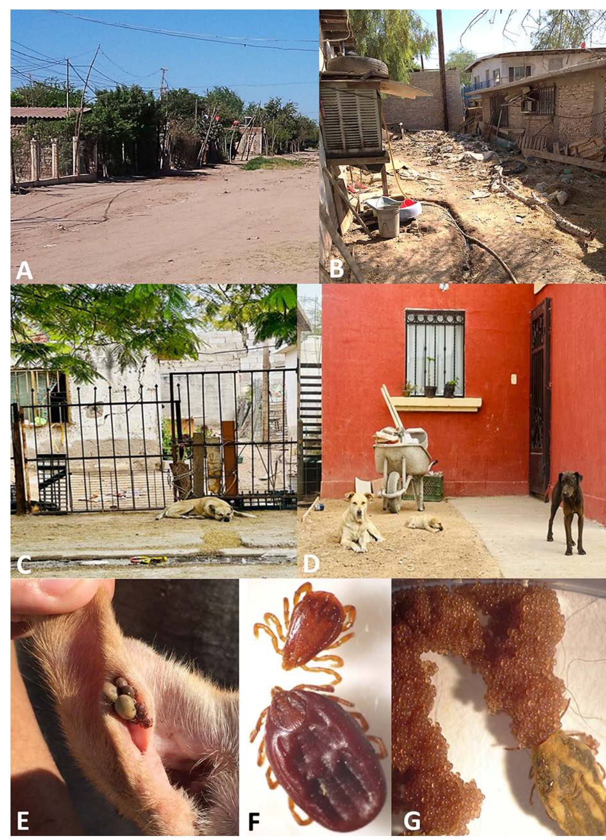

Figure 4—Ecological characteristics of RMSF in northern Mexico. A—Typical residential area in a community with hyperendemic RMSF in the state of Sonora (Alvarez-Hernandez et al 2023). B—Yard in a neighborhood of Mexicali, a city in Baja California with hyperendemic RMSF (Zazueta et al[51]). C and D—Free-roaming and pet dogs comingling around homes in the city of Hermosillo in the state of Sonora. E—Ear of a dog parasitized by *Rhipicephalus sanguineus*, the brown dog tick. F—Male (top) and female (bottom) specimens of *Rhipicephalus sanguineus*. G—Oviposition by female *Rhipicephalus sanguineus*. Depending on the amount of blood taken from its host, a single gravid female can lay as many as 4,000 eggs. Image (G) is courtesy of Francisco Martinez Ibáñez, DVM, National Agri-Food Health, Safety and Quality Service, Morelos, Mexico; other credits are for María Cárdenas-López, Sonora Health Department, Sonora, Mexico.

PCR-positive and some are infected with other rickettsiae such as *Rickettsia massiliae.*[48,52,68]

Strategies to Protect Human and Animal Health against RMSF

Management of amplifying hosts

Impacts of canine hosts on RMSF ecology, particularly from stray or free-roaming dogs, can be mitigated by encouraging owners to keep fewer dogs and to restrain the dogs to their property and spaying and neutering programs. Culling of free-roaming dogs has been employed in some countries to address outbreaks of canine-associated zoonoses[70] although culling is extremely unpopular among the public. The WHO discourages culling in favor of licensing, public education, and fertility control.[71] Culling can contribute to changes in behavior (including aggressiveness) and social and territorial behavior (often increasing contact rates).[72] Reduced population size temporarily increases population growth rates and increases the proportion of the population that is susceptible to disease. Restraining dogs more successfully reduces disease and other dog-related problems.

A meta-analysis of canine population control efforts across 15 countries found the greatest impact is achieved through fertility control.[73] For some species, a trap-neuter-release strategy could fill available niche space with neutered individuals, potentially reducing the population growth rate to zero. However, the carrying capacity for dog populations is largely set by human decisions such as providing food resources, buying or adopting dogs, and allowing dogs to roam. Trap-neuter-release is resource intensive, requiring trained personnel. However, it promotes an older, more disease-resistant population. Dogs that were infected previously with less virulent spotted fever group rickettsiae, such as *R massiliae*, contribute to herd immunity.[74] In the *A aureolatum*–infested dogs in São Paulo, spay and neuter efforts and education programs addressing responsible ownership are challenged by the continuous abandonment of dogs.[36]

Amblyomma sculptum abundance is associated with capybara abundance.[62,75] Although often protected by law, capybaras may be hunted for meat and hides and increasingly for population management, in part to protect public health. However, this culling may largely promote population turnover unless done very aggressively. One study[75] in an RMSF-endemic park area in southeastern Brazil demonstrated that culling the entire population of capybaras eliminated *A sculptum* population in 2 years[75] but required that the residential park be completely fenced (including streams that flowed into and out of the area), preventing colonization by nearby capybaras. The impact of capybaras on public health can be reduced by maintaining intact wild lands to reduce human-wildlife interaction. Fencing that keeps capybaras from croplands could reduce interactions and the capybara carrying capacity.

Fertility control appears to be the most feasible and impactful for controlling capybara populations including surgical sterilization[75] and immunocontraception.[76] One model found that the greatest reduction in RMSF was achieved through control of the capybara birth rate by 60%.[77] The entire niche space can be filled with neutered individuals, limiting population growth. Moreover, capybaras are extremely territorial, so this largely sterile population can prevent new colonization.

Management of tick populations

Rickettsia sanguineus sl is notoriously difficult to eradicate as it spends 95% of its time off-host in sequestra including on dirt floors, under debris, in porous concrete or stucco, or in cracks in walls or ceilings.[78] Reinfestation occurs due to reintroduction and inadequate initial kill. Acaricide may not permeate deeply enough, roaming dogs can repeatedly reintroduce ticks, and *Rhipicephalus sanguineus* sl can climb walls, actively migrating between semidetached houses.[79] Some folk remedies (eg, garlic, flea spray, and herbal remedies) have no efficacy for tick control, yet even correctly used acaricides may fail to control *Rhipicephalus sanguineus* sl due to acaricide resistance.[80] Resistance has been documented to fipronil, permethrin, deltamethrin, ivermectin, cypermethrin, dichlorodiphenyltrichloroethane, coumaphos, amitraz, and chlorpyriphos-methyl.[81–91]

Oral isoxazolines are effective against ticks as is the combination of flumethrin and imidacloprid delivered by collar. However, cost and limited availability challenge use in some homes and scalability for larger control. Acaricides are part of integrated approaches along with aligning residents' and health workers' expectations with the difficulty of the task, repeated and regular interventions, and postapplication assessments of efficacy. Other tick control measures such as sealing cracks and crevices can be helpful. [78]

Controlling populations of *A sculptum* and *A mixtum* remains challenging due to broad host ranges, and capybaras are difficult to handle to apply any product. Automatic devices to apply acaricides to capybaras are hindered by their semiaquatic behavior and unintended risk of environmental damage. In some RMSF-endemic areas, *A sculptum* populations are sustained by horses, and in those areas, environmental control of the ticks can be achieved through pyrethroid acaricides on horses[92] and vegetation management. There are reports of *A mixtum* from Mexico and *A sculptum* from Brazil with resistance to amidines and pyrethroids.[93–95] Integrated vector management can include creating environmental buffer zones, managing landscaping, and encouraging personal protection.[96] Pasture management, mowing grass close to the soil and yearly summer reforming of pasture leaves ovipositing *A sculptum* and their egg masses vulnerable to the changed soil microclimate.[97]

Prospects for control with vaccines

An effective vaccine against *R rickettsii*, a vaccine that inhibits feeding of the tick, or both could dramatically reduce community and urban-level RMSF.[98] Vaccinating amplifying hosts could reduce overall tick numbers and *R rickettsii*–infected ticks. A promising whole-killed *R rickettsii* vaccine protected dogs from death but not rickettsemia, although pathogen DNA load was greatly reduced.[99] Live attenuated vaccines could be produced through mutations of less pathogenic but immunologically cross-reactive rickettsiae such as *Rickettsia parkeri.* Naturally avirulent rickettsiae such as *Rickettsia amblyommatis* can serve as a vaccine. Subunit vaccines could interfere with rickettsial physiology, including attachment to and invasion of host cells but have not yet proven protective.[98] Two promising targets are the surface proteins OmpA and OmpB.

Anti-tick vaccines could allow for reduced acaricide use, lower environmental contamination, reduced acaricide resistance, and potential protection against multiple tick species. The BM86 vaccine protects cattle from *Rhipicephalus* (*Boophilus*) spp ticks by stimulating anti-*Boophilus* spp antibodies that reduce tick fecundity and survival.[100] However, genetic variability in the gene reduces universal efficacy. A crude tick gut extract showed slight efficacy against *Rhipicephalus sanguineus* sl in dogs.[101] Numerous other target proteins such as aquaporin and subolesin show efficacy above 50%.[102]

Vaccination campaigns face multiple challenges. Epidemiological calculations such as those used for rabies[103] can predict the proportion of the population that must be vaccinated against *Rickettsia* spp to achieve herd immunity based on data on population turnover and the basic reproduction number (R_{oo}). Logically, achieving control of *Rhipicephalus sanguineus* sl with an anti-tick vaccine on dogs would require almost 100% vaccination rates, because unvaccinated dogs could otherwise contaminate the environment with ticks. These same considerations apply to capybaras, with additional complications of darting and capturing them or creating an oral bait delivery system.

Protecting people against RMSF

Limited knowledge about RMSF, particularly the need to initiate appropriate antimicrobial therapy within the first 4 to 5 days, is the principal risk factor for a fatal outcome.[1,32] It is crucial to educate clinicians about RMSF in their region and that treatment should be based entirely on clinical acumen.[7,104] This requires that human and veterinary medical and vector professionals track local cases, exchange information, and promote public awareness about RMSF. Public awareness is crucial regardless of dog ownership, as cases of RMSF in households without dogs can occur because of roaming dogs or ticks moving from neighboring properties.[48,52]

Health education shortcomings may occur if content is delivered too infrequently or messaging lacks impact.[105] We should consider novel behavioral science and strategies of education such as environmental education for children, diverse learning models, motivational interviews, diffusion of innovation, social media, social marketing, gamification, and other cutting-edge techniques.

We provide a cautionary tale about the role of information dissemination in protecting the public against RMSF. In late 2023, the CDC issued an RMSF health alert regarding the newly emerging RMSF in Tecate, Mexico, with the spillover of fatal cases in the US. Yet, 2 years earlier, our team had found PCR-positive dogs in the local animal shelter, and epidemics were raging in nearby Mexicali and Tijuana.[106] In 2024, a series of 7 pediatric cases were reported in San Diego, CA, with travel or residence in Mexico; despite a very high standard of care, 2 were discharged with persistent neurological disease.[107]

Despite the urgency, rigorous evaluation of RMSF intervention campaigns is rare. In Arizona, comprehensive intervention in small tribal towns with epidemic RMSF included education, acaricide (on dogs and around homes), dog spay/neuter, and encouraging restraint of dogs to property.[108,109] Outcomes of tick numbers and cases were favorable but required ongoing highly resource-intensive intervention. A similar campaign was undertaken in a heavily affected area in Sonora. Compared to a control area, there was a significant decrease in tick infestation of dogs and no human RMSF cases.[49,50] Importantly, however, it is unknown which specific components of the interventions were most impactful or critical. Because of this, we have developed an in silico tool to test various combinations of intervention.[110] Another novel, intervention in Sonora that reduced *Rhipicephalus sanguineus* sl was paint with microencapsulated, slow-release pesticide.[49]

Summary

Anthropogenic and ecological circumstances that create disproportionately high numbers of amplifying hosts of *R rickettsii*, coupled with massive peridomestic populations of vector tick species, have resulted in hyperendemic levels of RMSF in many communities and cities in multiple countries of the Americas, particularly in Latin America. Managing these vertebrate amplifying host species is a key part of integrated control and preventive programs for RMSF. Managing tick vectors poses considerable challenges, but integrated pest management, the promise of effective canine vaccines, and other innovations are needed to mitigate the burden of RMSF. Most fatal cases stem from a lack of awareness of the disease among clinicians and the public that results in delays in diagnosis and initiation of appropriate antimicrobial treatment. In many areas where the burden of RMSF is greatest, most at-risk people are highly marginalized. This aspect of urban and community-level RMSF must also be addressed to effectively reduce the morbidity and mortality associated with this life-threatening disease.

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