Spotted Fever Group *Rickettsia* and How It “Bugs” Us

**What is Spotted Fever Group (SFG) *Rickettsia*?**

*Rickettsia* species are Gram-negative obligate intracellular bacteria, but SFG *Rickettsia* is a genera of rickettsial bacteria specifically dependent on ectoparasitic arthropods for their life cycle (Socolovschi *et al.*, 2009). The main arthropod vectors of SFG *Rickettsia* are ticks, mites, and fleas, with tick-borne rickettsial infection being the most prevalent of the SFG diseases. Rocky Mountain spotted fever (RMSF) is the SFG disease of highest concern, as the disease can be fatal if not treated properly or early enough. The fatality rate of RMSF has declined significantly over the past few decades, but the number of cases has been increasing. In the year 2000 only about 500 cases were reported nationwide in the United States, and by 2017 almost 6500 cases were reported (CDC, 2019). Other tick-borne SFG diseases of concern include Mediterranean spotted fever, which can be fatal as well, and African tick bite fever, the most commonly transmitted SFG disease amongst international travelers. Cat flea rickettsiosis and rickettsialpox, the single human SFG diseases noted to be transmitted by fleas and mites respectively, are of mild concern despite the wide spread of these arthropods.

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| Insect |  | Disease (pathogen) | Region |
| **Tick:** | *Hyalomma marginatum m.*  *H. m. rufipes*  *Rhipicephalus appendiculatus* | Rickettsiosis  (*Rickettsia aeschlimanii*) | South Africa, Morocco, Mediterranean littoral |
|  | *Amblyomma hebraeum*  *A. variegatum* | African tick-bite fever  (*R. africae*) | Sub-Saharan Africa, West Indies |
|  | *Ixodes holocyclus*  *I. tasmani* | Queensland tick typhus  (*R. australis*) | Australia, Tasmania |
|  | *Rhipicephalus sanguineus* | Mediterranean spotted fever/Boutonneuse fever  (*R. conorii*) | Southern Europe, southern and western Asia, Africa, India |
|  | *Dermacentor silvarum* | Far Eastern spotted fever  (*R. heilongjiangensis*) | Far East of Russia, Northern China, eastern Asia |
|  | *Ixodes elveti*  *I. ovatus*  *I. persulcatus*  *I. monospinus* | Aneruptive fever  (*R. elvetica)* | Central and northern Europe, Asia |
|  | *Ixodes granulatus*  *Aponomma hydrosauri*  *Amblyomma cajennense* | Flinders Island spotted fever/Thai tick typhus  (*R. honei*) | Australia, Thailand |
|  | *Haemaphysalis flava*  *H. longicornis*  *Dermacentor taiwanensis*  *Ixodes ovatus* | Japanese spotted fever  (*R. japonica*) | Japan |
|  | *Rhipicephalus sanguines*  *R. turanicus*  *R. muhsamae*  *R. lunulatus*  *R. sulcatus* | Mediterranean spotted fever-like disease  (*R. massiliae*) | France, Greece, Spain, Portugal, Switzerland, Sicily, central Africa, Mali, Argentina |
|  | *Ixodes ricinus* | Mediterranean spotted fever-like illness  (*R. monacensis*) | Europe, North Africa |
|  | *Amblyomma maculatum*   1. *americanum* 2. *triste* | Maculatum infection/Tidewater spotted fever/American boutonneuse fever  (*R. parkeri*) | North and South America |
|  | *Dermacentor silvarum*  *D. reticulatus*  *D. marginatus*  *D. nuttalli* | Tickborne lymphadenopathy/ *Dermacentor*-borne necrosis and lymphadenopathy  (*R. raoultii*) | Europe, Asia |
|  | *Dermacentor variabilis*  *D. andersoni* | Rocky Mountain spotted fever/Brazilian spotted fever  (*R. rickettsi*) | North, Central, and South America |
|  | *Dermacentor nuttalli*  *D. marginatus*  *D. silvarum*  *Haemaphysalis concinna* | North Asian tick typhus/Siberian tick typhus  (*R. sibirica*) | Russia, China, Mongolia |
|  | *Hyalomma asiaticum*  *H. trunicatum* | Lymphangitis-associated rickettsiosis  (*R. sibirica mongolotimonae*) | Southern France, Portugal, China, Africa |
|  | *Dermacentor marginatus*  *D. reticulatus* | Tickborne lymphadenopathy (TIBOLA)/*Dermacentor*-borne necrosis and lymphadenopathy (DEBONEL)  (*R. slovaca*) | Southern and eastern Europe, Asia |
| **Flea:** | *Ctenocephalides felis* | Cat flea rickettsiosis  (*R. felis*) | Europe, North and South America, Africa, Asia |
| **Mite:** | *Liponyssoides sanguines* | Rickettsialpox  (*R. akari*) | Countries of former Soviet Union, South Africa, Korea, Turkey, Balkan countries, United States |

**Figure 1: Arthropod vectors of SFG *Rickettsia* human diseases and worldwide presence (Brown *et al.*, 2016; CDC, 2017; Parola *et al.*, 2005; Saini *et al.*, 2004).**

**Disease Transmission: The Vector-borne Disease Triangle**

To further know how SFG rickettsial diseases are spread, there are a few key factors to understand about the framework behind disease transmission. Disease transmission is often explained by the “disease triangle,” in which 3 main components identified as contributory to the success of disease transmission: pathogen, vector, and host.

The first component is the pathogen itself, which plays a role in infecting both the host and the vector. Not only does the pathogen have to be present, but it has to possess certain characteristics that enable it to operate, survive, and replicate within the vector and host. The pathogen also plays a role in adapting to immune responses from the vector or host, or preventative measures such as antibiotics. If unable to adapt to such conditions, the pathogen would be halted from spreading, therefore the disease would no longer be present. In order to increase its potential for transmission, a pathogen will also be selective to vectors that inevitably expose the pathogen to the desired host, and will sometimes be transmittable by multiple vector species.

The second component is the vector, which must function as the “middle man” between the pathogen and the host. Without the vector, the pathogen is unlikely to come into contact with the desired host, and therefore cannot survive. In order for a vector to successfully transmit a pathogen, the vector must be able to acquire the pathogen, provide a favorable environment to the pathogen for survival or development, and be able to inoculate a host with the pathogen. There are multiple cases in which organisms are able to acquire a pathogen, but cannot transfer it to a host due to their immune response or physiology, eliminating the organism as a vector.

The third component is the host, which is any organism on or in which another organism can live. In a sense, this means that the vector also functions as a host to the pathogen. The pathogen is highly dependent on its ability to overcome the immune response of a host, and if it cannot then the pathogen cannot survive. The pathogen must also be able to persist within the host so that the pathogen can later be acquired by a vector to further transmission. The host also plays a role in attempting to protect itself from the vector. This includes examples such as wearing pest repellents or swishing tails, or even just staying away from the environments in which the vector is found. For example, a person who is active outside or possesses a lot of pets is more likely to come into contact with arthropod vectors. This also means that lower populations of the host result in lower transmission spread of the pathogen. Without the ability of the vector to come into contact with the host, then the pathogen is unable to reach the host.

The patterns of disease present in today’s world are evidence of the manipulation of these three factors identified in the disease triangle. Some diseases have been subdued by the efforts of the human hosts, often by means of interference with the vector or pathogen. At the same time, some diseases are steadily growing due to adaptive measures of both the pathogen and the vector against host preventative measures. Even if human interference were eliminated, these fluctuations would still be prevalent in disease transmission systems. While the disease triangle itself was created by mankind, it exists within the natural order of the planet’s inhabitants to survive.

**Figure 3. Example of the Vector-borne Disease Triangle for Rocky Mountain Spotted Fever (RMSF).**

**Arthropod vectors of SFG *Rickettsia***

Biological vectors are living organisms that can transmit a disease to a host, like a mosquito infecting a human with malaria. However, before getting into the specific transmitters of SFG *Rickettsia*, it is important to understand the classification of these arthropod vectors (see Figure 3). Arthropods, or members of Arthropoda, are a phylum of thekingdom Animalia. Arthropods include crustaceans, insects, centipedes, spiders, ticks, and various other invertebrate organisms, making up over 80% of known species in the animal kingdom (New World Encyclopedia contributors, 2012). Arthropods are specifically grouped by their exoskeleton (external skeleton; also known as cuticle), paired jointed appendages, and segmented body.

Within Arthropoda are subphylum such as Crustacea, Chelicerata, and Hexapoda. Crustaceans are characterized by having 3 body segments and 5-7 pairs of legs, with primitively branched two-parted (biramous) limbs. Within Chelicerata is the class Arachnida, or spiders, mites, ticks, and scorpions, which are known for having 8 pairs of legs, no antennae, two body regions and chelicera for mouthparts. Hexapoda has the class Insecta, which includes the insects, and organisms of this class characteristically have 3 pairs of legs, a pair of antennae, and 3 body regions. In this chapter we will be focusing on organisms from the classes Arachnida and Insecta due to their relationship with SFG *Rickettsia*.

**Ticks**

Ticks are of the order Ixodida in the class Arachnida, with three families: Ixodidae, Argasidae, and Nuttallidae. Only one species of tick exists in Nuttallidae, though it is of no medical or veterinary importance. Argasidae consists of the leathery “soft ticks,” which are mostly parasites of birds or bats. Members of Ixodidae are known as “hard ticks,” possessing a hard cuticular plate, or scutellum, in contrast to the softer cuticle of the Argasidae. The scutellum is the region of the tick just before the mouthparts that is often shaped like a “u” that cups the head-like portion of the tick. Ixodidae ticks are the largest of the tick families and of larger medical and veterinary importance (Nicholson *et al.,* 2009). In fact, it is the Ixodidae ticks that are the vectors of SFG *Rickettsia* diseases.

**Mites**

Mites are split between two different superorders, or classifications above orders, within Arachnida: Parasitiformes and Acariformes. Mites are fairly similar to ticks, but unlike ticks, which strictly live on animal hosts, mites can feed on either plants or animals. Mites are also known for their microscopic size, making them difficult to see with the naked eye. *Liponyssoides sanguines*, the only mite vector of SFG *Rickettsia*, is found in the superorder Parasitiformes along with ticks, and is in the order Mesostomata along with other predatory mites. *L. sanguines* is an ectoparasite that lives primarily on house mice, however they can feed on other animals as well, including humans.

**Fleas**

Siphonaptera, or fleas, are the only order of Insecta discussed in this chapter, though many more insect vectors of disease exist. Fleas are small, wingless and laterally compressed insects that often parasitize small animals and birds. The bilateral compression of fleas means that they are taller than they are wide, as opposed to the dorso-ventral compression of mites and ticks that causes them to be wider than they are tall. The compression of these arthropods are an adaptation for them to move easily amongst the hairs of the host, as well as be more difficult for the host to remove. Fleas are most commonly associated with their ability to jump long distances rapidly. *Ctenocephalides felis*, more commonly known as the cat flea, is a member of the family Pulicidae and the only flea vector of SFG *Rickettsia*. It is responsible for the transmission of Cat flea rickettsiosis, a minor SFG human disease. *C. felis* is also the most important flea pest of humans and many domestic animals. It feeds on a wide host range, and is commonly present on domestic animals such as cats and dogs.

**Figure 3. Taxonomy of arthropods discussed in chapter down to order level.**

**The Function of Arthropods as Vectors of SFG *Rickettsia***

Arthropods are highly effective vectors of diseases, accounting for more than 17% of all infectious diseases and more than 700,000 deaths annually (WHO, 2017). There are various reasons for which an arthropod could serve as an effective vector. Reasons for effectivity range from life cycles, feeding behaviors, host preferences, immune responses, and opportunistic relationships. In general, arthropods are highly widespread and reproduce quickly. Arthropods also adapt easily to changes in their environments or exposure to potentially harmful organisms. Their ability to reproduce quickly is largely responsible for their wide range, high population densities, and adaptability. Their small size is also advantageous because they require less resources for survival and can evade host threats. Perhaps one of the lesser qualities of arthropod vectors is their ability to acquire and transmit multiple pathogens at a given time within a single vector. The use of multiple vectors for a single pathogen is also an advantage in transmission because different arthropod species will have variations in preferred hosts and environments. Some blood-feeding arthropods are known to vary between host species at each feeding point, increasing the risk for a pathogen to be transmitted to a susceptible host This results in a wider coverage of the potential for the pathogen to be acquired and transmitted.

As shown in **Figure 1**, ticks are especially beneficial to SFG *Rickettsia* transmission and serve as the primary vector for most SFG diseases. When looking at the various tick vectors of SFG diseases, perhaps the largest contributor to vector efficiency of ticks is their need for a blood meal in order to develop. Some ticks utilize 3 different hosts in their lifecycle, while others carry out their entire life cycle on one host. The necessity of some ticks to feed on three different hosts increases the transmissibility of a pathogen to a host from this vector, and is a factor for most SFG *Rickettsia* tick transmitters. For example, *Dermacentor variabilis*, a main vector of Rocky Mountain Spotted Fever, feeds on hosts ranging in size from mice to deer, and even humans. Ticks that transmit *Rickettsia sp.* can also produce infected offspring, increasing the efficiency of ticks as Rickettsia disease vectors. Fleas and mites are also effective arthropod vectors because of their small size, variable host feeding and high reproductive rates. Both groups are fairly difficult to control, and can persist in high densities on a host for extended periods of time. Fleas have developed a specialized mechanism in order to leap far distances in a rapid manner, aiding in their ability to spread between hosts. The microscopic size of mites can make it difficult for the host to rid itself of them, and is typically shaped so as to fit closely to the surface of the host.

**References**

Brown, Lisa D. and Macaluso, Kevin R. “*Rickettsial felis*, an Emerging Flea-Borne Rickettsiosis.” Current Tropical Medicine Reports. 3 : 27-39. (2016). doi: 10.1007/s40475-016-0070-6.

Centers for Disease Control and Prevention. “Rocky Mountain Spotted Fever (RMSF).” CDC Diseases and Conditions. (2019). Available at https://www.cdc.gov/rmsf/stats/index.html.

Centers for Disease Control and Prevention. “Chapter 3: Rickettsial (Spotted and Typhus Fevers) & Related Infections, including Anaplasmosis & Erlichiosis.” CDC Yellow Book 2018: Health Information for International Travel. (2017).

Durden, Lance A. and Hinkle, Nancy C. “Chapter 9: Fleas (Siphonaptera).” Medical and Veterinary Entomology. 2 Ed. : 115-135. (2009).

Mediannikov, Oleg, Matsumoto, Kotaro, Samoylenko, Irina, Drancourt, Michel, Roux, Véronique, Rydkina, Elena, Davoust, Bernard, Tarasevich, Irina, Brouqui, Philippe, Fournier, Mullen, Gary R. and OConnor, Barry M. “Chapter 25: Mites (Acari).” Medical and Veterinary Entomology. 2 Ed. : 433-492. (2009).

New World Encyclopedia contributors. “Arthopod.” New World Encyclopedia. (2012). Available at https://www.newworldencyclopedia.org/entry/Arthropod.

Nicholson, William L., Sonenshine, Daniel E., Lane, Robert S., Uilenberg, Gerrit. “Chapter 26: Ticks (Ixodida).” Medical and Veterinary Entomology. 2 Ed. : 493-542. (2009).

Parola, Philippe, Paddock, Christopher D., and Raoult, Didier. “Tick-Borne Rickettsioses around the World: Emerging Diseases Challenging Old Concepts.” Clinical Microbiology Reviews. 18 (4): 719-756. (2005). doi: 10.1128/CMR.18.4.719–756.2005.

Pierre-Edouard. “*Rickettsia raoultii* sp. nov., a spotted fever group rickettsia associated with *Dermacentor* ticks in Europe and Russia.” International Journal of Systematic and Evolutionary Microbiology. 58: 1635-1639. (2008). doi: 10.1099/ijs.0.64952-0.

Saini, Ritu, Pui, John C. and Burgin, Susan. “Rickettsialpox: Report of Three Cases and a Review.” Journal of American Academy of Dermatology 51(5): s137-s142. (2004). doi: 10.1016/j.jaad.2004.03.036.

Socolovschi, Cristina, Mediannikov, Oleg, and Parola, Philippe. “The relationship between spotted fever group *Rickettsiae* and Ixodid ticks.” Veterinary Research. 40:34 (2009): 1-20. DOI: 10.1051/vetres/2009017.

World Health Organization. “Vector-borne diseases.” WHO Fact Sheet. (2017). Available at https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases.