



Rickettsial Diseases

Hinduja Healthcare Hospital, India

Rickettsial Diseases

Rickettsia is a genus of nonmotile, Gram-negative, nonspore-forming, highly pleomorphic bacteria that may occur in the forms of cocci (0.1 μm in diameter), bacilli (1–4 μm long), or threads (up to about 10 μm long). The term “rickettsia” has nothing to do with rickets (which is a deficiency disease resulting from lack of vitamin D); the bacterial genus *Rickettsia* was named after Howard Taylor Ricketts, in honor of his pioneering work on tick-borne spotted fever. Properly, *Rickettsia* is the name of a single genus, but the informal term “rickettsia”, plural “rickettsias”, usually not capitalised, commonly applies to any members of the order Rickettsiales. Being obligate intracellular parasites, rickettsias depend on entry, growth, and replication within the cytoplasm of living eukaryotic host cells (typically endothelial cells). Accordingly, *Rickettsia* species cannot grow in artificial nutrient culture; they must be grown either in tissue or embryo cultures; typically, chicken embryos are used, following a method developed by Ernest William Goodpasture and his colleagues at Vanderbilt University in the early 1930s.

Rickettsia species are transmitted by numerous types of arthropod, including chigger, ticks, fleas, and lice, and are associated with both human and plant diseases. Most notably, *Rickettsia* species are the pathogens responsible for typhus, rickettsialpox, boutonneuse fever, African tick-bite fever, Rocky Mountain spotted fever, Flinders Island spotted fever, and Queensland tick typhus (Australian tick typhus). The majority of *Rickettsia* bacteria are susceptible to antibiotics of the tetracycline group.

Classification

The classification of *Rickettsia* into three groups (spotted fever, typhus, and scrub typhus) was initially based on serology. This grouping has since been confirmed by DNA sequencing. All three of these groups include human pathogens. The scrub typhus group has been reclassified as a related new genus, *Orientia*, but they still are in the order Rickettsiales and accordingly still are grouped with the rest of the rickettsial diseases. *Rickettsias* are more widespread than previously believed and are known to be associated with arthropods, leeches, and protists. Divisions have also been identified in the spotted fever group and this group likely should be divided into two clades. Arthropod-inhabiting rickettsiae are generally associated with reproductive manipulation (such as parthenogenesis) to persist in host lineage

In March 2010, Swedish researchers reported a case of bacterial meningitis in a woman caused by *Rickettsia helvetica* previously thought to be harmless.

Spotted fever group:

- *Rickettsia rickettsii* (Western Hemisphere)
- Rocky Mountain spotted fever
- *Rickettsia akari* (USA, former Soviet Union)
- *Rickettsialpox*
- *Rickettsia conorii* (Mediterranean countries, Africa, Southwest Asia, India)
- Boutonneuse fever
- *Rickettsia sibirica* (Siberia, Mongolia, northern China)
- Siberian tick typhus or North Asian tick typhus
- *Rickettsia australis* (Australia)
- Australian tick typhus
- *Rickettsia felis* (North and South America, Southern Europe, Australia)
- Flea-borne spotted fever
- *Rickettsia japonica* (Japan)
- Oriental spotted fever
- *Rickettsia africae* (South Africa)
- African tick bite fever
- *Rickettsia hoogstraalii* (Croatia, Spain and Georgia USA)
- Unknown pathogenicity

Certain segments of rickettsial genomes resemble those of mitochondria. The deciphered genome of *R. prowazekii* is 1,111,523 bp long and contains 834 genes. Unlike free-living bacteria, it contains no genes for anaerobic glycolysis or genes involved in the biosynthesis and regulation of amino acids and nucleosides. In this regard, it is similar to mitochondrial genomes; in both cases, nuclear (host) resources are used.

ATP production in *Rickettsia* is the same as that in mitochondria. In fact, of all the microbes known, the *Rickettsia* is probably the closest relative (in a phylogenetic sense) to the mitochondria. Unlike the latter, the genome of *R. prowazekii*, however, contains a complete set of genes encoding for the tricarboxylic acid cycle and the respiratory chain complex. Still, the genomes of the *Rickettsia*, as well as the mitochondria, are frequently said to be “small, highly derived products of several types of reductive evolution”.

The recent discovery of another parallel between *Rickettsia* and viruses may become a basis for fighting HIV infection. Human immune response to the scrub typhus pathogen, *Orientia tsutsugamushi*, appears to provide a beneficial effect against HIV infection prog-

ress, negatively influencing the virus replication process. A probable reason for this actively studied phenomenon is a certain degree of homology between the rickettsiae and the virus, namely, common epitope(s) due to common genome fragment(s) in both pathogens. Surprisingly, the other infection reported to be likely to provide the same effect (decrease in viral load) is the virus-caused illness dengue fever.

Comparative analysis of genomic sequences have also identified five conserved signature indels in important proteins, which are uniquely found in members of the genus *Rickettsia*. These indels consist of a four-amino-acid insertion in transcription repair coupling factor Mfd, a 10-amino-acid insertion in ribosomal protein L19, a one-amino-acid insertion in FtsZ, a one-amino-acid insertion in major sigma factor 70, and a one-amino-acid deletion in exonuclease VII. These indels are all characteristic of the genus and serve as molecular markers for *Rickettsia*.

Rickettsial infections are an important cause of undifferentiated febrile illness in tropics. *Rickettsiae* are a rather diverse collection of organisms with several variations; this prohibits their description as a single homogenous group. *Rickettsia* is maintained in nature through a cycle involving reservoir in mammals and arthropod vectors. The public health impact of these on lives or productivity lost is largely unmeasured but suspected to be quite high worldwide. The rickettsial diseases were believed to have disappeared from India are reemerging and recently their presence has been documented in at least 11 states of India. Many cases of rickettsial diseases go unnoticed due to the lack of diagnostic tools. Greater clinical awareness, a higher index of suspicion and better use of available diagnostic tools will increase the frequency with which rickettsial diseases are diagnosed. Specified IgM ELISA or DNA PCR are preferred tests. New or emerging rickettsial diseases, tickborne lymphadenopathy (TIBOLA) and Dermacentor borne necrosis eschar lymphadenopathy (DEBONEL) related to *Rickettsia slovaca* infection have been described. Rickettsial diseases are one of the many causes of PUO cases (Pyrexia of Unknown origin). Even if advanced diagnostic facilities are not available, simple and easy to perform Weil Felix test can aid in the diagnosis of rickettsial infections.