Worldwide Research on Human and Animal Diseases Caused by Tickborne Rickettsiae

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In an analysis of ticks as vectors of rickettsial agents, a prominent European rickettsiologist who recently referred to early investigations on Rocky Mountain spotted fever (RMSF) stated that the relationships between *Rickettsia rickettsi* and its vectors have been studied so intensively that unsolved problems no longer exist. Also, because the dynamics of infections in the vectors of other tickborne rickettsial diseases were similar to those of RMSF, he considered the role of ticks as vectors of rickettsiae no longer of primary interest as a research problem.

True, the mechanisms by which the spotted fever agent, *R. rickettsi,* is maintained in nature have been the subject of intensive investigations for more than half a century. However, because of their complexity, many questions raised by Ricketts as early as 1909 have not been answered until quite recently or are still under investigation. Considerable advancement in our knowledge of the ecology of *R. rickettsi* was made during the past 6 years as a result of intensive field and laboratory studies in western Montana (Burgdorfer et al. 1962), Utah (Vest et al. 1965), and Virginia and Maryland (Shirai et al. 1961, Bozeman et al. 1967). For the first time strains of *R. rickettsi* were isolated from several species of wild animals, and serological data indicated the presence of complement-fixing antibodies to spotted fever antigen in a large variety of animal species, including birds.

In epizoological studies on infectious diseases in wild animals in Utah, development and persistence of rickettsemias in small mammals and birds indigenous to that State were determined (Lundgren and Thorpe 1966; Lundgren et al. 1966, 1968). Following inoculation with highly virulent strains of *R. rickettsi,* several species of rodents, birds, and lagomorphs had rickettsemias for 1–16 days. These observations led to the conclusion that certain species of mammals and birds have the potential of contributing to the dissemination of *R. rickettsi* by providing infective blood meals for ticks.

Although these results are very interesting, it should be emphasized that the strains used were isolated from ticks in western Montana and were of a virulence never found among strains so far isolated in Utah. These strains undoubtedly behave differently in indigenous rodents and birds than do the virulent strains from Montana.

At the Rocky Mountain Laboratory (RML) we have so far failed to demonstrate rickettsemias in various wild animals inoculated with avirulent or "mild" strains of *R. rickettsi,* and all attempts to infect normal ticks by feeding them on such animals were unsuccessful. Also, the fact that rickettsiae circulate in the blood of a tick's host does not necessarily prove the animal to be a source of organisms for infecting ticks. In our laboratory it was established (Burgdorfer et al. 1966) that a minimum amount of 10–100 guinea pig infectious doses per 0.5 ml of blood was required to infect 50% of larval Rocky Mountain wood ticks, *Dermacentor andersoni* Stiles, with virulent rickettsiae. Certain species of rodents, such as Columbian ground squirrels *Citellus columbianus columbianus;* golden-mantled ground squirrels, *C. lateralis tescorum;* chipmunks, *Eutamias amoenus;* and meadow mice, *Microtus pennsylvanicus,* when bitten by infected larval ticks developed rickettsemias that lasted from 6 to 9 days. During this time, rickettsiae in concentrations up to 1000 guinea pig infectious doses per 0.5 ml of blood circulated in the blood stream. Normal ticks that were allowed to feed during peak rickettsemias invariably had high infection rates, while those feeding during initial or final stages ingested an insufficient number of rickettsiae to establish permanent infection.

Indeed, the phenomenon of virulence variation of *R. rickettsi* and its significance in the natural history of RMSF continues to be a challenging research project. At least 4 different strains, with graded virulence for guinea pigs, occur in the United States, where they are said to be genetically true and to exist independently of one another (Price 1954). Of particular interest to us are the avirulent or "mild" strains that can be isolated from ticks but are no longer pathogenic for laboratory animals or any wild host animals so far tested. We have not yet been able to solve the question of where ticks become infected with such strains. Until a susceptible animal is found in nature, one may only speculate that these "mild" strains of *R. rickettsi* are nonpathogenic derivatives of originally virulent strains and are maintained in the tick population by transovarial passage. In support of this hypothesis are recent findings in the Bitter Root Valley of western Montana indicating that large percentages (as high as 35%) of adult *D. andersoni* contain rickettsia-like organisms related to *R. rickettsi* but nonpathogenic for chick embryos and guinea pigs (Burgdorfer, unpublished data). In distribution and growth within the tick, these organisms were found to behave similarly to pathogenic *R. rickettsi:* they invade all tissues and are transmitted ovarially. However, in contrast to pathogenic spotted