

Persistence of *Orientia tsutsugamushi* in humans

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Scrub typhus is known to be an acute infectious disease caused by *Orientia tsutsugamushi* and can be effectively treated with antibiotics. Previous studies using animal inoculation have revealed that *O. tsutsugamushi* does not persist in humans, and polymerase chain reaction (PCR)-based studies indicate that *O. tsutsugamushi* DNA in blood disappears gradually over 1 month after antibiotic treatment. It has not been clarified whether the DNA detected by PCR represents dead or viable bacteria, and the relevance of the DNA persisting after the disappearance of symptoms of scrub typhus has not been extensively investigated.

Although persistence of *O. tsutsugamushi* in humans has been reported sometimes, these cases are thought to be exceptional. Persistence of *O. tsutsugamushi* is a common finding in mice and has been documented an *in vitro* study. Chloramphenicol, doxycycline, azithromycin, and even rifampin show bacteriostatic effects against *O. tsutsugamushi* in mice or *in vitro*; therefore, theoretically antibiotics cannot eradicate the bacterium from the human body. Although the immune system is known to be involved in the recovery of an individual from scrub typhus, it is never been proven that this system can completely eradicate *O. tsutsugamushi* from the human body.

Viable *O. tsutsugamushi* were cultivated from blood samples of all 4 scrub typhus patients at 4 to 18 months after the completion of doxycycline treatment. At the time of obtaining samples for blood cultures, all patients were negative for symptoms of scrub typhus.

This finding suggests that *O. tsutsugamushi* causes chronic persistent infection that is characterized by an acute symptomatic phase, i.e., scrub typhus, followed by asymptomatic latent infection. Currently, relapse is the only known manifestation of latent infection. This new concept of *O. tsutsugamushi* infection being a chronic persistent infection rather than an acute infectious disease necessitates the revision of the current concepts of the epidemiology, clinical manifestations, diagnosis, and treatment of *O. tsutsugamushi* infection.