

Orientia tsutsugamushi

Disease Agent:

- *Orientia tsutsugamushi* (*Rickettsia tsutsugamushi* until 1995)

Disease Agent Characteristics:

- Rickettsiae are obligate intracellular, Gram-negative bacteria. The organism exhibits extensive genomic and antigenic heterogeneity that may lead to the definition of multiple species in the genus.
- Order: Rickettsiales; Family: Rickettsiaceae
- Size: 0.5-0.8 × 1.2-3 μm intracellular bacteria
- Nucleic acid: Rickettsial genomes are among the smallest of bacteria. The *Orientia* genome is approximately 2000 kb.
- Physicochemical properties: Information specific to *Orientia* was not found. The rickettsiae are susceptible to 1% sodium hypochlorite, 70% ethanol, glutaraldehyde, formaldehyde, and quaternary ammonium disinfectants. Sensitive to moist heat (121°C for at least 15 min) and dry heat (160-170°C for at least 1 h).

Disease Name:

- Scrub typhus, tsutsugamushi fever, mite-borne typhus fever

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Low, but absent in the US
- Public concern regarding disease agent: Absent

Background:

- Endemic across extensive parts of Asia, South Asia, Australia, and the Pacific
- Clinically described in the Far East more than 1500 years ago
- Scrub typhus may be the most prevalent human rickettsial infection, with over 1 billion people living in endemic areas and as many as 1 million infections annually.
- Localized, rural foci of risk are recognized where the vector (larval stages of trombiculid mites, referred to as chiggers) occurs and where natural environments are disturbed, as well as in rice paddies, atolls, and plantations.
- US experience related to exposure of military personnel during World War II, the Korean conflict, and the Vietnam war
- Disease prevalence is stable in endemic areas

- “Tsutsugamushi” = “dangerous mite” in Japanese
- Infection provides prolonged immunity to the specific strain of *O. tsutsugamushi* causing infection. Recurrent disease only occurs with other strains.

Common Human Exposure Routes:

- The bite of larval trombiculid mites (chiggers)
- Chiggers attach, take a blood meal over several hours, and then detach, often leaving a pruritic rash.
- Chiggers acquire infection transovarially or from rodent reservoirs.

Likelihood of Secondary Transmission:

- Vertical transmission during pregnancy has been alleged based on clinical illness and serology in the mother and the presence of IgM antibody in the infant.

At-Risk Populations:

- Residents of endemic areas, military personnel, and tourists

Vector and Reservoir Involved:

- *O. tsutsugamushi* is maintained in nature by highly efficient transovarial transmission in larval trombiculid mites (chiggers).
- Rodent reservoirs can also harbor the bacterium.

Blood Phase:

- Bacteremia occurs during the symptomatic phase and for 1-3 days before symptom onset.
- Although chronic infection of lymph nodes occurs, there is no evidence of bacteremia during this phase.

Survival/Persistence in Blood Products:

- Persistence and survival of *O. tsutsugamushi* in whole blood is well established.
- Survival in RBCs for 10, but not 30 days, and survival for at least 45 days in frozen and deglycerolized RBCs demonstrated in spiking studies.

Transmission by Blood Transfusion:

- Theoretical; a case report alleges transfusion-transmission, but proof is lacking.

Cases/Frequency in Population:

- Estimated 1 million cases per year in endemic areas
- Rare introduction into the US

Incubation Period:

- Usually 10-12 days; abrupt onset of illness 6-21 days after infected larval mite bite

Likelihood of Clinical Disease:

- Assumed to be very high

Primary Disease Symptoms:

- Abrupt onset of febrile illness
- Headache, myalgia, sweats, conjunctival injection, lymphadenopathy (may be tender), and mental changes (cognitive dysfunction to delirium and coma)
- Eschar develops at the site of mite bite and lymphadenopathy in nodes draining area may be prominent. The recognition of cutaneous findings varies greatly.
- Late in first week, a transient (few days) pale macular to maculopapular rash may be observed, most prominent on the trunk and spreading to the extremities.
- Hepatomegaly and splenomegaly may occur.
- Cough and x-ray evidence of pneumonia are common.
- Leukopenia/lymphopenia and thrombocytopenia are common.
- In severe disease, multiple organ involvement and disseminated intravascular coagulation with hemorrhage may occur.
- Febrile illness lasts for approximately 2 weeks without specific treatment. Prompt clinical response to tetracyclines
- Relapse is common but less severe.

Severity of Clinical Disease:

- The severity is very dependent on the particular strain of *O. tsutsugamushi*, area of acquisition, previous exposure, and host characteristics.

Mortality:

- Case-fatality rates vary from less than 1% with appropriate treatment to 60%.

Chronic Carriage:

- Viable organisms can be isolated from lymph nodes for up to 1-2 years after untreated infection.
- There is no evidence of long-term persistence after adequate therapy.

Treatment Available/Efficacious:

- Prompt clinical response to tetracyclines (e.g., doxycycline) or alternatively chloramphenicol, even with short courses
- Clinical evidence of antibiotic resistance is being described in South Asia.

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because transfusion transmission has not been definitively demonstrated.
- No sensitive or specific question is feasible.

Laboratory Tests Available:

- No FDA-licensed blood donor screening test exists.
- Serologic tests are the mainstay of laboratory diagnosis, but antibody appears after clinical illness and would not be useful for donor screening.
 - Specific IgM identified by IFA is the test of choice.
 - An immunoperoxidase test is available as an alternative.
 - EIA tests have been developed, and these have been found to be closely equivalent to IFA for early detection of antibody.
 - The complement fixation (CF) test for *O. tsutsugamushi* antibodies is strain specific, so all suspect strains must be included in the reagent.
 - Dot blot assays for antibody are available but are also strain specific.
- Direct detection:
 - Isolation in cell culture, animals, and embryonated chicken eggs
 - Immunofluorescence and immunoperoxidase staining can demonstrate organisms in tissue.
 - Monoclonal antibodies are now available for strain identification.
 - PCR has been used to detect *O. tsutsugamushi* in skin biopsies, peripheral mononuclear cells, whole blood, blood clots, and serum.
 - Nested PCR with specific primers allows determination of particular strains.
 - PCR is the only potentially rapid and specific practical approach to early diagnosis.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists, but malaria deferral will exclude many at-risk donors.
- Prudent practice would be to defer donor until signs and symptoms are gone and a course of treatment is completed.

Impact on Blood Availability:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:

- A mouse model suggests current filters can remove as many as 10^5 *O. tsutsugamushi* organisms from packed red blood cells spiked with infected mononuclear cells.

Pathogen Reduction Efficacy for Plasma Derivatives:

- No specific data are available for this organism, but fractionation and inactivation techniques in use for plasma derivatives should be robust against intracellular bacteria.

Other Prevention Measures:

- Tick avoidance measures (e.g., long pants, long sleeves, insect repellent)
- Riboflavin and light have been demonstrated to reduce infectivity by a factor of 10^5 in RBCs, platelets, and plasma in a mouse model.
- Amotosalen and UV light (INTERCEPT) used to treat platelet concentrates reduced infectivity in mice by a similar amount.

Suggested Reading:

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