Rickettsia is a genus of non-motile, non-spore forming, obligate intracellular, gram negative bacteria that can present as cocci, rods, or thread-like. Rickettsia can only live in eukaryotic host cells (e.g. endothelial cells, tissue or embryo cultures). Serologically, Rickettsia is classified into three groups (spotted fever, typhus, and scrub typhus). This grouping has since been confirmed by DNA sequencing. However, recently, the scrub typhus group has been reclassified into a new genus, Orientia.

**The Clinical Manifestations**

The taxonomical order of Rickettsia is:

- **Phylum**: Proteobacteria
- **Class**: Alphaproteobacteria
- **Order**: Rickettsiales
- **Family**: Rickettsiaceae
- **Genus**: Rickettsia, Orientia

**Species**:

- To name a few: R prowazekii, R rickettsii, R akari (spotted fever group/SFG), O tsutsugamachi (scrub typhus group)

**Antigen-based detection (serology)** includes enzyme-linked immunosorbent assay (ELISA) or detecting antibody expressed by infected blood specimens. An ELISA plate reader measures the fluorescence intensity, where higher fluorescent level (visible deeper color, Figure 7A) corresponds to higher antibody titer. Rickettsial infection is confirmed when fourfold rise of IgG between samples taken at the acute period of infection and during the convalescent time points (at least 14 days apart) is observed; or, if there is a significant increase in IgM titer. However, the current 'gold standard' of rickettsial detection is Immuno-fluoresence assay (IFA).

**Antigen-based detection** can be done by culturing the bacteria that can present as cocci, rods, or thread-like. Rickettsia can only live in eukaryotic host cells (e.g. endothelial cells, tissue or embryo cultures). Serologically, Rickettsia is classified into three groups (spotted fever, typhus, and scrub typhus). This grouping has since been confirmed by DNA sequencing. However, recently, the scrub typhus group has been reclassified into a new genus, Orientia. ELISA measures the expression of immunoglobulin G (IgG) and immunoglobulin M (IgM) against rickettsiae. An ELISA plate reader measures the fluorescence intensity, where higher fluorescent level (visible deeper color, Figure 7A) corresponds to higher antibody titer. Rickettisial infection is confirmed when fourfold rise of IgG between samples taken at the acute period of infection and during the convalescent time points (at least 14 days apart) is observed; or, if there is a significant increase in IgM titer. However, the current 'gold standard' of rickettsial detection is Immuno-fluorescence assay (IFA). The presence of rickettsia-specific antibody is shown as green fluorescent bodies (Figures 7B). Since antibody development at least five days after symptoms appear, confirmation of rickettsial infection by ELISA or IFA may not be used to guide treatment.

**Antigen-based detection (PCR)** fills in this gap because bacterial multiplication has started even before symptoms appear (Figure 6). Polymerase chain reaction (PCR) detects rickettsia in clinical specimens by amplifying a portion of the bacterial DNA multiple times. Detection of fluorescence during PCR cycles confirms the presence of rickettsia DNA. More copies of DNA (more bacteria) correspond with lesser values of Ct (cycle threshold). PCR is advantageous compared to serological assay in terms to confirm rickettsial infection in the early stages of disease, such that patients can obtain appropriate treatment. It is also highly sensitive (theoretically it can detect down to 1 DNA copy), which unfortunately makes it prone to cross-contamination leading to false positive result.

**Laboratory confirmation tests for rickettsial infection are not available at the hospitals in Indonesia for the following several reasons: the need of living media and high biohazard level; the delicate nature and costly materials/instruments of PCR, ELISA or IFA; the need for high-skilled technicians to perform these assays; and the lack of accurate rapid diagnostic tests. Consequently, rickettsia is rarely diagnosed as the cause of infectious diseases. It is reflected in INA-RESPOND’s acute fever requiring hospitalization (AFIRE) study where more than 5% of acute fever were confirmed rickettsial infections.**

**The treatment and prevention**

Early treatment with appropriate antibiotics (first week of illness) is highly effective. Fever usually disappears in 1-3 days after treatment. As well as the causative agent of murine typhus, R. typhi has been observed within the X cheopis fleas in East Java, West Java, East Kalimantan, and North Sulawesi. Seroreactivity either to murine typhus (R. typhi), SFG (R. rickettsii and R. conorii), or scrub typhus (O. tsutsugamushi), was shown in rodent population of Jayapura (Papua) as well as in human population of Malang (East Java) and Gag Island (Papua). Human cases have been confirmed serologically by two studies in Semarang and molecularly by several returning travelers. Our study confirmed that Rickettsia is rare in Indonesia. It is reflected in INA-RESPOND’s acute fever requiring hospitalization (AFIRE) study where more than 5% of acute fever were confirmed rickettsial infections. Rickettsia bacteria, we need to avoid getting bitten by the vectors (ticks, fleas, mice, chiggers) by covering our skin from exposure and using insect repellent when doing outdoor activities. At home, we need to keep our home clean of rats and to ensure that our pets are free from fleas.

**The situation in Indonesia and future steps**

In Indonesia, the endemicity of the three biotypes has been reported. The circulation of R. typhi and other rickettsiae as well as the causative agent of murine typhus, R. typhi, has been observed within the X cheopis fleas in East Java, West Java, East Kalimantan, and North Sulawesi. Seroreactivity either to murine typhus (R. typhi), SFG (R. rickettsii and R. conorii), or scrub typhus (O. tsutsugamushi), was shown in rodent population of Jayapura (Papua) as well as in human population of Malang (East Java) and Gag Island (Papua). Human cases have been confirmed serologically by two studies in Semarang and molecularly by several returning travelers. Our study confirmed that Rickettsia is rare in Indonesia. It is reflected in INA-RESPOND’s acute fever requiring hospitalization (AFIRE) study where more than 5% of acute fever were confirmed rickettsial infections. Rickettsia bacteria, we need to avoid getting bitten by the vectors (ticks, fleas, mice, chiggers) by covering our skin from exposure and using insect repellent when doing outdoor activities. At home, we need to keep our home clean of rats and to ensure that our pets are free from fleas.

**Further Reading**


**The Confusion between Typhus Fever & Typhoid Fever**

Typhus and typhoid fever were two diseases that people (including health care workers) often confuse and use interchangeably. To clarify, here are the differences.

- **Typhus Fever**
  - It is introduced by Pavoluk de Lasavage in 1879 to explain ‘confusional mania or delirium’ [Greek ‘typho’, meaning ‘smoke’, ‘mist’ or fog’].
  - Typhus fever (menacing typhus fever) was introduced by Pierre Charles Rocha in 1880 to describe the clinical and pathological aspects of the disease with mental fogging.

- **Typhoid Fever**
  - The first species of Rickettsia, which caused epidemic fever, was found by Rocha Lima, a Brazilian physician and named it Rickettsia prowazekii, after his friend Rickettsia prowazekii.
  - Rickettsia prowazekii was isolated in 1880 by Karl Joseph Eberth. The term ‘Salmonella’ was named after a US veterinary pathologist, Daniel E. Salmon.

**Transmission**

- Vector bites
- Food contamination (linal-linal)

**Diagnoses assays**

- **Bacterial culture in animals, embryonated egg or cell lines**
- **PCR, ELISA and IFA**

**Treatment**

- Doxycycline, Fluoroquinolones, Chloramphenicol
- Antimicrobial, Ceftriaxone, Ciprofloxacin, Chloramphenicol, Amoxicillin, Trimethoprim/Sulfamethoxazole

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