Rickettsia prowazekii

Basic agent information

Section I- Infectious Agent
Risk Group:
- RG3
Synonym or Cross reference:
- Louse-borne typhus fever, Louse-borne epidemic typhus, LBET, Epidemic typhus, exanthematic typhus, historical typhus, classic typhus, sylvatic typhus, red louse disease, jail fever, Brill Zinsser disease
Characteristics:
- SELECT AGENT
- Rickettsia prowazekii is an obligate intracellular bacterium of the Rickettsiaceae family. It is a small, gram-negative α-proteobacteria and is a coccobacillus

Section II- Dissemination
Reservoir:
- Humans are necessary to maintain the infection; however, flying squirrels may also be a potential reservoir for the disease
Zoonosis:
- The flying squirrel may spread the disease to humans indirectly via infected lice or infective lice feces in aerosol form
Vectors:
- The body louse, Pediculus humanis corporis is the main vector for epidemic typhus although it has been proposed that head lice, Pediculus humanis capitis, could also be a vector

Research use considerations

Section III- Laboratory Hazards
Laboratory-Acquired Infections:
- 56 laboratory-acquired infections with 3 deaths caused by epidemic typhus have been reported although all of these are prior to 1968. There were 57 cases additional of unidentified typhus within that same period of time
Sources/Specimens:
- Infective lice, their tissues and their feces may contain the infective agent. Flying squirrels may also be a direct source of infection
Primary hazards:
- Accidental parenteral inoculation and exposure to infectious aerosols or animals
Special Hazards:
- None
Section IV- Stability and Viability

Susceptibility to Disinfectants:
- Susceptible to many disinfectants - Clidox, 5% bleach, 70% ethanol, formaldehyde, glutaraldehyde, iodines

Physical Inactivation:
- Sensitive to moist heat (121°C for at least 15 min) and dry heat (160-170°C for at least 1 hour)

Survival Outside Host:
- Stable in lice feces for up to 100 days and can be viable in a blood sample for several years if kept at -70 °C

Section V- Recommended Precautions

Containment Requirements:
- Biosafety level 3 practices, containment and facilities for all manipulations of cultures and for experimental animal studies

Protective Clothing:
- Impervious gloves when direct contact with infectious materials is unavoidable; gloves and gown (with tight wrists and tie in back), PAPR when working at BSL3/ABSL3

Other Precautions:
- Animal Biosafety Level 3 facilities and practices

Health and Medical

Section VI- Health Hazard

Pathogenicity:
- Epidemic typhus is usually characterized by 1-3 days of malaise before abrupt onset of severe headaches and fever (40 °C). Symptoms include myalgia, arthralgia, abdominal pain, anorexia, chills, trachypnea, diarrhoea, myocarditis and tachycardia.
- In 20-40% of cases, non-confluent erythematous rashes start in the axilla and then spread to the rest of the body with the exception of the face, palms of hands and soles of feet.
- Up to 80% of cases have CNS complications such as delirium, seizures, coma, meningeal irritation, confusion, drowsiness, and hearing loss. Cough has been reported in 38- 70% of cases and gangrene and necrosis of fingers and toes have occurred.
- The disease usually lasts for two weeks, although it may take months to fully recuperate. The mortality rate is estimated at 4% if the patient is treated with the appropriate antibiotics but the mortality rate is higher in individuals who are over the age of 60. A milder recurrent form of typhus called Brill Zinsser disease may occur in a patient that has previously had epidemic typhus and this form has a mortality rate of 1%

Epidemiology:
- The disease is found in areas with cold weather, homelessness and poverty. It is a particular problem during famine, conflict and natural catastrophes as cramped conditions and lack of hygiene facilitate the spread of body lice. In the past 25 years, cases have been reported in Africa (Ethiopia, Nigeria and Burundi), Mexico, Central America, South
America, Eastern Europe, Afghanistan, Northern India, China and the United States. Since 1976, 39 cases of epidemic typhus were reported in the United States and at least one third of the cases were related to contact with flying squirrels.

**Host Range:**
- Humans, flying squirrels (*Glaucomys volans*) and body and head lice have been shown to contain the infectious agent in their tissues. Livestock and donkeys have also been found to have *Rickettsia prowazekii* antibodies in their systems.

**Infectious Dose:**
- <10 organisms

**Natural Mode of Transmission:**
- The infection is caused by the contamination of a louse bite site, superficial abrasion, conjunctivae or mucous membranes with louse feces or crushed louse tissues. The disease can also be transmitted by inhalation of infectious aerosols (like louse fecal dust), which poses a potential risk for healthcare workers and laboratory personnel. The body louse is infected when feeding on an infected human and the flying squirrel may be infected by fleas and lice.

**Incubation Period:**
- From 10 to 14 days

**Communicability:**
- Although human-to-human transmission does not occur, proximity to an infected individual increases the chances of exposure to infected body lice. Humans remain infective for life and can pass the disease to lice. The lice tend to leave sick individuals and go towards healthier hosts. Lice become infective 5-7 days after exposure and remain so for life; however, they tend to die 1 week after contracting the bacteria. The lice feces remain infective for 100 days as aerosols and this is the proposed mode of transmission between flying squirrels and humans.

**Section VII- Medical**

**Surveillance:**
- Anyone with a splash or aerosol exposure or inoculation injury or just develops fever should report to OCMED or the ER after reporting to their supervisor and PI on the project.
- The infection can be identified by PCR, latex agglutination test, or immunological tests (i.e. enzyme-linked immunoabsorbent, immunoperoxidase, dot blot, Western blotting, and IFA assays, CF and latex agglutination tests).
- Microbiological diagnosis is usually based on serology, where a four-fold rise in titer in paired samples is considered diagnostic.
- The organism can be isolated following culture of clinical samples (blood or skin biopsy) and visualized using microscopy following Gimenez staining or immunofluorescence.

**Immunization:**
- No vaccine is currently commercially available; however, some experimental vaccines are being developed for high-risk individuals (such as healthcare workers and scientists)
Drug Susceptibility:
- Susceptible to tetracyclines, chloramphenicol, or doxycycline. Therapy with doxycycline for 5-7 days, or 2-4 days after defervescence, is recommended to preclude relapses. In outbreak situations, a single oral dose of doxycycline can be given.

Prophylaxis:
- Post-exposure prophylaxis after a needle stick or splash is not routinely recommended.

Clinical Monitoring, including fever watch:
- Serologies
- Blood for culture and PCR (EDTA-anti-coagulated whole blood, sent to CDC)
- Skin biopsy for PCR or immunohistochemical staining (CDC)

Treatment:
- Successful treatment is achieved with doxycycline (200 mg/day) or cipro (1.5 g/d for 5-7 days). Chloramphenicol 2 g/day for 7-10 days, although chloramphenicol is not used for treatment in the Western world (even though chloramphenicol resistance is NOT an approved marker for use in the laboratory).
- Pregnant women should receive a macrolide, azithro or clarithro.

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