

Rickettsial Agents

Agent: *Coxiella burnetii*

Of the rickettsial agents, *Coxiella burnetii* probably presents the greatest risk of laboratory infection. The organism is highly infectious and remarkably resistant to drying and environmental conditions.⁽¹⁾ The infectious dose of virulent Phase I organisms in laboratory animals has been calculated to be as small as a single organism. The estimated human ID₂₅₋₅₀ (inhalation) for Q fever is 10 organisms.⁽²⁾ Pike's summary indicates that Q fever is the second most commonly reported laboratory-associated infection, with outbreaks involving 15 or more persons recorded in several institutions.⁽³⁾⁽⁴⁾ A broad range of domestic and wild mammals are natural hosts for Q fever and may serve as potential sources of infection for laboratory and animal care personnel. Exposure to naturally infected, often asymptomatic, sheep and their birth products is a documented hazard to personnel.⁽⁵⁾⁽⁶⁾ Although rare, *C. burnetii* is known to cause chronic infections such as endocarditis or granulomatous hepatitis.

Laboratory Hazards: The necessity of using embryonate eggs or cell culture techniques for the propagation of *C. burnetii* leads to extensive purification procedures. Exposure to infectious aerosols or parenteral inoculation are the most likely sources of infection to laboratory and animal care personnel.⁽⁷⁾ The agent may be present in infected arthropods, and in the blood, urine, feces, milk, and tissues of infected animal or human hosts. The placenta of infected sheep may contain as many as 10⁹ organisms per gram of tissue⁽⁸⁾ and milk may contain 10⁵ organisms per gram.

Recommended Precautions: Biosafety Level 2 practices and facilities are recommended for nonpropagative laboratory procedures, including serological examinations and staining of impression smears. Biosafety Level 3 practices and facilities are recommended for activities involving the inoculation, incubation, and harvesting of embryonate eggs or cell cultures, the necropsy of infected animals and the manipulation of infected tissues. Since infected guinea pigs and other rodents may shed the organisms in urine or feces,⁽⁹⁾ experimentally infected rodents should be maintained under Animal Biosafety Level 3. Specific clonal isolates of avirulent (Phase II) strains may be considered for lower containment conditions⁽¹⁰⁾

Recommended precautions for facilities using sheep as experimental animals are described by Spinelli⁽¹¹⁾ and by Bernard.⁽¹²⁾ An investigational new Phase I, Q fever vaccine (IND) is available from the Special Immunizations Program, U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID), Fort Detrick, Maryland. The use of this vaccine should be limited to those who are at high risk of exposure and who have no demonstrated sensitivity to Q fever antigen. Individuals with valvular heart disease should not work with *C. burnetii*.

Transfer of Agent: For a permit to import this agent, contact CDC. Contact the Department of Commerce for a permit to export this agent. Laboratory registration with CDC is required before sending or receiving this select agent. An importation or domestic transfer permit for this agent can be obtained from USDA/APHIS/VS.

Agent: *Rickettsia prowazekii*, *Rickettsia typhi* (*R. mooseri*), *Orientia* (*Rickettsia*) *tsutsugamushi* and Spotted Fever Group agents of human disease; *Rickettsia rickettsii*, *Rickettsia conorii*, *Rickettsia akari*, *Rickettsia australis*, *Rickettsia siberica*, and *Rickettsia japonicum*

Pike reported 57 cases of laboratory-associated typhus (type not specified), 56 cases of epidemic typhus with three deaths, and cases of murine typhus.⁽¹³⁾ More recently, three cases of murine typhus were reported from a research facility.⁽¹⁴⁾ Two of these three cases were associated with handling of infectious materials on the open bench; the third case resulted from an accidental parenteral inoculation. These three cases represented an attack rate of 20% in personnel working with infectious materials.

Rocky Mountain spotted fever is a documented hazard to laboratory personnel. Pike reported 63 laboratory-associated cases, 11 of which were fatal.⁽¹⁵⁾ Oster reported 9 cases occurring over a 6-year period in one laboratory, which were believed to have been acquired as a result of exposure to infectious aerosols.⁽¹⁶⁾

Laboratory Hazards: Accidental parenteral inoculation and exposure to infectious aerosols are the most likely sources of laboratory-associated infection.⁽¹⁷⁾ Successful aerosol transmission of *R. rickettsii* has been experimentally documented in nonhuman primates.⁽¹⁸⁾ Five cases of rickettsial pox recorded by Pike were associated with exposure to bites of infected mites.⁽¹⁹⁾

Naturally and experimentally infected mammals, their ectoparasites, and their infected tissues are potential sources of human infection. The organisms are relatively unstable under ambient environmental conditions.

Recommended Precautions: Biosafety Level 2 practices and facilities are recommended for nonpropagative laboratory procedures, including serological and fluorescent antibody procedures, and for the staining of impression smears. Biosafety Level 3 practices and facilities are recommended for all other manipulations of known or potentially infectious materials, including necropsy of experimentally infected animals and trituration of their tissues, and inoculation, incubation, and harvesting of embryonate eggs or cell cultures. Animal Biosafety Level 2 practices and facilities are recommended for the holding of experimentally infected mammals other than arthropods. Level 3 practices and facilities are recommended for animal studies with arthropods naturally or experimentally infected with rickettsial agents of human disease.

Because of the proven value of antibiotic therapy in the early stages of infection, it is essential that laboratories working with rickettsiae have an effective system for reporting febrile illnesses in laboratory personnel, medical evaluation of potential cases and, when

indicated, institution of appropriate antibiotic therapy. Vaccines are not currently available for use in humans (see following Surveillance section).

Transfer of Agent: For a permit to import these agents, contact CDC. Contact the Department of Commerce for a permit to export these agents. Laboratory registration with CDC is required before sending or receiving these select agents.

Surveillance of Personnel for Laboratory-Associated Rickettsial Infections

Under natural circumstances, the severity of disease caused by rickettsial agents varies considerably. In the laboratory, very large inocula are possible, which might produce unusual and perhaps very serious responses. Surveillance of personnel for laboratory-associated infections with rickettsial agents can dramatically reduce the risk of serious consequences of disease.

Experience indicates that infections adequately treated with specific anti-rickettsial chemotherapy on the first day of disease do not generally present serious problems. Delay in instituting appropriate chemotherapy, however, may result in debilitating or severe acute disease ranging from increased periods of convalescence in typhus and scrub typhus to death in *R. rickettsii* infections. The key to reducing the severity of disease from laboratory-associated infections is a reliable surveillance system which includes: 1) round-the-clock availability of an experienced medical officer, 2) indoctrination of all personnel on the potential hazards of working with rickettsial agents and advantages of early therapy, 3) a reporting system for all recognized overt exposures and accidents, 4) the reporting of all febrile illnesses, especially those associated with headache, malaise, and prostration when no other certain cause exists, and 5) a non-punitive atmosphere that encourages reporting of any febrile illness.

Rickettsial agents can be handled in the laboratory with minimal real danger to life when an adequate surveillance system complements a staff which is knowledgeable about the hazards of rickettsial infections and uses the safeguards recommended in the agent summary statements.

References

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