VIRAL HEMMORHAGIC FEVERS

ALL SUSPECT CASES OF TULAREMIA MUST BE REPORTED IMMEDIATELY TO THE HEALTH AND HUMAN SERVICES COMMUNICABLE DISEASE CONTROL:

During business hours: (916) 875-5881
After hours (Health Officer On call): (916) 875-5000

Etiologic Agents: Arenaviradae (Lassa, Junin, Machupo, Guanarito, and Sabia), Filoviradae (Marburg and Ebola), Bunyaviradae (Congo-Crimean hemmorhagic fever virus and hantaviruses)and Flaviradae (yellow fever and Dengue) can all cause viral hemmorhagic fever (VHF)

Epidemiology:

- Highly infectious after aerosolization
- Infectious dose can be as low as 1-10 organisms
- Risk of person-to-person transmission depends on virus

Clinical:

- Incubation period is 4 – 21 days, depending on virus
- Clinical presentation would vary by viral agent; however, dominant clinical features of all are a consequence of microvascular damage and changes in vascular permeability. Fever, myalgia, and prostration may evolve to shock, generalized mucous membrane hemmorhage, and neurologic, hematopoietic, or pulmonary involvement.

Laboratory Diagnosis:

- Viral isolation should be handled in a Biosafety Level 3 or 4 facility and may take 3 – 10 days
- ELISA or reverse transcriptase PCR available for most VHF viruses
- Contact the Sacramento County Public Health Laboratory for assistance.

Patient Isolation:

- Isolation room with contact precautions.

Treatment:

- Ribavirin (30 mg/kg IV x 1, then 15 mg/kg IV q 6 h x 4 days, 7.5 mg/kg IV q 8 x 6 days) may be helpful for Congo-Crimean hemmorhagic fever or arenaviruses

Prophylaxis:

- Licensed vaccine available only for yellow fever

SACRAMENTO COUNTY

HEALTH AND HUMAN SERVICES

COMMUNICABLE DISEASE CONTROL

Medical Treatment and Response to Suspected Q-Fever:

Information for Health Care Providers During Biologic Emergencies

ALL SUSPECT CASES OF Q FEVER MUST BE REPORTED IMMEDIATELY TO THE SACRAMENTO COUNTY HEALTH AND HUMAN SERVICES, COMMUNICABLE DISEASE CONTROL:

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I. KEY SUMMARY POINTS

Epidemiology:

- *Coxiella burnettii* is highly infectious by the aerosol route
- Q Fever is **rarely** transmitted from person to person

Clinical:

- Incubation period is 10-40 days
- Acute infection may be asymptomatic or a self-limited febrile illness
- Chest x-ray evidence of pneumonia is present in up to 50% of cases
- Mortality rate is less than 2%
- Contact the Sacramento County Public Health Laboratory at (530) 8889-7141 for assistance.

Diagnosis:

- Requires serologic confirmation (IFA or ELISA)
- Isolation of organism is not recommended due to significant hazards from handling bacterial cultures in the laboratory

Treatment:

- Illness usually resolves **without** treatment
- Tetracyclines are the antibiotics of choice for more severe illnesses

Prophylaxis:

- Tetracycline antibiotics are very effective if administered **8 to 12 days AFTER exposure**
- Starting prophylaxis <u>immediately</u> after exposure can delay symptom onset but does not prevent illness

Patient Isolation:

- Universal precautions. Patients do **not** require isolation rooms

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II. Introduction/Epidemiology

Q fever is a zoonotic disease caused by *Coxiella burnetii,* a rickettsia-like organism. *C. burnetii* is unable to replicate outside host cells, but there is a spore-like form of the organism that is extremely resistant to heat, dessication and many standard antiseptic compounds. The organism can persist in the environment for long periods under harsh conditions. Despite the inherent resilience of *C. burnetii* and its ease in transmissibility, generally by inhaled aerosols, the acute clinical disease of Q fever is usually benign, although temporarily incapacitating.

Coxiella burnetii is extremely infectious. Humans have been infected most commonly by contact with domestic livestock, particularly goats, cattle and sheep but household pets, notably cats, have also been associated with infection. The risk is highest when humans are exposed to these animals at parturition, presumably via aerosolization of the organism from the uterus during birthing. *Coxiella* organisms can persist in the local environment, and produce infection, for weeks or months after contamination.

Q fever has VERY RARELY been transmitted from person-to-person (specifically, transmission has occurred to attendants during autopsies and from an infected patient to the attending obstetrician during delivery). **Persons exposed to an aerosol of *Coxiella burnetii* do not present a risk for secondary transmission to others or for re-aerosolization of the organism.**

III. Significance as a Potential Bioterrorist Agent

- The spore-like form of the organism is resistant to heat and dessication, and can persist in the environment for long periods of time.

- Highly infectious when aerosolized and inhaled; a single organism may cause clinical illness

- Aerosolized *Coxiella burnetii* can result in an incapacitating respiratory illness; however, severe illness and fatalities are rare.

IV. Clinical Manifestations

During an act of bioterrorism, release of an aerosol will be the most likely route of transmission.

A. Acute Q Fever

Incubation period - 10 - 40 days, duration of the incubation period is inversely correlated with the size of the inoculum.

Symptoms - Acute disease is **not** clinically distinct, and illness resembles viral respiratory infections or atypical pneumonias. Can be divided into 3 main categories: (1) asymptomatic infection (seroconversion) - occurs in up to 50% of exposed persons, (2) self-limited febrile flu-like illness without pneumonia lasting 2 to 14 days and (3) pneumonia. Hepatitis, meningo-encephalitis, myocarditis, and pericarditis may be present acutely but are relatively uncommon.

Symptomatic patients exhibit any combination of the following (in order of decreasing frequency of appearance):

SYMPTOM	RELATIVE FREQUENCY (%)
fever (present in all symptomatic patients)	80-100
chills, rigors	75-100
severe headache, **retroorbital pain (may be a useful clue to diagnosis)**	50-100
fatigue, anorexia, weight loss	50-85
cough	50-60
myalgia	45-84
pleuritic chest pain	40-50
nausea, vomiting	15-20
diarrhea	5-20
neck stiffness	5-7

Pneumonia -Chest x-ray evidence of pneumonia may be present in up to 50% of patients. There are three possible presentations: (a) atypical pneumonia (dry nonproductive cough) (b) rapidly progressive pneumonia (often mimicking Legionnaire's disease), or (c) pneumonia with fever but no pulmonary symptoms [most common clinical scenario for acute Q fever]. *Radiographic findings*: Variable;

may have pleural-based opacities, multiple rounded opacities, about 35% have pleural effusion, hilar adenopathy is uncommon.

Duration - 2 days - 2 weeks

Mortality - Low, estimated to be about 2% (usually in patients with co-morbid conditions)

B. Chronic Q Fever

Chronic infection due to Q fever is uncommon, occurring in less than 1% of acute infections. Endocarditis is the usual manifestation of Q fever but a wide array of syndromes have been described including: infection of vascular grafts, osteomyelitis, infectious arthritis, chronic hepatitis, pseudotumor of the lung, chronic pulmonary fibrosis, infection during pregnancy with miscarriage and prolonged fever.

Incubation period - varies, can be months to several years

Symptoms - Variable depending on specific clinical syndrome. Most often diagnosed in patients with either a cardiovascular abnormality (valvulopathy, prosthesis or aneurysm) or an underlying immunocompromised state (i.e., HIV infection or cancer).

Laboratory Diagnosis

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The diagnosis of Q Fever requires a high index of suspicion since the disease often presents with nonspecific symptoms which can be difficult to distinguish from viral illnesses or atypical pneumonia. The diagnosis is generally confirmed serologically; most laboratories are not equipped to isolate *Coxiella burnetii* and isolation of the organism is not recommended due to the significant hazards from handling bacterial cultures in the laboratory.

- **Serology**

  Several assays are available; antibody detection by indirect fluorescent antibody (IFA) or ELISA are used most commonly and appear to be the most sensitive. Significant IgM antibody does not appear until 2-3 weeks into illness and may persist for years. Acute and convalescent (2-3 months after onset of illness) antibody titres show a four-fold rise. In acute Q fever, antibodies to phase II antigens are higher than those to phase I antigens, in chronic Q fever the reverse occurs. Antibodies of the IgM type are usually observed for the first 6-12 months after infection, with IgG persisting afterward.

- **Contact the Sacramento County Public Health Laboratory at (916) 874-9231 for assistance.**

V. Handling Laboratory Specimens

Laboratory staff handling specimens from persons who might have Q fever must wear surgical gloves, protective gowns, and shoe covers. Laboratory tests, such as serological examinations and staining of tissue impression smears, can be performed in Biological Safety Level 2 cabinets; although not recommended, blood cultures should be maintained in a closed system. Every effort should be made to avoid splashing or creating an aerosol. Biosafety Level 3 practices and facilities should be used for inoculation, incubation and harvesting of cell cultures and the manipulation of infected tissues.

Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (0.05% hypochlorite, 5% peroxide, or 1:100 solution of Lysol). All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation, or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

VI. Treatment

A. Acute Q Fever

Pneumonia usually resolves without treatment in 15 days; therefore, in the event of a bioterrorist attack, therapy may only be required for persons with more severe illness. Several antibiotics have been evaluated as therapeutic agents for acute Q fever -- tetracyclines have been shown to shorten the duration of illness and are considered the **drug of choice**, particularly for severe infection:

- ***Adult dosages:***

  Doxycycline 100 mg every 12 hours po or IV for 15-21 days or **tetracycline** 500 mg po every 6 hours for 15-21 days. (**NOTE:** For milder illnesses, 5-7 days of therapy may be sufficient)

  Alternatives:
  Quinolones, chloramphenicol, trimethroprim-sulfamethoxazole are also probably effective.

  Studies of erythromycin (500 mg - 1 gram every 6 hours p.o. or IV) have shown conflicting results, and erythromycin is probably not preferred for cases of severe pneumonia. Azithromycin appears to be another option but little clinical information is available. Beta-lactam antibiotics are generally ineffective.

- ***Pediatric dosages:***
  For more severe illnesses, when benefits outweigh the risks, consider use of doxycycline (or co-trimoxazole or chloramphenicol).

If > or = 8 years of age:	**Doxycycline:**	
		If > 45 kg - 100 mg IV or po every 12 hours
		If < 45 kg - 2.2 mg/kg IV or po every 12 hours
If < 8 years of age:	**Co-trimoxazole**	4 mg/kg IV or orally every 12 hours
	Chloramphenicol	25 mg/kg orally every 12 hours
Newborns up to age 2 months:	**Ciprofloxacin**	10-20 mg/kg orally twice daily, do not exceed 1 gram/day.

- ***Pregnant Women Post-Exposure Prophylaxis*** - Co-trimoxazole [1 DS tablet orally twice daily], is the preferred antibiotic, except at term, when the risk of kernicteris is greatest -- use fluoroquinolones [ciprofloxacin 500 mg orally twice daily]

B. Chronic Q Fever

Endocarditis requires combination therapy, usually with doxycycline plus rifampin or possibly a quinolone plus rifampin. The duration of therapy is for years and a valve replacement is often necessary.

VII. Isolation of Patients

Q fever is not transmissible from person-to-person. Standard precautions should be followed for all patients. Respiratory isolation rooms are not required.

VIII. Disposal of Infectious Waste

Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

IX. Autopsy and Handling of Corpses

All postmortem procedures are to be performed using Respiratory Precautions. Efforts should be made to avoid aerosolization.

- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal protective equipment) as delineated by O.S.H.A. guidelines.

- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as 10% hypochlorite or 5% phenol (carbolic acid).

X. Management of Exposed Persons

An exposed person is defined as a person who has been exposed to the release of a *Coxiella burnetii* containing aerosol.

Post-exposure prophylaxis: Antibiotic prophylaxis is very effective and will prevent clinical disease **if administered 8-12 days AFTER exposure** (doxycycline 100 mg po every 12 hours or tetracycline 500 mg po every 6 hours) for 5 days. **Starting prophylaxis immediately after exposure can delay onset of disease but not prevent symptoms from occurring.**

Pediatric Post-Exposure Prophylaxis with Doxycycline:

If > or = 8 years of age:		If > 45 kg - 100 mg orally every 12 hours for 5 days If < 45 kg - 2.2 mg/kg orally every 12 hours for 5 days
If < 8 years of age:	**Co-trimoxazole**	4 mg/kg orally every 12 hours for 5 days
	Chloramphenicol	25 mg/kg orally every 12 hours for 5 days
Newborns up to age 2 months:	**Ciprofloxacin**	10-20 mg/kg orally twice daily for 5 days, do not exceed 1 gram/day

XI. **Reporting to the Health Department**

Confirmed or suspect Q Fever cases must be reported immediately to the Sacramento County Health and Human Services Communicable Disease Control:

- **During business hours**

  Sacramento County Health and Human Services Communicable Disease Control at (916) 875-5881

- **After business hours**

  Sacramento County Health Officer On call, at (916) 875-5000

XII. **References**

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