Health Advisory:

Q Fever Cases in Missouri

March 27, 2014

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SUBJECT: Q Fever Cases in Missouri

Q fever is a zoonotic disease caused by the bacteria *Coxiella burnetii*. *C. burnetii* is distributed worldwide and causes sporadic infections and outbreaks in animal species and humans. In 2013, 22 human Q fever cases were reported to the Missouri Department of Health and Senior Services (DHSS). The purpose of this DHSS Health Advisory is to increase awareness among health care providers of Q fever, and to provide guidance on the epidemiology, diagnosis, and treatment of Q fever, including the identification of persons who are at higher risk of Q fever infection and its complications.

Background

C. burnetii are spore-forming bacteria that can survive for long periods of time in the environment. The primary sources of Q fever are infected cattle, sheep, and goats, which shed the organism in feces, milk, nasal discharge, placental tissue, and amniotic fluid. *C. burnetii* is known to be present in roughly 20-30% of goat herds, and is also endemic in cattle and sheep. Infection of humans usually occurs by inhalation of *C. burnetii* from air that contains airborne barnyard dust contaminated by infected animals. Inhalation of just a single organism is sufficient to cause infection. Cases of Q fever have been documented among people living downwind from infected livestock without having direct exposure to infected animals. Other, less common routes of transmission include: the consumption of raw dairy products, human-to-human transmission (baby infected during delivery by infected mother, exposure during autopsy), or a blood transfusion from an infected donor. Ticks can harbor *C. burnetii*, but infections acquired through a tick bite are rare. Because of the high infectivity of this organism, *C. burnetii* is designated a Category B bioterrorism agent.

Human cases are rare, with typically fewer than 200 Q fever cases reported annually in the United States, and 0-5 cases per year reported in Missouri between 2008 and 2012. However, because Q fever may resemble other diseases, be mild, or even cause no symptoms (asymptomatic seroconversion occurs in 50-60% of infected persons), cases of human Q fever are likely under-recognized. Q fever outbreaks associated with animal farms have been reported in the United States.

Q fever can cause acute and chronic illness in humans. Illness onset typically occurs 2-3 weeks after exposure to the organism. Symptoms may include: high fever (104°-105° F), chills and/or sweats, severe headache, malaise, myalgia, non-productive cough, chest pain, and possibly gastrointestinal symptoms such as nausea, vomiting, diarrhea, or abdominal pain. Most acute Q fever cases will recover completely, but some persons experience serious illness and severe complications, including: pneumonia, granulomatous hepatitis, myocarditis, and central nervous system complications. Pregnant women who are infected may be at risk for pre-term delivery or miscarriage. The estimated case fatality rate is < 2% of hospitalized patients. Early treatment with an appropriate antibiotic may shorten the duration of illness and lessen the risk of complications.

Chronic Q fever is a severe disease occurring in < 5% of acutely infected patients. It may occur as early as six weeks after an acute infection, or may manifest years later. Chronic Q fever is a risk for anyone with a history of acute Q fever illness, particularly those persons

with **valvular disease**, **blood vessel abnormalities**, **immunosuppressed** persons (such as may occur through cancer treatments, advanced HIV infection, prior organ transplants, or some medications), and women who were **pregnant** when they became infected. Endocarditis is the major form of chronic disease, comprising 60-70% of all reported cases, and with an estimated case fatality rate in untreated patients of 25-60%. Other forms of chronic Q fever include aortic aneurysms and infections of the bone, liver, or reproductive organs, such as the testes in males.

Post-Q fever fatigue syndrome has been reported to occur in 10-25% of some acute patients. This syndrome is characterized by constant or recurring fatigue, night sweats, severe headaches, photophobia, pain in muscles and joints, mood changes, and difficulty sleeping.

Diagnosis

Healthcare providers must use their judgment to treat patients based on clinical suspicion alone. While Q fever should be considered in patients who have close contact with domestic ruminants and cats, such an exposure may not always be reported. Information such as recent travel to rural or agricultural communities where infected livestock may be present, or employment in high risk occupations such as veterinarians or farmers, can be helpful in making the diagnosis. Clues such as a prolonged fever with low platelet count, normal leukocyte count, and elevated liver enzymes are suggestive of acute Q fever infection. Diagnosis can later be confirmed using specialized confirmatory laboratory tests. *Treatment should never be delayed pending the receipt of laboratory test results, or be withheld on the basis of an initial negative laboratory result.*

Laboratory Diagnosis

Clinical diagnoses of Q fever are confirmed by **serological** testing or **polymerase chain reaction** (PCR) where available.

Antibody titers to *C. burnetii* are usually detectable by 7-10 days after illness onset, and a negative test during the first week of illness does not rule out Q fever as a cause of illness. There are two distinct antigenic phases (Phase I and Phase II) to which humans develop antibody responses. In acute infection, an antibody response to *C. burnetii* Phase II antigen is predominant and is higher than Phase I antibody response; the reverse is true in chronic infection which is associated with a rising Phase I IgG titer that is often much higher than Phase II IgG. The gold standard serologic test for diagnosis of acute Q fever is the indirect immunofluorescence assay (IFA) using *C. burnetii* antigen. The first sample should be taken as early in the disease as possible, preferably in the first week of symptoms, and the second sample should be taken 2 to 4 weeks later. IgM antibodies usually rise at the same time as IgG near the end of the first week of illness and remain elevated for months or longer. Also, IgM antibodies are more likely to result in a false positive result. **Physicians should request both Phase I and Phase II IgG and IgM serologic titers** for diagnostic confirmation of acute and chronic Q fever. Approximately 3% of currently healthy people in the U.S. general population and up to 20% of people in high-risk professions (veterinarians, ranchers, etc.) have elevated antibody titers due to past exposure to *C. burnetii*. Therefore, **if only one sample is tested it can be difficult to interpret the findings. Paired samples** taken 2-4 weeks apart demonstrating a significant (four-fold) rise in antibody titer provide the **best evidence** for a correct diagnosis of acute Q fever. Diagnosis of chronic Q fever is confirmed by elevated Phase I IgG antibody (current U.S. case definitions >1:800 and higher than Phase II IgG) **and** an identifiable persistent focus of infection (e.g., endocarditis). Elevated Phase I titers alone do not confirm a chronic Q fever diagnosis.

During the acute phase of illness, a sample of whole blood can be tested by PCR assay to determine if a patient has Q fever. PCR is most sensitive in the first week of illness, and decreases in sensitivity following the administration of appropriate antibiotics. Although a positive PCR result is helpful, a negative result does not rule out the diagnosis, and treatment should not be withheld due to a negative result.

Culture isolation of *C. burnetii* is only available at specialized laboratories; **routine hospital blood cultures cannot detect the organism.**

The Missouri State Public Health Laboratory (MSPHL) can perform PCR assays on whole blood samples taken during the first week of illness and prior to initiation of antibiotic therapy, with prior arrangements. Testing requested on additional samples other than blood will be conducted at the Centers for Disease Control and Prevention (CDC) in Atlanta, GA. Please contact the Virology unit at MSPHL by calling 573/751-3334 for assistance.

Treatment

Doxycycline is the first line treatment for all adults and for children with severe illness. Treatment should be initiated immediately whenever Q fever is suspected. Use of antibiotics other than doxycycline or other tetracyclines is associated with a higher risk of severe illness. Doxycycline is most effective at preventing severe complications if it is started early in the course of disease. Failure to respond to doxycycline suggests that the patient's condition might not be due to Q fever.

Recommended Dosage for Acute Q fever

Doxycycline is the first line treatment for children with severe illness of all ages and adults:

- Adults: 100 mg every 12 hours
- Children under 45 kg (100 lbs): 2.2 mg/kg body weight given twice a day

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Standard duration of treatment is 2-3 weeks.

Recommended Dosage for Chronic Q fever

- Adults: Doxycycline 100 mg every 12 hours and hydroxychloroquine 200 mg every 8 hours.

Standard duration of treatment is 18 months.

The use of doxycycline is recommended to treat Q fever in children of all ages who are hospitalized or are severely ill. Children with mild illness who are less than 8 years of age may be treated with co-trimoxazole, but therapy should be switched to doxycycline if their course of illness worsens.

Treatment of pregnant women diagnosed with acute Q fever with once daily co-trimoxazole throughout pregnancy has been shown to significantly decrease the risk of adverse consequences for the fetus.

Patients at highest risk for progression to chronic Q fever should be serologically and clinically monitored at intervals of 3, 6, 12, 18, and 24 months after diagnosis of acute Q fever. Patients without obvious risk factors for chronic Q fever should receive a clinical and serologic follow-up approximately 6 months after diagnosis of acute illness to identify potential progression to chronic disease.

The prophylactic antimicrobial treatment for prevention of Q fever after a known exposure and prior to symptom onset is not indicated. Attempts at prophylaxis will likely extend the incubation period but will not prevent infection from occurring.

Please report any suspected Q fever cases within 1 day to your local public health agency (LPHA), or to DHSS at 573/751-6113.

References:

1. Centers for Disease Control and Prevention (CDC). Notes from the Field: Q Fever Outbreak Associated with Goat Farms — Washington and Montana, 2011. *Morbidity and Mortality Weekly Report* 2011; 60(40); 1393. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6040a5.htm.

2. Centers for Disease Control and Prevention (CDC). Diagnosis and Management of Q Fever — United States, 2013: Recommendations from CDC and the Q Fever Working Group. *Morbidity and Mortality Weekly Report* 2013; **62(RR03);1-23.** Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6203a1.htm.

3. Centers for Disease Control and Prevention (CDC). Q fever Homepage. Go to http://www.cdc.gov/qfever/.