Public Health Agency of Canada | Agence de la santé publique du Canada

Upcoming changes to Q fever testing at the National Microbiology Laboratory Branch

February 15, 2024

Dear Colleagues,

The National Microbiology Laboratory Branch (NMLB) is committed to providing support for the detection and diagnosis of zoonotic pathogens, including *Coxiella burnetii*. The Arbovirus, Rabies, Rickettsia and Related Zoonotic Diseases section at the NMLB provides Q fever serological and molecular testing as a diagnostic and reference service in Canada.

As a result of recent discussions with a number of provincial laboratories, we would like to inform you that effective March 31, 2024, IgM serological testing for Q fever will no longer be performed by the NMLB. Please see the attached **Q fever NMLB Testing Statement,** which provides an overview of this decision. For molecular testing requests, symptom onset date and clinical history must be provided on the requisition. Specimens submitted without this information will be rejected. For the updated requisition, please refer the National Laboratory Guide to Services https://cnphi.canada.ca/gts/laboratory/1020.

Please do not hesitate to contact us if you have any questions or require additional information.

Sincerely,

Wood, Heidi

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Canada

Q fever Testing Statement
The National Microbiology Laboratory Branch (NMLB)
February 2024

Summary:

1. **IgM testing is not recommended for the diagnosis and management of acute or chronic Q fever. The NMLB will no longer be accepting IgM submissions effective March 31, 2024.**
2. **Acute and convalescent serum samples tested in parallel for IgG are the gold standard for the serological diagnosis of acute Q fever. PCR can also be used for the diagnosis of acute fever in the early stages of infection.**
3. **Testing for chronic Q fever, which can include PCR and/or IgG serology, should be reserved for patients with a consistent history and clinical presentation.**

Q fever is caused by *Coxiella burnetii*, an obligate intracellular, Gram-negative bacterial pathogen. *C. burnetii* is highly infectious and can persist in the environment for prolonged periods. Sheep, goats and cattle are the primary reservoirs but a wide range of domestic and wild animals can be infected. History that indicates past exposure to livestock is an important component of the diagnosis. Person-to-person transmission is rare.

The typical incubation period for acute Q fever is 2-3 weeks, during which time initial serology can often be negative. Many individuals with acute Q fever will not develop symptoms, while those that do often develop non-specific symptoms, making diagnosis challenging. Chronic Q fever may develop months to years after acute illness, even in individuals without a history of symptoms. Chronic Q fever is a risk for anyone with a history of acute Q fever, but is more frequent in persons with valvular disease, blood vessel abnormalities, immunosuppressed persons, and women who were pregnant when they became infected.

Overview of serological testing

The immunofluorescence assay (IFA) is the reference method for the serological diagnosis of Q fever. The interpretation of Q fever IFA results can be challenging. *C. burnetii* exists in two different phases, phase I and phase II, depending on the structure of the LPS antigen. There are different patterns of antibody response to these antigens during acute and chronic Q fever. In acute infection, the phase II antibody response to *C. burnetii* appears first and is higher than the phase I antibody response. Chronic Q fever is associated with increasing phase I IgG titers that often become higher than phase II IgG titers.

Acute and convalescent serum samples tested in parallel represent the gold-standard for the serological diagnosis of acute fever. 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 3 to 6 weeks later. A significant or 4-fold rise in the phase II IgG titer confirms an acute infection. A titer of ≥ 1:256 to phase II IgG in a single serum sample is suggestive of recent exposure to *C. burnetii* in a patient with clinically compatible symptoms.

The diagnosis of chronic Q fever should not be established based on the phase I:phase II IgG ratio alone. It is not uncommon for patients with an acute Q fever infection to develop serological profiles consistent with chronic Q fever that eventually regress. The diagnosis of chronic Q fever is most accurately made based on PCR and serology of appropriate specimens along with a consistent clinical presentation. Patients with suspected chronic Q fever should have PCR on EDTA whole blood or serum performed because they can experience a recurrent bacteremia similar to acute Q fever. Serologic testing typically shows the phase I IgG titer rising to levels ≥1:1024 and exceeding the phase II titer.

IgM testing of a single serum sample is not reliable for the diagnosis of acute Q fever due to low specificity, with false-positive results reported due to cross-reactions with other pathogens and autoimmune antibodies. Based on an analysis of results from samples submitted to the NMLB from 2019-2022, 70/71 IgM positive results from paired submissions were classified as false-positives, using the manufacturer's recommended cut-off, based on a lack of seroconversion in the convalescent serum. An analysis of the NMLB data also indicated that raising the cut-off above the manufacturer-recommended threshold for positivity from 1:16 to 1:64 for phase II IgM reduced the false-positivity rate. However, IgM testing in non or low-endemic areas may still lead to a substantial number of false-positive IgM results when a single serum sample is tested. Notably, approximately 60% of all samples submitted to the NMLB for Q fever serology are single serum samples. Importantly, IgM antibodies may also persist for more than a year in some patients. As a result, a solitary IgM positive result is not a reliable indicator of acute Q fever. **Given these limitations, IgM testing is no longer recommended by the NMLB for the diagnosis and management of Q fever. This is consistent with recommendations from other public health laboratories including the US Centers for Disease Control and Prevention.**

Changes to NMLB's Requisition for Q fever testing

The NMLB will be updating the requisition for Q fever testing. The following changes will be implemented:

- Molecular testing – symptom onset date and clinical history **must** be provided. Specimens submitted without this information will be rejected.
- Serology – all fields should be completed; include specimen number for previously submitted samples from the same patient.