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Editorial

Q Fever Reporting: Tip of the Iceberg?

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Two articles by Dahlgren and others in the current issue of the *Journal* provide a much needed epidemiological update on Q fever in the United States from the Centers for Disease Control and Prevention (CDC).[1,2] It has been over 10 years since the last substantial report on Q fever in the United States.[3] Aside from increased awareness related to service members potentially being infected in Iraq and a large-scale outbreak in the Netherlands, Q fever has remained for the most part a disease linked to certain occupations (veterinarians, slaughterhouse workers, and farmers).[4] The current articles provide new data related to incidence and outcomes in terms of hospitalization and mortality. The reports raise the question of how common is Q fever and what are the outcomes of acute and chronic disease.

The first article summarizes the reported cases through two national surveillance systems (National Notifiable Disease Surveillance System [NNDSS] and Case Report Forms [CRF] sent to CDC) in the United States from 2000 to 2012.[1] There were a total of 1,366 confirmed and probable cases reported through the NNDSS with an incidence rate of 0.36 cases per million person-years. Infection was slightly more common in males (3:1 incidence ratio), and patients from the Mountain and West North Central divisions were more likely to be infected. There were 709 cases reported to CDC through CRF, although only 474 (67%) were unique cases defined as not being a duplicate of another report meeting the case definition. This included 110 chronic cases from 2008 to 2012. The most common occupation was rancher (17%) followed by military (8%); however, 36% of cases were classified as having an occupation related to agriculture. Interestingly, 66% of cases reported exposure to animals, but only 39% reported exposure to the animals most commonly associated with infection (sheep, cattle, and goats). The hospitalization rate was 62% and there were nine fatalities (9 of 428 cases with known outcomes, 2.1%). Based on statistical modeling, the authors estimated that for every case reported by a CRF there are 13 or more cases that go unreported.[1]

The second article examined case fatality through the Multiple Causes of Death (MCD) database (summary of death certificates in the United States) and CRF from 2000 to 2011. There were 33 unique cases (1 case was a match between the systems) of fatal Q fever reported during this period. This included 9 and 25 fatal cases reported through CRF and MCD, respectively. A statistical estimation of the total number of deaths during this period was made using the Chapman estimator for population size. The authors estimated that deaths were underreported by a factor of 5 and 14 for the MCD and CRF, respectively. By comparing the two data sources, the authors estimated that 129 fatal cases (confidence interval of 62–1,250) occurred between 2000 and 2011. Although these numbers are small in comparison to some other infectious diseases, early recognition and treatment may avert a poor outcome. The fact that there is such an underestimating of reporting at least raises the question as to whether some potentially treatable cases are being missed.

It is worth pointing out that only 25% of the acute and 48% of the chronic cases met the CDC definition for a confirmed case.[1] Confirmation requires a clinically compatible illness with laboratory confirmation. Of note, the CDC definition changed slightly between the reporting periods (2000–2007 and 2008–2012). It is possible that some of these cases were in fact not Q fever. For acute disease, patients may not return for follow-up serology, although Q fever is one disease where follow-up serology is recommended given the risk of chronic infection.[5] Even with repeat testing, confirmation can be difficult given issues surrounding Q fever serologies. Unfortunately, serological results can vary between laboratories and can be difficult to interpret. One study comparing results from three reference laboratories showed only a 35% concordance.[6] Consequently, when considering or confirming the diagnosis, if there is a question related to the result, the sample should then be sent to a reference laboratory such as the CDC. This is particularly important for chronic cases when decisions related to treatment are being made. Serology alone should not be used to determine if a patient has chronic disease, rather it should be used in conjunction with the overall clinical picture. The CDC published recommendations in 2013 to help providers deal with these decisions.[5]

Despite the problems with confirming the diagnosis, the evidence from the newly published studies in this issue supports that Q fever is significantly underreported. Recent serosurveys further suggest cases go unrecognized and/or not reported. Anderson and others[7] reported the seroprevalence for *Coxiella burnetii* in the United States was 3.1% (95% confidence interval of 2.1–4.3%) among 4,437 adults that took part in the 2003–2004 National Health and Nutrition Examination Survey cycle. Although the military had numerous reported cases including those in the work presented here, it is likely they were underreported as well. A seroprevalence study of 909 service members presenting with compatible illness to a combat support hospital showed a 10% (88 cases) seroconversion rate.[8] Another study of deployed service members reported a 7% rate of seroconversion during an outbreak, and 2.1% seroconversion rate in another population used to determine a background rate.[9]

Although 60% of cases in the current study were hospitalized, many patients have minimal symptoms.[1] In general, patients who have a mild flu-like illness are unlikely to seek care or are seen on an outpatient basis. They often are treated empirically and diagnostic testing is not conducted unless they

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fail to improve. Furthermore, the diagnosis of Q fever can be challenging as it is indistinct clinically from many other more common illnesses (community acquired pneumonia, influenza, and tick-borne illness among others). It is very likely that without a specific history of exposure to animals or a high risk occupation (slaughter house, veterinarian) that the disease is not even considered. In the past, authors have suggested that a lack of exposure to farm animals could rule out the infection.[10] The current report shows that exposure history alone, while a clue to diagnosis, should not preclude clinicians from considering the diagnosis.[1] Only a third of the cases in the current report had exposure. Coupling this with another article suggesting that *C. burnetii* is more common in the environment than we think should make us broaden our perspective as to when to consider Q fever as a possibility in our differential diagnosis.[11]

Therefore, where are we to go from here? A thorough history and physical examination still remains vital to the diagnosis. Knowledge of occupational hazards or exposure during travel could aid in the diagnosis. Additionally, the presence of a compatible clinical syndrome should prompt physicians to consider the diagnosis. Patients commonly present with fevers, headache, and myalgias and often have liver enzyme abnormalities. Q fever presents similar to other atypical pneumonias, although is most consistent with Legionella. Headache tends to be a common complaint so considering the diagnosis in a patient who presents with a Rickettsial like illness is prudent. For chronic infection, Q fever remains on the differential diagnosis and should be checked for all culture-negative endocarditis patients and patients with unexplained vascular graft infections.

Ultimately, Q fever remains a relatively uncommon diagnosis, but one that deserves more attention. The two studies in the current issue of the *Journal* are a nice step forward, but many questions remain. More research is needed both in terms of incidence and outcomes for both acute and chronic disease to determine where exactly we are on the epidemiological iceberg.

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