



REVIEW ON Q FEVER

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ABSTRACT

Q fever is a zoonotic disease considered as emerging or re-emerging in many countries. It is caused by *Coxiella burnetii*, a bacterium developing spore-like forms that are highly resistant to the environment. *Coxiella burnetii* is most commonly transmitted to humans by direct contact with the reproductive tissues of cattle, sheep, and goats in which the causative organism reaches exceptionally high titers. Q fever has been reported worldwide with the exception of New Zealand. The overall mortality rate for Q fever is 1-2% in untreated cases, and lower in those who are treated. Humans infected with *C. burnetii* often seroconvert without clinical signs or develop a mild, self-limited, flu-like illness. Animals are thought to become infected during direct contact, via routes such as inhalation and ingestion, or by aerosols. Infectious airborne particles have been reported to travel up to 11 miles.

KEYWORDS

Introduction, history, pathophysiology, diagnosis, treatment, Doxycycline

INTRODUCTION

Q fever has long been considered a rare and regionally restricted disease. In recent years, spectacular advances have been made in the knowledge of this disease and its causative agent, *Coxiella burnetii*. First, the worldwide role of *Coxiella burnetii* as a cause of endocarditis has been recognized in most countries performing systematic serology. Moreover, the classification of *C. burnetii* by the CDC as a potential bioterrorism agent resulted in the disease becoming reportable in many countries, such as in the United States, which revealed that the disease is more common than previously thought. [11] Third, the recent war in the Middle East and research in the tropics have shown that Q fever may be a very common cause of fever in the intertropical area. [9,3] Finally, a very large outbreak in the Netherlands has shown that this disease could become a major public health problem. [8] Furthermore, knowledge about *Coxiella burnetii* has evolved, with the sequencing of multiple genomes of bacterial strains and their culture in axenic medium. This break-through enables genetic transformation and opens a new era. Moreover, redefining the clinical forms of Q fever is necessary, because of a lack of consensus on the distinction between acute Q fever and chronic Q fever. [10] Many reports describe the survival of the *Coxiella* cells on wool at room temperature for up to 1 year, in milk for more than 3 years, and in fresh meat for 4 weeks. [23]

HISTORY

It was first described by Edward Holbrook Derrick in abattoir workers in Brisbane, Queensland, Australia. The "Q" stands for "query" and was applied at a time when the causative agent was unknown; it was chosen over suggestions of "abattoir fever" and "Queensland rickettsial fever," to avoid directing negative connotations at either the cattle industry or the state of Queensland [1,4]. The pathogen of Q fever was

discovered in 1937, when Frank Macfarlane Burnet and Mavis Freeman isolated the bacterium from one of Derrick's patients. It was originally identified as a species of Rickettsia. H.R. Cox and Gordon Davis isolated it from ticks in Montana, USA in 1938. *Coxiella burnetii* is no longer regarded as closely related to Rickettsiae, but as similar to Legionella and Francisella, and is a proteobacterium.[2,6] *R. burnetii* reached Northern Ireland between 1957 and 1962, probably as a result of the importation of infected ewes from England (Connolly, 1968), and the Republic of Ireland at about the same time, though the first known case of Q fever there seems to have occurred in 1966 (Hillary, Shattock & Meenan, 1971).[21]

Causes

Q fever can be transmitted through following ways-[19]

- Aerosols: Inhalation of contaminated aerosols is the main mode of transmission
- Ingestion of raw dairy products
- Vertical (mother to fetus) transmission has been reported
- Parenteral
- Tick bites

Signs and symptoms

The common signs and symptoms of Q Fever are:

- High fever up to 105 F
- Severe headache, nausea
- Diarrhea
- Dry cough
- Muscle and joint pain
- Chills, sweating
- General feeling of sickness, fatigue
- Loss of appetite
- Abdominal pain, chest pain
- Rashes

Sometimes, the following symptoms may occur:

- Hepatitis or liver disease (jaundice)
- Endocarditis: Inflammation of the heart cavity
- Pneumonia[22]

DIAGNOSIS

In most instances, the diagnosis is confirmed serologically since most laboratories do not have the facilities to work with *C. burnetii*. The microagglutination, complement fixation, micro immune fluorescence, and the enzyme-linked immunosorbent assay (ELISA) have all been used for this purpose.[13-15] The ELISA is the most sensitive, but the IFA is easier to perform and for detection IgM antibodies at an early phase of infection and after 12 months of follow-up. A fourfold rise in antibody titer between acute and convalescent phase serum samples is diagnostic of acute Q fever [12, 16-18]. IgM antibodies can persist for six to eight months in some patients, so determination of IgM antibodies on a single serum should not be used in the diagnosis of acute Q fever [12]. In chronic Q fever, the antibody titers are usually much higher than those seen in acute Q fever, and phase I antibodies are higher than or equal to phase II antibody titers. In acute Q fever, the phase II antibody response predominates. ELISA has several advantages because it is easy to perform, the assay can be automated, and it is mainly used for diagnosis of acute and chronic Q fever. [23]

TRANSMISSION

The major route for acquiring *C. burnetii* infection is by uptake of a contaminated aerosol, while consumption of contaminated raw food materials, e.g., milk, etc. is the minor source of transmission. Occasionally, the infection may occur after skin or mucosal contact with contaminated products, blood transfusion or mating[25] Aerogenic transmission of the disease from contaminated sites to humans depends on atmospheric dispersion and the impact of environmental factors on deposition and re-aerosolization [26]

PATHOPHYSIOLOGY

The *Coxiella*'s life cycle contains 2 forms of development – large-cell (LCV) or the active replicating form found during the log phase and small-cell variant (SCV) that are typical for the stationary phase. The infection has two phases, which correlate to changes in the lipopolysaccharide of *C. burnetii*:^[21] it can last

for 586 days, in dried blood at room temperature it can last for 5 months, in dust 120 days in wool 12-16 months at 4-6 C, and in milk more than 30 days[24]

- Phase I: Characterized by a smooth lipopolysaccharide capsule. Despite being less efficient in the invasion of host cells, antibodies against phase I are always isolated from acute Q fever patients.
- Phase II: Characterized by a rough lipopolysaccharide capsule. Antibodies against phase II have been isolated from chronic Q fever patients..[20]

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.^[5] Doxycycline is most effective at preventing severe complications from developing if it is started early in the course of disease. Therefore, treatment must be based on clinical suspicion alone and should always begin before laboratory results return. If the patient is treated within the first 3 days of the disease, fever generally subsides within 72 hours. In fact, failure to respond to doxycycline suggests that the patient's condition might not be due to Q fever. Severely ill patients may require longer periods before their fever resolves. Resistance to doxycycline has not been documented.^[5] In cases of life-threatening allergies to doxycycline and in pregnant patients, physicians may need to consider alternate antibiotics. 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.^[7] Recommended treatment for Chronic Q fever in Adults is: Doxycycline 100 mg every 12 hours and hydroxyl chloroquine 200 mg every 8 hours. Standard duration of treatment is 18 months.^[5] There are no unique programs for animals vaccination; it is done related to the epidemiological situation in a certain region.

CONCLUSION

Although described 60 years ago, Q fever is still a poorly understood disease. Its reservoirs seem to be related to any mammal, but ticks may also be reservoirs. The clinical presentation is very pleomorphic and includes severe forms with a poor prognosis. Most often, acute cases present as asymptomatic infections, as a flu-like syndrome, as a pneumonia, or as hepatitis. Host factors probably play an important role in the development of chronic disease, which may present as a blood-culture-negative endocarditis or as an infected aneurysm. The best tests for diagnosis are those which permit the direct detection of bacteria. They include shell vial cell culture, PCR amplification, and immunodetection with tissue biopsy specimens. All these techniques require a level 3 biosafety laboratory and trained personnel due to the extreme infectivity of *C. burnetii*. In chronic cases, the techniques that allow the direct detection of *C. burnetii* in blood or tissues should be used before the beginning of therapy. As for indirect specific diagnosis, the technique to be used should be very sensitive and should detect antibodies early in the course of the disease.

REFERENCE

- [1] E. H. Derrick, "'Q' fever, a new fever entity: clinical features, diagnosis and laboratory investigation," *Reviews of Infectious Diseases*, vol. 5, no. 4, pp. 790–800, 1983.
- [2] F. M. Burnet and M. Freeman, "Experimental studies on the virus of Q fever," *Medical Journal of Australia*, vol. 2, pp. 299–305, 1937.
- [3] Eldin C, Mahamat A, Demar M, Abboud P, Djossou F, Raoult D. 2014. Qfever in French Guiana. *Am J Trop Med Hyg* 91:771–776. <https://doi.org/10.4269/ajtmh.14-0282>.
- [4] "Historical aspects of Q fever," in *Q Fever, Volume I: The Disease*, T. J. Marrie, Ed., CRC Press, Boca Raton, Fla, USA, 1990.
- [5] <http://www.cdc.gov/qfever/symptoms/index.html>
- [6] G. E. Davis and H. R. Cox, "A filter-passing infectious agent isolated from ticks. I. Isolation from *Dermacentor andersonii*, reactions in animals, and filtration," *Public Health Reports*, vol. 53, no. 52, pp. 2259–2282, 1938.
- [7] X. Carcopino, D. Raoult, F. Bretelle, L. Boubli, and A. Stein, "Q fever during pregnancy: a cause of poor fetal and maternal outcome," *Annals of the New York Academy of Sciences*, vol. 1166, pp. 79–89, 2009.
- [8] Delsing CE, Kullberg BJ, Bleeker-Rovers CP. 2010. Q fever in the Netherlands from 2007 to 2010. *Neth J Med* 68:382–387.

- [9] Angelakis E, Mediannikov O, Socolovschi C, Mouffok N, Bassene H, TallA, Niangaly H, Doumbo O, Znazen A, Sarih M, Sokhna C, Raoult D. 2014. Coxiella burnetii-positive PCR in febrile patients in rural and urban Africa. *Int J Infect Dis* 28:107–110. <https://doi.org/10.1016/j.ijid.2014.05.029>.
- [10] Million M, Raoult D. 2015. Recent advances in the study of Q fever epidemiology, diagnosis and management. *J Infect* 71(Suppl 1):S2–S9. <https://doi.org/10.1016/j.jinf.2015.04.024>.
- [11] White B, Brooks T, Seaton RA. 2013. Q fever in military and paramilitary personnel in conflict zones: case report and review. *Travel Med Infect Dis* 11:134–137. <https://doi.org/10.1016/j.tmaid.2012.11.001>.
- [12] Worswick D, Marmion BP. Antibody responses in acute and chronic Q fever and in subjects vaccinated against Q fever. *J Med Microbiol* 1985; 19: 281-296.
- [13] Field PR, Hunt JG, Murphy AM. Detection and persistence of specific IgM antibody to Coxiella burnetii by enzyme-linked immunosorbent assay: A comparison with immunofluorescence and complement fixation tests. *J Infect Dis* 1983; 148: 477-487.
- [14] Fiset P, Ormsbee RA, Silberman R, et al. A microagglutination technique for detection and measurement of rickettsial antibodies. *Acta Virol* 1969; 13: 60-66.
- [15] Murphy AM, Field PR. The persistence of complement fixing antibodies to Q fever (Coxiella burnetii) after infection. *Med J Aust* 1970; 1: 1148-1150.
- [16] Peter O, Dupuis G, Burgdorfer W, et al. Evaluation of the complement fixation and indirect immunofluorescence test in the early diagnosis of primary Q fever. *Eur J Clin Microbiol* 1985; 4: 394-396.
- [17] Peter O, Dupuis G, Peacock MG, et al. Comparison of enzyme-linked immunosorbent assay and complement fixation and indirect antibody tests for detection of Coxiella burnetii antibody. *J Clin Microbiol* 1987; 25: 1063-1067.
- [18] Hunt JG, Field PR, Murphy AM. Immunoglobulin response to Coxiella burnetii (Q fever): Single-serum diagnosis of acute infection using an immunofluorescence technique. *Infect Immun* 1983; 39: 977-981.
- [19] Marrie TJ (1990). "Q fever - a review". *Can. Vet. J.* **31** (8): 555-63. PMC 1480833. PMID 17423643.
- [20] C. Michael Gibson, M.S., M.D. Ahmed Younes M.B.B.Ch [2]. **“Q fever pathophysiology**
- [21] R. J. C. HART M.B., M.R.C.Path. The epidemiology of Q fever, Public Health Laboratory, Church Lane, Heavitree, Exeter EX2 5AD
- [22] <https://www.dovemed.com/diseases-conditions/q-fever/>
- [23] <http://daekitech.com/coxiella-burnetii-how-deadly-could-be-the-q-fever/>
- [24] Scientific opinion: Scientific Opinion on Q fever: EFSA journal, 8, 5, 1595, 2010.
- [25] Ullah, Q.; Jamil, H.; Qureshi, Z.I.; Saqib, M.; Neubauer, H. Sero-epidemiology of Q Fever (Coxiellosis) in small ruminants kept at government livestock farms of Punjab, Pakistan. *Pak. J. Zool.* **2019**, *51*, 135–140. [Google Scholar] [CrossRef]
- [26] Van Leuken, J.P.G.; Swart, A.N.; Brandsma, J.; Terink, W.; Van de Kasstele, J. Droogers, P.; Sauter, F.; Havelaar, A.H.; Van der Hoek, W. Human Q fever incidence is associated to spatiotemporal environmental conditions. *One Health* **2016**, *2*, 77–87. [Google Scholar] [CrossRef] [PubMed] [Green Version]