

## Epidemiology, Zoonoses, Control and Prevention Methods of Q-Fever

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### Abstract

Q fever is a zoonotic disease, caused by Gram negative bacterium *C. burnetii*, which imparts significant socio-economic burden due to production and reproductive loss (abortion, stillbirth, and infertility) in ruminants and debilitating clinical disease in human populations. The geographical distribution of Q fever is worldwide except New Zealand. The main reservoirs for human infections are cattle, goat, sheep, and pets and ticks are the natural primary reservoir for animal. *Coxiella burnetii* in ruminant cause reproductive problems like miscarriage, infertility and reduced milk production. The organism can be found in the milk, urine, feces placenta and birth fluids of animals. The airborne transmission of *C. burnetii* associated with its highly resistance to environments and the ability to easily produce huge quantities of *C. burnetii* in the after birth of aborted ewes or goats have led to classify *C. burnetii* as a Category-B, biological terrorism agent. The incubation period of Q fever is depending on the size of infectious. The recommended treatment for ruminant administering two injection of Oxytetracycline during the last month of gestation, also Doxycycline is the best drug. *C. burnetii* can be reduced in the farm environment by regular cleaning and disinfection of animal facilities. Q fever is global health problem and it is an OIE notifiable disease. Q fever is one of infectious disease which is considered as being having economic and public health importance in Ethiopia. Therefore, awareness creation and, application of prevention and control method has paramount importance in reduce the hazardous effect of this disease.

**Keywords:** Epidemiology, Prevention and Control, Q Fever, Zoonoses.

### Introduction

Q fever, a zoonotic disease transmitted from animals to humans, is a significant public health problem worldwide. It is mostly occupationally acquired, and despite the availability of a vaccine for human use, at least in Australia, some countries continue to bear a substantial disease burden [1]. The disease is caused by *Coxiella burnetii*, an obligate gram-negative intracellular bacterium. Q fever occurs worldwide; Most commonly reported in southern France and Australia [2].

*Coxiella burnetii* infects various hosts, including humans, ruminants (cattle, sheep, goats), and pets—and, in rare cases, reptiles, birds, and ticks. This bacterium is excreted in urine, milk, feces, and birth products [3]. Q fever is a mainly airborne zoonosis; infection is most acquired by breathing infectious aerosols or contaminated dust. Infection can occur

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also in individuals not having direct contact with animals, such as persons living along a road used by farm vehicles or those handling contaminated clothing [4]. The infection result from inhalation of endospores and from contact with the milk, urine, feces, vaginal mucus or semen of infected animals [5]. The pathogen is highly resistant to adverse physical conditions and chemical agents, so it can survive for months and even years in the environment which create conducive condition for infection [6].

Because of its sporelike-life cycle, *C. burnetii* can remain viable and virulent for months. Infection can be acquired via inhalation or skin contact, and direct exposure to a ruminant is not necessary for infection. Rare human-to-human transmissions involving exposure to the placenta of an infected woman and blood transfusions have been reported [7].

In more recent dates Q fever is classified as a “Category “B” critical biological agent” by the Centre for Diseases Control and Prevention(CDC) and is considered a potential weapon for bioterrorism. The disease so is considered has having public health concern throughout the world alongside with its economic importance. On top this, although Q-fever is an OIE notifiable disease, it remains poorly reported and its surveillance is frequently severely neglected [8]. Review of the disease epidemiologic status, public health significance is lacking in different countries, including Ethiopia. Therefore, the objectives of this seminar paper are:

\* To review Q-Fevers Epidemiology, Zoonoses, control and prevention methods of the disease

To highlight current status of Q fever in Ethiopia

## Q-Fever

### History

It was first described by Edward Holbrook Derrick in abattoir workers in Brisbane, Queensland, Australia [9]. 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 [10]. 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 [3].

### Etiology

*C. burnetii* is a gram-negative, pleomorphic, and obligate intracellular bacterium [11]. Due to its ability to enter cells and replicate, it was taxonomically classified in past decades within the Rickettsiae group due to the impossibility of its isolation in an axenic medium and its ability to infect arthropods. Although there are some similarities with *Rickettsiae*, current knowledge confirms that *C. burnetii* does not belong to the group, mainly due to its placement in phylogenetic inferences using sequences of the 16S rRNA

gene where *Coxiella* showed a close relationship to the order *Legionellales*, distancing it from the *Rickettsiales* [11]. In addition, several factors, including metabolism, infectivity, morphological variations during infection, and the ability to form spores, also support the reclassification into the *Coxiellaceae* family [12].

### Epidemiology

**Occurrence:** Q-fever may occur in sporadic as well as epidemic forms. It may be emerging disease, probably related to climate changes [13]. Q fever is an endemic zoonosis with worldwide distribution, except Antarctica and New Zealand. The patterns of transmission make the epidemiology of *C. burnetii* complex, there are two major ways of spread involving wild animals and their ectoparasites, mainly ticks and the other involving domestic ruminants, independent to wild animal cycle [5]. The broad host range and complicated vector born transmission cycle have led to the ubiquity of *Coxiella burnetii* among arthropods annelid, poikilotherms, and the homoeothermic reservoirs in disparate habitat. Although Q fever is ubiquitous, they occur more frequently in area where domestic animals are prevalent [14].

**Host and susceptibility:** *Coxiella burnetii* is a well-established infectious agent that has reached a state of balanced pathogenicity in a plethora of host. Human are unnatural and usually dead-end-host. The microorganism generally maintained in a less pathogenic form in separate cycle existing independently among wild mammals and their haematophagus arthropods, principally tick and in domestic animals [15]. The reservoir hosts vary depending on the geographic location, and include domestic and wild animals, and their ectoparasites [16]. The primarily reservoir hosts for *C. burnetii* are ticks, both Ixodid and Argasid, which facilitate wild life cycle in rodents, large animals, and birds [15]. Bird may serve as reservoirs; there was one outbreak associated with exposure to aerosol of pigeon faces and bite from tick feeding on these birds. Wildlife and farm animal species may be the reservoir hosts for domestic pets [5].

### 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 [17]. However, in animals, ticks may play an active role in disease transmission [18]. Body secretions and excretions, e.g., milk, saliva, parturition products, aborted materials, urine and feces, contain a large number of *C. burnetii*, which may result in sexual and vertical transmission of the disease. These discharges can dry and combine with dust, ultimately leading to human exposure through aerosols [17].

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 [19]. Although human-to-human transmission of Q fever is rare, it may occur following contact with parturient women. Transplacental transmission, cutaneous

inoculation and postpartum spread of *C. burnetii* do occur in sporadic cases. The disease is reported in more than 40 species of ticks from the families Ixodidae and Argasidae, and some other arthropods that feed on animals [17].

### Clinical sign of the disease

The symptoms of this disease are very different in humans, and about 60% of carriers of the disease are asymptomatic [15]. Clinical symptoms of the acute Q fever include a sudden headache, fever, pneumonia, fatigue, chills, headache, muscle aches, sweating, coughing, nausea, vomiting, chest pain, diarrhea, skin rash, neurological signs, cardiac involvement, bone marrow involvement, cholecystitis, acute lymphadenitis, dermatological signs, myocarditis, pericarditis, meningoencephalitis, and even death. In chronic forms of the infection, endocarditis, bone and joint involvement, vascular infections, chronic lung infection, and chronic fatigue syndrome have repeatedly been reported [20]. Furthermore, *C. burnetii* infection may lead to premature deliveries, stillbirth, or abortions in pregnant women. Although, Q fever is a benign disease, its mortality in patients with chronic disease is reported to be between 1% to 11% [3].

### Diagnosis

Diagnosis is based on established clinical-epidemiological and laboratory criteria. Laboratory diagnosis involves direct and indirect methods, depending on the sample type, the period in which it was collected, and the species of origin [21].

### Direct diagnostic methods

**Bacterial isolation in cell culture:** *The material of choice for isolation will also depend on the clinical presentation of the patient; however, blood, plasma, cerebrospinal fluid, bone marrow, heart valves, aneurysms, vascular prostheses, liver biopsies, and placenta are usually suitable materials. Embryonic lung fibroblasts are most often used for culture because they are more susceptible to infection. Isolation of C. burnetii should only be performed in a biosafety level 3 laboratory because of its extreme infectivity [22].*

**Bacterial isolation by axenic media (ACCM2):** *The material of choice will depend on the patient's clinical presentation, and this is a recent method under evaluation. It is a semisolid medium that supports robust growth of C. burnetii via colony formation on agarose plates [23]. It has the advantage of overcoming the need for purification required for further molecular analysis of isolates and reducing animal use for isolating the bacteria. However, it has been reported that some genotypes (ST1-7/30, ST8, and ST9-10/27-28/30 groups) do not grow in this medium. All these strains have a QpRS plasmid. Hence, its use for primo isolation from clinical samples may not be indicated [21].*

**Molecular diagnosis:** *the primary technique used by specialized laboratories, both for the acute and persistent phases, is real-time polymerase chain reaction (qPCR), where the target of the reaction is usually the IS1111 gene due to its high diagnostic sensitivity [24]. This method allows detection of the agent from serum, blood, cerebrospinal fluid, tissue and*

*milk samples. Molecular diagnosis is the most sensitive method for detecting recent infections when serology cannot be used due to the absence of antibodies. However, after 17 days of infection, the DNA of C. burnetii becomes undetectable by the technique because as antibodies are produced, the bacteria stop circulating, limiting molecular diagnosis [21].*

### Indirect diagnostic methods

**Serological diagnosis:** *laboratory confirmation of acute Q fever is defined by the presence of Anti-Phase II antibodies approximately 7 to 21 days post-infection when seroconversion occurs with IgG titers equal to or greater than 200 and IgM titers equal to or greater than 50 (Porter et al., 2011). Persistent Q fever (formerly known as chronic Q fever) is defined by the presence of Anti-Phase I antibodies with IgG titers equal to or greater than 800, and when lower, this titer is considered the result of residual antibodies and not of a properly active infection [25].*

**Indirect Immunofluorescence Reaction (RIFI):** *the gold standard for diagnosing the disease in humans. Phase I and II strains of C. burnetii are used to perform the technique. The technique presents superior sensitivity and specificity compared to ELISA for IgM and IgG. Paired sample collections are preferred, with 2 to 3 weeks between collections, to establish a more effective diagnosis by comparing the increase of titers over a period of time. In summary, it is the method of choice for the clinical monitoring of infected patients [26].*

**Indirect Enzyme Immunoassay (i-ELISA):** *the gold standard for diagnosing the disease in animals has also been widely used to diagnose the disease in humans. Some commercial kits detect the different immunoglobulins produced against Phase I and Phase II [25].*

**Complement Fixation Test (CFT):** *In veterinary medicine, CFT was the method of reference for serological diagnosis according to OIE. CFT usually utilizes phase 2 antigens only [27]. It is capable of detecting approximately 65% of infected subjects during the second week after initial clinical signs and 90% during the fourth week. CFT is more laborious, less specific, and less sensitive than indirect immunofluorescence assay (IFA) or ELISA (described hereafter). A study by Rousset et al. on goats originating from different herds reported that CFT results obtained on sera of aborting goats and of non-aborting goats were not significantly different and confirmed the lack of sensitivity of CFT compared to ELISA. CFT, on the contrary to ELISA, is incapable of detecting all IgG subclasses [28].*

### Treatment

In non-pregnant women and other patients with acute Q fever, treatment consists in a daily dose of 200mg doxycycline for 14 to 21 days. Hydroxychloroquine can be associated with doxycycline. Hydroxychloroquine increases the pH of the phagolysosomes, and its association with doxycycline has a bactericidal effect. Rifampin, erythromycin, clarithromycin, and roxithromycin can also be used as an alternative treatment. Fluoroquinolones are recommended in cases of meningoencephalitis as their penetration into the central nervous system is better compared to doxycycline [13].



## Prevention and control

To prevent and reduce the animal and environmental contamination, several actions can be proposed. When introducing a new animal into a Q fever free flocks, in order to avoid the spread of infection, specific care taken. An antibody investigation for Q fever should be performed in the flock of the seller and animals from seropositive flocks can only be introduced in seropositive or vaccinated flocks. *C. burnetii* can be reduced in the farm environment by regular cleaning and disinfection of animal facilities, with particular care of parturition areas, using 10% sodium hypochlorite [29]. In the UK, Health Protection Agency guidelines mention the use of 2% formaldehyde, 1% Lysol, 5% hydrogen peroxide, 70% ethanol, or 5% chloroform for decontamination of surfaces. Pregnant animals must be kept in separate pens, placentas and aborted fetuses must be removed quickly and disposed under hygienic condition to avoid being ingested by dogs, cats or wildlife. Since parturition is critical for the transmission of the disease, in infected flocks, birth must take place in a specific location, which must be disinfected as well as every utensil used for delivery [29].

Appropriate tick control strategies and good hygiene practice can decrease environmental contamination. Infected fetal fluids and membranes, aborted fetuses and contaminated bedding should be incinerated or buried. In addition, manure must be treated with lime or calcium cyanide 0.4% before spreading on fields; this must be done in the absence of wind to avoid spreading of the microorganism faraway. The best methods available for prevention and control of Coxiellosis are antibiotic treatment and vaccination. In-feed addition of tetracycline or injectable oxytetracycline pre-partum has not been shown to prevent *C. burnetii* shedding in feces, milk and vaginal secretions [30].

Human-to-human transmission is extremely rare and Q fever is mainly an airborne disease, measures of prevention are aimed at avoiding the exposure of humans and particularly persons at risk, to animal and environmental contamination. At human level, prevention of exposure to animals or wearing gloves, boots, and masks during manipulation of animals. Pasteurization at 72 °C during 15 s, or sterilization of milk from infected flocks is regularly recommended even if the oral route is not the main one [13]. *C. burnetii* is able to survive for long periods in the environment and in wild animals. The only way to really prevent the disease in ruminants is to vaccinate uninfected flocks, with an efficient 16 vaccines. Three types of vaccine have been proposed for providing human protection against Q fever: the attenuated live vaccine (produced and trialled in Russia but subsequently abandoned because of concern about its safety); chloroform-methanol residue extracted vaccine or other extracted vaccines (trialled in animals but not humans); and the whole-cell formalin-inactivated vaccine, which is considered acceptably safe for humans [6].

**4.8.1 One health approach in Q fever control:** The One Health approach can be defined as 'the collaborative efforts of multiple disciplines to optimize human, animal, and environmental health'. A crucial aspect of this approach

is that the different disciplines working on human, animal, and environmental health collaborate and integrate their knowledge, while taking into account the nature of the three domains. The goal is to realize better solutions for the system as a whole compared to a monocentric approach. In the control of zoonotic diseases in humans, the One Health approach can be really well applied, as it takes into account knowledge from the human, veterinary, and environmental domains. Q fever is an example of this 'par excellence': Humans become infected from the animal reservoir from which the Q fever bacterium is transported to humans via the environment [31].

## Public Health Importance of Q Fever

Q fever is a global public health concern, as is reported from more than 59 countries of the world [13]. Human infections occur after inhalation of aerosols generated from contaminated dust resulting from contaminated manure and desiccation of infected placenta [30]. The incubation period has been estimated to be approximately 20 days (range, 14–39 days). There is no typical form of acute Q fever and the clinical signs vary greatly from patient to patient. The most frequent clinical manifestation of acute Q fever is probably a self-limited febrile illness (91%) which is associated with severe headaches (51%), myalgias (37%), arthralgias (27%) and cough (34%) [32].

The main symptoms fever, pulmonary signs, and elevated liver enzyme levels can coexist. Of 323 hospitalized patients with acute Q fever in France, 25% presented with the three symptoms, 40% presented with fever and elevated liver enzyme levels, 17% presented with fever and pulmonary signs, and 4% presented with only fever, pulmonary signs, or elevated liver enzyme levels. Atypical pneumonia is also a major clinical presentation and abnormal chest X rays can be found in 27% of the patients. After primary infection, 60% of the patients will exhibit a symptomatic seroconversion, and only 4% of the symptomatic patients will be admitted to hospitals. A chronic disease will develop in at risk patients. Prolonged fever Prolonged fever is usually accompanied by severe headaches. The fever may reach from 39 to 40 °C, usually remaining elevated all day. Fever typically increases to a plateau within 2–4 days, and then after 5–14 days the temperature returns rapidly to normal. However, in untreated patients, fever may last from 5 to 57 days [9]. The duration of fever is longer in elderly patients [33].

When a woman is infected by *C. burnetii* during pregnancy, the bacteria settle in the uterus and in the mammary glands. The consequences are of great importance: there is an immediate risk for the mother; there is an immediate risk for the fetus as 100% of the fetuses' abort when the infection occurs during the first trimester and there is a risk of preterm delivery, or low birth weight if infection occurs during the second or third trimester; there is a long-term risk of chronic Q fever in the mother [34].

## 6. Status of Q Fever in Ethiopia

In Ethiopia, the existence of antibody against *Coxiella burnetii* was reported in goats and sheep slaughtered at Addis Ababa abattoir, and its peri-urban zone. A seroprevalence of

6.5% was also reported in Addis Ababa abattoir workers according to [35]. A seroprevalence of 31.6%, 90%, and 54.2% of *C. burnetii* was recorded in cattle, camels and goats respectively in South Eastern Ethiopian pastoral zones of the Somali and Oromia regional states as reported by Abebe. And also a cross-sectional study with a cluster sampling design was conducted in South Eastern Ethiopian pastoral zones of the Somali and Oromia regional states They reported seroprevalences of *C. burnetii* were 31.6% , 90.0% and 54.2% in cattle, camels and goats, respectively [36].

Ticks were tested for *C. burnetii* in Ethiopia by quantitative real time polymerase chain reaction targeting two different genes followed by multispacer sequence typing (MST). An overall prevalence of 6.4% of *C. burnetii* was recorded. *C. burnetii* was detected in 28.6% of *Amblyomma gemma*, 25% of *Rhipicephalus pulchellus*, 7.1% of *Hyalomma marginatum rufipes*, 3.2% of *Amblyomma variegatum*, 3.1% of *Amblyomma cohaerens*, 1.6% of *Rhipicephalus praetextatus*, and 0.6% of *Rhipicephalus (Boophilus) decoloratus*. Significantly higher overall frequencies of *C. burnetii* DNA were observed in *Amblyomma gemma* and *Rhipicephalus pulchellus* than in other tick species as reviewed by [30]. Abortion is one of the most important reproductive health problems of dairy cows in Ethiopia in terms of economic impact. Both infectious and non-infectious agents may cause abortion in cattle. Q fever is one of infectious disease which cause abortion in Ethiopia.

## Conclusion and Recommendations

Generally, Q fever is a zoonotic bacterial disease of worldwide distribution. All people in the world should concern because of its importance causing abortion, still birth and birth of poorly viable newborns especially in sheep. *Coxiella burnetii* is highly infectious to human; even a single organism can cause infection and clinical disease is limited largely to humans; therefore, even greater concern should be paid for its importance as a zoonosis. Because of its stability in the environment, the ease with which it can be transmitted by aerosol, and very low infectious dose and variable clinical presentations even it can be considered as a potential agent for bioterrorism. Therefore, on the basis of the foregoing conclusion, the following recommendations are suggested:

- \* Animal producers should be aware concerning the economic effect and public health significance of coxiellosis.
- \* Hygienic measures such as disinfection of utensils, destruction of placenta, contaminated bedding and dung should be made.
- \* In countries like Ethiopia, more investigation of the disease and epidemiological study should be needed

Prevention of the disease through ONE HEALTH approach.

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