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Q FEVER IN CAMELIDS WITH OWN INVESTIGATIONS IN DROMEDARIES

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ABSTRACT

Q fever has been neglected as a zoonosis for many years but has recently emerged in many countries including Holland, Japan and Australia who have reported outbreaks in their human population. In humans, infection is primarily by inhalation of contaminated dust. Rats seem to play an important role as reservoir for QF. Many serological investigations found high prevalence up to 80% in dromedaries, but preliminary investigations have shown that fresh unpasteurised camel milk does not seem to be a source of infection.

Key words: Antibody, camelids, ELISA, Q fever

Q fever (QF), caused by *Coxiella (C.) burnetii*, is a zoonosis although primary infection in humans is asymptomatic in more than half of number of cases infected. The disease is distributed worldwide except in New Zealand. *C. burnetii* can infect a wide spectrum of animal species and antibodies against QF have been detected in camelids.

Aetiology

C. burnetii is an obligate intracellular, pleomorphic coccobacillus. Historically, it belonged to the order Rickettsiales, family Rickettsiaceae, tribe Rickettsiae, in the Coxiella genus, together with the genera Rickettsia and Orienta. However, the gene sequence analysis classifies now *C. burnetii* in the order Legionellae, family Coxiellaceae. *C. burnetii* displays 2 antigenic phases, phase I and phase II. Phase I organisms are more infectious.

Zoonotic implication

Q fever has been neglected as zoonosis for many years but is now a significant infectious disease threat in many countries (Porter *et al,* 2011), and even to US military personnel deployed to Iraq (Anderson *et al,* 2011).

C. burnetii is the organism responsible for QF, a zooanthroponosis. In humans, infection is primarily by inhalation (ECDC, 2010). Sources of infection include diverse materials like soil, air-borne dust, wool, bedding and other materials contaminated by urine, faeces or birth products of animals. The role of rodents and domesticated animals as hosts or reservoirs for infection in humans has long been established. The camel is no exception. Reusken *et al* (2011) determined the occurrence of *C. burnetii* in rats captured at different locations during the QF outbreak in the Netherlands, and found the highest percentage of QF rat-positive locations around goat farms (50%) and cattle farms (14.3%). The authors also believe that rats act as true reservoirs for *C. burnetii* capable of maintaining infection cycles. Numerous authors (Maurice and Gidel, 1968; Mathur and Bhargava, 1979) have indicated the danger of QF in humans due to close contact with dromedaries. The greatest danger is most likely from the consumption of raw camel milk (Wernery and Kaaden, 2002).

Several severe outbreaks of QF have occurred in different parts of the world in humans. In humans, symptoms are shown in high fever, severe headache, malaise, myalgia, sore throat, chills, sweat, nausea, stomach and chest pain. *C. burnetii* can be transmitted either by ticks or by inhaling contaminated dust. A single inhaled organism may produce illness.

In primates, the dose to kill 50% of primates was found to be 1.7 organisms (Lille *et al,* 1941). Infection of humans usually occurs by inhalation of air that contains airborne barnyard dust contaminated by dried placental material, birth fluids and excreta of infected herd animals. Outbreaks have recently occurred in veterinary students working on a sheep farm in Slovenia, and in South Australia caused by a nearby goat abattoir (Promed, 2007a, b). Another QF outbreak in humans occurred in a Scottish slaughterhouse and cutting plant (Wilson *et al,* 2010). A major outbreak occurred in 2007 in the south

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province of Netherlands, where around 170 people fell ill. Since then, there have been more than 4000 cases including 11 deaths in 2010 (Promed, 2011). The symptoms in humans are febrile illness, sometimes accompanied by pneumonia or hepatitis. Chronic QF is uncommon, but may cause life-threatening endocarditis. Acquisition of QF can also occur through the consumption of raw milk. It is not known with certainty if a pasteurisation of 72°C for 15 seconds will destroy *C. burnetii* in the milk (Quinn *et al,* 1994).

Epidemiological investigations of QF in Japan revealed that shedding of *C. burnetii* in milk by domestic ruminants has a very limited impact as raw milk is very rarely consumed by the Japanese population. Clinical cases in children are more frequently reported in this country than elsewhere, and *C. burnetii* is one of the causative cause of a typical pneumonia of immunity-acquired pneumonia. It is believed that cats are a significant source of *C. burnetii* of QF in humans in association with parturition of foetuses.

Epidemiology

The organisms can be resistant to heat, drying, and many common disinfectants. These features enable the bacteria to survive for long periods in the environment. The very stable form of *C. burnetii* is associated with compact small cell variants of the organism that are produced during standard replication along with the less resistant large cell form, metabolically dormant, and spore-like (Norlander, 2000). So far no disease has been attributed to QF in camelids, but many serological investigations have been carried out (Table 1).

Recent seroprevalence studies in Egypt, Chad and the UAE diagnosed a high percentage of reactors to QF. The seroprevalence of 80% in Chad has not been reported in the literature before. Afzal and Sakhir (1994) and Elamin *et al* (1992) stated that camels are to be considered as an important source of QF, although despite the high prevalence in Chad, seroprevalences in humans were relatively low with 1%. However, Schelling *et al* (2004) calculated a significant higher risk factor for QF seropositivity in Chad camel breeders compared to cattle breeders. They also found that camels in Chad had the highest QF seroprevalence among livestock species.

In cattle it was found, that there is no relationship between serological response and excretion. Most animals that shed *C. burnetii* in vaginal mucous, faeces or milk are seronegative. On the other hand 6 bulk milk samples (50%) were positive in PCR and 10 (83%) were positive in ELISA from samples of 12 bovine dairy herds tested by real-time PCR assay and antibody-ELISA (Muskens *et al,* 2011). In the same study, the uterine content of 45 dairy cows with metritis was tested for *C. burnetii* with a real-time PCR assay, but only one uterine sample tested PCR (highly) positive. Guatteo *et al* (2011) found the seroprevalence with 20% (animal level) and 38% (herd level) slightly higher in cattle

Table 1. Literature survey regarding QF antibodies in camelids in %.

C. burnetii	Blanc *et al*	1948	Morocco	
	Giroud *et al*	1954	Chad	22.2
	Rafyi and Maghani	1954	Iran	2.0
	Veeraghavan and Sukumaran	1954	India	
	Kalra and Taneja	1954	India	
	Elyan and Dawood	1955	Egypt	13.9
	Brown	1956	Kenya	20.0
	El-Nasri	1962	Sudan	0.0
	Imamov	1964	Kazakhstan	4.8
	Maurice *et al*	1967	Chad	13.6
	Sabban *et al*	1968	Egypt	4.8
	Bares	1968	Chad	
	Maurice and Gidel	1968	Central Africa	
	Pathak and Tanwani	1969	India	11.9
	Choudhury *et al*	1971	India	23.8-26.9
	Harbi and Awad El Karim	1972	Sudan	12.2-12.8
	Kulshreshtha *et al*	1974	India	17.3
	Burgemeister *et al*	1975	Tunisia	15.8
	Ghosh *et al*	1976	India	5.6
	Schmatz *et al*	1978	Egypt	
	Mathur and Bhargava	1979	India	6.7-7.7
	Addo	1980	Nigeria	12.0
	Harrak	1986	Tunisia	
	Abbas *et al*	1987	Sudan	14.5
	Djegham	1988	Tunisia	3.06
	Gallo *et al*	1989	Tunisia	0.0
	Soliman *et al*	1992	Egypt	66
	Schelling *et al*	2003	Chad	80
	Mazyad and Hafez	2007	Egypt	13.3
	Probst *et al*	2011	Germany	4.6
	Wernery *et al*	2012	UAE	45, dairy camels

than in small ruminants (15.0% animal level; 25% herd level). They recognised the ELISA and indirect immunofluorescence (IIF) to be more sensitive than the CFT or the agglutination for detection of serum antibodies.

In the Middle East also wildlife might play a role in the epidemiology of QF, since late-stage abortion associated with *C. burnetii* infection in Dama gazelle (*Gazella dama*) occurred in the United Arab Emirates (Lloyd *et al,* 2010). Antibodies to *C. burnetii* were also present in 18.3% of 227 sand gazelles, 7.3% of 232 mountain gazelles and 46.9% of 96 Arabian oryx reared in captivity in Riyadh, Saudi Arabia (Hussein *et al,* 2011).

DNA of *C. burnetii* was detected in 5.1% of roe deer (*Capreolus capreolus*), 4.3% of wild boar (Sus scrofa), 9.1% of European hare (Lepus europaeus), and among wild birds, in 11% of vultures (*Gyps fulvus*) and 14% of black kites (*Milvus migrans*) in Spain (Astobiza *et al,* 2011). However, all of the 340 adult ticks collected from these animals were negative for *C. burnetii*-PCR, suggesting that ticks do not play an important role in the transmission of *C. burnetii* in this area.

In dromedaries, it was observed that a higher seroprevalence of QF was detected among animals with no history of abortion as compared to animals with miscarriages (Shelling *et al,* 2003). Despite a high seroprevalence of 45% in dairy camels in the UAE (Wernery *et al,* 2012), no abortions have been observed and testing with PCR is currently conducted if the bacteria are excreted through milk. If tests are positive, it would be of tremendous interest to investigate if the bacteria are viable after pasteurisation or if they have been destroyed. However, this is a difficult and laborious task to perform because these investigations would need culturing of the bacteria.

Clinical signs

Most infected ruminants remain asymptomatic. Abortion occurs in sheep and goats during the latter part of the gestation, but is extremely rare in cattle. It has not been reported in camelids despite the often high seroprevalence (Wernery and Kaaden, 2002). *C. burnetii* can also induce pneumonia in cattle, but it is not known if QF pneumonia also develops in camelids.

Diagnosis

Clinical signs of QF are not specific; hence an accurate diagnosis requires an appropriate laboratory testing. The diagnosis of abortion caused by *C. burnetii* is performed by detection of bacteria on smears of placenta stained by the Gimenez, Stamp or Macchiavello methods in connection with a serology test like CFT, ELISA or microagglutination (Table 2). Recently the detection of *C. burnetii* DNA in placenta and vaginal mucous by PCR has radically changed the diagnosis of QF in veterinary medicine (Jones *et al,* 2010). PCR is the only method to demonstrate the shedding of bacteria which is essential to identify the herds, which may present a public health risk. This is important in dairy farms. Detection of bacteria in bulk tank milk samples using PCR is a useful and simple way of assessing milk shedders (Muskens *et al,* 2011). Recently, it was done for the first time in camel dairy farms (Rahimi *et al,* 2011). One of 70 (1.4%) camel bulk milk samples from 22 camel breeding farms was found positive for *C. burnetii*.

The combination of PCR and ELISA is nowadays the most effective way of diagnosing QF.

However, like in paratuberculosis none of the ELISAs have been evaluated for use in camels so far. It is essential to screen any potential anti-species IgG for camelid diagnostic use, using a panel of positive and negative sera in order to minimise false positive and false negatives. Soliman *et al* (1992) for example tested camel sera for QF using an in house cELISA and a HRP protein A ELISA. Their data showed a 50% less sensitivity for the protein A ELISA compared to the cELISA.

Treatment and control

Antibiotic treatment with tetracyclines is often used to reduce the number of abortions and the excretion of *C. burnetii* shed at parturition. However, the efficacy of such treatment is doubtful. During QF

Table 2. Laboratory diagnosis of Q fever

Disease	Laboratory diagnosis	Appearance of agent in Giemsa-stained smears
Q fever (*Coxiella burnetii*)	Fluorescent antibody (FA) or Giemsa-stained smears from placenta. PCR from placenta or milk. Paired serum samples for serology (CFT, ELISA or microagglutination). Antibody rise 2-3 weeks post-infection	Small purple-red cocci (0.2-4 µm) or short rods within cells. Similar in appearance to *Chlamydia psittaci* when stained with Giemsa stain

outbreaks, sanitary measurements should be put in place to reduce contamination of the environment to avoid it becoming a constant source of re-infection. Therefore, after birth material and dead foetuses must be removed and destroyed. After birth, the area should be disinfected to avoid aerosols and airborne infection. Manure is the main source of contaminated dust, and therefore the manure pit must be covered.

Several inactivated vaccines have been developed but none has been used in camelids.

Own investigation in dromedaries

Serology

For a serological survey of Q fever we have used an indirect commercial QF ELISA (Checkit Q fever, IDEXX, France), because to the best knowledge of the author, no competitive ELISA is currently available. This commercial assay works with an anti-ruminant conjugate. In total 69 sera were withdrawn from dairy dromedaries belonging to the Emirates Industry for Camel Milk Products (EICMP), and tested with the indirect ELISA. The results of this indirect ELISA were compared using the same ELISA with HRP protein A and a goat anti-camel conjugate. When anti-ruminant was used as conjugate 30% (21/69) of the dromedary sera showed antibodies to QF, whereas 25% (17/69) and 58% (40/69) had antibodies when conjugates containing protein A and goat anti-camel were used.

This showed again that the best results were achieved in indirect ELISAs when a homologous system is used (Wernery *et al,* 2012 in prep.).

Milk PCR

Individual fresh, unpasteurised camel milk samples from 30 serologically positive as well as 30 serologically negative QF dromedaries belonging to EICMP where tested with the PCR for the presence of QF organisms. The tests were conducted at CVRL and the Central Veterinary Institute in Wageningen, Holland. In both laboratories all 60 milk samples were negative, indicating that *C. burnetii* is not excreted through camel milk and therefore camel milk is a negligible source of infection. However, further investigations are necessary to substantiate these findings.

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