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The rise and control of the 2007–2012 human Q fever outbreaks in the Netherlands☆

Piet Vellema*, René van den Brom

Department of Small Ruminant Health, Animal Health Service, PO Box 9, 7400 AJ Deventer, The Netherlands

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ABSTRACT

Q fever is an almost ubiquitous zoonosis caused by *Coxiella burnetii*, which is able to infect several animal species, as well as people. Cattle, sheep and goats are the primary animal reservoirs. In small ruminants, an infection may result in abortion and stillbirth. Infected animals can shed the organism in faeces, milk and mainly in foetal membranes and foetal fluids. Transmission to humans mainly occurs through the aerosol route.

Q fever was described as a febrile illness, which had started to occur in 1933 in abattoir workers in Brisbane, Australia. Since the first documented outbreaks, Q fever has been described in many countries all over the world, and in 1955 its existence was reported in 51 countries on five continents. In the Netherlands, Q fever was diagnosed for the first time in humans in 1956, and became a notifiable disease in 1978. Between 1978 and 2006, the average number of notifications per annum was seventeen. In 2007, the first year of what later turned out to be one of the largest recorded community outbreaks of Q fever, an outbreak occurred with 168 human patients notified, and in 2008 and 2009, 1000 and 2354 human Q fever patients were notified, respectively, and dairy goats were suspected to be the source.

In 2005, *C. burnetii* was diagnosed for the first time as a cause of abortion at two dairy goat farms in the Netherlands. In 2006, 2007, 2008, and 2009, six, seven, seven, and six new abortion waves at dairy goat farms were confirmed, respectively. The infected dairy goat farms were mainly located in the same area where human cases occurred and they were considered the most plausible source of human infection. In the same period, cases of abortion caused by *C. burnetii* were confirmed at two dairy sheep farms.

Since 2007, a large multidisciplinary research portfolio has started, aimed at generating better knowledge about this disease. In June 2008, Q fever in small ruminants kept for milk production became notifiable in the Netherlands for farms with an abortion rate of more than five per cent. In the autumn of 2008, a voluntary vaccination campaign in goats was made possible in the high-risk Q fever area in the south of the Netherlands with the so far unregistered phase I vaccine containing inactivated *C. burnetii* (Coxevac®, CEVA Santé Animale). From 2009 onwards, vaccination became compulsory for dairy sheep and dairy goat farms in the south of the country, and was compulsory in the whole country from January 2010 onwards for dairy sheep and dairy goat farms, and for small ruminant farms offering recreational activity. Since February 2009, a stringent hygiene protocol became mandatory for all dairy goat and dairy sheep farms, and on 1 October 2009, bulk milk monitoring became mandatory on farms with more than

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* Corresponding author.
E-mail address: p.vellema@gddeventer.com (P. Vellema).

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fifty dairy goats or dairy sheep, and *C. burnetii* PCR positive bulk milk has since been used as an additional criterion for veterinary notification of Q fever. At the end of 2009, it was decided to cull all pregnant animals on farms with a *C. burnetii* PCR positive bulk tank milk. Since 2010, there was a sharp decline in the number of notified human cases with 504, 81, and 66 cases notified in 2010, 2011, and 2012, respectively. In combination with a rise in the human population with antibodies against *C. burnetii*, the implemented control measures most likely have ended this large outbreak.

1. Introduction

Q fever is an almost ubiquitous zoonosis caused by *Coxiella burnetii*, an aerobic Gram-negative highly resistant bacterium which is able to infect several animal species, as well as people. Cattle, sheep and goats are the primary animal reservoirs (Zeman et al., 1989; Damoser et al., 1993; Maurin and Raoult, 1999; Hatchette et al., 2001). In small ruminants, an infection may result in abortion, mainly in late pregnancy, and stillbirth. Infected animals can shed the bacterium in faeces, milk and, in particularly high concentrations, mainly in foetal membranes and foetal fluids (Maurin and Raoult, 1999; Wouda and Dercksen, 2007). Placentas of infected small ruminants can contain over 10^9 hamster infective doses or bacteria per gram of tissue (Babudieri, 1959; Fournier et al., 1998). Transmission to humans mainly occurs through the aerosol route (Marrie, 1990b; Maurin and Raoult, 1999; Schimmer et al., 2009, 2010).

Q fever was described as a febrile illness which had started to occur early 1933 in abattoir workers in Brisbane, Queensland, Australia (Derrick, 1937). Burnet and Freeman (1937) reproduced the disease in guinea pigs, mice, monkeys and albino rats with an emulsion of infectious guinea pig liver received from Derrick, and demonstrated rickettsial organisms in spleen sections from infected mice. In the same period, Davis and Cox (1938), working on the possible vectors of Rocky Mountain spotted fever, allowed *Dermacentor andersoni* ticks collected near Nine Mile Creek, Montana, to feed on guinea pigs and found that some guinea pigs developed a febrile illness with enlarged spleens. The 'Nine Mile agent' was demonstrated intravacuolarly in infected tissue culture (Cox, 1938, 1939) and was able to cause an infection in man (Dyer, 1938). In 1938, *Rickettsia diaporica*, the proposed name for the organism (Cox, 1939) incorporating both rickettsial features and the ability of the organism to pass a bacteriological filter, was propagated in tissue cultures and in developing chicken embryos (Cox, 1939; Cox and Bell, 1939). Derrick (1937) proposed the name Q fever or query fever for this disease.

The American and Australian groups started working together and demonstrated that the Australian Q fever agent, the zoonotic agent, and the Nine Mile agent were in fact isolates of the same microorganism, *Rickettsia burnetii* (Derrick, 1939; Maurin and Raoult, 1999), later renamed as *C. burnetii* (Philip, 1948), a name which honours both Cox and Burnet as Q fever pioneers.

Since the first documented outbreaks, Q fever has been described in many other countries all over the world. Kaplan and Bertagna (1955) reported its existence in 51 countries on five continents, mainly in cattle, sheep, goats, and man. In New Zealand, Poland, the Scandinavian countries, and the Netherlands no confirmed cases had been found at that time.

This article describes abortion waves in sheep and goats in the Netherlands caused by *C. burnetii* which started to occur in 2005, causing environmental contamination and a subsequent rise in human Q fever cases. A large multidisciplinary research portfolio was developed and implemented aimed at generating better knowledge about this disease to be able to take adequate control measures. Finally, this article presents and discusses measures taken which, in combination with a rise in the human population with antibodies against *C. burnetii*, most likely resulted in a control of this outbreak at the end of 2012.

2. Abortion waves in sheep and goats

C. burnetii can infect several animal species, as well as humans (Babudieri and Moscovici, 1952; Babudieri, 1959; Marrie, 1990a; Maurin and Raoult, 1999; Arricau-Bouvery and Rodolakis, 2005; Muskens et al., 2007). Cattle, sheep and goats are the primary animal reservoir (Zeman et al., 1989; Damoser et al., 1993; Maurin and Raoult, 1999; Hatchette et al., 2001; Wouda and Dercksen, 2007) although cats have also been described as a major source of infection (Marrie et al., 1988). In cattle, an infection is usually asymptomatic but may occasionally result in abortion, fertility problems and metritis (Arricau-Bouvery and Rodolakis, 2005). Infected small ruminants may deliver live or dead lambs but infection may also result in large abortion waves, mainly at the end of gestation (Arricau-Bouvery and Rodolakis, 2005; Wouda and Dercksen, 2007; Roest et al., 2012).

Historically, the seroprevalence of Q fever in ruminants in the Netherlands was considered to be low, and in a survey held between 1951 and 1953, and in 1954, all 524 (Wolff and Kouwenaar, 1954) and 745 ruminants tested (Dekking and Zanen, 1958), respectively, were seronegative. In a survey in 1987, using an indirect ELISA, antibodies against *C. burnetii* were demonstrated in 3.5% of 3603 sheep from 191 flocks. A total of 52 flocks (27.2%) had one or more seropositive sheep. This limited survey also included 498 goats of 0.5–1 year old, and 96 adult goats, and showed that less than 1% of goats had antibodies against *C. burnetii* (Houwers and Richardus, 1987).

The sheep industry in the Netherlands has been more or less stable in recent decades, with a little less than one million breeding ewes. In recent years, commercial dairy sheep are kept on forty farms, and the number of animals per farm