

# The largest Q fever outbreak ever reported

P. Speelman

Department of Internal Medicine, Academic Medical Centre, Amsterdam, the Netherlands,  
e-mail: p.speelman@amc.uva.nl

Since 2007, the Netherlands has experienced the largest Q fever outbreak ever reported in the literature. From 2007 till today approximately 4000 people have been affected and at least 14 of these patients, nearly all of them with severe underlying conditions, have died. The clinical details of the patients who died are described by Kampscheur *et al.* in this issue of the Journal.<sup>1</sup>

It all started in May 2007 when medical specialists in a hospital in the southern part of the Netherlands and a general practitioner in the same region reported a substantial number of patients with pneumonia not responding to amoxicillin, whereas patients did well on moxifloxacin. Soon it became clear that these pneumonias were caused by *Coxiella burnetii*. During 2007, 168 patients were reported. Although an association with intense goat farming was already suggested in 2007<sup>2</sup> and experts warned that the outbreak could recur, a limited number of preventive measures were taken. The experience that earlier reported outbreaks were usually limited in time and did not recur in the following years may have played an important role. In 2008, however, the epidemic recurred and 1000 patients were reported. This prompted more preventive regulations. In June 2008, Q fever finally became a notifiable disease for the veterinary sector as well. A ban on the spread of manure from farms with Q fever was issued and (voluntary) vaccination of non-pregnant goats on dairy goat farms in the region was advised. In 2009 compulsory hygiene measures in farms with more than 50 goats or sheep were instituted and compulsory vaccination of goats and sheep in farms with more than 50 animals was ordered. Later that year testing for *Coxiella burnetii* on bulk milk was started and transport of cattle was prohibited. In December 2009 breeding on infected farms was prohibited. After a lot of political pressure and a critical documentary on national television, it was decided to start culling more than 50,000 pregnant goats on infected farms. In January 2010 compulsory vaccination for all goats and sheep was instituted. In 2010 up to 3 November, 492 patients with Q fever (not confirmed yet) have been reported. Since several measures have been instituted simultaneously it is difficult

to speculate which measures have been most effective. It is very likely that the culling of all pregnant goats has had an important impact. It is clear, however, that most interventions were issued too late. Retrospectively, we know that Q fever was already a problem in the veterinary sector in 2005 and 2006 but that this knowledge was not communicated to the human health sector.

Approximately 4000 people were affected. Among the admitted patients fever and flu-like symptoms with headache and cough were the most important symptoms. Most inpatients had an infiltrate on the chest X-ray. CURB scores on admission day were 0 +/- 1, indicating mild pneumonia.<sup>3</sup> As reported by Delsing *et al.* in this issue of the Journal<sup>4</sup> acute Q fever may be followed by a chronic fatigue syndrome. A recently published case-control study among 54 patients who contracted Q fever in 2007 reported severe fatigue, one year after acute Q fever, in over 50% of the cases compared with 26% of controls.<sup>5</sup> Chronic Q fever may develop in 1 to 2% of patients after acute Q fever. Although endocarditis is a feared complication, in the Netherlands infected aneurysms and infected vascular prosthesis were more frequently reported and therefore screening of patients with aortic aneurysms has been advocated.<sup>6</sup> Delsing *et al.* estimate that over the last three years 40 to 50 cases of chronic Q fever have been diagnosed.

A French study in pregnant patients with Q fever reported obstetric complications in 80% of patients, compared with 44% of patients who were treated with co-trimoxazole.<sup>7</sup> Other studies, however, did not find an association between seropositivity for *Coxiella burnetii* and adverse pregnancy outcome. A retrospective study in the Netherlands did not find a correlation between seropositivity during early pregnancy and adverse pregnancy outcome.<sup>8</sup> A randomised controlled trial has started this year aimed at providing conclusive data on the need to screen pregnant women in high incidence areas.

Recently the Health Council of the Netherlands has advised the Minister of Health to provide the only available vaccine (Q-VAX, developed and registered in Australia) for

certain high risk groups (<http://www.gezondheidsraad.nl/nl/adviezen/vaccinatie-van-mensen-tegen-q-koorts-eerste-advies>). These people should be tested serologically and with a skin test since previous exposure to *Coxiella burnetii* may lead to serious side effects. Since the data on efficacy and safety are limited the vaccine should not be administered to pregnant women and people below the age of 15 years.

An extremely important question still remains unanswered. How is it possible that so many people became infected and that an epidemic of historic proportions could develop?

Factors that may have played a role include the high number of goats in highly populated areas, environmental factors and the possible introduction of a more virulent strain of *Coxiella burnetii*. The number of dairy goats in the Netherlands has increased from 98,000 in 2000 to 231,000 in 2009. The number of farms with more than 100 goats increased from 33 to 58. In the Netherlands there are hardly any goat farms without many people living in the proximity of the farm. From earlier studies and also from a recent study it is known that the relative risk for people to contract Q fever is directly related to the distance between the infected farm and their house. Environmental factors may also play a role, e.g. weather conditions. In 2007 we had a long dry period without rain. Recently Hunink *et al.* reported a correlation between vegetation density and higher groundwater levels and lower transmission of Q fever from infected farms in various regions of the Netherlands (RIVM report no. 90, 1 January 2010). Studies on isolated strains of *Coxiella burnetii* are ongoing. The Central Veterinary Institute has reported that one MLVA type prevails on many dairy goat farms in the southern part of the Netherlands, possibly indicating clonal spread in this area. In a new project whole genome sequencing will be used to distinguish between *Coxiella* bacteria from different sources.

Infectious diseases remain important. New infectious diseases appear and old infectious diseases re-emerge. Approximately 75% of the re-emerging infectious diseases are zoonoses. In a densely populated country with an extremely high concentration of farm animals suitable systems have to be available for timely recognition of emerging zoonotic diseases in humans and farm animals. The recently published report 'Emerging zoonoses: early warning and surveillance in the Netherlands' is an important step on the road to an effective human-veterinary early warning system (EMZOO rapport: Emerging zoonoses: Early warning and surveillance in the Netherlands; <http://www.rivm.nl/bibliotheek/rapporten/330214002.pdf>)

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