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A Q fever outbreak in a psychiatric care institution in The Netherlands

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SUMMARY

In May 2008 the Nijmegen Municipal Health Service (MHS) was informed about an outbreak of atypical pneumonia in three in-patients of a long-term psychiatric institution. The patients had been hospitalized and had laboratory confirmation of acute Q fever infection. The MHS started active case finding among in-patients, employees of and visitors to the institution. In a small meadow on the institution premises a flock of sheep was present. One of the lambs in the flock had been abandoned by its mother and cuddled by the in-patients. Samples were taken of the flock. Forty-five clinical cases were identified in employees, in-patients and visitors; 28 were laboratory confirmed as Q fever. Laboratory screening of pregnant women and persons with valvular heart disease resulted in one confirmed Q fever case in a pregnant woman. Of 27 samples from animals, seven were positive and 15 suspect for *Coxiella burnetii* infection. This outbreak of Q fever in a unique psychiatric setting pointed to a small flock of sheep with newborn lambs as the most likely source of exposure. Care institutions that have vulnerable residents and keep flocks of sheep should be careful to take adequate hygienic measures during delivery of lambs and handling of birth products.

Key words: Community outbreaks, coxiellae, zoonoses.

INTRODUCTION

Q fever is a zoonosis caused by *Coxiella burnetii*, a small, pleomorphic Gram-negative obligate intracellular bacterium. Ruminants, mainly sheep, goat and cattle are the most common reservoir. *C. burnetii* infections in animals are usually asymptomatic, but may cause abortions in sheep and goats. High

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concentrations of *C. burnetii* can be found in birth products of infected mammals [1]. Humans can acquire infection by inhaling contaminated dust and aerosols. The incubation period varies from 1 to 6 weeks depending on the number of inhaled organisms, with most patients becoming ill within 3 weeks of exposure [2]. About half of those infected with *C. burnetii* show signs of clinical illness, and 20% develop a more severe infection complicated with pneumonia, hepatitis or another clinical diagnosis. Fatal infections are rare [1, 2]. About 5% of cases are hospitalized but, in a previous large outbreak in The Netherlands, this reached more than 20% [3]. Certain conditions such as pregnancy, heart valve and other vascular abnormalities predispose individuals to chronic Q fever [4].

In The Netherlands, acute Q fever is notifiable. Between 2001 and 2006 the annual number of cases varied from 5 to 19 per year. In 2007 and 2008, 191 and 1000 cases were notified, respectively [3]. In other countries, such as Switzerland, Germany and the UK several community outbreaks of Q fever in rural areas due to aerosolized spread have been described [5–10]. In most cases these outbreaks were attributed to sheep, although sometimes no source was detected. Other outbreaks have been associated with goats, cattle, pigeons, cats and rabbits [11–15]. Outbreaks have also been described in abattoirs [16, 17].

Boschini and colleagues described an outbreak in an Italian residential ('closed') facility for the rehabilitation of drug users [18]. No other Q fever outbreaks in a healthcare setting have been described.

OUTBREAK INVESTIGATION

Outbreak alert

On 9 May 2008, a physician in a long-term psychiatric institution located south-east of the city of Nijmegen reported to the regional Municipal Health Service (MHS) that three residents of the institution had been hospitalized with atypical pneumonia. (For CXR of one of the residents see Supplementary Fig. S1, available online.) Symptoms included high fever, headache, cough and chills. The physician suspected an outbreak. In all three patients the diagnosis of Q fever was confirmed by polymerase chain reaction (PCR) on throat swabs or sputum samples. No other infections, including *Legionella* and influenza were diagnosed. Because of their presence on the premises of the institution, sheep and birds were considered as likely sources. Upon the alert day (day 0) MHS Nijmegen started an outbreak investigation to determine the source and extent of the outbreak.

Outbreak setting

A total of 127 in-patients were resident in this long-term psychiatric care institution; in addition, there were 1285 ambulatory patients. Most patients suffered from chronic psychiatric disorders such as schizophrenia and bipolar disorders. The institution had 350 employees. The institution was openly accessible to visitors.

Case finding

The MHS immediately started active case finding among residents and employees of the institution. The nursing staff were asked to be on the alert for clinical symptoms in their in-patients. All staff of the psychiatric institution and nearby surrounding institutes were also asked to be alert for possible cases. In addition, local and regional general practitioners and appropriate hospital clinicians were warned to be aware of possible cases, both in patients residing at the institution as well as those in the local community. Case finding of ambulatory patients and visitors was not actively performed.

Case definitions

A suspected case was defined as a person who had been living or working at the psychiatric institution or in one of the neighbouring organizations on the same premises; or had visited the premises; or lived within 500 m of the area in the 6 weeks prior to the alert and who, in addition, had fever ($>38{\cdot}5\ ^{\circ}C$) and three or more of the following symptoms: severe headache, pneumonia (clinical or radiological), chills, sweats, coughing, aching muscles, diarrhoea, fatigue or malaise. A case was confirmed if *C. burnetii* was detected in throat swab and/or blood samples using PCR, and/or a fourfold rise in serum antibody titres to *C. burnetii* complement fixation test (CFT), and/or detection of IgM using an immunofluorescence assay (IFA).

PCR tests of clinical specimen (both blood samples and throat swabs) of suspected cases, CFTs for IgG, and phase 1 (IgM) and phase 2 antibody IFAs were performed.

From each confirmed case the following information was obtained: general characteristics (age,

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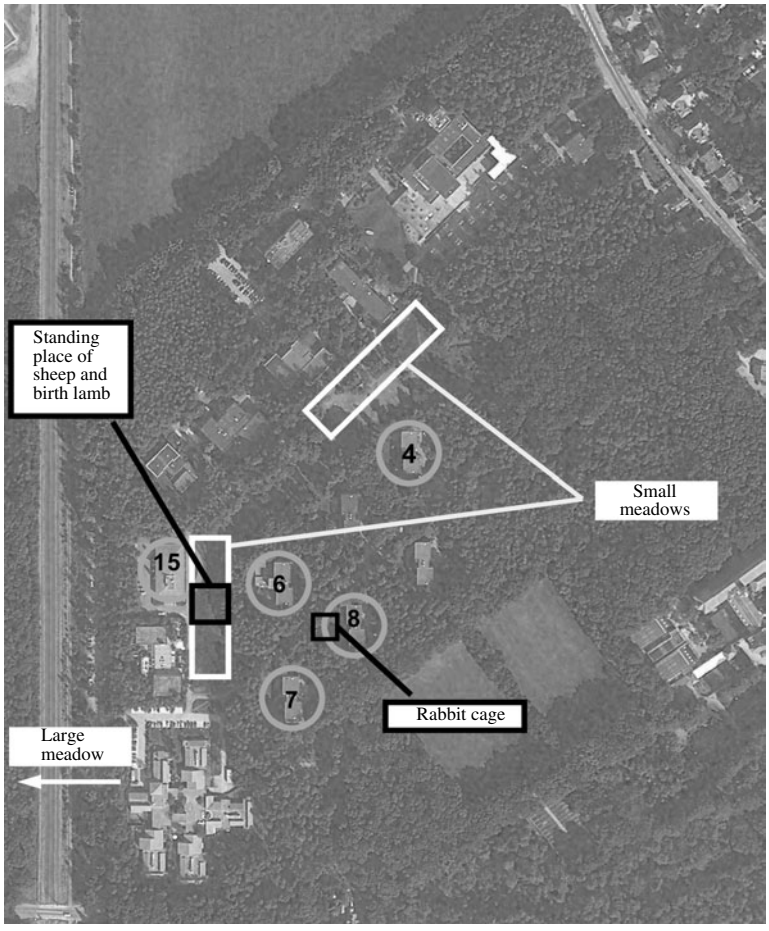

Fig. 1. Map of the psychiatric institution, Nijmegen. Location of the meadows where the flock of sheep was grazing (white), location of the birth of the abandoned lamb, rabbit cage (black) and client residences with confirmed Q fever clients (grey circles) are indicated. Attack rate (AR) per building: building 4, AR 4/25 (16%); building 6, AR 1/26 (4%); building 7, AR 2/26 (8%); building 8, AR 1/21 (5%); building 15 AR 1/68 (1%).

gender, place of residence), medical status (medical history), and exposure information (contact with animals at or around the premises of the institution). At 10 weeks after Q fever diagnosis, 17 cases were followed up and asked whether they still had symptoms. In addition to the active case finding, active screening of pregnant women and persons with valvular heart disease linked to the institution was performed.

Epidemiological investigation

During the epidemiological investigation two main hypotheses were explored. First, a flock of six sheep present in a small meadow on the institution premises for 5–6 years was considered a possible source of the outbreak. Since this flock produced five lambs in the weeks prior to the outbreak alert [the first born in the beginning of April (day 38), the last on 8 May (day 1)] it was the most likely source. In-patients and outpatients could have been infected by inhaling contaminated aerosols after close animal contact, particularly with pregnant or newborn animals. One of the lambs, born on 14 April (day 25), was abandoned by its mother and was adopted by one of the in-patients, who took it into her bedroom and living room (building 4, Fig. 1) and bottle-fed it six times a day. Several in-patients cuddled this lamb. Three days after its birth, it was placed in a rabbit cage on the premises of the institution, and cared for by in-patients and employees.

The other hypothesis was that cases were infected by a large flock of sheep in a large meadow directly opposite the main entrance of the institution. A flock of about 200 sheep had grazed there until 1 April (day 38). Two shepherds and the wife of one of the shepherds had been confirmed as Q fever cases with onset in March 2008. The hypothesis was that infection could have occurred by windborne spread from

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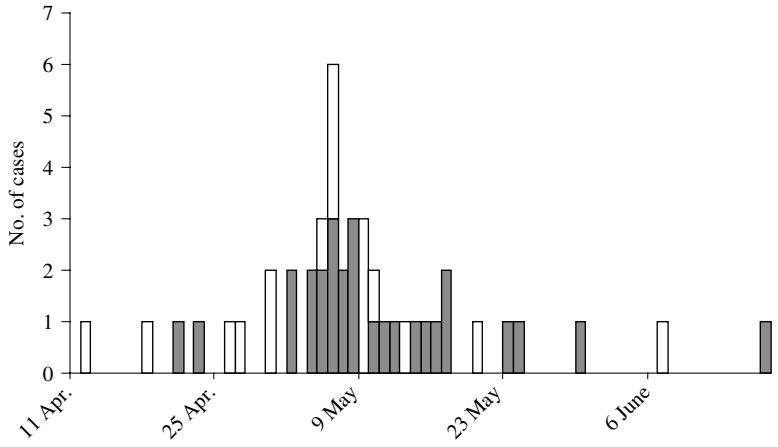

Fig. 2. Confirmed (■) and possible (□) Q fever cases in a psychiatric care institution by day of illness onset, April–June 2008 ($n = 45$).

the meadow, or by introduction of contaminated animal products from this flock (such as straw, hay, or compost), or by wild animals. Considering windborne spread, the MHS assumed human Q fever cases could have also occurred in the neighbouring community.

A detailed map of the institution premises was used to plot cases, calculate attack rates (ARs) for each building and indicate environmental information such as the location of the meadow, the rabbit cage and the predominant wind direction (Fig. 1).

Veterinary and environmental investigation

In order to identify the source of the outbreak an environmental and veterinary investigation was undertaken by the Food & Consumer Safety Authority and by scientists of the Laboratory of Zoonoses and Environmental Microbiology of the National Institute for Public Health and the Environment (RIVM). Animal samples were collected from: (i) rabbits (anal and oral swabs) at the psychiatric institution, (ii) the sheep and lambs (vaginal and udder swabs) who had been residing at the institution, but had now moved, and (iii) the flock of sheep opposite the entrance of the institution. Environmental samples taken included faecal samples from the rabbit cage and meadow (sheep) at the institution, and faecal samples and wool from the flock of sheep opposite the institution. All samples were sent for PCR testing at the RIVM using a newly developed multiplex Q-PCR [19]. MLVA (multiple locus VNTR analysis) typing was used for some of the human and animal specimens.

RESULTS

Q fever cases

Through active case finding 45 persons were identified as suspected cases. Of those 28 (62%) were confirmed by laboratory tests, as per the case definition. Of the other 17 persons screened, all laboratory results (PCR, CFT, IFA) were negative. Of the confirmed cases there were 16 employees (one from a neighbouring organization), 10 in-patients, one friend of an employee who had visited the institution and walked in the meadow, and one person living nearby (< 500 m) (Fig. 2). The friend of the employee and the person living nearby did not have close contact with the lamb or sheep. The average mean age of the confirmed cases was 42 years (range 15–63 years). Fifteen of the 28 cases were male.

The dates of onset of illness extended from 21 April (day 18) to 17 June (day 39). Follow-up of 17 cases showed that the median duration of illness was 2 weeks (range 0·5–3·5 weeks). At 10 weeks after infection, 7/17 cases reported to be still suffering from fatigue (a common sequela of Q fever). In all, 29% (8/28) of cases were hospitalized, six of whom were in-patients and two employees of the institution.

The overall clinical AR was 7·9% (10/127) in in-patients residing at the institution and 4·6% (16/350) in employees. The ARs appeared to be highest (16%) in building 4 (Fig. 1). This is probably due to the fact that the lamb was placed in building 4 directly after delivery. Nine of 10 confirmed cases resided in five of the 15 buildings on the premises. These five buildings were close to the small meadows where the sheep were grazing. Denominators for the number of employees

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per building were unavailable, and ARs for employees per building could not be calculated. The buildings with confirmed Q fever residents were in general closer to one of the small meadows or the rabbit cage (or harboured the abandoned lamb, building 4) compared to the other buildings.

Screening of employees pregnant or with valvular lesions

Screening of 24 asymptomatic pregnant employees of the institution resulted in one positive Q fever infection in a woman who was 38 weeks pregnant. This woman was hospitalized and labour was induced, because of the risk of placentitis. A healthy infant was born and PCR on birth products was negative. None of the six screened persons with valvular heart disease became infected.

Results of the veterinary and environmental investigation

Of 27 animal samples analysed, five were negative, 15 were suspect for Q fever, with one or two out of three genomic targets positive in Q-PCR, but concluded to be negative, and seven were found to be positive (all three genomic targets positive in Q-PCR). The positive samples were obtained from three ewes and the abandoned lamb from the small meadow. Vaginal and udder swabs were found to be positive in two ewes. A vaginal swab and a wool sample were found to be positive in a third ewe. The abandoned lamb was found to be positive from a throat swab. No other potential wild or domestic animal sources were identified. Of the flock of sheep that had been grazing outside the premises 10 were tested; all were negative.

DISCUSSION

To our knowledge, this is the first reported outbreak of Q fever related to lambing, in an open healthcare institution. Our investigation pointed to a small flock of sheep with newborn lambs on the premises of the institution as the most probable source of exposure. Due to the unique and restricted setting of this outbreak in a psychiatric care institution, exhaustive screening of risk groups was feasible. However, an analytical study in this type of setting was not possible. Urgent outbreak control was also paramount.

This outbreak investigation was thus limited to descriptive analyses on active case finding and active screening of risk groups, and it was not possible to investigate exposure of asymptomatic cases or involve controls.

Our outbreak investigation nevertheless strongly suggested that the flock of sheep and its newborn lambs were the most likely sources of the outbreak, in accord with other studies [5, 8, 18, 20]. During the Q fever outbreak in The Netherlands, which has been ongoing since 2007, MLVA typing of samples from patients, ewes and lambs showed similar relationships between each other. In this study a swab specimen from a newborn lamb showed an identical MLVA genotype to that from a patient who developed severe pneumonia after close cuddling with a lamb in another incident [21].

It is possible that other, untested lambs of the small flock, that were born before or after the birth of the abandoned lamb, were carriers of *C. burnetii* and caused illness. Presuming the abandoned lamb was the main source of this outbreak, the infectious potential of this one lamb was comparable to that of entire flocks in different settings as described in the study of a superspreading ewe [20]. If the abandoned lamb at birth on 14 April 2008 was the main source of this Q fever outbreak, the mean incubation period of the cases was 27 days (range 7–64 days), which is higher than the incubation period of 3 weeks found in comparable studies [9, 20]. This suggests that transmission could have taken place during delivery, but in addition also after delivery. The rejection by the mother offered an opportunity for the psychiatric patients to have frequent and in some instances, intensive contact with the abandoned lamb. In addition, the possibility of infection by inhalation of contaminated dust (from manure or birth products) by in-patients and employees should be considered, taking into account that the first day of illness of some cases exceeds the maximal incubation time of 6 weeks after the birth of the lamb.

The observed overall ARs in in-patients (7·9%) and employees (4·6%) are comparable with those described in a recent study of an outbreak in a German village, which showed an AR of 4·3% in citizens living in the area within 400 m of a suspected meadow [8].

The proportion of clinical cases hospitalized was 29%, which is similar to a 25% hospitalization rate in the outbreak caused by a superspreading ewe in a market in Germany [20], but substantially

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higher than the average of 9% found in other studies [6, 9, 18].

Markedly, 60% (6/10) of Q fever cases in in-patients were hospitalized, compared to 13% (2/16) of the employees. Possibly, case finding in employees was more complete and included milder cases.

Future preventive measures should focus on reducing contact with lambing sheep and increase awareness in personnel and occupational health professionals of the potential health risks posed in similar settings. After a study of a large outbreak of Q fever at a farmers' market in Germany [20] the authors recommended that pregnant sheep should not be displayed in public during the third trimester, and that animals in petting zoos should be tested regularly for *C. burnetii* [20]. Another study recommend not keeping sheep within 500 m of residential areas and that lambing of sheep should not occur outdoors [8]. Care institutions with vulnerable residents maintaining flocks of sheep should be made to take adequate hygienic measures during delivery of the sheep and handling of birth products.

NOTE

Supplementary material accompanies this paper on the Journal's website (http://journals.cambridge.org/hyg).

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DECLARATION OF INTEREST

None.

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