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An outbreak of sheep-associated Q fever in a rural community in Germany

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Abstract. In spring 1996, an outbreak of Q fever occurred among residents of a rural town (population: 300) in Germany. A retrospective cohort study was conducted to ascertain the extent of the outbreak and to assess potential risk factors for illness. In July 1996, all residents ⩾15 years received a self-administered questionnaire and were offered *Coxiella burnetii* antibody testing. Residents were considered to have probable Q fever if they had a positive result for IgM *C. burnetii* antibodies by ELISA or possible Q fever if they had fever ⩾39 °C lasting >2 days and ⩾3 symptoms (chills, sweats, severe headache, cough, aching muscles/joints, back pain, fatigue, or feeling ill) after 1 January 1996. Two hundred (84%) of the 239 residents aged ⩾15 years either completed the questionnaire or submitted blood for antibody testing. Forty-five (23%) of these 200 met the probable or possible case definitions. Onsets of illness occurred in January–June 1996. Cases were geographically distributed throughout the town. Persons reporting contact with sheep (32% vs 18%, RR: 1.8, 95% CI: 1.1–2.9) and walking near a large sheep farm located next the town (34% vs 8%, RR: 4.5, 95% CI: 1.7–12.2) were more likely to have met the case definition than those without these exposures. Fifteen of 20 samples from the large sheep flock were positive for *C. burnetii* antibodies. The sheep had lambed outdoors in December 1995–January 1996 while the weather was extremely dry. The timing of the outbreak after lambing, the uniform distribution of cases thoughout the town and the absence of risk factors among most case-persons suggest airborne transmission of *C. burnetii* from the large sheep farm.

Key words: Cohort study, *Coxiella burnetii*, Outbreak investigation, Q fever

Introduction

Q fever is a zoonotic disease caused by the rickettsial organism *Coxiella burnetii* [1–3]. The most common reservoirs for *C. burnetii* are domesticated ruminants, primarily cattle, sheep, and goats. Humans typically acquire Q fever by inhaling infectious aerosols and contaminated dust generated by animals or animal products.

Although Q fever usually occurs sporadically, occupational exposures have caused outbreaks in abattoirs and among staff in research facilities using sheep as experimental animals [4–9]. In Europe, large outbreaks of Q fever involving people without occupational exposure in communites have been rarely reported [7, 10–12]. Indirect exposure to sheep flocks passing populated areas was shown to be a determinant of the outbreaks in Switzerland and Northern Italy [10,12]. In Great Britain, one urban outbreak was related to passage of farm vehicles containing contaminated straw and manure, and another to windborne spread from farmlands near an urban area [7, 11]. Dry periods may enhance desiccation and aerosolization of contaminated material, and thus may promote the occurrence of community Q fever outbreaks [2, 13]. However, data on the relationship of weather to Q fever are scarce.

This report describes an investigation of an outbreak of Q fever with a high attack rate among residents of a small rural town in Hessen, Germany during the spring of 1996. The investigation indicated that the outbreak was caused by airborne transmission of *C. burnetii* to town residents following lambing at a nearby sheep farm. An exceptionally dry period during the lambing could have contributed to the occurrence and extent of the outbreak.

Methods

Background

In May 1996, the local health authorities in Hessen, Germany, became aware of a cluster of persons with high and persistent fever. Most persons lived in a rural town, Rollshausen (population approximately 300), although ill persons also lived in five surrounding towns located 1–3 km from Rollshausen, in the district of Lohra in Hessen. Serologic testing of some patients suggested that these persons had Q fever. In Germany, Q fever is a reportable disease and, in 1995, no persons were reported to have had Q fever from Lohra. There were two sheep flocks near Rollshausen before the cluster. One flock, with 1000–2000 sheep, had pastured on the farm property northwest of Rollshausen from October 1995 to May 1996. Lambing occurred indoors and outdoors in December 1995 and January 1996. The second flock, with 20 sheep, has been located northeast of Rollshausen since 1995.

Retrospective cohort study of Rollshausen residents ⩾15 years of age

The study cohort consisted of the 239 Rollshausen residents 15 years of age and older. These persons were given a self-administered questionnaire and were offered phlebotomy for *C. burnetii* antibody testing. The questionnaires, distributed to each household on 10 July 1996, gathered information about the onset, duration and characteristics of symptoms since 1 January 1996, demographics, occupation, livestock exposure, consumption of raw milk, tick bites, and outdoor activities. Persons who did not return questionnaires received a second questionnaire on 26 July 1996 by mail. The Rollshausen residents had been notified of the availability of *C. burnetii* antibody testing by letter on 4 July 1996 and also when the questionnaire was distributed on 10 July 1996. Phlebotomy for all willing residents was carried out at a central location in Rollshausen on 11 July 1996. In addition, we contacted family doctors and local hospitals serving Lohra to identify all Rollshausen residents with possible Q fever who had sought medical care since January 1996. During July 1996, we then attempted to retest all identified persons for *C. burnetii* antibody and administer the questionnaire.

Case ascertainment for non-Rollshausen residents

Residents of the surrounding towns with possible Q fever were identified by reviewing medical records of the family doctors and local hospitals. These persons were also offered *C. burnetii* antibody testing and were given the same questionnaire used in the retrospective cohort study of Rollshausen residents.

Case definitions

Persons were considered to have laboratory evidence of *C. burnetii* infection if they had a positive result for IgM *C. burnetii* antibodies and were considered to have clinical evidence of *C. burnetii* infection if they had had fever ⩾39 °C lasting >2 days and ⩾3 of the following symptoms (chills, sweats, severe headache, cough, aching muscles/joints, back pain, fatigue or feeling ill) after 1 January 1996. Based on these criteria, persons were classified as having probable *C. burnetii* infection if they had laboratory evidence of *C. burnetii* infection, regardless of their clinical symptoms. Persons were classified as having possible *C. burnetii* infection if they had clinical evidence of *C. burnetii* infection but did not have bood obtained for laboratory testing. Persons who had negative IgM results were not counted as possible cases, regardless of whether they met the clinical criteria or not.

Laboratory analysis

The laboratory of the Institute for Hygiene and Infectious Diseases of Animals of the Justus-Liebig University performed *C. burnetii* antibody testing on serum samples collected from humans and animals by an enzyme-linked immunosorbent assay (ELISA) [14]. Human sera were tested both for IgG and IgM antibodies; in animal samples IgG and IgM were not distinguished. The IgM cutoff value for the ELISAs was 400 ELISA units (abs. 405 nm = 0.4) and the IgG cutoff value 200 ELISA units, except for sheep (600 ELISA units). Before testing human sera for IgM, a rheumatic factor absorption was done because of possible nonspecific reaction due to a rheumatic factor.

Environmental investigation

Twenty serum samples from the large sheep flock, nine from the small flock and 12 from other animals including cows, horses, dogs, cats and goats obtained in May–July 1996 were tested for *C. burnetii* antibody by ELISA. The weather report data of Lohra (strength and direction of wind, rainfall, temperature) from spring 1996 and the three previous years were obtained from the German Weather Service/Climate and Environmental Evaluation.

Statistical analysis

Univariate statistical analysis of the categorical data was performed using the χ^2 test and Fischer's exact test, as appropriate. Confidence interval (CI) for relative risks (RR) were calculated using EpiInfo. Multivariate analyses were performed by multiple logistic regression analysis using SPSS software. The population attributable risk, which is the proportion of cases in a population presumably attributable to a given risk

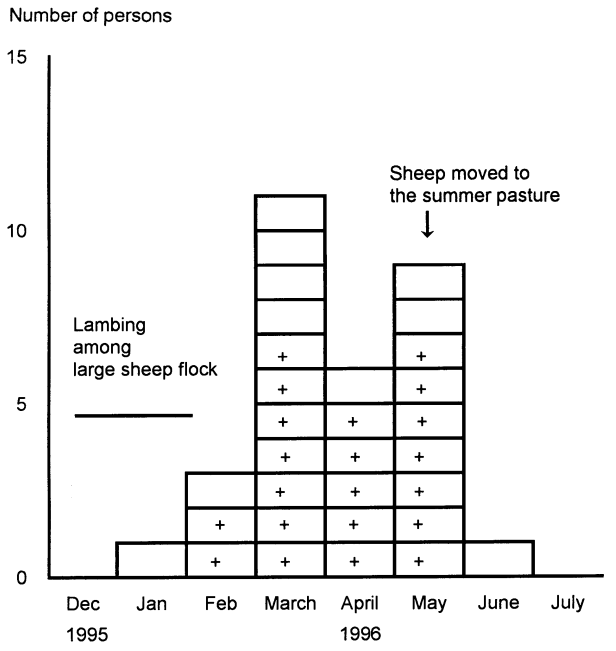

Figure 1. Number of Rollshausen residents with Q fever, by month of symptom onset, January–June 1996. Note: + = person with probable Q fever; no sign = person with possible Q fever.

factor, was calculated for those risk factors associated with illness by univariate analysis [15].

Results

Cohort study of Rollshausen residents

Two hundred (84%) of the 239 residents ⩾15 years of age either submitted a blood sample (n = 120, 50%) or completed the questionnaire (n = 193, 81%). Of the 120 persons submitting a blood sample, 35 (29%) had a positive IgM antibody result and 20 (17%) had evidence of past infection (IgG+, IgM–). Of the 193 completing a questionnaire, 35 (18%) had clinical evidence of *C. burnetii* infection.

Forty-five (23%) of the 200 persons were considered to have probable (35) *C. burnetii* infection because of a positive IgM antibody test or possible (10) *C. burnetii* infection based only on the clinical criterion. To estimate how many of the 10 persons defined as possible cases would have met the probable case definition if they had blood samples obtained, we considered the 25 persons who had clinical evidence of *C. burnetii* infection and who also had blood samples obtained for antibody testing. Of these persons, 21 (84%) had a positive IgM antibody result which suggests that the positive predictive value of the clinical criterion was 84%. Therefore, among the 10 persons meeting the possible case definition and who did not have blood obtained for antibody testing, at least eight would have been expected to have met the probable case definition if they had blood obtained for testing. Of the 35 persons who had laboratory evidence of *C. burnetii* infection, 21 (60%) met the clinical criterion of *C. burnetii* infection, 8 (23%) had some symptoms but did not meet the clinical criterion and 6 (17%) were asymptomatic.

Symptom onsets among persons with probable or possible *C. burnetii* infection who met the clinical criterion (i.e. for whom symptom onsets were available) were from January to June (Figure 1). Besides fever, the most common symptoms reported by the 45 probable and possible case-persons were fatigue, feeling ill, sweats, and aching muscles or joints (Table 1). Four were hospitalized with radiologically confirmed pneumonia.

In all further analyses, the attack rates (AR) were defined as the proportion of persons having probable or possible *C. burnetii* infection among the 200 persons who either submitted a blood sample or completed the questionnaire. The 45 persons who met the case definition were geographically distributed throughout Rollshausen (Figure 2). ARs did not vary by gender, age, or household size. Persons who reported contact with sheep (i.e. been near a sheep stable or pasture) were nearly twice as likely to have met the case definition as those who had not had this exposure (Table 2). In addition, persons who reported to have been walking near the large sheep farm (the area called Haidekopf, see Figure 2) were nearly twice as likely to have met the case definition as those who had not been walking there. However, population attributable risk calculations indicated that either of these risk factors could account for less than 30% of the cases (22% for contact with sheep and 26% for walking in Haidekopf). Walking as a leisure activity did not increase the probability of meeting the case definition;

Table 1. Symptoms reported among 45 persons with Q fever in Rollshausen, 1996

Symptom	No.	(%)
Fatigue	35	(78)
Feeling ill	33	(73)
Fever ⩾ 39 °C	32	(76)
Sweats	32	(71)
Aching of muscles/joints	30	(67)
Back pain	27	(60)
Chills	25	(57)
Severe headache	24	(53)
Cough	17	(38)
Nausea	13	(29)
Diarrhea	9	(21)
Vomiting	8	(18)

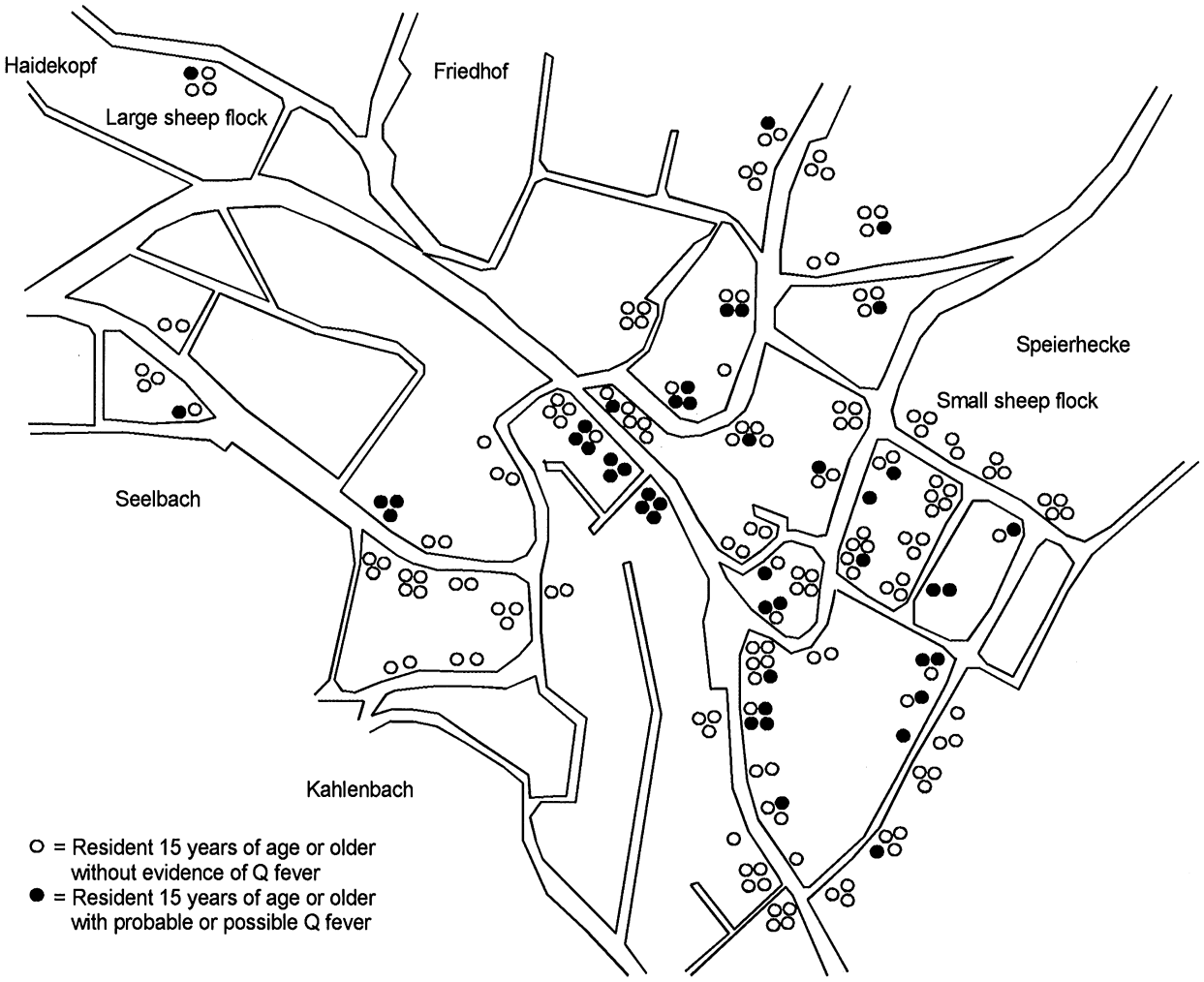

Figure 2. Each circle represents the location of residence of the 200 Rollshausen inhabitants participating in the cohort study. Black circles represent those 45 having probable or possible *C. burnetii* infection. The locations of the walking areas (Haidekopf, Friedhof, Seelbach, Kahlenbach, Speierhecke), the farm with the large sheep flock, and the small sheep flock are indicated.

however, among the 121 persons who reported walking as a leisure activity, those who walked in Haidekopf were more than four times more likely to have met the case definition than those who did not report walking there (AR 34% vs 8%, RR: 4.5, 95% CI: 1.7–12.2). A stepwise logistic regression model indicated that neither contact with sheep nor walking in Haidekopf were significant risk factors by themselves. However, the odds of Q fever were 3.4 times higher among persons who had reported both contact with sheep and walking in the area near the large sheep farm (adjusted OR 3.4, 95% CI: 1.6–7.0, $p = 0.0012$) compared to those with only one or neither of these exposures.

Q fever cases in other towns

We identified 11 persons living in towns other than Rollshausen who had laboratory evidence of *C. burnetii* infection. Ten of the 11 persons also had clinical evidence of *C. burnetii* infection. Of the 11 persons, four were from Gießen, a town about 30 km south from Rollshausen. These four persons had been spending weekends in a cottage next to the large sheep farm in Rollshausen; all four became febrile during March 1996. Of the 10 persons who met the clinical criterion, nine (90%) had symptom onsets from March through May. Two required hospitalization. All but one of these 11 case-persons had been in the vicinity of Rollshausen before their onset of illness.

Results of environmental investigation

Fifteen of the 20 samples tested from the large sheep flock were positive for antibodies to *C. burnetii* by ELISA. All nine samples from the small sheep flock were negative. Of the 12 samples from the animals other than sheep, one from a cow was positive. Between December 1995 and April 1996, compared to the three previous years, there was less rain in Rollshausen (Ta-

Table 2. Risk factors among people ⩾15 years of age during the outbreak of Q fever in Rollshausen in spring 1996

Exposure	Exposed			Not exposed			RR	95% CI
	No. cases	Total	AR (%)	No. cases	Total	AR (%)		
Contact with farm animals								
Sheep	21	66	32	24	132	18	1.8	1.1–2.9
Cattle	17	52	33	28	145	19	1.7	1.0–2.8
Pig	11	32	34	34	167	20	1.7	1.0–3.0
Goat	2	10	20	43	189	23	0.9	0.3–3.1
Contact with parturient animals	3	8	38	41	190	22	1.7	0.7–4.4
Living a farm with cattle, sheep or goats	7	28	25	38	168	23	1.1	0.6–2.2
Walking areas								
Haidekopf	25	83	30	19	114	17	1.8	1.1–3.1
Friedhof	36	140	26	9	59	15	1.7	0.9–3.3
Seelbach	25	87	29	20	112	18	1.6	1.0–2.7
Kahlenbach	17	64	27	26	132	20	1.4	0.8–2.3
Speierhecke	17	71	24	28	127	22	1.1	0.6–1.8
Walking ways								
Road	33	122	27	12	78	15	1.8	1.0–3.2
Path	38	155	25	7	45	16	1.6	0.8–3.3
Farm path	30	133	23	15	65	23	1.0	0.6–1.7
Track	19	83	23	26	115	23	1.0	0.6–1.7
Direct in forests	19	70	27	26	130	20	1.4	0.8–2.3
Across country in fields	15	59	25	30	141	21	1.2	0.7–2.1
Freetime activities								
Farming	12	32	38	33	168	20	1.9	1.1–3.3
Walking	27	121	22	18	79	23	1.0	0.6–1.7
Jogging	2	14	14	43	185	23	0.6	0.2–2.3
Biking	8	54	15	37	145	26	0.6	0.3–1.2
Gardening	28	114	25	17	85	20	1.2	0.7–2.1
Hunting	1	2	50	44	197	22	2.2	0.6–9.2
Drunk raw milk	1	12	8	43	185	23	0.4	0.05–2.4
Tick bites	5	25	20	37	162	23	0.9	0.4–2.0

ble 3). January 1996 was especially dry. From December 1995 through April 1996, the wind blew from the northwest (from the direction of the sheep farm to Rollshausen) an average of 17 (57%) days per month.

Discussion

Our investigation shows that there was an outbreak of Q fever among at least 45 Rollshausen residents and among at least 11 persons from the neighboring towns. Several lines of evidence suggests that the large sheep farm was the source of this outbreak and that the principal mode of transmission of *C. burnetii* was airborne. First, the lambing period in December and January shortly preceded the outbreak and the first persons with documented IgM antibody had onsets of illness in February, consistent with the average 20-day incubation period for Q fever [1]. Outbreaks of Q fever occur after lambing because *C. burnetii* is reactivated in ewes in pregnancy and due to multiplication of *C. burnetii* in the placental villi, placentae and birth fluid contain large amounts of coxiellae [1–3, 13].

Table 3. Rainfall in millimeters by month in 1992–1996 in Lohra-Rollshausen

Month	Rainfall in millimeters			
	1992–1993	1993–1994	1994–1995	1995–1996
December	40	149	67	48
January	85	81	96	4
February	17	32	69	45
March	7	68	61	26
April	38	51	44	10
May	58	64	54	100
June	29	83	23	33
Total	274	528	414	266

Second, the high attack rate (23%) of Q fever and the nearly uniform distribution of ill residents throughout the town suggest a ubiquitous exposure consistent with airborne transmission. This is plausible as the lambing at the sheep farm occurred outdoors, there was an exceptionally dry period at the beginning of the outbreak, and the prevailing wind direction was from the large sheep farm to the town. During lambing, infected birth products can contaminate the ground. Since *C. burnetii* is highly resistant and little affected by extreme environmental conditions, it can form a highly infectious dust [2, 13]. Unusually dry periods have been proposed to encourage the formation and propagation of infectious dusts and aerosols [2]. Moreover, *C. burnetii* is extremely infectious for humans; a single viable inhaled organism is able to cause infection [8].

Other associated factors include the high percentage of ewes (75%) that tested positive for *C. burnetii* antibody and the fact that the people who had been in contact with sheep and walking in the areas near the large sheep farm were more likely to have met the case definition than those who had not had those exposures. The occurrence of Q fever among the four persons who had spent weekends next to the large sheep farm also supports this hypothesis of the sheep as a source of the outbreak. In addition, the high rate of people hospitalized with pneumonia suggests that the infection was acquired by inhalation. The route of infection has been shown to determine the clinical manifestation (respiratory versus gastrointestinal) of acute Q fever in animal models [16].

Although the participation rate in our study was high, several factors may have influenced our results. Symptomatic persons were probably overrepresented as we actively contacted the persons who possibly had had Q fever since January and those who were symptomatic may have been more willing to take part in the study. These facts would lead to an overrepresentation of symptomatic persons in our sample particularly among those with *C. burnetii* antibody testing. This would tend to artificially lower the percentage of persons who had asymptomatic infection or who had minimal symptoms. Despite this bias, 40% of persons with IgM antibody did not meet the clinical case definition, suggesting that many Rollshausen residents were infected but had minimal or no symptoms. Moreover, IgG antibody testing indicated that 20% of the residents had evidence of past infection and thus may have been immune. Therefore, the AR of Q fever among susceptible residents was probably even higher than 23%. Recall concerning sheep and the large sheep farm could have been biased by local media accounts of the outbreak.

This is the first reported community outbreak of Q fever in Europe which occurred shortly after lambing. Two previously reported community outbreaks in Switzerland and Italy were associated with the transport of infected sheep flocks from and to alpine pasture, but neither outbreak was directly linked to lambing [10, 12]. In neither of the two community outbreaks of Q fever reported from Great Britain was an animal source detected, although one was thought to be related to windborne spread from farmlands near an urban area [7, 11].

The results of this outbreak investigation suggest that Q fever should be considered as a possible cause of unexplained fever in Germany, particularly among persons who have travelled or lived near rural areas in the state of Hessen. Further study of the extent of *C. burnetii* infection in sheep and humans is required to define the optimal strategies for prevention of similar outbreaks in Germany.

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