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An epidemiological study of an outbreak of Q fever in a secondary school

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SUMMARY

Five cases of clinical Q fever were identified amongst students and staff of a Somerset secondary school between 23 October 1987 and 21 December 1987. Five goats which were kept at the school were found to have antibodies to *Coxiella burnetii* phase II.

A cross-sectional study was conducted at the school in July 1988. A single CF test was used to identify evidence of prior infection, and a self-administered questionnaire was used to collect data on exposure variables and illness during 1987.

Four hundred and ninety-nine eligible subjects took part in the study, and serological information was obtained from 461 of these. Eighty-seven subjects (18·9%) had CF titres of 20 or greater. It was estimated that only 1 in every 30 individuals with evidence of past *C. burnetii* infection had been recognized as a clinical case of Q fever.

Antibody positive subjects were more likely to have been off school sick and to report having suffered chest pain than negative subjects.

Contact with school animals, specifically cleaning the school poultry, collecting their eggs and visiting a school goat on the day of kidding, was associated with the presence of antibodies to *C. burnetii*. However a large proportion of the antibody positives (24·2%) had no known contact with the school animals. Spread of organisms, either wind-borne or in straw or manure, may have been responsible for the high prevalence of unexplained infection.

INTRODUCTION

Q fever is a zoonosis caused by the rickettsia *Coxiella burnetii*. Human cases occur sporadically and in outbreaks primarily as a result of direct or indirect contact with infected animals or their products [1, 2]. The infection is widespread amongst animal species including cattle, sheep and goats and is also seen in dogs, cats, birds and ticks. Serological surveys suggest that 2–3% of cattle and 2–6% of sheep in the United Kingdom have antibody to Q fever [3–5].

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Occupational exposure in abattoirs and laboratories handling sheep and goats accounts for many outbreaks [6–11]. Surveys indicate that 8–12% of abattoir workers and veterinarians have serum antibody to *C. burnetii* [12, 13]. Other outbreaks have been associated with skins, straw, manure and dust from animals and vehicles [14–19], and, most recently, parturient cats [20, 21]. Often the source of infection has not been identified [22–24].

The symptoms of acute Q fever include severe headache, retrobulbar pain, myalgia, arthalgia, fever, dry cough, chest pains and general malaise. Many cases are thought to be subclinical [1, 9, 12]. The incubation period is 14–39 days [1]. Aerosol transmission is the most important route of spread although ingestion of infected milk and person-to-person contact have also been implicated [1, 2, 12, 25]. Patients with acute Q fever almost invariably recover but convalescence can take several months [1, 9, 12]. Rarely chronic cases develop endocarditis or granulomatous hepatitis [1, 2, 12, 26].

The current outbreak began when Q fever was diagnosed in two 15-year-old schoolgirls from Street, Somerset, during the last week in November and first week in December 1987. Their only common contact with animals was at the local secondary school. A small flock of chickens and ducks, a hive of bees and 5 goats, 3 does and 2 kids, were maintained by the Rural Science Department for teaching purposes. The three does were lactating, having kidded between April and July 1987. They were considered the most likely source of infection and were examined by a senior veterinary investigation officer from the Ministry of Agriculture. All five had complement fixing (CF) antibody titres of 16 or 32 to *C. burnetii* phase II antigens and in view of the potential risk to the school population the goats were destroyed in mid-December 1987. Attempts to culture *C. burnetii* from milk from these animals proved unsuccessful.

Medical practitioners in the area were advised to consider Q fever in the differential diagnosis of influenza-like illness in pupils and teachers from the School. Three additional clinical cases of Q fever (ie. symptomatic patients with a serial fourfold rise in antibody titre or a single titre of greater than 80) were diagnosed, one of whom had a raised titre on 23 October, and symptoms dating back to early August 1987. Of a further 21 patients with symptoms, 8 had CT titres of 20–40. These results suggested that subclinical infection had occurred but provided no clue to the prevalence of infection within the total population at risk or the proportion of subclinical infections. A cross-sectional study was undertaken to answer these questions and to investigate the source and route of infection.

MATERIALS AND METHODS

Study population

All staff and pupils attending Crispin School in July 1988 were informed of the study and encouraged to participate. Parental consent was obtained for school pupils. Those who consented to take part were given a self-administered questionnaire and after completion, a 5 ml blood sample was taken. The study took place in the school between 4 and 13 July 1988. Pupils who had arrived at the school after 1987 were excluded from the study. All study subjects or their parents were informed of the results by letter. General practitioners were also informed of their

patients' results and were given guide-lines for the management of those with serum antibody to *C. burnetii*. In view of the possibility of the development of chronic Q fever, tetracycline (Doxycycline 100 mg daily for 2 weeks) was advised for these patients. The well recognized effect of tetracycline on developing teeth ceases before the age of 10 years when all teeth have developed although they may not have completely erupted.

Questionnaire

A three-page questionnaire was used to obtain information on demography, illness during 1987 and exposure to possible sources of infection at home, school or overseas. The questionnaires were completed in individual school classes in the presence of two of the authors. Explanation and completion took about 20 min.

Blood samples

Blood samples were held at 4 °C overnight, centrifuged and the serum removed and used in doubling dilutions in a microcomplement fixation assay starting at 1/10. Samples were analysed using phase I and phase II *C. burnetii* antigens of the Nine Mile strain with normal yolk sac as a control.

Analysis

Data entry and analysis were performed on an IBM compatible microcomputer. The Yates corrected Chi squared test was used to detect differences in proportion between antibody-positive and negative subjects [27] and odds ratios and 95% confidence limits were calculated by Cornfield's method [28]. Where an expected value was less than 5, Fisher's exact test [29] was used and the exact confidence limits calculated. Unconditional logistic regression was used to obtain maximum likelihood estimates for odds ratios and their 95% confidence limits adjusted for potential confounders.

RESULTS

Response rates

Five hundred and seven (61%) of a total of 831 students and staff in the school participated in this study. Eight had arrived at the school after the outbreak and were excluded, leaving a total of 499 study subjects.

The study sample was representative of the school population in terms of sex and school year distribution. There were 248 males and 251 females. Forty-six participants (9.2%) were staff members and 453 (90·8%) were first to fourth year students. The fifth year students had left school by July 1988 and could not be included.

Serum antibody to C. burnetii *in the general population of the area*

Records of the samples submitted to the Taunton Public Health Laboratory for routine virology were examined and the date of submission, sex and age of the patients with CF titres > 20 recorded. Fifty-two samples from a total of 2773 (1·9%) examined during 1987 were positive. A starting dilution of 1:20 was used routinely and hence there was no information available on the prevalence of lower titres amongst these samples.

Table 1. *Distribution of CF titres to* C. burnetii

Phase I			Phase II		
Titre	Freq.	Percent	Titre	Freq.	Percent
< 10	455	98·7	< 10	354	76·8
10	4	0·9	10	20	4·3
20	2	0·4	20	59	12·8
			40	14	3·0
Total	461	100·0	80	10	2·2
			160	1	0·2
			320	3	0·7
			Total	461	100·0

Antibody to C. burnetii *in the school population*

Four hundred and sixty-one samples were analysed for antibody to *C. burnetii*. No serum sample was obtained from the remaining 38 subjects who completed a questionnaire, either because a vein was unobtainable (22 subjects), because of refusal to give blood (13 subjects) or because the blood samples were mislabelled (3 subjects).

The distribution of CF titres to *C. burnetii* phase I and phase II antigens is shown in Table 1. Eighty-seven participants (18·9%) had phase II titres of 20 or greater. Only six of these (1.3%) had any detectable antibody to phase I antigen and only two of them (0·4%) had titres of 20.

Twenty subjects (4·3%) had phase II titres of 10. The significance of these titres was uncertain because there was no estimate of their prevalence in the general population of the area. Such low titres could indicate non-specific reactions or infection in the distant past. These and the 38 participants with no serum sample were excluded from the comparison of participants with and without serum antibody, leaving a total of 441. These exclusions did not alter the age, sex or school year distribution of the sample significantly, or the proportion of the subjects who had had contact with the school animals.

Changes in serum antibody titres with time

Serum from 13 subjects had been submitted for testing at the time of the outbreak, 6–8 months before the study. Comparison of these paired samples was used to give an indication of the decay in antibody titre with time. Seven subjects (including four clinical cases) who had previously had phase II titres of 40 or greater were still positive with titres of 20–40.

Two subjects who had previous titres of 20 now had titres of less than 10. These subjects would have been defined as having serum antibody 6 months earlier but were included in the negative group for further analysis. None of the four subjects who were negative in December 1987 had seroconverted.

Association between serum antibody and exposure to possible sources of infection

There were a number of associations between the presence of antibody to *C. burnetii* and contact with school animals (Table 2). The most significant both before and after adjustment for age, sex and school years were with cleaning out

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Table 2. *Serum antibodies to* C. burnetii *and exposure to school animals*

Variable	No. reporting/ total no. (%) Antibody Positive	Negative	Crude odds ratio, Cornfield 95% confidence limits and *P* value	Maximum likelihood estimates, adjusted for age, sex and school year
Studied Rural Science elective 1987	8/87 (9·2)	16/338 (4·7)	OR 2·14 CL 0·81–5·54 *P* 0·11	OR 1·80 CL 0·65–5·03 *P* 0·26
Visited the Rural Science compound	52/84 (61·9)	230/332 (69·3)	OR 0·72 CL 0·43–1·22 *P* 0·25	OR 0·61 CL 0·35–1·07 *P* 0·09
Touched the school goats	43/85 (50·6)	163/331 (49·2)	OR 1·06 CL 0·64–1·75 *P* 0·92	OR 0·91 CL 0·55–1·50 *P* 0·71
Helped look after the school goats	13/86 (15·1)	28/352 (8·0)	OR 2·06 CL 0·96–4·38 *P* 0·07	OR 1·93 CL 0·92–4·04 *P* 0·08
Helped milk the school goats	6/85 (7·1)	12/351 (3·4)	OR 2·15 CL 0·69–6·40 *P* 0·13	OR 2·26 CL 0·78–6·53 *P* 0·13
Helped clean the school goats' pens	11/87 (12·6)	30/352 (8·5)	OR 1·55 CL 0·70–3·40 *P* 0·33	OR 1·67 CL 0·77–3·59 *P* 0·19
Helped look after the school poultry	9/85 (10·6)	21/352 (6·0)	OR 1·87 CL 0·76–4·50 *P* 0·20	OR 2·08 CL 0·88–4·90 *P* 0·10
Helped clean the school poultry's pens	7/87 (8·0)	8/352 (2·3)	OR 3·76 CL 1·12–12·21 *P* 0·02*	OR 5·61 CL 1·83–17·15 *P* 0·002*
Helped collect the school poultry's eggs	9/86 (10·5)	16/351 (4·6)	OR 2·45 CL 0·91–6·13 *P* 0·06	OR 2·41 CL 0·99–5·87 *P* 0·05*
Helped look after school flowerbeds	16/85 (18·8)	54/345 (15·7)	OR 1·25 CL 0·64–2·40 *P* 0·59	OR 1·29 CL 0·65–2·57 *P* 0·47
Visited a goat on the day of kidding	13/81 (16·0)	23/327 (7·0)	OR 2·53 CL 1·14–5·53 *P* 0·02*	OR 2·18 CL 1·00–4·77 *P* 0·05*
Visited a goat on the day after kidding	8/73 (11·0)	22/320 (6·9)	OR 1·67 CL 0·65–4·16 *P* 0·35	OR 1·69 CL 0·69–4·16 *P* 0·25
Visited a goat within a week of kidding	26/78 (33·3)	78/300 (26·0)	OR 1·42 CL 0·80–2·51 *P* 0·25	OR 1·09 CL 0·62–1·93 *P* 0·90

* Significant at the 5% level.

the school poultry (Adj. odds ratio 5·61, $P = 0·002$); collecting their eggs (Adj. odds ratio 2·41, $P = 0·05$); and visiting school goats on the day of kidding (Adj. odds ratio 2·18, $P = 0·05$).

Approximately 50% of subjects exposed to these activities had serum antibody to *C. burnetii*. However, few subjects carried out these activities and in only 5–7% of the school population could the presence of serum antibody be attributed to this exposure.

These three exposure variables were entered into an unconditional logistic regression model to evaluate their independent effects. Sex, age and school years were also included in the model. None of the three retained significance when any one diverse variable was included in the model. This was due to a high degree of collinearity, particularly amongst the poultry variables. Hence it was not possible to separate out the independent effects, if any, of individual variables.

Two exposure variables were of border line significance: looking after school goats (Adj. odds ratio 1·93, $P = 0·08$) and consuming an unpasteurized goat milk-shake on school sports day in July 1987 (Adj. odds ratio 1·98, $P = 0·08$).

A number of other exposures were investigated including pet ownership, type of pet, exposure to parturient dogs or cats, occupational exposure of household members to animals or animal products, contact with newborn lambs, calves, and goat kids, consumption of milk products or contact with animals or animal products either at home or overseas and tick bites. None were associated with the presence of serum antibody to *C. burnetii*. Interestingly, living on a farm was not associated with the presence of serum antibody. In fact those with farm animals at home tended to have no serum antibody to *C. burnetii*, although this difference was not significant (Adj. odds ratio 0·56, $P = 0·26$).

Association between serum antibody and other variables

Illness (Table 3)

The presence of serum antibody to *C. burnetii* was associated with reported absence from school for 2 days or more (Adj. odds ratio 1·89, $P = 0·03$). A total of 226 subjects (45·3%) reported being off school for 2 days or more (Table 3).

One hundred and ninety-three subjects (38·7%) reported seeing a doctor and 17 reported staying overnight in hospital but neither of these were associated with the presence of serum antibody to *C. burnetii*.

Symptoms

Subjects were asked whether they had suffered from a bad headache, an asthma attack, a sore throat, a fever, vomiting, diarrhoea, a runny nose, a cough or chest pain during 1987. Of the 499 subjects 469 (94·0%) reported at least one symptom.

The most common symptom was a running nose (418), followed by sore throat (289), cough (276), and bad headache (242). The least common symptom was an asthma attack (27). None of these was associated with the presence of serum antibody. Nineteen of 74 antibody positive and 56 of 300 negative subjects reported suffering chest pain. There was a marginally significant association between antibody positivity and chest pain (Adj. odds ratio 1·79, $P = 0·07$).

Demographic associations

There was a strong association between the presence of antibody and age (χ^2 on 7 D.F = 23·4, $P = 0·0015$). When the distribution according to school years was examined the association was even stronger (χ^2 on 4 D.F. = 22·7, $P = 0·000\,15$). A model containing school years alone fitted the data better than one containing age. Fitting age to the school year did not improve goodness of fit (likelihood ratio statistic on 1 D.F. = 0·705, $P = 0·40$) suggesting school year rather than age to be the critical factor. The proportion of antibody positives in the first year was low,

Table 3. *Serum antibodies to* C. burnetii *and illness during 1987*

Variable	No. reporting/ total no. (%) Antibody Positive	Negative	Crude odds ratio (OR), Cornfield 95% confidence limits (CL) and *P* value		Maximum likelihood estimates, adjusted for age, sex and school year	
Off school for 2 days or more	45/69 (65·2)	151/299 (50·5)	OR CL *P*	1·84 1·03–2·58 0·04*	OR CL *P*	1·89 1·06–3·35 0·03*
Visited a GP	37/39 (46·8)	134/319 (42·0)	PR CL *P*	1·22 0·79–2·05 0·52	OR CL *P*	1·26 0·75–2·11 0·34
Stayed overnight in hospital	2/85 (2·4)	15/346 (4·3)	OR CL *P*	0·53 0·08–2·50 0·54	OR CL *P*	0·55 0·12–2·54 0·44

* Significant at the 5% level.

Table 4. *Serological status and school year*

Year	CF ⩾ 20 +	−	Total	Odds ratio	95% CL	*P* value
1	6	95	101	1·00		
2	28	65	93	6·82	2·56–21·10	< 0·001**
3	17	90	107	2·99	1·06–9·64	0·040*
4	24	71	95	5·35	1·98–16·73	< 0·001**
Staff	12	33	45	5·76	1·80–19·99	0·001**
Total	87	354	441			

* Significant at the 5% level.
** Significant at the 1% level.
Yates corrected χ^2 on 4 D.F. = 22·65.
P values = 0·000 15.

5·9% (6/101). The proportion amongst other years and staff ranged from 15·9–30·1% and there was no significant difference between these groups (χ^2 on 3 D.F. = 6·1, $P > 0·1$) (Table 4).

The proportion of students with serum antibody also varied between school classes, ranging from 0–90·9%. Although students with serum antibody appeared to be clustered in some classes, the numbers were too small to allow meaningful analysis.

The majority of participants (84·0%) lived either in Street or in the villages spread between Street and Bridgwater. There was no significant association between antibody status and place of residence, sex or social class.

Familial association

The study sample contained 62 pairs of siblings and one set of 3 siblings. Antibody titres of 53 of the pairs were classified as positive or negative. Thirty-six pairs consisted of 2 negative subjects, 15 of 1 positive and 1 negative subject and there were 2 pairs of 2 positive subjects. The set of 3 siblings comprised 1 positive and 2 negative subjects. Hence there was no evidence of clustering of positives within

families; the distribution of antibody positives over the pairs was almost identical to that expected assuming a uniform seroprevalence of 18·9%.

DISCUSSION

The prevalence of CF antibody to *C. burnetii* phase II antigen of 20 or more amongst the study sample was 18·9%. A CF titre of 20 is that normally taken to indicate specific exposure to *C. burnetii* in this laboratory. The proportion of the general population in Somerset with this level of serum antibody is unknown but 52/2773 (1·9%) of the samples submitted to the Taunton Public Health Laboratory in 1987 were positive. This figure excludes the students and staff of Crispin School. The prevalence in the general population is likely to be even lower as most of these samples come from patients with symptoms similar to those of Q fever. This provides good evidence to suggest that the outbreak of Q fever was confined to the school. For this reason we were able to conduct a survey of the prevalence of infection in the entire population at risk and to estimate the proportion of unrecognized infection.

When the 13 subjects with prior serological results were excluded, the prevalence was 16·5%. If we assume that the only clinical cases were those identified, and that the sample was representative of the school population, the total population of 831 contained an estimated 149·6 subjects with serum antibody who had not been detected as clinical cases (95% confidence limits 126·6–174·5). The ratio of clinical cases to those with serum antibody was 1/29·9 (95% confidence limits 1/24·9–1/34·9). Thus only 1 of every 30 individuals infected by *C. burnetii* was recognized as a clinical case of Q fever. This is the first time that such a quantitative estimate of subclinical infection has been made.

The effect of excluding the Fifth Year on the prevalence of serum antibody to *C. burnetii* could not be estimated. Although no clinical cases of Q fever had come from the Fifth Year, six of the students had been previously tested of whom two had serum antibody to *C. burnetii*. If the prevalence of antibody positives in the Fifth Year had indeed been similar to that in other years, the ratio of antibody positives to clinical cases would have been slightly higher.

There were a number of problems in interpretation of the serum antibody levels. The time lag between the cross-sectional study and the outbreak meant that evidence of past, rather than current, infection was obtained. Thus a positive result meant only that infection had occurred some time in the past. Although in the majority of cases antibodies to *C. burnetii* appear to persist for over a year, they can decline quite rapidly [30, 31]. In the present study, two subjects who had been antibody positive at the time of the outbreak were now negative. Thus an unknown number of individuals who had been infected may have fallen into the antibody negative group.

The identification of 20 subjects with CF titres of 10 also raised problems because the significance of such titres was uncertain. These subjects were excluded from the analysis. It is likely that both of these effects would result in a dilution of any real associations.

The finding that antibody positives were more likely to have been off school sick for 2 days or more, but were not more likely to have visited a general practitioner

suggests that *C. burnetii* infection may have been associated with mild non-specific disease. In the school population an estimated 5·18% of self-reported absences from school for 2 days or more during 1987 could be attributed to the presence of serum antibody.

Self-reporting of symptoms is notoriously inaccurate. In the present study, recall bias was minimized by collecting data on illness before most subjects were aware of their serological status. Subjects with serum antibody were marginally more likely to report chest pain, but no other symptoms were associated with serum antibody. Symptoms frequently seen in Q fever, such as fever, headache and coughing, were commonly reported by both positive and negative subjects and the ubiquity of these symptoms may have obscured any real association with positivity.

In this as in many other Q fever episodes, a single source of infection could not be elucidated. The low prevalence of serum antibody amongst the First-Year students, who arrived in September 1987, suggested that they had less exposure to the infectious organisms than students in other years. The school goats were still present at that time.

Subjects with serum antibody were clustered in some school classes but the numbers in these classes were too small for meaningful analysis.

The presence of serum antibody was associated with specific types of contact with the school animals, notably cleaning the school poultry, collecting their eggs and visiting the school goat on the day of kidding. These associations were consistent with previously reported sources of *C. burnetii* infection, which have included the products of conception and contaminated straw and dust [6–11, 14–21]. Although the school goat kidded in April–July 1987, well before the identification of the school outbreak, symptoms predated diagnosis of Q fever in all clinical cases. In at least one case, symptoms could be traced back to early August. Three of the school poultry examined at the time of the study were antibody negative but this does not exclude poultry as the source of infection.

The three significant exposure variables were highly correlated and their independent effects could not be separated, suggesting that perhaps only one was important or that all were merely imperfect measures of some other exposure. Only small numbers of subjects participated in these activities. They accounted for only 5–7% of the school population with serum antibody.

Exposure to school animals during the entire year 1987 were included, though it is probable that infection occurred over a few months at the most. This would also tend to dilute any real associations.

A large proportion of the subjects with serum antibody to *C. burnetii* (24·2%) had no known contact with school animals. This could be explained by wind-borne spread, as most of the population passed the Rural Science compound on their way to the playing areas. Goat manure was also spread on the flower beds, although looking after the flower beds was not associated with serum antibody. Straw was used as litter for both goats and poultry and might have been a source of infection. There might also be another unidentified source, either within or outside the school.

Another intriguing possibility is that person-to-person spread took place. This would explain the clustering of antibody positives within school classes. However,

there was no evidence of clustering within families so person-to-person spread was unlikely.

The low prevalence of serum antibody amongst students admitted to the school in September 1987 suggests that whatever the source of infection, it is no longer present in the school, and as a result of this outbreak new guide-lines for the keeping of animals at schools in Somerset have been drawn up.

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