The risk of acquiring Q fever on farms: a seroepidemiological study

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Abstract

Objectives—To determine the occupational risk of Q fever.

Design—Cohort study.

Setting—Community: five English local authority districts.

Subjects and methods—Prevalence and incidence of immunoglobulin G (IgG) specific antibody to *Coxiella burnetii* phase II antigen was measured in a representative (study) cohort of farm workers in the United Kingdom, and detailed exposure data were collected. Also seroprevalence of Q fever in a (control) cohort of police and emergency service personnel was measured.

Results—Prevalence was significantly ($P < 0.01$) higher in the study cohort (105/385 v 43/395). During the first 12 month period after enrolment no seroconversions were found (upper 95% confidence limit: 1318/100 000/year). During the second 12 month period after enrolment two seroconversions were found, equalling an incidence of 813/100 000/year (95% confidence interval (95% CI) 98–2937/100 000/year). No association was found between seroprevalence and age. In the study cohort, extent of total contact with farm animals seemed more important than exposure to any specific animal: full time employees were more than four times more likely to be antibody positive than part time employees ($P < 0.05$). Exposure to cattle, but not sheep, goats, cats, raw milk, and hay (all reported sources of Q fever) was associated with being positive to *Coxiella burnetii* IgG by univariate analysis but this association was not independent of total farm animal contact.

Conclusions—The risk of Q fever on live-stock farms is related to contact with the farm environment rather than any specific animal exposure. The absence of an increasing prevalence with age suggests that exposure may occur as clusters in space and time (outbreaks).

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illness or pneumonia. Endocarditis may complicate one in 10 of those clinically affected.¹ The most common animal reservoirs are thought to be sheep, goats, and cattle, but infection in these hosts is almost always sub-clinical and consequently of little economic concern. It might be expected that those at greatest risk of infection would be people in close and frequent contact with domestic ruminants or their products. Recent outbreaks have been attributed to such diverse exposures as parturient cats,^{2–5} straw,⁶ and wild rabbits.⁷ In other outbreaks, and in many sporadic cases, a history of animal exposure is not always elicited.⁸

To study the importance of Q fever as an occupational disease, seroprevalence and seroincidence of Q fever antibodies was measured in a well characterised representative cohort of farm workers and their family contacts in the United Kingdom. Associations between Q fever and occupational exposures to animals were examined in detail. Seroprevalence of Q fever antibodies in the study group was also compared with that of a control cohort of police and emergency service personnel.

Subjects and methods

SUBJECTS

A sample of 404 people was recruited from 255 farms randomly selected from the Ministry of Agriculture, Fisheries, and Food (MAFF) lists of agricultural holdings for the English local government districts of Hereford City, South Hereford, Leominster, Preston, and Lancaster. Each participant provided a 10 ml venous blood sample at enrolment and at 12 and 24 months after enrolment. Participants kept an illness diary in the 12 months between samples and completed three questionnaires. The occupation and farm type of the participants were coded as in the MAFF June census. Sampling, recruitment, and measurement of exposure are described elsewhere.⁹

Data on cigarette smoking and alcohol consumption were obtained from participants 24 months after enrolment ($n = 341$).

CONTROL COHORT

Stored serum samples were made available from two previous cross sectional surveys of hepatitis B in emergency ambulance service personnel ($n = 163$) and police officers ($n = 232$) employed in Lancashire.^{10 11}

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Q fever is a zoonosis of worldwide distribution. In humans infection may be subclinical or may cause a self limiting influenza like

SEROLOGY

Serum was separated from samples and stored at -20°C. Concentrations of serum IgG specific antibody to *Coxiella burnetii* phase II antigen were measured at Bristol Public Health Laboratory with an indirect immunofluorescence antibody test. Serum samples with a titre of 32 or more were taken as positive. Samples taken at 12 months after enrolment were screened. All samples found to be IgG positive were retested in parallel with samples taken from the same subject at enrolment. Samples taken at 24 months after enrolment were screened for IgG to provide a repeat measure of incidence. Samples from the cohort of police and emergency service personnel were screened for IgG.

ANALYSIS

The age, sex, occupation, and farm type of those study subjects who were seropositive were described. Seropositive people within the control cohort were similarly characterised. Seroprevalence of Q fever in the study and control cohorts were compared with the Mantel-Haenszel version of the χ^2 test,¹² stratified for age.

Associations between Q fever seroprevalence and specific categorical (yes or no) exposures (table 1) were examined in the study cohort with the Mantel-Haenszel version of the χ^2 test. Seropositive and seronegative subjects were compared (table 1) for the extent of animal contact, exposure to silage,

straw, slurry, feed, and hay (each ranked from 0-4), numbers of animals contacted, numbers of cigarettes a day and number of alcohol units a week, by the Mann-Whitney two sample test.

All variables found by univariate analysis to give an increased risk of seropositive Q fever, together with age, sex, and number of cigarettes a day, were examined by logistic regression.¹³ These were: regular hired farm worker (as opposed to another occupational group), working or living on a mainly dairy farm (as opposed to any other farm type—including specialist dairy), being full time employed (as opposed to part time employed), dairy cattle contact, beef cattle contact, milking contact, attending calving, and handling conception products of cattle.

Results

A second blood sample was provided by 385 people (95%). Of these, 105 (27.3%) were seropositive for *Coxiella burnetii* IgG antibodies 12 months after enrolment. When the enrolment serum samples of the 105 seropositive people were examined none had become seropositive during the first year. The 246 people who were IgG negative at 12 months after enrolment provided a third blood sample. Two of these were positive.

Seroprevalence rates of IgG in men (80/285; 28.1%) and women (25/100; 25.0%) were not significantly different. Although IgG seroprevalence was highest in the 60-69 age group (13/29), there was no trend with age (table 2) and there was no significant difference between the ages of positive subjects (mean (SD) age 44.6 (12.9), median 45) and negative subjects (mean age 44.5 (12.0), median 45).

Working or living on a "mainly dairy" farm was associated with seropositivity (attack rate (AR) 48/133; relative risk (RR) 1.59; 95% confidence interval (95% CI) 1.15-2.19; $P < 0.01$). No other farm type was a significant risk (including working or living on a "specialist" dairy farm). Being a regular hired worker (as opposed to any other category of employment) was significantly associated with being seropositive (AR 8/16; RR 1.90; 95% CI 1.13-3.20; $P < 0.05$). Full time employment (as opposed to part time employment) was significantly associated with the presence of antibodies (AR 100/334; RR 3.05; 95% CI 1.31-7.13; $P < 0.01$).

Seroprevalence of IgG antibodies to *Coxiella burnetii* was significantly higher in the study group (105/385) than in the comparison cohort (43/395) (RR = 2.51; 95% CI 1.81-3.47; $P < 0.01$). This effect was independent of age and sex.

All subjects in the study cohort reported at least some animal contact, and 98% reported contact with either sheep, goats, or cattle. Attending calving (AR 80/255; RR 1.63; 1.10-2.42; $P < 0.05$) and handling the products of conception of cattle (AR 72/228; RR 1.45; $P < 0.05$) increased the risk of having Q fever IgG antibody. Seropositive subjects

Table 1 Exposures examined

Categorical variable (yes or no)	Working or living on a specialist dairy farm, working or living on a mainly dairy farm, occupation regular hired worker, occupation full time employed, any animal contact, any ruminant contact (sheep, goats, or cattle), contact with sheep, goats, beef cattle, dairy cattle, pigs, dogs, cats, horses, rats, other wild rodents, deer, badgers and foxes, attending calving, handling the products of conception of cattle, having a pigeon loft, reporting a rat problem, drinking untreated milk, and drinking untreated water.
Ordinal variable	Contact with sheep, goats, cattle, pigs, dogs, cats, horses (ranked 0-5)*; milking exposure (ranked 0-5)**; contact with silage, straw, slurry, feed, and hay (ranked 0-4).***
Continuous variable	Numbers of sheep, goats, cattle, pigs, dogs, cats, horses on farm of residence or occupation, numbers of cigarettes a day and number of alcohol units a week.

*Ranked as previously described.
**Ranked by cows milked a week (0 = 0, 1 = <100, 2 = 100-200, 3 = 200-400, 4 = 400-800, 5 > 800).
***Ranked by frequency of contact (0 = never, 1 = occasionally, 2 = monthly, 3 = weekly, 4 = most of every day).

Table 2 Prevalence of IgG antibody to Q fever in three occupational groups

Age	Farm		Ambulance		Police	
	n	Positive n(%)	n	Positive n(%)	n	Positive n(%)
10-19	5	2 (40)	—	—	—	—
20-29	43	13 (30)	18	1 (6)	53	2 (4)
30-39	87	25 (29)	65	9 (14)	83	6 (7)
40-49	111	27 (24)	58	12 (21)	73	11 (15)
50-59	105	24 (23)	22	0 (0)	21	2 (10)
60-69	29	13 (45)	—	—	—	—
70+	5	1 (20)	—	—	—	—
Not known	—	—	—	—	2	0 (0)
Total	385	105 (27)	163	22 (13)	232	21 (9)

Table 3 Exposures associated with presence of IgG antibody to Q fever by univariate (n = 385) and multivariate (n = 341) analysis by logistic regression

Exposure	Univariate analysis OR (95% CI)	Multivariate analysis	
		Adjusted for age, sex, and cigarettes/day OR (95%CI)	Adjusted for age, sex, cigarettes/ day, and all other variables in table OR (95%CI)
Full time employed	3.9 (1.5–10.2) *	5.5 (1.8–16.5) *	4.3 (1.4–13.2) *
Working or living on a mainly dairy farm	1.9 (1.2–3.1) *	2.0 (1.2–3.2) *	1.9 (0.8–4.3)
Occupation regular hired worker	2.8 (1.0–7.7) *	3.5 (1.1–10.5) *	3.1 (1.0–9.6)
Dairy cattle contact	1.1 (1.0–1.2) *	1.1 (1.0–1.2) *	1.0 (0.8–1.2)
Beef cattle contact	1.2 (1.0–1.3) *	1.1 (1.0–1.3) *	1.1 (1.0–1.3)
Milking exposure	1.1 (1.0–1.3) *	1.1 (1.0–1.3) *	1.0 (0.7–1.2)
Attending calving	1.9 (1.2–3.2) *	1.8 (1.0–3.0) *	1.3 (0.4–3.7)
Handling cattle conception products	1.7 (1.0–2.7) *	1.6 (0.9–2.6)	0.9 (0.3–2.3)

*P < 0.05.

had significantly more exposure to milking (more frequent milking of more cattle) than negative subjects ($P < 0.05$), significantly more exposure to beef cattle ($P < 0.05$) and significantly more exposure to dairy cattle ($P < 0.05$). No other animal exposures gave a significantly increased risk of being seropositive by univariate analysis, nor did drinking raw goats' or cows' milk, drinking untreated water, smoking, drinking alcohol, handling rats, reporting a rat problem, having a pigeon loft, or being present at lambing or farrowing. Contact with goats was associated with a lower prevalence of *Coxiella burnetii* (AR 1/19; RR 0.19; 95% CI 0.03–1.26; $P < 0.05$). Seropositive people reported significantly less exposure to goats ($P < 0.05$) and exposure to significantly fewer goats ($P < 0.05$).

After stratifying for each of those exposures significant at the $P = 0.05$ level by univariate analysis, and by age, sex, and number of cigarettes a day, only handling products of conception from cattle was no longer significant at the $P = 0.05$ level (table 3).

With backward elimination only "employed full time" remained a risk factor still significant at the $P = 0.05$ level (odds ratio (OR) 4.27; 95% CI 1.38–13.20; $P < 0.05$).

The two subjects who became seropositive during the second year were women, one spent most of her time indoors with animal contact, the other indoors without animal contact. Neither reported clinical illness in the year between the second and third samples. One reported exposure to sheep (exposure score 5), cattle (score 5), dogs (score 2), cats (score 3), ducks and geese (score 2), and reported drinking untreated cows' milk, and handling rats. The other reported exposure to sheep (score 3), cattle (score 2), dogs (score 5), cats (score 2), and horses (score 5). One reported a pigeon loft on the farm, the other reported no pigeon loft but doves roosting in a barn on the farm. Neither had been overseas, or been bitten by a tick in the previous year.

Discussion

Risk of having antibodies to *Coxiella burnetii* increases with exposure to a farm environment. The prevalence of IgG was significantly

higher in the study cohort than in ambulance and police workers. Further, full time farmers were at least three times more likely to have acquired antibodies than part time farmers, and prevalence was highest in regular hired workers—those having the closest and most frequent animal contact. This result is similar to a study from the Basque country of Spain that found that seroprevalence was significantly higher among residents in the least populated areas, and among those working in agriculture or animal husbandry.¹⁴

These findings are consistent with what is known of the biology of Q fever. *Coxiella burnetii* differs from other rickettsiae crucially in its resistance to physical conditions—such as extremes of temperature and desiccation. As a consequence, infection in an animal reservoir may result in wide dissemination of the organism in the environment. Transmission of Q fever to humans is thought to occur primarily through inhalation of contaminated aerosols. This wide air borne dissemination hampers epidemiological study, particularly in outbreaks, by confounding statistical associations with any specific exposures.¹⁵

It proved impossible to differentiate the effect of exposure to any animals from living or working on a farm, because all subjects reported animal exposure of some kind. No investigations were made of the prevalence of Q fever in the animals on the farms.

By univariate analysis cattle exposures did increase risk: being present at calving, contact with beef and dairy cattle, and milking were significant risks. Whereas the magnitude of the relative risks were low (< 2), the fact that several specific cattle exposures were significantly associated with the likelihood of being seropositive makes biological sense. The highest numbers of organisms have been reported as being present in the mammary glands (= milking) and placentas (= attending calving) of domestic ruminants.

Exposure to raw milk, ticks, cats, lambing, hay, and straw were not associated with increased risk. These have all been reported as sources of Q fever.⁸ Further, neither did contact with sheep and goats, also thought to be important sources of infection. Indeed, exposure to goats was negatively associated with Q fever. This finding is of interest as recent outbreaks have been attributed to exposure to goats.^{16 17} It may reflect that goat owners in this cohort had less lifetime exposure to animals overall. It is also possible that the small numbers of goats in contact with this cohort were simply free of *Coxiella burnetii*.

It should be noted that observed associations are between current exposures and past infection. The use of current exposure as a proxy for lifetime exposure is broadly reasonable given the relative stability of farming communities in the United Kingdom. The study has not shown any effects attributable to specific animal exposures. Although unlikely, changes in the type of animals kept or the contact with them, after illness remains a theoretical explanation.

No subjects became seropositive in the first year suggesting that incidence of Q fever among farmworkers in the two geographical areas that year was less than 1318/100 000 (upper limit of the 95% CI assuming a poisson distribution). Two subjects became seropositive during the second year giving an incidence of 813/100 000 a year (upper limit of the 95% CI = 2937/100 000 assuming a poisson distribution). The source of infection of the two subjects who seroconverted is not known although both were exposed to several animals including cattle.

Assuming age as a proxy for duration of exposure, and dividing prevalence by the mean age of the cohort, annual incidence over the lifetime of study subjects may be estimated as 614/100 000 a year. Given that this calculated incidence falls within the 95% CIs of the observed incidences, it is necessary to consider why there is a lack of association between age and seroprevalence in the study cohort. It should be noted that farm dwellers under 16 years were not recruited to this study. It would seem, therefore, that incidence in adults with exposure to animals on farms is not constant over time, but rather transmission occurs in outbreaks (clusters in space and time affecting a range of ages). Only by collecting longitudinal seroincidence data over several years can this question be answered.

Exposure to *Coxiella burnetii* is common in farm workers and their families in the United Kingdom. Disease, however, seems to be mild or subclinical. It is possible that the severity of Q fever has been overestimated from cases identified by clinicians or ascertained by public health agencies (no clinical endocarditis was found in this cohort), and that the clinical spectrum may be wider than currently thought.¹⁸ More should be learned about the frequency and severity of any long term

sequelae of *Coxiella* infection. Awareness of this common and, of course, treatable disease should be increased among farm workers.

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