An outbreak of Q fever associated with parturient cat exposure at an animal refuge and veterinary clinic in southeast Queensland

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Abstract

Objective: To determine the source of a Q fever outbreak in humans at an animal refuge and veterinary clinic in southeast Queensland from October to December 2016.

Methods: Case interviews and a retrospective cohort study of animal refuge and veterinary clinic staff using a self-administered questionnaire related to clinical history of Q fever, Q fever vaccination status and workplace activities during the exposure period.

Results: Seven cases (six confirmed, one probable) were identified. Forty-three questionnaires were completed (92% response rate). Workplace activities associated with the greatest risk of illness were the disposal of deceased cats or dogs (RR, 14.0; 95%CI, 1.9–104.1) and participating in euthanasia of cats or dogs (RR, 4.6; 95%CI, 1.3–16.9). Five feline birthing events occurred at the animal refuge from 25 September to 19 October 2016, each with subsequent euthanasia of the queen cat and litter. All cases had likely exposure to a specific queen cat and her litter that were euthanised the same day as the birthing event.

Conclusions: A parturient cat was the most likely source of the outbreak.

Implications for public health: Occupational groups and others with regular exposure to feline or canine parturient products should receive Q fever vaccine.

Key words: Q fever, outbreak investigation, zoonoses, occupational health, vaccine-preventable disease

Q (query) fever is caused by the intracellular bacterium *Coxiella burnetii* and was first described among Queensland abattoir workers in 1937.[1] Transmission occurs through inhalation of *C. burnetii*-contaminated aerosols, usually generated from parturient products or the slaughtering of infected animals.[2] As *C. burnetii* can survive in the environment for prolonged periods, infection can occur in those without direct animal contact.[2] The most commonly identified reservoirs are cattle, sheep and goats.[2,3] Human outbreaks and cases are therefore generally reported in abattoir workers or those with livestock exposure,[1,2,4,5] although many cases have no clear risk factors for transmission identified.[5-7] In Australia, Q fever vaccine (Q-Vax, CSL Limited) is recommended for abattoir workers and other high-risk groups.[8]

Serological evidence of *C. burnetii* infection has also been found in cats, dogs, kangaroos, flying foxes, bandicoots and ticks.[2,4,9] Human outbreaks have been associated with exposure to both infected parturient cats[10-15] and dogs.[16] Australian estimates of *C. burnetii* seroprevalence range from 0–7.8% in cats[9,17] and 1.9–21.8% in dogs.[9,18,19] Despite moderate *C. burnetii* seropositivity in Australian feline and canine populations, reports of local human Q fever cases attributed to cat or dog exposures are rare. The only documented Australian outbreak reported nine cases after a caesarean section was performed on an infected cat at a small animal veterinary clinic near Sydney in 2011.[14] A combination of the high proportion of asymptomatic Q fever infections[2] and low index of clinical suspicion in patients without a history of livestock exposure could lead to cat- and dog-related human Q fever being an unrecognised phenomenon in Australia.

On 17 November 2016, the Metro South Public Health Unit (MSPHU) in Brisbane received laboratory notification of Q fever in an animal refuge worker. Routine follow-up by MSPHU staff revealed that the case had been hospitalised and other animal refuge employees, as well as two staff members at an adjacent veterinary clinic, were experiencing non-specific febrile illnesses. An outbreak investigation was initiated after laboratory-confirmed infection in a second animal refuge. Our investigation focused on the most likely sources of infection – livestock, cats and dogs.

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Methods

Outbreak setting

The animal refuge had a livestock area that routinely kept sheep, goats, geese, ducks and kangaroos. Dogs and cats were kept in separate impounds that were not accessible to the public. The veterinary clinic was adjacent (but not connected) to the animal refuge, and was not near the livestock area. Veterinary clinic staff regularly attended the animal refuge to perform euthanasia of cats and dogs.

Case definitions and exposure period

Confirmed and probable case definitions were developed (see Box 1). The incubation period for *C. burnetii* (four days[13] to six weeks) was used to define a likely common exposure period for cases.[2]

Case-finding

Animal refuge and veterinary clinic staff who were unwell prior to or during the investigation were encouraged to contact MSPHU and request their usual medical practitioner perform testing for Q fever. All cases of Q fever notified to MSPHU during the outbreak investigation (in people who were not employees of the animal refuge or veterinary clinic) were asked if they had visited an animal refuge in southeast Queensland during their exposure period. Neighbouring public health units were alerted to the outbreak and requested to also determine if new Q fever cases had visited an animal refuge.

Case interviews

All confirmed and probable cases were interviewed using the standard Queensland Health Q fever Case Report Form[20] and dates of work were ascertained for the common exposure period.

Box 1: Case definitions used during a Q fever outbreak at an animal refuge and veterinary clinic in southeast Queensland, 2016.

Confirmed case

From 15 September to 31 December 2016, any animal refuge or veterinary clinic staff with either:

1. Detection of C. burnetii through nucleic acid testing

OR

2. Presence of IgM antibodies to C. burnetii AND a clinically compatible illness.

Probable case

From 15 September to 31 December 2016, any animal refuge or veterinary clinic staff with:

1. A clinically compatible illness

AND

2. No previous clinical history of Q fever

AND

3. No previous record of receiving Q fever vaccine.

Animal records

Records of livestock present at the animal refuge from mid-September until the onset date of the earliest case were reviewed. Euthanasia records for cats, kittens and dogs at the animal refuge for the same time period were also examined to explore the potential likelihood of transmission events. Euthanasia records included dates of birth for kittens born at the animal refuge and the names of the veterinary staff who performed the euthanasia.

Site visit

MSPHU staff alerted Workplace Health and Safety Queensland (WHSQ) of the outbreak. WHSQ subsequently performed a site visit of the animal refuge in late November 2016.

Employees of the animal refuge and veterinary clinic were offered Q fever pre-vaccination screening (intradermal hypersensitivity test and serum complement-fixation antibody test). Q fever vaccine was offered to those with negative results to both screening tests.

Self-administered questionnaire

We conducted a retrospective cohort study among animal refuge and veterinary clinic staff to determine workplace activities associated with Q fever infection. A paper-based, self-administered questionnaire with questions related to clinical history of Q fever, Q fever vaccination status and workplace activities from 15 September to 31 October 2016 was developed. The questionnaire was delivered to animal refuge and veterinary clinic management for distribution among staff members (including Q fever cases) and collected one week later.

Data analysis

Individuals who reported receiving Q fever vaccine more than six weeks prior to the onset of the first case were deemed to be at low risk of infection[21] and were excluded from analysis. Risk ratios were calculated, comparing cases and non-cases, for visiting the livestock area, cat impound and dog impound, and for specific workplace activities within these areas. Individuals who reported not visiting the livestock area, cat impound or dog impound were excluded from further analysis of workplace activities specific to that area. Fisher's exact *p*-values were calculated for corresponding risk ratios, with $p<0.05$ considered significant. For exposures with a risk ratio of infinity, exact logistic regression was used to calculate an odds ratio and the lower bound of the 95% confidence interval.

Individuals who underwent Q fever pre-vaccination screening after the investigation commenced, and reported receiving the vaccine negative screening results, were classified as susceptible non-cases. To control for the potential misclassification of asymptomatic cases or inclusion of individuals with pre-existing immunity, a sensitivity analysis was performed comparing exposures of cases to susceptible non-cases. All analyses were performed using Stata 14 (Stata Corp, USA).

Ethics approval

This investigation was carried out under the Queensland *Public Health Act 2005* in response to an acute threat to public health to determine the likely source of disease transmission and potential ongoing risk to staff and the public. Ethics approval was therefore not obtained.

Results

Cases

Seven cases (six confirmed, one probable) were identified, with illness onset dates from 21 October to 20 November 2016 (Figure 1). Two confirmed cases had *C. burnetii* detected through nucleic acid testing. The probable case had a non-specific febrile illness with elevated inflammatory markers, elevated liver enzymes, no previous clinical history of Q fever and no record of receiving Q fever vaccine. Confirmatory testing was unable to be performed for the probable case. Two (29%) cases were hospitalised as a result of their illness (Case 1, for five days; Case 4, for two days). The common exposure period was from 9 to 17 October (Figure 2). No visits to an animal refuge were reported among notified cases of Q fever in southeast Queensland (who were not animal refuge or veterinary clinic staff) during the investigation.

Case interviews

Five cases (83%) were animal refuge workers with varying roles including management, cleaning of animal areas and disposal of deceased animals after euthanasia. Case 1

handled cats and kittens during euthanasia and also attended to laundry at the veterinary clinic. Multiple staff reported that personal protective equipment (PPE) was not routinely used in the handling of animals or newborn kittens during euthanasia.

Animal records

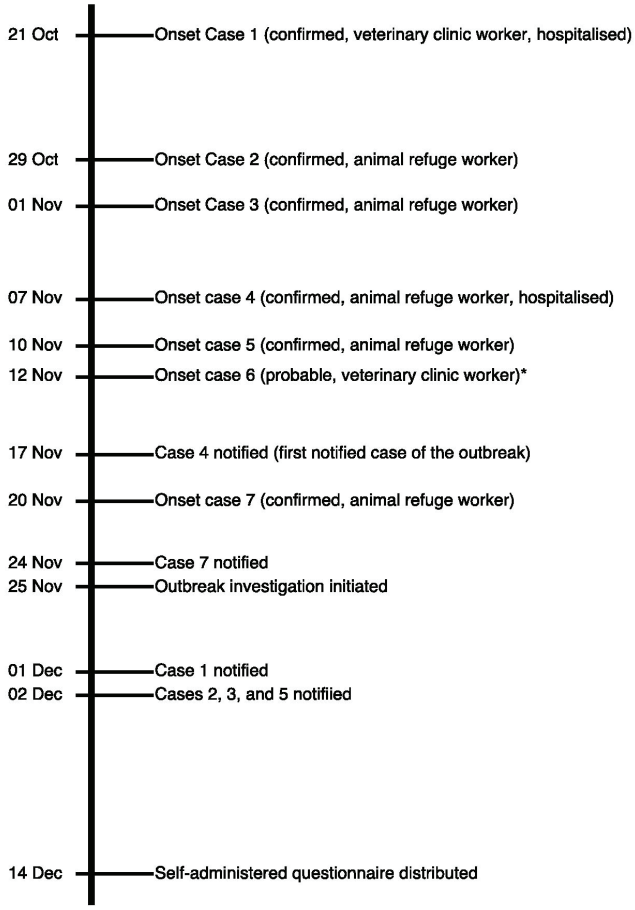
Veterinary clinic staff attended the livestock area in mid-September to review an unwell three-month-old goat. The goat was kept at the animal refuge for less than one week before being transferred for adoption and was unavailable for Q fever testing. No livestock births occurred during the common exposure period and livestock slaughtering did not occur at the animal refuge.

From 25 September to 19 October, there were records of five feline birthing events at the cat impound where the queen cats and their litters were eventually euthanised by veterinary clinic staff. A birthing event on 7 October – when all cases were present at work – involved a cat that had been caught in a trap by the local council on 5 October. This cat delivered her litter prematurely and they were all subsequently handled and euthanised the same day. As a common exposure, this event equates to maximum incubation periods of 14 and 44 days for Cases 1 and 7, respectively. The four other occasions where a queen cat and her litter were euthanised occurred on days when either all cases were not present at work, euthanasia was not performed on the same day as the birthing event, euthanasia was performed by a susceptible non-case, or the corresponding incubation periods fell outside the known range. The origin of these four queen cats was not ascertained during the investigation. There were no reports of euthanised puppies in the records reviewed. Animal cadavers were collected and disposed of on a weekly basis and were therefore unavailable for testing.

Self-administered questionnaire

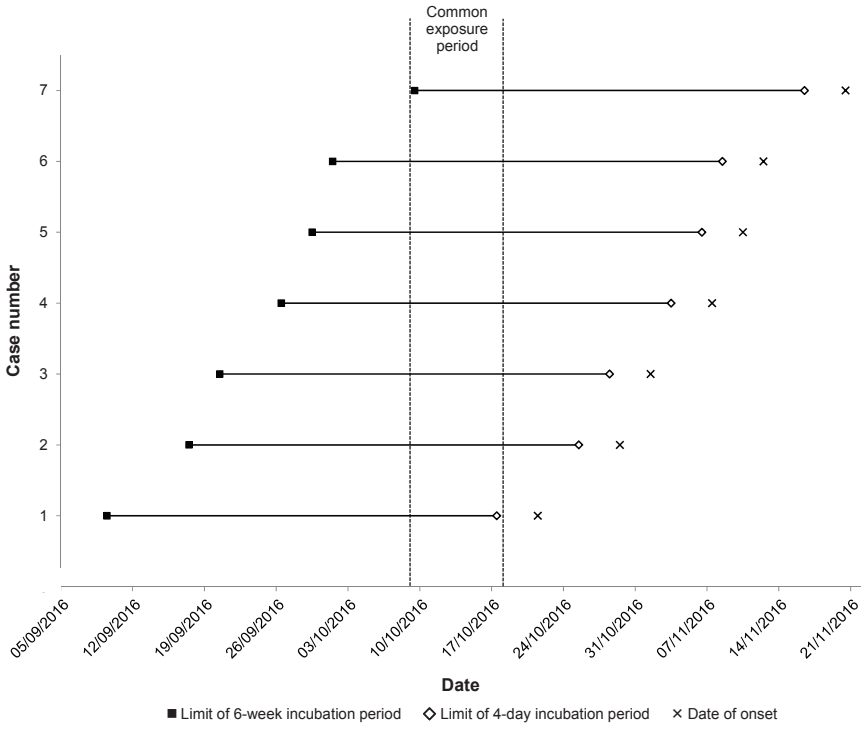
Forty-three (92% response rate) questionnaires were completed by workers at the animal refuge (38) and veterinary clinic (5). Three animal refuge workers reported receiving Q fever vaccine more than six weeks prior to the onset date of Case 1 and were excluded from the analysis. All cases reported attending each of the livestock area, cat impound and dog impound between 15 September and 31 October.

Figure 1: Timeline of Q fever outbreak at an animal refuge and veterinary clinic in southeast Queensland, 2016.



*Note: * The probable case (case 6) was not notified and came to attention through follow-up of other notified cases.*

Figure 2: Exposure periods for cases of Q fever (confirmed and probable) during an outbreak at an animal refuge and veterinary clinic in southeast Queensland, 2016.



Activities associated with the greatest risk of illness were the disposal of deceased dogs or puppies, the disposal of deceased cats or kittens, providing or assisting with euthanasia of dogs and providing or assisting with euthanasia of cats or kittens (Table 1). After aggregating dog- and cat-related activities, disposal of deceased animals (RR, 14.0; 95%CI, 1.9–104.1, p=0.001) and providing or assisting with the euthanasia of animals (RR, 4.6; 95%CI, 1.3–16.9, p=0.03) remained the activities associated with highest risk of illness.

Twenty individuals reported receiving Q fever vaccine after commencement of the investigation. The sensitivity analysis, including only susceptible non-cases and all cases, demonstrated a similar pattern of risk ratios reported in Table 1. However, the exposures with the highest associated risk, disposal of deceased dogs or puppies (RR, 4.2; 95%CI, 1.0–17.2, p=0.06) and disposal of deceased cats or kittens (RR, 3.6; 95%CI, 0.9–14.6, p=0.07), were no longer statistically significant.

Conclusions

We found descriptive and epidemiological evidence that this outbreak of Q fever was likely caused by exposure to parturient products of an infected cat. The most plausible source was the queen cat that delivered her litter prematurely on 7 October, all of which were subsequently euthanised the same day. *C. burnetii* has been detected in cats having an abortion or delivering stillbirths, and associated with prematurity and abortion in other animals.[22] If this was a point-source outbreak, the range of incubation periods was 14–44 days. The upper limit of this range is similar to the previously reported extreme,[23] although environmental contamination with delayed transmission is also possible. Case 1, with the earliest onset of illness, was likely to have had the highest exposure dose to infectious material through assisting with euthanasia of cats and attending to laundry at the veterinary clinic – consistent with the dose-dependent incubation period of acute Q fever infection[1,24] and known transmission routes.[11]

The origin of the implicated queen cat (from a council trap) is of potential interest, as feline subpopulations are likely to differ in their potential for acquiring *C. burnetii* infection. Of two previous Australian *C. burnetii* seroprevalence studies, one found the highest seropositivity among cattery-confined cats, with zero seropositivity in feral and shelter cats,[17] while the other examined urine samples from domesticated cats at a veterinary surgery.[9] The seroprevalence of *C. burnetii* among shelter and feral cats in Australia is therefore unknown, and requires further investigation to determine the risk of human Q fever infection from this source.

While six of the seven cases reported having direct contact with livestock, the absence of livestock birthing events, slaughtering and corresponding risk ratios for livestock-related activities makes this an unlikely source of disease transmission. Disposal of deceased dogs or puppies and assisting with the euthanasia of dogs were associated with an increased risk of illness. However, only one case reported exposure to dogs giving birth during the exposure period, making this an unlikely mode of infection. For most cases, cat- and dog-related activities were correlated, providing an explanation for the significant association with some dog-related activities in the absence of a high-risk exposure event for Q fever in the dog impound. The lack of other plausible sources of transmission supports our conclusion that this outbreak was due to an infected parturient cat.

Outbreaks of Q fever associated with parturient cats have been reported in the United States,[12] Canada,[10,11,15] and Australia.[14] Our outbreak was detected following the hospitalisation, Q fever testing and subsequent laboratory notification of two cases. This outbreak likely would have gone undetected had these two cases developed a milder clinical illness not requiring hospitalisation. A history of exposure to parturient domestic animals should serve as

Table 1: Attack rates and risk ratios for workplace-related exposures of Q fever cases (confirmed and probable) and non-cases during an outbreak at an animal refuge and veterinary clinic in southeast Queensland, 2016.[a]

	Exposed			Unexposed					
	Total	Cases	Attack rate (%)	Total	Cases	Attack rate (%)	Risk ratio	95%CI	p-value†
Livestock area									
Visit to livestock area	29	7	24.1	11	0	0.0	4.4‡	0.6–∞	0.16
Contact with any livestock (sheep, goat, horses, poultry)	25	6	24.0	4	1	25.0	1.0	0.2–6.0	1.00
Cleaning of livestock area or animal pens	10	2	20.0	19	5	26.3	0.8	0.2–3.2	1.00
Cat impound									
Visit to cat impound	31	7	22.6	9	0	0.0	3.3‡	0.4–∞	0.18
Direct contact with cats or kittens	28	7	25.0	3	0	0.0	1.2‡	0.1–∞	1.00
Handling cats or kittens at birth, or present during birthing events	13	4	30.8	18	3	16.7	1.8	0.5–6.9	0.41
Providing or assisting with euthanasia of cats or kittens	9	4	44.4	22	3	13.6	3.3	0.9–11.7	0.15
Disposal of deceased cats or kittens	11	5	45.5	20	2	10.0	4.5	1.1–19.7	0.07
Cleaning of cat impound, cages or changing cat litter	12	3	25.0	19	4	21.1	1.2	0.3–4.4	1.00
Dog impound									
Visit to dog impound	34	7	20.6	6	0	0.0	1.0‡	0.2–∞	0.57
Direct contact with dogs or puppies	32	6	18.8	2	1	50.0	0.4	0.1–1.8	0.37
Handling dogs or puppies at birth, or present during birthing events	6	1	16.7	28	6	21.4	0.8	0.1–5.3	1.00
Providing or assisting with euthanasia of dogs	8	4	50.0	26	3	11.5	4.3	1.2–15.4	0.04
Disposal of deceased dogs or puppies	9	5	55.6	25	2	8.0	6.9	1.6–29.7	0.007
Cleaning of dog impound, cages or dog waste	14	3	21.4	20	4	20.0	1.1	0.3–4.1	1.00

a: The outbreak occurred from October–December 2016 and the workplace-related exposures were reported from 15 September–31 October 2016. †Fisher's exact P value. ‡Odds ratio and lower bound of the 95% confidence interval calculated using exact logistic regression.

an indication for Q fever testing in patients with an unexplained, non-specific febrile illness.

Q fever vaccination for all veterinarians, veterinary nurses and veterinary students and the use of personal protective equipment (PPE) during exposure to parturient products was recommended in the first (2011)[25] and two subsequent (2013, 2017)[26,27] editions of the Australian Veterinary Association *Guidelines for Veterinary Personal Biosecurity*. Surprisingly, none of the veterinary clinic staff and only three animal refuge workers had previously received Q fever vaccine. Additionally, PPE was not reported as being used by animal refuge or veterinary clinic workers involved with euthanasia, even when exposed to parturient products. These practices are consistent with previous reports demonstrating a relatively low perceived risk of Q fever among Australian veterinary workers[28] and cat breeders.[29] Additionally, *The Australian Immunisation Handbook* recommends Q fever vaccine for professional dog and cat breeders,[8] although other occupations with exposure to parturient cats and dogs are not currently included in this recommendation. Given our finding that feline birthing events were a relatively common occurrence in the cat impound, workers in these settings are likely to experience a similar exposure risk to that of professional dog and cat breeders. Animal refuge workers and others with regular exposure to parturient cats or dogs should therefore also be included in the recommendation to receive Q fever vaccine after undergoing pre-vaccination screening. Ongoing communication regarding the risk of Q fever infection – reinforcing the use of PPE and Q fever vaccination – should be provided to those in the veterinary and non-veterinary workforces with routine exposure to parturient cats or dogs. Promoting the use of PPE as part of routine infection control practices in veterinary and non-veterinary workforces is also of importance, given the potential for infection with other zoonoses.

Our investigation was limited by the lack of Q fever serological testing for all workers at the animal refuge and veterinary clinic, resulting in potentially misclassifying asymptomatic cases and including non-cases with pre-existing immunity. However, sensitivity analyses, including only the cohort who underwent Q fever pre-vaccination screening and subsequently received Q fever vaccination as susceptible non-cases, revealed a similar pattern of risk ratios for workplace exposures when compared to the primary analysis. As this investigation was undertaken as part of an acute public health response in a busy metropolitan public health unit, a more comprehensive approach involving serum sampling of all at-risk staff was not feasible.

We were also limited by the inability to test for markers of *C. burnetii* infection, as was performed during the previous Australian cat-related outbreak, in the cat implicated in this outbreak.[14] This testing would have provided additional evidence to either support or refute our conclusions.

Implications for public health

Parturient cats and dogs are potentially unrecognised sources of sporadic Q fever cases and outbreaks in Australia. A history of exposure to feline or canine parturient products should increase clinical suspicion for Q fever in patients with an unexplained, non-specific febrile illness. Q fever vaccine should be provided to susceptible individuals with occupational or other regular exposure to parturient cats or dogs.

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