Sexually Transmitted Q Fever

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We report the sexual transmission of *Coxiella burnetii* from a man with occupationally acquired Q fever to his wife. Fifteen days after coitus, his wife also developed serologically proven acute Q fever. *C. burnetii* DNA sequences were detected by polymerase chain reaction (PCR) performed on semen samples obtained from the husband at 4 and 15 months after the onset of acute Q fever, but PCR results were variable at 23 months, indicating the presence of few organisms.

Humans with acute primary Q fever caused by the obligate intracellular bacterium *Coxiella burnetii* present with a high fever, severe fatigue, myalgia, arthralgia, profuse sweats, rigors, and marked loss of weight. Some patients develop pneumonia, and the presence of anicteric hepatitis is common. Less frequently, the bone marrow, ovary, testis, or CNS may be involved. The incubation period is 14–60 days but usually is ~20 days [1]. After primary infection occurs, *Coxiella* organisms may persist in the host and give rise to subacute endocarditis, chronic hepatitis, and osteoarticular lesions. Persistence may also be related to a prolonged postinfection fatigue syndrome [1, 2].

Cattle, sheep, and goats are the main reservoirs for *Coxiella* organisms that cause infection in humans in Australia, although such organisms are also present in macropods, small bush animals, and ticks. Transmission of *C. burnetii* from animal to animal, or from animal to human, most frequently occurs via inhalation of dust or droplets that contain *Coxiella* organisms [3–6]. Person-to-person transmission is rare [1].

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Studies done since the late 1940s have shown that, after initial infection, *C. burnetii* may persist in sheep, cattle, or laboratory animals; female animals may have a recrudescence during the late stage of pregnancy, with organisms shed in large numbers in the products of conception at parturition. An analogous sequence sometimes occurs during human pregnancy and may cause damage to the fetus or neonate [7].

Q fever infection of the male reproductive tract is less well documented, although sexual transmission of *C. burnetii* or the presence of such organisms in the reproductive tract has been observed in laboratory animals and cattle [8–10]. A recent report on sexual transmission of *C. burnetii* among humans described the initial infection of Polish sheep shearers in Spain and the subsequent infection of the shearers' wives when they returned to their home country [11].

Our report adds to the latter experience and describes the transmission of *C. burnetii* from a man in the late recovery phase of acute Q fever to his wife. PCR detected genomic DNA of *C. burnetii* in the man's semen samples twice during the 15 months after his onset of acute Q fever but showed variable results at 23 months after onset.

Methods. Q fever is a notifiable disease in South Australia. A case is defined as a clinically compatible illness with serological evidence of current infection, optimally by demonstration of a $\geqslant$4-fold increase in antibody titer to the antigens of *C. burnetii* during the course of the illness.

In South Australia, notified cases of Q fever are mostly occupationally acquired. From January 1990 through November 2000, 57% of notified cases were directly or indirectly linked to large domestic and export meat plants (Communicable Disease Control Branch, Adelaide, South Australia, unpublished data).

The cases of Q fever noted in the index patient and his wife formed part of a cluster of 5 cases of Q fever that occurred in a rural South Australian town. Patients were interviewed by the staff of the Communicable Disease Control Branch to determine a possible common source of infection. A semistructured questionnaire was used that covered exposure to all known risk factors during the month before the individuals became ill. Information was collected regarding occupation, visits to farms, visits to wildlife parks and rural areas, exposure to farm animals, exposure to parturient cats or dogs, contact with domestic animals, pet ownership, consumption of unpasteurized milk, sexual history, and laundering of work clothes. Questions were also asked about routes taken to work from home and about other travel associated with work.

Table 1. Serum titers of antibody to *Coxiella burnetii* phase I and phase II antigens in the index patient and his wife.

Subject, time from onset of illness to titer assessment	Serum titers of antibody to *C. burnetii* antigens					
	IgG		IgM		IgA	
	Phase I	Phase II	Phase I	Phase II	Phase I	Phase II
Index patient						
9 days	<10	<10	<10	<10	<10	<10
22 days	<10	**1280**	**10**	**640**	<10	<10
36 months	**320**	**1280**	**10**	<10	**20**	<10
Wife of index patient						
19 days	<10	**160**	<10	**640**	<10	<10
55 days	<10	**160**	**40**	**160**	<10	<10

NOTE. Titers were measured by means of indirect immunofluorescence and use of conjugates against the IgG, IgM, and IgA. Values shown in boldface type are positive.

Laboratory confirmation of Q fever was made by examination of serum samples collected at various intervals after the onset of illness. These samples were titrated for antibody on microdots of *C. burnetii* phase I and II antigens on microscope slides, by means of indirect immunofluorescence with conjugates against IgG, IgM, and IgA [12].

C. burnetii DNA was detected in the index patient's semen samples by means of a highly sensitive PCR amplification of a target sequence in the transposon or insertion element IS*IIII*a present in the *Coxiella* genome in ~20 copies; the assay is able to detect <5 *Coxiella* cells. PCR product (amplicon) was identified by sizing on gel electrophoresis in comparison with a known DNA standard and also by specific binding of probe in the ABI 7700 sequence detection system (Taqman; Perkin-Elmer) [13].

Results. The index patient was a 57-year-old man who was employed to drive tiptrucks for road construction. His work depot was located 600 m from a livestock sale yard. It is postulated that his exposure occurred as a result of inhalation of infected aerosols or dust from the nearby sale yard. Within 4 weeks of the onset of his illness, 3 more cases of Q fever in men were announced; 2 of the 3 affected men worked at the same depot. The third man who was affected was a livestock buyer who attended sales at the livestock sale yard every 2 weeks. He also traveled to farming properties on a regular basis. The livestock sale yard thus appeared to be the common source of infection for the index patient and the subsequent 3 patients. With the exception of the livestock buyer, who in theory might have been exposed to infection elsewhere, the patients did not identify other potential sources of exposure.

Approximately 6 weeks after the onset of Q fever in the index patient, his wife (the fifth patient in the cluster) was given a diagnosis of Q fever. She was employed as a support worker who visited the homes of intellectually and physically impaired people. Her office was not located near the sale yard or her husband's workplace. Thirty-five days after the onset of her husband's illness, she drove him to his workplace and remained in the car for ~5 min. Eight days after this visit, she developed Q fever. During the 7 weeks before the onset of her illness, the wife did not have contact with potentially contaminated work clothes used by the index patient because he was too sick to work and did not return to work until 8 weeks after the onset of his own illness. There were no other people in the household. Twelve days before the onset of her illness, the wife had traveled to the north of South Australia with her husband, but she did not have any contact with animals and did not remember passing trucks used for the transport of livestock. No other risk factors were identified, and her only overt exposure appeared to be sexual contact with her infected husband.

The index patient and his wife did not have sexual intercourse until 29 days after the onset of his illness. Three days after they had intercourse, the index patient developed orchitis, and 15 days after coitus, his wife developed symptoms of Q fever. The orchitis lasted for 2 weeks, and during this time, the index patient and his wife did not have sexual contact.

Table 1 shows the results of serological assays performed on serum samples obtained from the 2 patients. From days 9 through 22 of his illness, the index patient showed a >4-fold increase in titers of antibody to *C. burnetii* phase II antigen in IgM and IgG, a finding that confirms that his illness was a current attack of Q fever. His antibody levels have remained high. The wife's first serum sample was obtained on day 19 after the onset of illness, when IgM and IgG antibodies to phase II antigen were already present at titers of 640 and 160, respectively. By day 55 after the onset of her illness, the IgM antibody titer showed a significant decrease to 160, but there was a 4-fold increase in IgM antibody to phase I antigen; antibody to this antigen is known to increase later in the course of illness than does antibody to phase II antigen. The overall

pattern of antibody responses clearly indicated that the wife's illness was acute Q fever.

Semen samples were donated by the index patient at 4, 15, and 23 months after the onset of the acute illness. The first 2 samples were readily found to be positive for *C. burnetii* DNA by PCR assay, but the third sample gave variable results on repeated testing, which probably indicated the presence of small numbers of organisms and inhibition of PCR by host DNA [13].

Discussion. We conclude that the index patient (and the other male patients) acquired Q fever as a result of airborne transmission of infection from the sale yard. The wife of the index patient had only one brief exposure to the sale yard, spending ~5 min in its vicinity while dropping off her husband at work 8 days before the onset of her illness. The incubation period of Q fever after natural exposure is 15–25 days. American experiments with human volunteers who were exposed to infective aerosols that contained graded doses of *C. burnetii* showed that the length of the incubation period was inversely proportional to the size of the dose [14]. To achieve an incubation period as short as 9 days, it would be necessary to give a dose of 1500 guinea pig median infective doses (ID_{50}); 1 to <5 guinea pig ID_{50} were sufficient to cause infection. It seems highly unlikely that the spouse could have been exposed to a dose of that size during her brief visit to an area located at least 600 m away from the sale yard and have had a resulting incubation period of 8 days. On the other hand, the onset of her Q fever 15 days after intercourse falls within the usual limits of the incubation period, particularly given the unusual route of inoculation. (Note that the incubation period for Q fever in the guinea pig is shorter after ip injection than after exposure via the respiratory tract [14].)

Although the presence of *C. burnetii* was demonstrated in the index patient's semen samples, it has been pointed out to us that sexual intercourse may also involve the exchange of other fluids (presumably blood, saliva, or urine) that might be the actual vehicle of infection. The bacteremic phase of Q fever, as judged by guinea pig inoculation, occurs during the primary fever and ceases with the formation of antibody [15]. At the time of intercourse, the index patient was afebrile, 29 days from the onset of illness, and had high levels of IgG and IgM antibody to *C. burnetii* phase II antigen (table 1). Similar time limitations apply to isolation of *C. burnetii* in urine, although sporadic isolations have been made later in convalescence [15]. Little information exists on excretion of *C. burnetii* in saliva or on infection of the nasopharynx.

There is good evidence of persistent infection in the genital tract of humans and animals. Kruszewska et al. [11] reported sexual transmission of Q fever in humans. Nine sheep shearers who acquired Q fever from sheep in Spain subsequently infected their spouses in Poland. *C. burnetii* was isolated from urine and semen samples obtained from 2 of the shearers. Increased levels of Q fever antibodies were found in 6 of the shearers' spouses.

Sexual transmission of Q fever has also been observed in laboratory animals. In infected mice, *C. burnetii* has been cultured from the spleen, liver, testis, epididymis, prostate, and semen. *C. burnetii* was isolated from the spleen, liver, and amniotic fluid of pregnant mice after they mated with infected male mice; the pregnant mice also had seroconversion [8]. Similarly, infection was detected in the testes and seminal vesicles of guinea pigs at 90 days after inoculation with *C. burnetii,* an illustration of persistent carriage of *C. burnetii* in the genital tract [10]. Attached cells of *C. burnetii* have been demonstrated on spermatozoa by means of immunofluorescence and scanning electron microscopy [8, 16]. Overall, in light of the information discussed here and in light of the presence of orchitis and *Coxiella* species in the genital tract of the index patient, the most economical hypothesis seems to be that infection was transmitted via semen during intercourse.

Contact with contaminated work clothing (e.g., laundering) is also recognized as an indirect mode of infection for the families of workers exposed to Q fever. In the episode that involved Polish sheep shearers, infected dust on clothing brought from Spain was unlikely to be a means of transmission because other household members were not infected [11]. In the present report, the index patient's wife had no exposure to work clothing for 7 weeks before the onset of her illness, and there were no other household contacts to test for antibody. Moreover, the index patient had not been working directly with animals but apparently had been infected by airborne transmission of *C. burnetii* over a distance of 600 m. The possibility that some level of direct contamination of the index patient's work clothes facilitated subsequent liberation of *Coxiella* organisms at a distant site is, therefore, highly improbable.

Orchitis is a recognized, often late complication of acute Q fever infection [17–19]; its rate of incidence varies from outbreak to outbreak. A patient in an abattoir-associated outbreak of infection in southeast Australia experienced persistent testicular swelling after an attack of Q fever that was suspected to be a testicular tumor and that was removed 6 months after the acute attack. Histological examination of the excised tissue showed only low-grade, nonspecific inflammation, but PCR examination revealed *C. burnetii* DNA sequences (P.A.S., R.J.H., and B.P.M., Adelaide Q Fever Group, unpublished data).

The use of phase I as well as phase II antigen in the immunofluorescence assay serotests enabled detection of a late, diagnostic increase in antibody titer in the wife of the index patient. PCR detection of the *C. burnetii* genome is rapid, sensitive, and specific. Strictly speaking, it does not differentiate between living and dead *Coxiella* organisms, but in both this study and the Polish study [11], infective organisms were clearly

present. Both husband and wife recovered; no overt chronic sequelae have been noted to date. More extensive observations are required to determine the frequency and duration of carriage of *Coxiella* organisms in the male genital tract after acute Q fever and also whether precautions are required to prevent transmission of Q fever between sexual partners in the convalescent phase of Q fever. Our findings should not be interpreted to imply that Q fever ranks with other infections regularly transmitted by the sexual route.

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