REVIEW ARTICLE

Q fever — A review

Thomas J. Marrie

Abstract

Q or "query" fever is a zoonosis caused by the organism *Coxiella burnetii*. Cattle, sheep and goats are the most common reservoirs of this organism. The placenta of infected animals contains high numbers (up to 10^9/g) of *C. burnetii*. Aerosols occur at the time of parturition and man becomes infected following inhalation of the microorganism. The spectrum of illness in man is wide and consists of acute and chronic forms. Acute Q fever is most often a self-limited flu-like illness but may include pneumonia, hepatitis, or meningoencephalitis. Chronic Q fever almost always means endocarditis and rarely osteomyelitis. Chronic Q fever is not known to occur in animals other than man. An increased abortion and stillbirth rate are seen in infected domestic ungulates.

Four provinces (Nova Scotia, New Brunswick, Ontario and Alberta) reported cases of Q fever in 1989.

A vaccine for Q fever has recently been licensed in Australia.

Résumé

La fièvre Q: une revue

La fièvre Q est une zoonose ayant pour étiologie *Coxiella burnetii*. Les réservoirs les plus communs de cet organisme sont les bovins, les ovins et les chèvres. Les placenta d'animaux infectés contiennent de nombreux organismes (jusqu'à 10^9/g), *C. burnetii*. Les aérosols transportent l'organisme au moment de la parturition et sont la source d'infection pour l'homme par inhalation. La maladie chez l'homme présente une variété de symptômes qui s'expriment dans les formes aiguës ou chroniques. La forme aiguë se caractérise plus fréquemment par des symptômes passagers ressemblant à l'influenza, mais peuvent inclure la pneumonie, l'hépatite ou la méningo-encéphalite. La forme chronique est presque toujours associée à l'endocardite et rarement à l'ostéomyélite. La forme chronique existe seulement chez l'homme. Une augmentation de la mortalité néonatale et des avortements est observée chez les ongulés domestiques infectés.

Quatre provinces (Nouvelle-Écosse, Nouveau-Brunswick, Ontario et Alberta) ont rapporté des cas de fièvre Q en 1989. Un vaccin contre la fièvre Q a été récemment homologué en Australie.

(Traduit par Dr Thérèse Lanthier)

Can Vet J 1990; 31: 555-563

History

In August 1935, Dr. E. H. Derrick (MD, Melbourne University, 1922), the Director of the Laboratory of Microbiology and Pathology of the Queensland Health Department at Brisbane, Australia, was asked to investigate an outbreak of undiagnosed febrile illness among abattoir workers in Brisbane (1). This illness he named "Q" for "Query" fever. Derrick inoculated guinea pigs with blood or urine from the "Q" fever patients. The guinea pigs became febrile. Derrick was unable to isolate the agent responsible for the fever so he sent a saline emulsion of infected guinea pig liver to Macfarlane Burnet in Melbourne. Burnet was able to isolate organisms which "appeared to be of rickettsial nature" (2). At about the same time Drs. Herald Rea Cox and Gordon Davis at Rocky Mountain Laboratory, Montana were working on the possible vectors of Rocky Mountain spotted fever and tularemia. Davis had ticks (the suspected vectors) feed on guinea pigs; the guinea pigs became ill.

In May 1938, Dr. Rolla Dyer, the Director of the National Institute of Health, visited Cox in Montana to challenge Cox's report that he had cultivated rickettsiae in large numbers in embryonated eggs. Ten days later he became ill with retro-orbital pain, fever, chills and sweats. Five mL of his blood drawn on the sixth day of his illness resulted in fever when injected into guinea pigs. Subsequent studies showed that this agent was identical to the Nine Mile agent isolated from ticks. In April 1938, Burnet sent Dyer spleens from mice infected with the Q fever agent, Dyer showed that the Q fever agent was identical to Nine Mile agent (3). Cox named the Nine Mile agent *Rickettsia diaporica* (diaporica means having the property or ability to pass through) a reference to the filterable property of the agent (4). Meantime in Australia, Derrick proposed the name of *Rickettsia burnetii* for the Q fever agent (5). In 1948 Cornelius B. Philip proposed that *R. burnetii* be considered as the single species of a distinct genus since it was now apparent that this organism was unique among the rickettsiae (6). He proposed the name *Coxiella* (6). The Q fever agent is now known as *Coxiella burnetii*. Cox and Burnet both died in 1986 (3).

Department of Medicine and Department of Microbiology, Dalhousie University, and Victoria General Hospital, 1278 Tower Road, Halifax, Nova Scotia B3H 2Y9.

Reprint requests to Dr. T.J. Marrie, Room 4090 A.C.C., Victoria General Hospital.

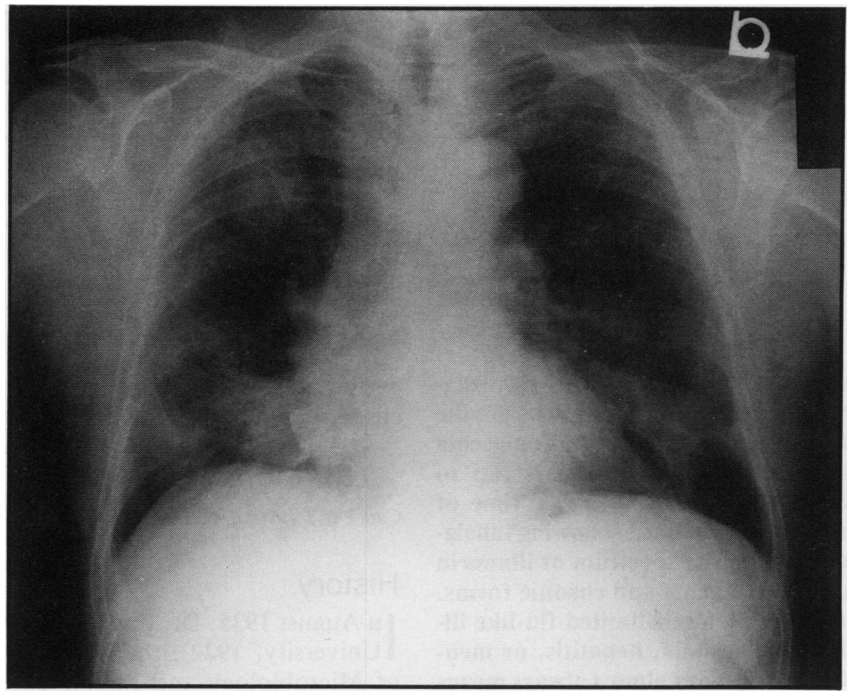

Figure 1. Chest radiograph of a patient with Q fever pneumonia. Note three opacities in the right lung and two in the left.

Epidemiology

The initial description of Q fever as an illness occurring among abattoir workers (1) was a strong portender of the epidemiology of this illness. The epidemiology of Q fever in man is linked to the epidemiology of Q fever in animals. Q fever is a zoonosis. Of all the animals infected by *C. burnetii*, man is the animal to usually develop illness as a result of infection (7). Man becomes infected following inhalation of *C. burnetii*. The desiccation-resistant organism is shed from infected animals, usually cattle, sheep, goats or cats, especially at the time of parturition. Air samples are positive for weeks following parturition and viable organisms are present in the soil for periods of up to 150 days (8).

Two characteristics of the organism are important in the epidemiology of the disease. These are its ability to withstand harsh environmental conditions, probably as a result of spore formation (9), and its extraordinary virulence for man. A single organism can cause disease in man (10). *Coxiella burnetii* has been a very successful pathogen. By 1955 Q fever had been reported from 51 countries on five continents (11). From the very beginning, outbreaks have dominated the epidemiology of Q fever. These can occur even following indirect exposure to contaminated aerosols, as was the case when 415 residents of a Swiss valley, who lived along a road over which sheep travelled to and from mountain pastures, developed Q fever (12). Occasionally, large outbreaks of Q fever may occur and the source of the infection may not be apparent. Recently, May to July 1989, more than 100 cases of Q fever occurred in the West Midlands of England, chiefly Birmingham. No common source has been found but, since the outbreak coincided with the lambing period of sheep and as the summer was early and dry, it is postulated that wind-borne contaminated dust resulted in the outbreak (13).

Institution-related outbreaks have been important from the early days of laboratory work with *C. burnetii* to the present. From 1938 to 1955, 266 laboratory workers world-wide developed Q fever (14). Since the 1960's, the epidemiology of institution-acquired Q fever has changed. Since then there have been several outbreaks of Q fever due to the use of infected pregnant sheep in research (15–17). Transportation of these infected sheep along heavily travelled corridors has resulted in infection of individuals who were not involved in the research.

Some studies have suggested that ingestion of raw (contaminated) milk is a risk factor for the acquisition of Q fever (18–20). Seroconversion, but not disease, did occur following ingestion of raw milk (21). It is likely that, in some populations, ingestion of infected material accounts for the high seropositivity rate. Ingestion of *C. burnetii* is probably important in the maintenance of Q fever in the animal population. Cats experimentally infected via the oral route did not become ill, whereas cats infected via the subcutaneous route became febrile and lethargic (22).

Percutaneous infection can occur (23,24), but accounts for very few cases of Q fever worldwide.

While *C. burnetii* has been isolated from human placentas (25), there is little to suggest that vertical transmission occurs in man.

Person-to-person transmission has been documented but it is very unusual. Pneumonia occurred among two pathologists, a nurse, and an autopsy attendant who performed a postmortem examination on a patient who had died from *C. burnetii* pneumonia (26). Twelve cases of Q fever occurred at the Institute of Pathology at Tubingen University — person-to-person

transmission is assumed to have occurred but the source of the infection was not found (27). Recently Mann *et al* (28) described what they feel is person-to-person transmission of Q fever in a family. I have not observed transmission of Q fever from patients to medical staff. There is no need to isolate patients hospitalized with this illness (29), however precautions should be taken in the handling or postmortem examination of infected cadavers (30).

Sexual transmission of *C. burnetti* has been demonstrated in mice in the laboratory (31), but whether Q fever can be transmitted sexually under natural conditions and in other animal species is unknown.

Worldwide, there is a remarkable diversity in the epidemiology of Q fever. In some areas there always seem to be human cases of Q fever, while in other areas with the same rate of infection in animals, spread to man does not occur (10,32). This may be due to a combination of microorganism (different strains) and host differences. Luoto (20) has speculated that there may be unrecognized factors which may contribute to or limit human disease. Countries with considerable Q fever activity at present include Uruguay (32), People's Republic of China (33), France (34,35), Germany (36), The Netherlands (37), Portugal (38), Spain (39), Switzerland (12), United Kingdom (40), USSR (41), Australia (42). Almost every country in the world has reported cases of Q fever. Three hundred and twenty-eight cases of Q fever were identified in Canada from 1980–1987 (Dr. S. Acres — personal communication). No cases were reported from Saskatchewan, Manitoba or Newfoundland. There was one case from British Columbia and two from New Brunswick. Most of the cases were from Ontario (60%) and Nova Scotia (26%). The number of cases from Nova Scotia (170 were identified but do not appear in the statistics) on a per capita basis was much higher than that for Ontario — (198 cases).

The occurrence of Q fever in Nova Scotia illustrates the epidemiology of this fascinating disease. In 1979 we began to study pneumonia — we soon began to diagnose cases of Q fever (44,45). Whether Q fever was present in Nova Scotia prior to this is unknown — certainly it was not recognized. In 1982, Kosatsky (46) investigated the first outbreak of Q fever in our province. Ten members of one family (and two friends) developed Q fever following exposure to a cat that had just given birth to kittens. Since then we have observed an additional 17 incidents of cat-associated Q fever; thirteen of these were recently described (47). We have observed only one outbreak of Q fever following exposure to an infected cow (48). Cases of Q fever in Nova Scotia have also followed exposure to infected rabbits (49) and to the contaminated [by new-born kittens] clothing of a worker in a truck repair facility (49). Many questions remain unanswered about the epidemiology of pneumonia in Nova Scotia. Why are cats so important in the epidemiology of infection in this province? How do the cats become infected? Pneumonia is the predominant manifestation of Q fever in Nova Scotia — why?

We have also found that infected cats have resulted in cases of Q fever in Prince Edward Island (47) and New Brunswick (TJ Marrie — unpublished observations). Whether or not cat-related Q fever is limited to Maritime Canada awaits further study.

Q fever occurs throughout the year in Nova Scotia, however only a few cases occur during the winter.

Fourteen percent of 1684 Nova Scotians had antibodies (indirect fluorescent antibody test) to phase II *C. burnetii* antigen. The rate of seropositivity among males and females was equal, but males outnumbered females by 2:1 among the 180 cases of acute Q fever that we have studied so far. The rate of seropositivity was highest among veterinarians — 49% of those tested had antibodies to phase II antigen (51).

It is likely that strain differences of *C. burnetii* are important in the epidemiology of Q fever. This may explain why the predominant manifestation of Q fever in Nova Scotia is pneumonia, while in Ontario granulomatous hepatitis occurs in addition to other manifestations of Q fever (52). This is probably the explanation of why the rate of chronic Q fever (mainly endocarditis) varies from country to country. Chronic Q fever is uncommon in the United States and Australia, whereas it is quite common in England and France.

The organism

Coxiella burnetii is a highly pleomorphic coccobacillus with a gram-negative cell wall. It measures 0.3 × 1 μm (53); unlike true rickettsiae it enters the cell by a passive mechanism. Within the cell it survives within the phagolysosome — the low pH of this environment is necessary for the metabolic functioning of *C. burnetii*. *Coxiella burnetii* undergoes phase variation (54). In nature and laboratory animals it exists in the phase I state. Repeated passage of phase I virulent organisms in embryonated chicken eggs leads to gradual conversion to phase II avirulent forms (53). These two antigenic phases differ in the sugar composition of their lipopolysaccharides (55,56), in their buoyant density in cesium chloride, and in their affinity for hematoxylin and basic fuchsin dyes. Plasmids have been found in both phase I and phase II cells. There are three different plasmid types varying in length from 36 to 45 kilobases (57).

Q fever in animals

Coxiella burnetii can infect a large number of animal species including livestock (58). These animals rarely become systemically ill from *Coxiella burnetii*, but abortion and stillbirths may occur. Endocarditis, the major form of chronic Q fever in man, does not seem to occur in other animals.

Coxiella burnetii localizes in the uterus and mammary glands of infected animals (58). In some instances, cattle have been resistant to infection by intranasal, intravenous, and intravaginal inoculation and by feeding contaminated bran (60), however in other studies intranasal infection of a pregnant cow by means of an atomizer did lead to infection (61) and recovery of the organisms from the placenta. *Coxiella burnetii* has been recovered from the placentas of naturally infected dairy cows (62).

Similarly, this organism has been isolated from the placentas of naturally infected (63) and experimentally infected sheep (64), and has been found in the amniotic fluid of these animals (63). *Coxiella burnetii* has been transmitted transplacentally in a guinea pig model of infection (65). Cows have been known to shed *C. burnetii* in milk for up to 32 months (66), while sheep shed the organism in feces for 11 to 18 days postpartum (8). Outbreaks of abortion due to *C. burnetii* were first reported in goats (58) and later in cattle (67). Inflammation of the placenta has been demonstrated in sheep and goats in instances where *C. burnetii* has caused abortion (68,69). Histological examination of the placenta shows trophoblasts distended with the bacilli and necrotic villi (69). Stresses such as overcrowding and the immune suppression of pregnancy are associated with multiplication of *C. burnetii* in the placenta (70). The placentas of infected sheep can contain 10^9 hamster infective doses per gram of tissue (63).

We have noted that the stillbirth rate among infected cats is high [up to 70%] (47) compared with the quoted background rate of 10% (71).

The following additional domestic animal species have been found to be infected by *C. burnetii* in some areas: pigs (58), horses (67,72,73), dogs (58,72).

Infected cattle, sheep and goats are most commonly associated with transmission of Q fever to man. We have shown that cats are the major source of Q fever for humans in Nova Scotia and Prince Edward Island (47). Dogs have been infrequently associated with transmission of *C. burnetii* to man; the reasons for this are not readily apparent. Interestingly enough, we could not demonstrate any infection by *C. burnetii* among dogs in Nova Scotia (74) despite the preeminence of cats in the epidemiology of Q fever in this province. This suggests that the behavior of these animals is important in their acquisition of *C. burnetii*. We postulate that cats acquire this infection by ingesting infected mice. Dogs soiled with sheep placenta have passively spread Q fever to their owners (75).

Wild animals may be very important in the epidemiology of Q fever. Doves are felt to be responsible for introducing *C. burnetii* to Northern Ireland (71). Carnivorous birds probably acquire the infection from their infected prey; granivorous and insectivorous birds feed and roost in close proximity to cattle and probably become infected via the aerosol route. A wide variety of fish, rodents and marsupials have been shown to be infected by *C. burnetii* (58).

Ticks are probably most important in keeping the cycle of *C. burnetii* going in nature (4,76,77). *Coxiella burnetii* multiplies in the cells of the midgut of the tick and is excreted in the feces of the tick during feeding. Early in the history of Q fever, Derrick felt that ticks were important in the epidemiology of this disease (78). An outbreak of Q fever occurred in a sheep station near Tambo, Australia involving 22 employees on the station (78). Shearing was carried out six months following parturition, so it was felt unlikely that shedding of *C. burnetii* by the sheep was responsible for the outbreak. The sheep were heavily infested with the tick *Amblyomma triguttatum* and one of the hypotheses was that the ticks laden with *Coxiella* might have contaminated the wool; however *C. burnetii* was not isolated from the ticks. We now know that dried tick feces is infectious for up to 586 days (30). Sheep wool becomes contaminated during parturition (79). These contaminated "wool-tags" and in some instances contaminated tick feces have probably led to outbreaks of Q fever in wool processing plants and the high rate of *C. burnetii* seropositivity among sheep shearers (79).

Table 1. Symptoms of acute Q fever (data represent a summary of patients reported in references 32, 46, 79, 80)

Symptom	Percent reporting this symptom	Comment
Fever	88–100	Duration 5–57 days may persist for weeks to months
Fatigue	98–100	
Headache	65–98	Clue to diagnosis
Chills	60–88	True rigors may occur
Myalgia	47–69	
Sweats	31–98	
Cough	24–90	Dry; mild
Nausea	22–49	
Vomiting	13–25	
Chest pain	10–34	May be pleuritic
Diarrhea	5–22	
Sore throat	5–14	Rare
Rash	4–18	"Nonspecific"

Q fever in man

Man is the only animal known to almost always develop illness following infection with *C. burnetii* (80). Several clinical syndromes result from this infection — these are: (81,82).

1. A self-limited febrile illness
2. Pneumonia
3. Hepatitis
4. Endocarditis
5. Osteomyelitis
6. Q fever in infancy
7. Neurological manifestations
8. Complications of acute Q fever

While some *C. burnetii* infections are totally asymptomatic (83), the majority are mild self-limited febrile illnesses. It is difficult to know just what proportion of Q fever is truly asymptomatic. Luoto *et al* (84) found no overt cases of Q fever among 315 residents in 90 infected premises in Rasalli County, Montana; 22 persons seroconverted in one year. Minor illnesses were encountered but none were identifiable as Q fever infection. How many of these minor illnesses were due to Q fever is unknown since these subjects were not investigated to determine the etiology of their minor illness. Stoeneer and co-workers (85) studied families with infected and noninfected herds in two areas of the state of Idaho. While seropositivity to *C. burnetii* was significantly greater among subjects with positive herds, the incidence of disabling febrile illness of two days or more was not greater. Even when illnesses

probably due to influenza were excluded, there was no difference between the two groups.

Acute Q fever, which may be manifest as pyrexia of unknown origin, pneumonia or hepatitis, is almost always of abrupt onset. The manifestations of acute Q fever vary from country to country (56) (Table 1). Severe headache is a characteristic feature, so much so that it prompts a lumbar puncture to rule out meningitis in some patients. Headache is more common with Q fever pneumonia than it is in pneumonia due to other agents (47).

Physical examination may be normal apart from an elevated temperature. Hepatomegaly and splenomegaly may be present (86). We have not noted these findings in patients with cat-associated Q fever. However, 51% of 111 patients with Q fever in Australia had hepatomegaly and 30% had splenomegaly (87), while 11% of 180 patients studied in northern California had hepatomegaly and 4% had splenomegaly (86). Relative bradycardia — pulse inappropriately slow for the degree of fever — has been reported by some workers (88,89). This feature however has been inadequately studied.

Pneumonia has been the predominant manifestation of Q fever in Nova Scotia. It accounted for 2.9% (21 of 719) of patients with community-acquired pneumonia admitted to an urban hospital (90), while it caused 20% of pneumonias admitted to rural hospitals in this province (91). *Coxiella burnetii* causes an "atypical" pneumonia. This term is used to distinguish this form of pneumonia from those due to conventional bacteria, e.g. *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, and aerobic gram-negative bacilli. Patients with atypical pneumonia (92) usually have a nonproductive cough and the radiographic findings tend to be more extensive than the physical findings would suggest. *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Chlamydia pneumoniae*, and various respiratory tract viruses are other causes of atypical pneumonia. Severe *C. burnetii* pneumonia cannot be distinguished from that due to *Mycoplasma* or *Legionella* on clinical and radiographic grounds. The chest radiograph will frequently show multiple rounded opacities in patients with Q fever pneumonia following exposure to infected parturient cats (Figure 1). Other features include increased reticular markings and atelectasis (93,94). Pleural effusions occur in 26% of patients (95) and, rarely, cavitation of pulmonary nodular opacities has occurred (96). The white blood cell count is increased in 30% of patients with acute Q fever — it is normal in the remainder. Thrombocytosis during the recovery phase of Q fever pneumonia is common. Abnormal liver function tests are present in about half of the patients — rarely jaundice may be one of the presenting manifestations of acute Q fever.

Uncommon features of acute Q fever include a variety of neurological manifestations: encephalitis, dementia, toxic confusional states, extrapyramidal disease (97), meningoencephalitis (98–100). Manic psychosis (101), polyradiculopathy and isolated neuritis of the cranial nerves are other manifestations (102). Optic neuritis due to Q fever is uncommon — it has been described in six patients, and three had other neurological manifestations as well (103–107).

Thyroiditis (108), myocarditis, pericarditis (109,110), bone marrow necrosis (111), bone marrow granuloma (112,113), mesenteric panniculitis (114), inappropriate secretion of antidiuretic hormone (115), orchitis, epididymitis, priapism, erythema nodosum (109) and splenic rupture (117) are all rare manifestations of acute Q fever.

In recent years, acute Q fever has been described in the immunocompromised host (118–121) including patients with Hodgkin's disease, leukemia, Crohn's disease and bone marrow transplant patients. Irradiation (122) and corticosteroid therapy (123) can result in reactivation of *C. burnetii* in experimental animals.

Q fever hepatitis (124–130) has three clinical presentations:

(a) as an infectious hepatitis picture,
(b) fever of unknown origin with characteristic granulomas being present on biopsy, or
(c) as an incidental finding in patients with Q fever pneumonia.

The typical granuloma consists of a dense fibrin ring and inflammatory cells surrounding a lipid vacuole. While these granulomas are highly suggestive of Q fever, they may also be seen in Hodgkin's disease, infectious mononucleosis and leishmaniasis.

Chronic Q fever

The strains of *C. burnetii* that cause chronic Q fever in man are probably different from those that cause acute disease (131,132). The major manifestation of chronic Q fever is endocarditis. An abnormal native heart valve or a prosthetic valve is usually infected, although infection of vascular grafts or aneurysms may also occur (133,134). Another important predisposing factor is paralysis of specific cell-mediated immunity. Lymphocytes from patients with Q fever endocarditis are unresponsive to *C. burnetii* antigens (135) — however this may be a secondary rather than a primary phenomenon. Phase I antibodies and antibodies in the IgA fraction predominate in Q fever endocarditis — this is not so in acute Q fever.

While chronic Q fever has been reported from many countries, the proportion of cases of chronic Q fever to acute Q fever varies considerably from country to country. In the United Kingdom, Q fever endocarditis accounts for 11% of all cases of Q fever (136), whereas this entity is extremely rare in the United States (137).

The clinical presentation of chronic Q fever is usually that of "culture-negative endocarditis". In areas where there is little clinical experience with this illness, diagnosis is usually delayed. Symptoms include malaise, weakness, fatigue, weight loss, chills, fever, anorexia and night sweats (36,40,133,138–151). However these patients are often afebrile by the time they consult a physician. The physical findings are nonspecific — clubbing of the fingers and toes is found in 1/3 of cases, splenomegaly in about 50%. Hepatomegaly is also common. A purpuric rash is noted on the extremities in 20% of cases. This is due to circulating immune complexes. Anemia is common, as

is an elevated erythrocyte sedimentation rate. The globulins are increased in about 90% of patients, sometimes markedly so. Rheumatoid factor is present and cryoglobulins are positive. Phase I antibody titers that are equal to or greater than the phase II antibody titers suggest chronic Q fever.

Diagnosis

In most instances, the diagnosis is confirmed serologically since most laboratories do not have the facilities to work with *C. burnetii*. The microagglutination (152), complement fixation (153), microimmunofluorescence (154), and the enzyme-linked immunosorbent assay (ELISA) (154) have all been used for this purpose. The ELISA is the most sensitive, but the IFA is easier to perform. A fourfold rise in antibody titer between acute and convalescent phase serum samples is diagnostic of acute Q fever (155–159). IgM antibodies can persist for six to eight months in some patients, so determination of IgM antibodies on a single serum should not be used in the diagnosis of acute Q fever (158).

In chronic Q fever, the antibody titers are usually much higher than those seen in acute Q fever, and phase I antibodies are higher than or equal to phase II antibody titers. In acute Q fever, the phase II antibody response predominates.

Treatment

Acute Q fever is readily treated with tetracycline (160). *In vitro* susceptibility testing of *C. burnetii* has been carried out by Yeaman *et al* (160) using persistently infected L929 fibroblast cells. In this system the most active agents were quinolones and rifampin. Chloramphenicol, doxycycline and trimethoprim had some activity, while tetracycline, gentamicin, streptomycin, erythromycin, sulfamethoxazole, penicillin G and polymyxin B had minimal to no activity. Some workers have reported that erythromycin is effective in the treatment of *C. burnetii* pneumonia (162,163) — this has not been our experience. In uncontrolled clinical trials we have found that rifampin is very effective in the treatment of acute Q fever.

The treatment of chronic Q fever is difficult. It is probably best to use two antibiotics for at least two years. Some authorities recommend treating chronic Q fever for life. Strain differences may be very important in the management of chronic Q fever. The Priscilla isolate is less sensitive than the Nine Mile isolate to quinolones and it is resistant to rifampin (163). We have treated eight patients with chronic Q fever with two years of tetracycline and cotrimoxazole; there have been no relapses. Surgical replacement of the infected valve is frequently necessary. The decision to replace the infected valve is made primarily on the basis of hemodynamic changes (increasing valvular insufficiency or stenosis).

Prevention

Early vaccines were complicated by occasional severe reactions consisting of an indurated mass at the vaccination site and the formation of a sterile abscess which was complicated by fistula formation requiring excision (164,165). *Coxiella burnetii* persists at the injection site resulting in prolonged antigenic stimulation (164). It was concluded that previously sensitized persons were at risk for severe reactions and that potential vaccinees should be screened for previous sensitization (166). In 1964, Ormsbee and co-workers showed that a phase I *C. burnetii* vaccine was 100 to 300 times more potent in protecting guinea pigs against experimental infection than a vaccine made from phase II cells (167).

The next step in the development of a Q fever vaccine was to develop methods to purify the *C. burnetii* phase I cells from yolk sac material and lipid (168,169). In recent years (1981 onwards) Marmion has used a formalin-inactivated *C. burnetii* phase I whole cell vaccine made from strain Henzerling. This vaccine has been shown to be protective (170). The rate of serious reactions to this vaccine was low. One percent of 2682 vaccinees developed an abscess at the inoculation site, and 1% had a lump at the site two months following vaccination (171).

Other measures that are of use in the prevention of Q fever are: using only seronegative pregnant sheep in research facilities and control of ectoparasites on livestock. The management of infected animals is important. In Cyprus, the prevalence of Q fever among sheep and goats was reduced by destroying infected aborted material, isolating infected dams and disinfecting the premises (172).

Concluding remarks

Q fever is present in Canada and while the number of cases varies from year to year, veterinarians and physicians must be aware of the epidemiology of this disease. Probably the best approach to management of Q fever is to investigate outbreaks and apply appropriate control measures if necessary. Serological surveys of cattle, sheep and goats should be done periodically to monitor the endemic level of the presence of *C. burnetii* in a region as measured by seropositivity among the traditional reservoirs of this organism for man. Disease in humans is readily diagnosed as long as the manifestations of the disease and the provincial epidemiology of the disease are known to practising physicians. Those at high (occupational) risk for this infection should also be aware of its signs and symptoms. CVJ

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