Q fever update

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Abstract

Infection in animals and humans from the bacterium *Coxiella burnetii* is responsible for significant disease risk. In sheep and goats it is an important cause of abortion, stillbirth, and neonatal weakness and mortality, although the organism may be present and shed in birth fluids, milk and feces without signs of disease. Infection in these species, as well as cattle, is widespread. Humans who work with infected ruminants are at risk of developing mild to severe disease, called Q fever. Chronic Q fever is particularly dangerous, with a high case fatality rate. Treatment with antimicrobials to control abortion or reduce bacterial shedding is unrewarding in sheep and goats. Vaccination has been shown to reduce abortions and degree of shedding, but currently no vaccine is licensed in the US or Canada. Measures to lower risk of infection in humans include lowering the level of contamination of the environment with the bacteria, understanding the signs in people so that treatment can be given promptly, and using protective wear to reduce exposure. This is an important zoonosis, and education of clients and service providers is a critical component of reducing the risk of Q fever.

Résumé

L'infection par la bactérie *Coxiella burnetii* peut causer une maladie grave appelée coxiellose (ou fièvre Q) chez les animaux et les humains. Chez les ovins et les caprins, c'est une cause fréquente d'avortements et de mortinatalité, ainsi que de faiblesse et de mortalité néonatales. Toutefois, le microorganisme causal peut être présent et sécrété dans les fluides excrétés à la naissance, dans le lait et les fèces sans causer de symptômes. L'infection chez ces deux espèces animales, tout comme chez les bovins, est très répandue. Les humains qui manipulent les ruminants infectés courent le risque de développer une forme modérée ou grave de la coxiellose. La forme chronique de cette maladie est particulièrement dangereuse, comme en témoigne son taux élevé de mortalité. Chez les ovins et les caprins, le traitement aux antimicrobiens pour prévenir l'avortement ou pour réduire l'excrétion dans les fèces s'avère peu efficace. Par contre, la vaccination se révèle efficace à réduire la fréquence des avortements et le degré d'excrétion mais, pour le moment, aucun vaccin n'est homologué à cette fin aux États-Unis et au Canada. Pour diminuer les risques d'infection chez les humains, on recommande de réduire la présence de la bactérie dans l'environnement, de bien comprendre les signes de la maladie chez les gens pour en permettre un traitement rapide et le port de vêtements de protection pour réduire l'exposition au microbe. La coxiellose est une zoonose grave et l'information des clients et des fournisseurs de services au sujet de cette maladie est un élément essentiel de la lutte contre celle-ci.

Introduction

Q fever is the name of the disease in humans caused by infection with the bacterium *Coxiella burnetii*. It can also cause disease in sheep, goats and cattle – the disease is called Q fever or coxiellosis. Infection in animals and humans appears to be widespread, and in some populations, very common. Disease is less common but when it occurs, the burden of illness is significant. A recent outbreak of Q fever in The Netherlands (2007 to 2010) was responsible for significant illness in over 4,000 people and was epidemiologically linked to nearby dairy goat farms. In Canada and the US, the disease in humans is reportable, but it is very likely that cases are under-reported.

The Agent

Coxiella burnetii is a gram-negative, intracellular bacterium which can infect a wide range of hosts including ruminants (cattle, sheep and goats), swine, guinea pigs, cats, dogs, wildlife, rodents and humans, as well as birds and ticks. It has two forms, the Large Cell Variant – which exists intracellular and grows logarithmically in an infected host, and the Small Cell Variant (SCV) – which is spore-like, is shed in birth fluids, semen, milk and feces, and exists outside the host. The SCV is very resistant to heat, freezing and desiccation, and can survive many months in dust, soil, and manure. It is this form that infects animals.

Distribution of Infection

Surveys of sheep, goats and cattle have found that herd-level infection rates are significantly high. In Ontario, based on bulk-tank milk polymerase chain reaction

(PCR), 30% of dairy goat herds and 60% of dairy cattle herds were positive, based on one sample. Prevalence was higher when two tests in parallel were interpreted (either test positive). More recent work in Ontario sheep flocks and goat herds found that on a herd basis, 42% of meat sheep, 64% of dairy sheep, 44% of meat goat, and 79% of dairy goat farms had a least one sero-reactor of 35 animals sampled, indicating infection. In a recent Ontario study of the causes of abortion in sheep and goats, *C. burnetii* was found to be the cause in about 20% of goat cases and about 10% of sheep cases submitted. However, the bacteria was found to be present on the placenta but not the cause of abortion in 76% of goat submissions and 80% of sheep submissions, strongly suggesting that *C. burnetii* infection is very common in sheep and goat farms in that province.

Clinical Picture – Animals

Goats appear to be most clinically affected, followed by sheep and then cattle. Abortion rates can vary from 5% to 35%. Severe suppurative placentitis along with abortion, stillbirth, and weak lambs or kids is commonly seen. Abortion in subsequent years is less common due to flock or herd immunity, although stillborn and weak lambs or kids may persist. Cattle may also abort, but it appears not to be as common as in sheep and goats. There is evidence that *C. burnetii* infection in cattle is associated with an increase in somatic cell counts (i.e., subclinical mastitis) but its role in infertility has not been determined. What is important to understand about this agent is that infection is much more common than disease. However, because with infection, the organism is readily shed into the environment, it is important to consider when determining appropriate control measures that include protecting the people that work with infected animals.

Transmission and Pathogenesis

Inhalation of contaminated air or dust, or mucous membrane contact with aborted materials, vaginal fluids, and membranes from normal birthing can serve as a source of infection. A cloud of organisms is present around aborting animals or even during normal parturition. Ticks may also shed the organism and contaminate the wool. The number of organisms shed is much higher when abnormal birth events occur, but can still be significant when birthing is normal. The organism is shed for weeks after an abortion or normal parturition, and for months in the feces and / or milk. Sheep intermittently shed the organism in the milk, but goats and cattle are persistent shedders – sometimes for several months, particularly cattle. Pasteurization will kill the bacteria in the milk. The organism can be present in the contaminated bedding and manure for months and be a source of infection when manure is spread on dry, windy days. The bacteria have been detected up to three miles (five km) downwind of an infected farm.

Diagnosis in Animals

It is important to be able to differentiate whether *C. burnetii* is the cause of disease or is present only as infection. When determining if it is the cause of abortion, demonstration by immunohistochemistry and / or PCR is a highly reliable method of diagnosis when combined with histopathology. There should be evidence of inflammation, and the pathologist should confirm that if intracellular bacteria are seen on histopathology, that they are confirmed as *C. burnetii* as they may be confused with intracellular *Chlamydophila abortus*. When *C. burnetii* is present but not the cause of abortion, the numbers of organisms, as determined by quantitative real-time PCR, is much lower than if it is the cause of abortion (median values for abortion in the range of 10^9 and when not the cause of abortion, only present at 10^2). Culture of the bacteria is rarely done, as it requires a Level 3 containment facility because of its zoonotic nature.

Serology can be done to support a suspected clinical diagnosis, as animals which have aborted due to *C. burnetii* are often – but not always – seropositive as determined by IFA or ELISA. However, an animal may be seropositive and have a normal kidding or lambing. Additionally, serological status is a poor predictor of shedding. Sheep and goats may shed vaginally, in the milk or in the feces and be seronegative. They may also be seropositive and not shed. For this reason, serology is only useful for establishing the infection status of the herd or flock, and not for determining which animals in the flock are infected and shedding. It should never be used in a test and cull program.

Treatment of Animals

The current level of knowledge suggests that long-acting oxytetracycline, when injected twice at 9.1 mg/lb (20 mg/kg) BW during mid to late gestation, is not effective in reducing the level of abortion due to *C. burnetii*. However, the studies have been small and more work should be done in this area. What is certain is that no administration of antimicrobials appears to influence the level of shedding of the organism. For these reasons, there is no justification to recommend the administration of antimicrobials in the feed or water, either in the short or long term, to control *C. burnetii* in an infected herd or flock.

Control of Infection in Animals

Because of the environmental contamination and the longevity of the organism in the environment, control should focus on lowering the level of challenge from the environment by lowering sources of contamination. As use of antimicrobials will not affect shedding in goats or sheep, nor prevent abortion – when most of the shedding occurs – then it is important to investigate the use of vaccines in those species. There is recent evidence that use of tetracycline at dry-off will reduce the risk of shedding at calving. No commercial vaccine is available in North America, although a phase I inactivated vaccine (Coxevax, CEVA Santé Animale) licensed in Europe appears to prevent abortion and reduces shedding in goats and cattle. The vaccine can be imported into Canada by use of a biological import permit obtained from the Canadian Food Inspection Agency. Less work has been published in sheep, and to date, long-term studies of efficacy have not been published in any species. However, there is sufficient evidence that at this time vaccination is recommended as a control measure for preventing abortion and reducing risk to humans. Cats and rodents may also be a source for continuing re-contamination of the environment. The organism can remain viable in a dried state in the environment for months and be a source of reinfection. So at this time, continued vaccination is recommended until further research indicates whether the organism can be eradicated from a premise.

Q Fever in Humans

The disease in humans makes this organism very important to control in livestock. Although most people who become infected do not become clinically ill (60%), approximately 40% develop flu-like illness, with about half of those becoming ill enough to seek medical attention. Approximately 5% of people with Q fever are hospitalized. A similar percentage may go on to develop chronic Q fever. The time from exposure to clinical signs is two to three weeks but many patients do not suspect Q fever, believing instead that they have the 'flu', and may delay seeking medical attention for another week or two. Signs of acute illness include undulating fevers, headaches, malaise, nausea, rashes, shortness of breath (indicating an atypical pneumonia), sometimes hepatitis and, more rarely, meningitis. Acute Q fever is very responsive to the appropriate antimicrobial therapy (usually doxycycline) if provided in a timely manner. Pregnant women who develop Q fever are at risk of severe fetal disease and should be treated as a medical emergency. Chronic Q fever is also very dangerous to the health of humans and more difficult to effectively treat, and has a high case fatality rate. It is associated with chronic fatigue syndrome and endocarditis in people with pre-existing heart valve problems. Diagnosis is based on serological response of the patient (from a serum sample), and the level of Phase I and Phase II IgG and IgM antibodies are measured and interpreted. In a very early case, PCR performed on blood may be positive before antibodies are detected. It is important to note that many physicians are unfamiliar with the disease, and the vagueness of the signs may delay appropriate therapy.

Control of Q Fever in Humans

Because of the degree of shedding, the highest risk for human infection is likely from working with parturient small ruminants, particularly if abortion is occurring. People may become infected from inhaling contaminated aerosols, handling infected placentas and lambs or kids, from being present in the barn during parturition, and from windborne organisms from infected premises or dried organisms in the dust of barns. Biosecurity precautions are very important to reduce risk to humans. Milk from dairy ruminants on infected farms is commonly infected with *C. burnetii*, and so the consumption of raw milk is discouraged because of this. Pasteurization temperatures will kill the organism.

It is prudent for people who are considered high risk for infection, such as people with weakened immune systems (e.g. the elderly and those on immunosuppressive drugs), have pre-existing heart valve conditions, are pregnant or are very young, to lower their risk. This can be done by not attending lambings or kiddings and staying out of the area of the barn where ewes or does are giving birth.

However, Q fever can occur in healthy young to middle-aged adults, so all people should consider that they are at risk. When in the barn, all people caring for livestock should wear protective clothing dedicated for animal use. This includes coveralls or overalls, boots, coats, mittens, hats or any other piece of clothing worn in the livestock areas of the barn. That clothing should remain in the barn and not be brought to the house except in a plastic bag for laundering. Laundering of the clothing should be done carefully with hot water and soap, and no other clothing items should be washed at the same time. All lambings, kiddings, or calvings should be done wearing shoulder-length plastic sleeves and afterwards, hands and arms should be washed thoroughly with a disinfectant soap (e.g. chlorhexadine). When potentially exposing themselves to aerosolized organisms (at birthing events or when moving manure or contaminated bedding), it is advisable to wear a fitted N95 respirator which will filter out the bacteria. A renovator's mask is not sufficient.

Manure should be composted for at least three months, and only moved or spread when winds are calm

to avoid creating contaminated dust. If moved off property, the manure should be covered while transported, again to avoid exposing people to the wind-borne bacteria. Aborted fetuses, placentas or stillborn kids and lambs should be properly disposed of – e.g. covered with composting or burning if allowed. They should not be disposed of in the manure pile.

Owners and employees on infected farms, as well as service providers that must handle the animals, such as veterinarians, shearers, livestock truckers, and abattoir workers, should consider themselves at high risk of becoming infected with *C. burnetii*. In addition to taking proper precautions, they should visit a physician if they have signs of fever, malaise, headaches or lower respiratory disease. Because many physicians are unfamiliar with the disease, it is advisable to provide fact sheets on signs of Q fever and its diagnosis and treatment to the physician at the office visit. Fact sheets can be obtained from a number of online sources including the Centers for Disease Control (USA), Public Health Agency of Canada (Health Canada), and the Ontario Ministry of Health and Long-Term Care. A human vaccine is not readily available in Canada or the US, although a licensed vaccine is marketed and widely used in Australia.

Management of a Q Fever Outbreak

On occasion, both animal and human disease due to *C. burnetii* infection is significant with more than one human case occurring in a short period of time, or evidence of spread of infection beyond one farm. The Q Fever Working Group of the National Association of State Public Health Veterinarians (NASPHV) is in the process of developing a document which can be used by veterinarians to assist in managing disease in animals as well as risk to humans. The document contains details beyond the scope of this article. At the time of this writing, the recommendations are still in draft form, but should be available to interested parties by the time of the meeting presentation.

Further Reading

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