Q Fever

Query Fever, Coxiellosis, AbattoirFever

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Importance

Q fever is a zoonotic disease caused by the intracellular bacterium *Coxiella burnetii*. Although it has a wide and diverse host range, in animals this organism is primarily known as a cause of reproductive losses in domesticated ruminants. Clinical cases seem to be most significant in sheep and goats, with sporadic losses and occasional outbreaks that may affect up to 50-90% of the herd. *C. burnetii* has also been implicated in abortions and stillbirths in some other mammals, though much of this research is still preliminary. Infected animals can be difficult to recognize: nonpregnant animals do not seem to have any obvious clinical signs, and seropositivity is not always correlated with shedding of the bacteria.

Humans infected with *C. burnetii* often seroconvert without clinical signs or develop a mild, self-limited, flu-like illness. However, this organism can cause more serious syndromes, including pneumonia and reproductive losses. A few people, generally those with pre-existing abnormalities of heart valves or blood vessels, develop life-threatening sequelae. Humans commonly acquire *C. burnetii* from parturient animals, especially ruminants, which can shed large numbers of bacteria in birth products. Aerosolized organisms from these animals are sometimes spread by the wind, occasionally travelling long distances. Windborne outbreaks can affect dozens to hundreds of people who have no direct exposure to animals. In one exceptional incident, more that 4000 clinical cases were recognized in the Netherlands between 2007 and 2010. Efforts to end this outbreak resulted in temporary breeding bans and the culling of more than 50,000 small ruminants. The current state of knowledge about *C. burnetii* is incomplete, and some aspects of infections in humans and animals are still debated or not well understood.

Etiology

Q fever, which is also known as coxiellosis in animals, results from infection by *Coxiella burnetii*. This small coccobacillus is an obligate intracellular pathogen in the family Coxiellaceae, order Legionellales and gamma subdivision of the Proteobacteria. *C. burnetii* has a biphasic life cycle, alternating between a large cell variant (LCV), which is the replicating form within a cell, and a small cell variant (SCV), the non-replicating, infectious form. The SCV has an unusual spore-like structure with highly condensed chromatin, and it is highly resistant to environmental conditions. *C. burnetii* also has two distinct antigenic phases, phase I and phase II, based on changes that occur in the organism during *in vitro* culture. The primary significance of these two phases is that antibodies to phase II antigens are made during the early stages of the infection, but antibodies to phase I antigens predominate if the organism persists longer. This switch is used to distinguish acute from chronic infections in people, although it is not currently employed in animals.

Other species of Coxiella *and their impact on* C. burnetii *epidemiology*

At one time, *C. burnetii* was thought to be the only member of the genus *Coxiella*. However, several candidate species have now been recognized in reptiles (*C. cheraxi*), birds (*C. avium*) and humans (*C. massiliensis*). *Coxiella*-like bacteria are also common in ticks, and one of these organisms was recently found in horses. The newly-recognized relatives of *C. burnetii* have the potential to alter some aspects of its epidemiology For instance, *C. burnetii* is often said to occur in more than 40 species of ticks; however, the current PCR tests can also amplify *Coxiella*-like bacteria, and whether all of these ticks were truly infected with *C. burnetii* is now in doubt.

Species Affected

C. burnetii primarily affects sheep, goats and cattle, but it has been implicated in reproductive losses in cats, dogs, horses, water buffalo, deer and captive exotic ungulates, including waterbuck (*Kobus ellipsiprymnus*), sable antelope (*Hippotragus niger*) and several species of gazelle. It is also proposed to affect camels. Infections occur in many additional species not known to have clinical signs. Direct and/or serological evidence for *C. burnetii* has been reported in rodents/ small mammals, pigs, wild boar, various lagomorphs (rabbits, hares, jackrabbits), foxes, coyotes

(*Canis latrans*), raccoons (*Procyon lotor*), skunks, opossums, badgers (*Taxidea taxus*), black bears (*Ursus americanus*), European wildcats (*Felis silvestris*), wild jaguars (*Panthera onca*), captive Egyptian mongooses (*Herpestes ichneumon*), marine mammals (including seals, sea lions and sea otters), various Australian marsupials, and wild or captive exotic ungulates. This organism has also been detected in asymptomatic birds including pigeons, swallows, parrots, crows, geese, vultures (*Gyps fulvus*), black kites (*Milvus migrans*) and other species, as well as in snakes, tortoises (*Kachuga* sp.) and monitors (*Varanus indicus*). Some reviews mention that *C. burnetii* can infect fish, although there does not appear to be any published documentation of this within the last 50 years.

Sheep, goats and cattle seem to be the major reservoir hosts for *C. burnetii*, but farmed red deer are also reported to maintain this organism. Some proposed wild animal reservoirs include deer, rodents/ small mammals and rabbits, as well as three-toed sloths (*Bradypus tridactylus*) in French Guiana, and western grey kangaroos (*Macropus fuliginosus*) in Australia.

Zoonotic potential

C. burnetii is pathogenic for humans.

Geographic Distribution

C. burnetii has been found in most countries that have conducted surveillance. However, a few countries or areas, such as New Zealand, Norway, Iceland and French Polynesia, report that they have not found any evidence of this organism in surveys to date.

Transmission

Animals are thought to become infected during direct contact, via routes such as inhalation and ingestion, or by aerosols. Infectious airborne particles have been reported to travel up to 11 miles. *C. burnetii* is shed in large amounts in birth products, such as the placenta. Organisms can be shed during normal pregnancies as well as after a reproductive loss. *C. burnetii* also occurs in vaginal secretions, milk, feces and urine, and it has been detected in the semen of some species (e.g. cattle, dorcas gazelle [*Gazella dorcas neglecta*], humans and experimentally infected mice). Sexual transmission was demonstrated in mice. Infected animals do not necessarily shed organisms by all routes at any given time, and some studies have suggested that different routes might predominate in different species. *C. burnetii* can persist in some tissues including the mammary glands, supramammary lymph nodes and uterus, and ruminants may shed it in milk, the placenta and reproductive discharges during more than one pregnancy and lactation. Bone marrow and adipose tissue have also been proposed as possible sites of persistence.

C. burnetii can be transmitted by ticks and possibly by other arthropods. It has been found in a number of tick species, and transstadial and transovarial transmission has been demonstrated in some species. The importance of ticks may vary with the situation, and they are generally thought to be more significant in wildlife than domesticated herds in developed countries. *C. burnetii* is also capable of infecting mites, fleas (*Xenopsylla cheopis*, *Ctenocephalides felis* and *C. canis*), human lice, bedbugs and flies. Whether most of these arthropods can transmit this organism is unclear; however, human lice and fleas were unable to infect animals in some laboratory experiments. *C. burnetii* is capable of growing in amoebae, but whether they have any role in maintaining it in nature is not known.

People usually seem to be infected via aerosols, often when they are exposed to an animal that has given birth. Organisms may also be acquired orally from unpasteurized milk or other contaminated material. The importance of tick-borne infections is unclear, although intradermal inoculation was reported to be an efficient route of transmission in human volunteers. Humans are reported to shed *C. burnetii* by similar routes as animals, but person-to-person spread seems to be rare. There are a few reports of people who became infected when assisting during childbirths or conducting autopsies, and one pregnant woman with periodic vaginal bleeding apparently transmitted the organism to her hospital roommate. Sexual transmission was suggested in a few cases, though other sources were also possible. Blood transfusions and bone marrow transplantation have been implicated rarely, but some studies suggest the risk of transmission in blood may be low.

C. burnetii can remain viable for prolonged periods in the environment. It is reported to survive for up to 30 days in dried sputum; 120 days in dust; 49 days in dried urine from infected guinea pigs; at least 19 months in tick feces; 42 months in milk or 12-16 months on wool at 4-6°C (39-43°F); and 7-10 months on wool at ambient temperatures. Nevertheless, experiences in the Netherlands suggest that windborne human outbreaks mainly seem to occur when animals are aborting, and new infections decrease quickly after the abortions stop.

Disinfection

C. burnetii is relatively resistant to disinfectants. The infective dose is also reported to be low. Agents reported to be effective with a contact time of 30 minutes include 70% ethanol and some quaternary ammonium-based disinfectants (e.g., MicroChem-Plus®, 5% Enviro-Chem®). This organism can also be inactivated with 5% hydrogen peroxide, or by gaseous formaldehyde, 5% chloroform or ethylene gas in a sealed, humidified chamber. Variable susceptibility has been reported for hypochlorite, phenolic disinfectants and formalin. U.S. Centers for Disease Control (CDC) guidelines note that sodium hypochlorite (1:100 dilution of household bleach) or 1% Virkon S® result in greater than 90% reduction in infectivity. Although 2% formaldehyde is reported to destroy *C. burnetii*, it has been isolated from tissues stored in formaldehyde for several

months. Sources also differ on the effectiveness of Lysol®, which has changed its formulation a few times.

Physical inactivation can be accomplished by gamma irradiation or high heat, including high temperature pasteurization of milk (e.g., 161°F/72°C for 15 seconds).

Infections in Animals

Incubation Period

The incubation period is variable, as reproductive failure is usually the only sign of illness in naturally infected animals.

Clinical Signs

In ruminants, significant clinical signs seem to be limited to pregnant animals, and are characterized by abortions, stillbirths, and the birth of small or weak offspring. Reproductive losses may occur as outbreaks in sheep and goats, but they seem to be sporadic in cattle. Most abortions are reported to occur near term. Anorexia, depression, agalactia and retained fetal membranes are possible, but they seem to be uncommon, and most abortions have no significant premonitory signs. Subsequent pregnancies might sometimes be affected. Links between infection with *C. burnetii* and endometritis/ metritis or infertility have been suggested in cattle and sheep, and a possible link with subclinical mastitis has been proposed in cattle, Additional research is needed to substantiate these associations.

C. burnetii has also been implicated as a cause of reproductive losses in horses, cats, dogs, water buffalo and farmed red deer (*Cervus elaphus*), as well as captive waterbuck (*Kobus ellipsiprymnus*), sable antelope (*Hippotragus niger*), dama gazelle (*Nanger dama mhorr*) and other species of gazelles. In some cases, this organism was found in the placenta, fetus and/or vaginal secretions; however, proving a causative role is difficult because it can also be found during normal births. *C. burnetii* was detected in uterine swabs from camels with a history of abortions and other reproductive problems, and it is possible that it affects this species. Abortions and perinatal deaths have been demonstrated in experimentally infected pregnant mice.

Naturally infected animals that are not pregnant, including domesticated ruminants, seem to be infected subclinically. However, one recent review mentions the possibility of respiratory and digestive disorders when rearing kids. Experimentally infected sheep and cattle developed fever, anorexia and mild respiratory signs (e.g., mild coughing, rhinitis, increased respiratory rates) in some early research. Horses inoculated with a low dose of the organism only had a fever, but higher doses resulted in respiratory signs, conjunctivitis and enteric signs (acute gastritis, enteritis). Experimentally infected cats had a brief, self-limited febrile illness with nonspecific signs (lethargy, anorexia), while nonhuman primates, inoculated via aerosols, developed a nonspecific febrile illness and radiological signs of pneumonia. Some experimentally infected rodents had hepatitis, splenomegaly and/or respiratory signs.

Post Mortem Lesions

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C. burnetii abortions in ruminants are characterized by placentitis primarily affecting the intercotyledonary areas. The placenta is typically leathery and thickened, and it may contain large amounts of mucopurulent or purulent exudates, especially at the edges of the cotyledons and in the intercotyledonary areas. Severe vasculitis is uncommon, but thrombi and some degree of vascular inflammation may be noted. Aborted fetuses tend to be fresh, though they are occasionally autolyzed. Fetal lesions are usually non-specific, although pneumonia and microscopic evidence of hepatic necrosis or granulomatous inflammation have been reported.

Diagnostic Tests

In clinical cases, *C. burnetii* or its nucleic acids may be found in vaginal discharges, the placenta, birth fluids and aborted fetuses (e.g., spleen, liver, lung, stomach contents). Shedding in milk and colostrum can be intermittent. Blood, urine, feces and vaginal swabs are reported to be useful in screening some animals, including wildlife, for this organism.

In the placenta, organisms may be visualized in exudates or areas of inflammation with modified Ziehl–Neelsen, Gimenez, Stamp, Giemsa or modified Koster stains, but they are not usually detected by Gram staining. *C. burnetii* is acid-fast, pleomorphic, small, and coccoid or filamentous. Care should be taken not to confuse it visually with *Chlamydophila abortus* or *Brucella*. Its identity can be confirmed by immunostaining as well as other methods.

Diagnostic laboratories usually use PCR to detect *C. burnetii* in secretions, excretions and tissues. Loop-mediated isothermal amplification (LAMP) assays have also been published. Nucleic acids of *C. burnetii* can occur in the placenta after a normal delivery, or concurrently with other pathogens; thus, caution should be used when attributing a clinical case to this organism. Histopathology and quantitative PCR may be helpful in establishing a causative role. Recently vaccinated animals can excrete vaccine strains during the first month.

Isolation of *C. burnetii* is dangerous to laboratory personnel, requiring BSL 3 conditions, and culture is rarely used for diagnosis. Embryonated chicken eggs do not work as well as cells, and are no longer recommended for the initial isolation. Laboratory animals, such as mice and guinea pigs, have occasionally been employed to isolate *C. burnetii*, mostly in the past. Various genotyping methods, such as multiple-locus variable-number tandem repeat analysis (MLVA), multispacer sequence typing (MST) and single-nucleotide-polymorphisms can be useful for linking outbreaks to their source.

Serological tests including indirect immunofluorescence (IFA), ELISAs, microagglutination and complement fixation can be used to help diagnose Q fever. However, some animals do not seem to seroconvert, and others shed organisms before they develop antibodies. Thus, serology may be most useful as a herd test. Animals can remain seropositive for several years after an acute infection.

Treatment

Although some practitioners recommend antibiotics (usually tetracyclines) in flocks or herds aborting due to *C. burnetii*, there is currently no clear evidence for their efficacy. Some sources are concerned that antibiotics may promote drug resistance, possibly complicating the treatment of clinical cases in people.

Control

Disease reporting

Veterinarians who encounter or suspect Q fever should follow their national and/or local guidelines for disease reporting. This disease is reportable in many U.S. states, and state regulations should be consulted for more specific information.

Prevention

Minimizing the introduction of new stock may decrease the risk of introducing *C. burnetii* to an uninfected farm; however, this organism is readily aerosolized and it may also be carried to the premises on a windy day or enter on fomites. In an infected flock or herd, standard abortion control measures such as the use of segregated lambing/ kidding areas, and burning or burying the placenta and reproductive membranes, are expected to decrease transmission between animals. Environmental control includes regular cleaning and disinfection, particularly of areas where animals give birth; good manure management; and avoidance of activities that may generate aerosolized bacteria, such as manure spreading, during windy conditions. Good tick control is also generally recommended. Vaccines, given to animals before their first pregnancy, are used to protect ruminants from clinical signs in some countries. They can reduce but do not eliminate shedding of the organism. Vaccination may need to be carried out for several years to be effective in reducing prevalence.

Morbidity and Mortality

Infections seem to be relatively common among domesticated ruminants, although some studies have found that, in some cases, only a small percentage of the animals in a herd is seropositive. A review of surveys in cattle, sheep and goats reports that at least 15-20% of animals and herds have been exposed to this organism in many countries. High exposure rates have also been found in some nonruminant species, such as camels in the Middle East and macropods in Australia. A limited number of surveys in dogs report seroprevalence ranging from <10% to 66%.

Reproductive losses in animals can occur either sporadically or as outbreaks. Outbreaks have mainly been reported in small ruminants, though they may be uncommon even in these species except when *C. burnetii* is first introduced to a farm. During an outbreak, reproductive losses have been reported to affect 5-50% of a sheep flock, and up to 90% of the animals in some goat herds. Sporadic reproductive losses also occur in cattle, but significant outbreaks have not been reported in this species. Surveys in Germany between 1993 and 1996 attributed 0.5-4% of all abortions in cattle to *C. burnetii*. Death of the dam is uncommon in all species.

Infections in Humans

Incubation Period

In humans, the incubation period for acute Q fever ranges from 2 days to 6 weeks, with most patients becoming ill within 2-3 weeks of exposure. Chronic Q fever is reported to develop months to years after infection, although some of the latter cases could result from delayed diagnosis. Studies from recent outbreaks in the Netherlands suggest that most cases of endocarditis can be detected within a few months to a year of infection.

Clinical Signs

Acute Q fever is usually a flu-like illness of varying severity, with symptoms that may include fever, chills, a headache, fatigue, malaise, myalgia, arthralgia and a cough. The headache is often retro-orbital and may be very severe in some cases. Gastrointestinal signs (e.g., vomiting, abdominal pain, nausea, diarrhea) and a rash have been reported, especially in children. In most cases, the illness is mild. Some people with Q fever develop atypical pneumonia, with respiratory signs and pneumonitis on X-ray. More severe cases of pneumonia are also possible, especially in elderly or debilitated patients. Other syndromes can include hepatitis (usually without jaundice) or clinically asymptomatic evidence of hepatic dysfunction. Atypical pneumonia is reported to be more common in some countries, while hepatitis is the predominant form in others. Fatalities are uncommon in acute Q fever. This illness is often self-limiting in healthy people, who typically recover within one to a few weeks; however, patients with atypical pneumonia can be ill for longer.

Pregnant women may develop complications if they become infected with *C. burnetii*, especially during the first trimester. Premature delivery, and/or a low birth weight fetus, abortions and stillbirths have been reported. Reproductive losses might also be possible during subsequent pregnancies, though this is thought to be unusual. Other complications are uncommon in acute Q fever; however, there are rare reports of cardiac involvement (e.g., pericarditis, valvular vegetations, myocarditis), neurological signs (aseptic meningitis, encephalitis, polyneuropathy, myelitis), optic neuritis and

other ocular signs, bone marrow involvement, thyroiditis, pancreatitis, acute acalculous cholecystitis lymphadenopathy that mimics lymphoma, and hemolytic-uremic syndrome. A serious systemic infection was reported in one transplant patient. Chronic fatigue, sometimes accompanied by myalgia, arthralgia and other vague signs, has been reported in some people who recovered from acute Q fever. In many cases, it seems to resolve within 6-12 months.

A small number of infected people develop clinical signs related to persistent, localized infections of heart valves, blood vessels or other tissues, months or years after becoming infected. This group of syndromes is traditionally called chronic Q fever, although some authors argue for the use of more specific terminology based on the tissues affected. Chronic Q fever can be seen in people who do not recall a preceding illness as well as in those who had acute Q fever. The two most common syndromes are vascular infections and endocarditis. They usually occur in people who have pre-existing damage to blood vessels (e.g., aneurysms, vascular grafts) or heart valves, respectively. Nonspecific signs such as low-grade fever, night sweats and weight loss may be early indications in cases of endocarditis. Similar early signs, often accompanied by lumbar or abdominal pain, may be seen in vascular disease. However, some patients with these conditions are asymptomatic until severe complications develop. Vascular lesions can spread to nearby tissues, aneurysms may rupture, and embolisms that form on affected valves can cause neurological signs or other complications. Some other syndromes that have been reported in chronic Q fever include osteoarthritis, osteomyelitis, tenosynovitis, spondylodiscitis, paravertebral abscesses, psoas abscess and pulmonary lesions. Some complications resulted from the extension of a vascular lesion; others occurred independently. One elderly immunosuppressed patient developed a disseminated infection affecting multiple organs. Reproductive losses have been reported in pregnant women with untreated chronic Q fever.

Diagnostic Tests

In humans, Q fever is usually diagnosed by serology and/or PCR. PCR assays may detect nucleic acids of *C. burnetii* in a wide variety of samples including blood, serum, throat swabs, cerebrospinal fluid, urine and tissue samples from affected sites. In acute Q fever, PCR is generally useful during the first 2 weeks of the illness. It is less likely to be diagnostic as antibody titers rise. PCR is also reported to detect nucleic acids in the blood of up to 50% of patients with chronic Q fever. As in animals, isolation of *C. burnetii* is rarely attempted.

IFA, ELISAs and complement fixation are often employed for serological diagnosis, but other tests have also been used. Rising titers can provide a definitive (retrospective) diagnosis in acute Q fever. Residual antibody titers can persist for years, and IgM titers can remain high for more than a year. Antibodies to phase I and phase II antigens are used to distinguish acute Q fever from chronic Q fever. Antibodies to phase II antigens usually predominate in acute Q fever, while high and persistent levels of IgG antibodies to phase I antigens, combined with steady or falling titers to phase II antigens, are suggestive of chronic Q fever. However, the diagnosis of Q fever by serology is complex. Endocarditis has been reported in some patients with low phase I titers, while temporarily high phase I titers have sometimes been reported in acute Q fever. There are also reports of people with chronic Q fever who had very high phase II IgG titers, even exceeding their phase I IgG titers.

Echocardiograms are used to help evaluate possible endocarditis, but the lesions are subtle. *C. burnetii* antigens may be detected in tissues, such excised heart valves, by immunohistochemical staining. However, the organism can be localized to a small area of the valve and the damage may be minimal.

Treatment

Antibiotics can shorten the course of acute Q fever, and may reduce its severity. Tetracyclines are recommended most often in nonpregnant patients, but other drugs (e.g., certain macrolides or quinolones) are sometimes used. Trimethoprim/ sulfamethoxazole (“cotrimoxazole”) is often employed in pregnant women to avoid side effects from other drugs. The optimal length of treatment during pregnancy has been debated.

Treatment of chronic Q fever is more difficult. Single antibiotics are not generally effective. Tetracyclines combined with hydroxychloroquine are traditionally employed, typically for 18-24 months, but tetracyclines combined with quinolones have also been used successfully. Surgical replacement is sometimes necessary for damaged valves. Surgery seems to be important in treating infected vascular grafts or aneurysms.

Prevention

Most human cases are associated with direct or indirect exposure to ruminants. However, the placentas of animals other than ruminants, including marine mammals, may also contain large amounts of *C. burnetii.* Animals exhibited in public places should be chosen with care, as some pregnant ruminants have infected large numbers of people when they gave birth.

In general, measures should be taken to minimize human contact with infectious materials, particularly birth products but also sources such as feces. Aerosolization should be avoided, for instance by not spreading manure during windy conditions. Some manure disposal and treatment methods (e.g., covering and natural composting, closed composting with CaO or CaCN2, pasteurization or prolonged covered storage of manure) may reduce the risk of exposure. Methods used to decrease *C. burnetii* prevalence in ruminants, such as vaccination and cleaning/

disinfection, are expected to be helpful. Some countries have employed additional measures to decrease public exposure during outbreaks in ruminants. They have included temporary breeding bans, indoor housing of animals giving birth, culling of pregnant animals, depopulation of infected farms, relocation of animals away from human villages, and movement restrictions. Most of these emergency measures are not sustainable long term. Because ingestion is a potential route of exposure, unpasteurized milk and milk products should be avoided.

CDC guidelines recommend either a face mask and eye protection or a face shield for obstetricians when delivering a child from an infected woman. Contaminated materials should be handled in ways that minimize the risk or aerosolization. For instance, soiled laundry should not be shaken. More stringent personal protection, including a respirator, may be necessary during medical procedures where aerosolization is an issue. Gloves and a mask have been suggested when assisting at the birth of puppies or kittens. Recommendations to reduce human risks (e.g., CDC guidelines) have also been published for specific settings, such as laboratories that study small ruminants.

A few countries offer or recommend vaccination for people at occupational risk of exposure, or for those at elevated risk of complications (e.g., people with abnormal heart valves). People who have already been exposed to *C. burnetii* can have significant local or systemic reactions to the current vaccines, so vaccination is always preceded by serology and skin testing. No commercial vaccine is available in the U.S., although an investigational vaccine was available for the military and some other risk groups in the past, and new vaccines are being investigated.

Some experts recommend *C. burnetii* screening and/or prophylactic treatment for certain groups at elevated risk of complications. Opinions currently differ on the value of these programs, compared to alternative measures to minimize the risk of Q fever complications.

Morbidity and Mortality

Seroprevalence rates vary widely between surveys, depending on the population, country sampled and test, but range from < 5% to approximately 25% in most cases, with sporadic reports of higher seroprevalence. Approximately 50-60% of these infections are thought to be asymptomatic. Estimates of the incidence of clinical Q fever in different countries range from approximately 1 to 30 cases per million. Clinical cases can occur sporadically or as outbreaks. Some occupational risk groups include farmers, abattoir workers, researchers, laboratory personnel, dairy workers and woolsorters. Small ruminants seem to be the most frequent sources of exposure for humans. Cattle are implicated less often, and occasional cases have been linked to other domesticated animals, such as cats or dogs, and wildlife (e.g., kangaroos, sloths, rabbits). Outbreaks can occur in people with no livestock exposures, for instance when climatic conditions are favorable for winds to disperse organisms from infected farms.

Some outbreaks in European countries, such as Bulgaria, have affected hundreds of people, with the largest outbreaks involving more than a thousand people. An exceptionally large epidemic occurred in the Netherlands between 2007 and 2010. It primarily affected urban populations with no livestock contact, who were apparently infected from nearby small ruminant (especially goat) farms. Approximately 4000 cases of Q fever were reported during this epidemic, and a follow-up study suggested that these cases may have represented only 10% of all infections.

The overall mortality rate for Q fever is 1-2% in untreated cases, and lower in those who are treated. Most cases of acute Q fever are mild. About 2-5% of adults, especially those with pre-existing health conditions, are estimated to develop severe illness and require hospitalization. Higher hospitalization rates have been reported in some outbreaks, although this may also reflect underreporting of milder cases. Serious illnesses seem to be uncommon in children. Unexpectedly severe cases of pneumonia, affecting even healthy people, have been seen in French Guiana since the 1990s. Whether this is the result of an unusually virulent strain or other factors is still unclear. Most acute Q fever complications are generally not fatal; however, myocarditis has a poor prognosis, with a 25% case fatality rate in one study. The frequency of pregnancy complications in women who develop acute Q fever is uncertain. Some researchers have suggested that there is a relatively high risk, but recent reports from several European countries suggest that reproductive losses are not common.

Chronic Q fever is thought to occur in < 1% to 2% of infections, with one older study estimating 5%. It is not known whether these complications evolve directly after the initial stages of the infection, or if the organism can become dormant and reactivate. Chronic Q fever can be seen in people with no apparent history of acute Q fever, as well as in those who were symptomatic. Groups at elevated risk include those with heart valve and vascular abnormalities, as well as people who are immunosuppressed. Estimates of the risk of endocarditis when there is a predisposing abnormality of the heart valves range from 39% to 100%. Estimates of the mortality rate in treated chronic Q fever currently range from < 5% to 10% in endocarditis, and 18% to 25% in vascular infections. Mortality was historically much higher, with untreated Q fever endocarditis reported to have a case fatality rate greater than 50%. There are few studies on the long-term consequences of chronic Q fever for pregnancy, but in one report, 7 women with treated chronic Q fever subsequently had normal pregnancies.

Internet Resources

HealthDirect, Australia. Q fever (links include information on human vaccine available in Australia)
https://www.healthdirect.gov.au/q-fever

Centers for Disease Control and Prevention (CDC). Q fever
https://www.cdc.gov/qfever/

CDC. Diagnosis and management of Q fever--United States, 2013: recommendations from CDC and the Q Fever Working Group.
https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6203a1.htm

European Centre for Disease Prevention and Control. Q fever
https://ecdc.europa.eu/en/q-fever

Emedicine. Q Fever: Practice Essentials, Background, Pathophysiology
http://emedicine.medscape.com/article/227156-overview

The Merck Veterinary Manual
http://www.merckvetmanual.com/

Public Health Agency of Canada. Pathogen Safety Data Sheets
http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

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