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Review Article

Zoonotic pathogens cause of animal abortion and fetal loss

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Summary

Abortion is one of the most common disorders that decrease reproductive performance in animals, and it results in considerable economic loss to the industry. A wide range of agents, either infectious or noninfectious, can be the cause of abortion. It seems that infectious agents of abortion are more frequent than non-infectious ones in the domestic animals. Some of the infectious agents are zoonotic that could transmit from animals to humans and have an important impact on human health. Several infectious agents can cause severe disease in humans. So, besides to economic loss of abortion in the herd, its zoonotic implications regard to human consumption of farm animal products or keeping pets must be considered. The infectious agents, such as *Brucella spp, Campylobacter spp*., *Listeria monocytogenes*, *Leptospira spp.*, *Aspergillus*, *Toxoplasma gondii*, *Chlamydia spp*, and *Coxiella burnetii* are zoonotic pathogens that cause abortion in the animals. This article provides a review of the zoonotic pathogens responsible for animal abortion. Parameters necessary for disease recognition and diagnosis in humans and animals, reservoirs of infection and transmission mode, and their treatment are emphasized and described that it can help reduce the risk of increasing of zoonotic disease.

Keywords: Abortion, Animal, Human, Zoonotic pathogens

Introduction

Failure of mechanisms that control pregnancy can result in loss of pregnancy. Abortion can be defined as the delivery of immature conceptus either live or dead, before completing of gestation period. A wide range of agents, either infectious or noninfectious, can be the cause of abortion. Noninfectious agents such as chemical, nutritional, physical, and toxic can result in abortion (Noakes et al., 2018). It seems that the infectious agents are a more frequent causes of abortion in domestic animals than other agents. One of the most

important aspects of abortion in farm animal breeding is its economic consequences. Beside to economic importance of abortion in the herd, its zoonotic implications regard to human consumption of farm animal products or keeping pets must be considered. These diseases are also a problem for international commerce, and a serious economic loss for farmers and can have wide consequences for public health. Infectious agents that resulted in abortion can be divided into protozoal, bacterial, viral, and fungal categories. With the aim of knowledge and control of these disorders, this review article has been focused on zoonotic agents of abortion in farm animals (Givens and Marley, 2008; Noakes et al., 2018).

1. Bacterial agents

1.1. *Brucella*

a gram-negative Intracellular coccobacillus microorganism which can affect many species, including farm animal as well as human (Capasso, 2002). The genus Brucella consists of six recognized species include: *B. melitensis*, *B. suis*, *B. ovis*, *B.abortus*, *B. neotomae*, and *B. canis*. Distribution of Brucella is worldwide, and the widest spared species are *B.abortus* and *B. suis* (Poester et al., 2013).

Infection with this bacterium in animals can result in abortion. The main pathogen in cattle is *B.abortus*, which is found worldwide (Poester et al., 2013). Although it must be mentioned, bovine brucellosis has been eradicated in most of the European countries such as Finland, Germany, Norway, Sweden, Denmark, Netherland, Belgium (Spinage, 2012). The prevalence of bovine brucellosis in dairy cattle is higher than beef cattle. The rout of infection in cattle is the ingestion of aborted material or genital discharge of aborted cow or contaminated pasture, water, or food (Aparicio, 2013; Enright, 1990). *B. abortus* causes inflammation of the endometrium and placenta and abortion. Retained placenta is a common consequence of Brucellosis in cattle (Aparicio, 2013). Sheep and goat brucellosis is a severe problem in the Mediterranean basin of Africa, Asia, and Europe (Thimm, 2013). *B.melitensis* causes abortion in late gestation, stillbirth and delivery of weak lambs. The lesions of the placenta are similar to those detected in infection with *B.abortus* in cattle. Inflammation of the placenta, necrotic, and edematous cotyledon and leathery appearance can be identified in the inspection of aborted materials (Aparicio, 2013; Blasco and Molina-Flores, 2011). In cases of horse infection, *B. suis* and *B. abortus* has been isolated. Clinical manifestations of brucellosis in horses are fistulous bursitis, “fistulous withers”, and “poll

evil." The occurrence of abortion in the horse is rare. Transmission of infection from cattle or swine to horse or inversely has been proven. Transmission of infection horse to horse is unknown. (Mair and Divers, 2009). Although in cases of canine Brucellosis, *B. abortus* and *B. suis* have been isolated, but the main pathogen in the dog is *B.canis* worldwide. The signs of canine brucellosis include prolonged Non-febrile bacteremia, abortion to day 50 of pregnancy, embryonic death in early gestation, prostatitis, scrotal dermatitis, lymphadenitis, and inflammation of the spleen. In some cases, dams delivery dead pups at the end of full-term pregnancy or pups die a few days after born (de Oliveira et al., 2019). Cat is resistant to Brucella infection, and the occurrence of the natural disease is unknown.

Brucellosis in human

Humans are susceptible to infecting by *B. melitensis*, *B. abortus*, and *B. suis*. The most invasive pathogen is *B. melitensis* that followed by *B. suis* and *B, abortus* in descending order. Generally, the incubation period is between 1 to 3 weeks, although it may last for several months. (Doganay and Aygen, 2003; Franco et al., 2007). Brucellosis in humans is a septicemic illness accompanied by an intermittent or continued fever, fatigue, and chills. The body temperature may be normal in the morning but may increase to 40 °C in the afternoon. Sweeting with a peculiar odor may occur at night. Other symptoms are sexual impotence, insomnia, constipation, headache, arthralgia, anorexia, and general malaise. The illness has considerable effects on the nervous system. Symptoms of nervous system impairment include nervousness, irritation, and depression. Hepatosplenomegaly and hepatomegaly are frequent in patients infected by *B. melitensis*. Enlargement of the peripheral lymph node is detectable in many patients who have been affected by brucellosis (Franco et al., 2007; Sohn et al., 2003). The duration of illness varies from a few weeks to several years. Brucellosis in humans can produce serious complications includes meningitis, encephalitis, spondylitis, peripheral neuritis, vegetative endocarditis, supportive arthritis, seminal vesiculitis, orchitis, and prostatitis. In some patients, chronic form of brucellosis may occur, which can last for many years. In chronic brucellosis, the localized foci of infection may present or not. Symptoms of this form are associated with hypersensitivity. It is usually hard to diagnosis chronic brucellosis. For the treatment of acute brucellosis, a daily dose of rifampicin (600 to 900 mg per day) combined with doxycycline (200 mg per day) for a period of time at least six weeks has been recommended. If antibiotic therapy is unsuccessful, a chronic form of brucellosis must be suspected, especially with *B.abortus*

and *B.suis* infection (Franco et al., 2007; Roushan et al., 2006).

Reservoirs of infection and transmission mode

The natural reservoirs of *B.suis*, *B. abortus*, *B.canis*, and *B.melitensis*, are respectively swine, cattle, dog, goat, and sheep. Transmission of infection from animal to human occurs through direct contact, inhalation of airborne microorganisms, and ingestion of farm animal products. The most common pathway for transmission of infection from animals to humans is the consumption of raw milk or fresh cheese from sheep and goat, which has infected by *B. melitensis*. Sporadic brucellosis occurs following the consumption of milk from a cow, which has infected by *B. abortus* or *B.suis***.** The bacteria rarely survive in sour cream, butter, sour milk or fermented cheese. Another possible pathway for transmission of infection is contaminated water with infected animals' excreta or raw vegetables. Human brucellosis is mostly an occupational disease of veterinarians, butchers, and slaughterhouse workers. Infection usually occurred in case of handling of a conceptus or fetal membranes, contact with excreta, carcasses of infected animals, and vaginal secretions. The bacteria can enter through the conjunctiva and skin abrasion (Doganay and Aygen, 2003; Franco et al., 2007).

1.2. *Leptospira*

Leptospirosis is also known as Weil's disease, rice field disease, swamp fever, cane-cutter's disease, and swineherd's disease. Leptospira is a spiral-shaped, motile, aerobic, and culturable bacteria. Leptospira has been distributed worldwide. Two species of *leptospira*, which has been recognized are *L. intterogans* and *L. biflexa*. *L. intterogans* is important in term of transmission between animal and man. This species has more than 200 serovars all over the world. Some of these serovars are universal, such as *L. intterogans* serovar canicola or serovar icterohaemorrhagiae. The prevalence of leptospirosis is high in tropical regions with neutral or alkaline soil and rainfall weather (Ellis, 2015).

Leptospirosis in animal

In cattle, at least 13 serovars has been recognized. Pomona, hardjo, and grippotyphosa are predominant serovars in cattle. Infection with Icterohaemorrhagiae and canicola is found in cattle (Ellis, 2015). Leptospirosis in cattle may remain clinically inapparent or cause acute or subacute disease. Clinical signs include fever, which lasts for 4 or 5 days, anorexia, diarrhea, and conjunctivitis (Ellis, 2015; Kingscote, 1985). With the formation of antibody, leptospires begin to disappearing and approximately one week later, completely disappeared form the

bloodstream because of humoral immunity. The chronic phase of infection begins with the harboring of survival leptospires in convoluted tubules of the kidney. Then leptospires shed with urination in the outside environment, especially in the first month of infection. This shedding of bacteria gradually decreases and finally ceased. In case of infection with hardjo serovar, two syndromes may occur. The first syndrome is a severe reduction in milk production or agalactia. The second syndrome is abortion or delivery of weak calves. Abortion usually occurs 1 to 3 weeks after the beginning of the disease. Up to 20% of aborted cows have retained fetal membranes (Yadeta et al., 2016). Recommended treatment for acute leptospirosis is the administration of high dose of tetracycline or penicillin G or Dihydrostreptomycin (12.5 mg/kg twice daily for a day) the intramuscular injection of sodium ampicillin (25 mg/kg twice a day) can be used. Epizootics in sheep and goats are not as frequent as in other species. The infection is characterized by fever, anorexia, anemia, and jaundice in some cases, hemoglobinuria, abortion, stillbirth, delivery of weak lambs, and infertility. The recommended treatment is an intramuscular injection of dihydrostreptomycin (25 mg/kg) (Ellis, 2015; Yadeta et al., 2016).

Leptospirosis in human

Humans are susceptible to infected by lots of serovars. Generally, the incubation period is between 1 to 2 weeks. The infection has two phases, contain the bacteremic phase, which lasts 7 to 10 days and the bacteriuric phase, which lasts one week to several months. Generally, two clinical types of illness are distinguished includes the icteric and anicteric. The anicteric type is much more frequent than icteric type (Weil's Disease). The onset of clinical manifestation of icteric type is sudden and include: fever, conjunctivitis, headache, myalgias, nausea, vomiting, and constipation or diarrhea. Petechiae on the integument, hemorrhages in the alimentary tract, and proteinuria are frequent. Jaundice and Hepatomegaly, renal insufficiency with considerable anuria or oliguria, electrolyte imbalance, and azotemia develop by the disappearance of bacteria form the bloodstream. With the improvement of patient condition, jaundice decreases, and diuresis is reestablished. In anicteric type, symptoms are milder than icteric type. The symptoms during bacteremia are fever, myalgias, conjunctivitis, nausea, and occasionally vomiting and stiffness of the neck are present. Leptospiruria may prolong for a week or several months after the elimination of clinical symptoms (Haake and Levett, 2015). For prevention of tissue lesions, treatment must be started as soon as possible. It has been reported amoxicillin and

Penicillin G are effective even one week later after the onset of a clinical symptom of the disease (Haake and Levett, 2015; Murray et al., 2004).

Reservoirs of infection and transmission mode

A week after leptospiremia, infected animals begin to shed bacteria by urination, contaminating the environment. The infection in animals and man is contracted directly through skin abrasions and the conjunctival, nasal and oral mucosa, or indirectly through exposure through soil, food, or water contaminated by infected animals' urine is the most probable route. Working with livestock often results in exposure to animal urine indirect route or as an aerosol. Domesticated animals, especially swine and cattle, are an important source of leptospire and frequently cause infection in humans in many countries. Water contamination by rodent urine may cause infection in rice-paddy workers (Haake and Levett, 2015; Steneroden et al., 2011).

1.3. *Listeria*

Geniuses of *Listeria* contain seven species. Two important species for humans and animals are *L.monocytogenes* and *L. ivanovii*. *L.monocytogenes* is a facultatively anaerobic, gram-positive bacillus that is distributed worldwide. This microorganism can be found in soil, the vegetables, animal, and human intestine (Gray et al., 2006; Letchumanan et al., 2018).

Listeriosis in animal

Listeriosis in ruminant may result in encephalitis, septicemia, and neonatal mortality. The most frequent clinical form of the disease is encephalitis (Erdogan et al., 2001; Wesley, 1999). Signs of listerial encephalitis contain depression, lack of coordination, fever, torticollis, paralysis and spasmodic contractions of the throat, and facial muscles, strabismus, conjunctivitis, profuse salivation, trying to lean against something while standing, and walk in circles. In the final stage of the disease, animals are recumbent and have characteristic chewing movements when trying to eat. Listerial encephalitis affects animals in all ages, but its occurrence is more frequent in the first three years of life. Septicemia in young animals is much more frequent than the adults. In general, the only sign of genital infection is abortion, which mainly occurs during the last month of pregnancy. The occurrence of uterine infection prior to the seventh month of gestation in cow results in retention of the macerated fetus in the uterus for several days. Retention of fetal membranes and metritis may occur as consequences of infection (Schweizer et al., 2006; Wesley, 1999). By the occurrence of infection during final month of gestation, fetus

shows no particular lesions. The occurrence of mastitis in a cow following infection with *L. monocytogenes* has been reported (Winter et al., 2004).

Listeriosis in human

Incidence of Listeriosis in human is low, but because of high mortality rate is an important disease. The most vulnerable group are newborns, followed by over 50 years of older people. The occurrence of the disease in the age range of 1 month to 18 years old is very rare. Listeriosis in pregnant women usually causes abortion in the second half of pregnancy, especially in the third trimester of gestation. Symptoms precede a few days or a week before abortion or birth, may include: increased body temperature, chills, slight dizziness, cephalalgia, and occasionally gastrointestinal symptoms (Craig et al., 2019; López et al., 2007; Mateus et al., 2013). These episodes of septicemia before delivery of a stillbirth fetus or the seriously ill neonate may be recurrent or not. Although after parturition mother does not show the symptoms of the disease, but *L. monocytogenes* can be isolated from urine, vagina, and cervix for a few days to several months. Infected Neonates who are born alive may show symptoms of sepsis or disseminated granulomatosis, which is less frequent, immediately after parturition or a few days later. The case fatality rate is high. In some cases, neonates born apparently healthy but after a few days or several months, fall ill because of meningitis. Meningoencephalitis or meningitis is the most frequent clinical form of listeriosis in adults. Additionally, listeriosis may cause endocarditis, endophthalmitis, internal, and external abscesses (Craig et al., 2019; López et al., 2007; Mateus et al., 2013). For the treatment of maternal-fetal listeriosis, ampicillin has been recommended. For other forms of listeriosis, ampicillin, tetracycline, chloramphenicol may be used (Lamont et al., 2011; Temple and Nahata, 2000).

Reservoirs of infection and transmission mode

The causal agent of infection is distributed widely in humans, animals, and the environment. *L. monocytogenes* has been isolated from soil, plants, stream, and wastewater (Buchholz and Mascola, 2001; Lamont et al., 2011). Many animal species, such as sheep and cattle, eliminating bacteria in their feces. Although the range of natural reservoirs is wide, but few humans get the infection. It has been clarified that many females who shed the bacteria in their stools delivery healthy babies. Concurrent Predisposing factors such as stress, disease or immunosuppressive treatments play an important role in initiating the infection. The infected mother is the source of infection for the newborn and fetus. Transmission through

oral route seems to be important regards to recent outbreaks (in human population) in Switzerland, France, and the USA. Ingestion of contaminated meat, vegetables, and milk, or milk products are the vehicle for transmission of the infection (Buchholz and Mascola, 2001; Lamont et al., 2011; McLauchlin, 1987).

1.4. *Chlamydia*

Genus *Chlamydia* has four species: C. *pneumonia, C. trachomatis, C.psittaci*, and *C. pecorum*. Chlamydia is an intracellular microorganism with a reproductive cycle that consists of two phases, which one of them is infectious. *C. trachomatis* cause keratoconjunctivitis and infection of the genital tract in humans. Infection with *C. pneumonia* results in pulmonary disease in humans. *C. psittaci* is the causative agent of psittacosis in birds and several illnesses in mammals. The human can infect by *C. psittaci* accidentally, so this species has zoonotic importance. *C. pecorum* causes bovine encephalitis, pneumonia, and enteritis and also ovine arthritis. Chlamydia is distributed worldwide (Shewen, 1980).

Chlamydiosis in animal

Infections with *C. pcittaci* in birds are mostly unapparent and latent. Since stress reduces the bird's resistance, it can predispose factors for clinical manifestation of the disease. The symptoms of the disease, such as fever, loss of appetite, diarrhea, and emaciation are not characteristic. *C. pcittaci* cause keratoconjunctivitis, abortion and other diseases in mammals. Chlamydophila abortus (formerly *C.pcittaci*) is one of the most important causes of abortion in sheep and goat. There are no signs of systemic disease in pregnant ewes. Although a small proportion of ewes abort in the first trimester of pregnancy, but most of the abortions occur in the last three weeks of pregnancy (Szeredi and Bacsadi, 2002). Chlamydial Abortion is in association with necrotizing placentitis. The necrotic changes in the cotyledons of ewes that have aborted close to term referred to infection with *C.pcttaci*. Infection with this microorganism in rams can result in orchitis and seminal vesiculitis. Infected rams are shedding the microorganism in their semen. Besides abortion, *C.pcittaci* may also cause polyarthritis and pneumonia in sheep and goat (Shewen, 1980).

Chlamydiosis in human

The period of incubation is ranging from one to two weeks and sometimes longer. Many infections have no clinical manifestation, while with others, the severity of clinical symptoms can vary widely. A mild form of infection resembles common respiratory disease, and consequently often goes

unnoticed. The onset of disease can be sudden, with fever, sweating, chills, loss of appetite, myalgia and headaches. The symptoms of the disease last for 7 to 10 days. In cases with atypical pneumonia, radiology shows infiltration and patch of consolidation (less often) of the inferior part of the lung, which can develop into bronchopneumonia. Patients who are over age 50 exhibit the most acute form of illness. Patients with the most severe form of illness may have vomiting, enlargement of the spleen and liver, constipation, diarrhea, disorientation, mental depression, insomnia, and even delirium. In countries such as Great Britain, where enzootic abortion is caused by *C.pcittaci* in sheep and goats, pregnant women can get the infection from these animals at any point of gestation (Meijer et al., 2004). In some these cases, fever, dysfunction of liver and/or kidney, and disseminated intravascular coagulation has been reported. The importance of early treatment for prevention of complications and shortening the duration of illness must be considered. Administration of tetracycline as long as the existence of fever and 10 to 14 days after that is recommended. Since tetracycline is contraindicated in child under the age of eight and pregnant women, erythromycin can be used. With proper treatment, the case fatality rate would be lower than 1% (Miller, 2006; Shewen, 1980).

Reservoirs of infection and transmission mode

The natural reservoirs of *C.pcittaci* are domestic and wild birds. This microorganism is the causative agent of enzootic abortion in ovine and caprine. These animals are shedding the microorganism in a large quantity through their placenta and feces. By handling these materials at the site of parturition or slaughterhouse by pregnant women, they would be infected. This infection is also seen in non-pregnant women and people who are in contact with these animals because of their occupations such as veterinarians. The infection can transmit from birds to humans by inhalation of an air-born microorganism in contaminated environments. Sporadic cases of Chlamydiosis in humans because of the transmission of the infection from psittacines and other decorative or companion birds, has been reported. Chlamydiosis, because of coming in contact with birds, is also an occupational illness of geese and duck pluckers, workers of turkey-processing farms, and pigeon breeders (Meijer et al., 2004; Shewen, 1980).

2-Fungal agents

Aspergillus

Aspergillosis is also known as pneumonomycosis and bronchomycosis (in animals). *A. fumigatus* and other species such *as A. flavus, A. niger, A. nidulans, and A. terreus* are saprophytic fungi. These funguses

are ubiquitous and distributed widely in the world. The occurrence of aspergillosis in humans is sporadically and uncommon. Sporadic occurrence of aspergillosis has been reported in many wild and domestic animals and birds. The economic aspect of the disease in cattle and fowl should be considered. Outbreaks in young turkeys and chicks can result in significant losses (Tell et al., 2019).

Aspergillosis in animal

Aspergillus is the cause of 75% of mycotic abortions in cattle. If campylobacteriosis, trichomoniasis, and brucellosis get under control, the relative role of mycotic agents as the cause of abortions increases. Abortion because of mycotic agents is mainly seen in stabled cattle, so it occurs in cold weather. Generally, abortion occurs in one or two cows of the herd. The pathogenesis of the infection has not been well clarified. It is thought that fungus is primarily localized in the digestive or respiratory tract, and then the agent could invade the placenta through the bloodstream and would result in placentitis. The fungus may invade to the fetus. Retention of the fetal membrane is a common sequel. Pulmonary aspergillosis in horses is relatively rare. As in cattle, the infection is associated with abortion. Disseminated aspergillosis rarely occurs in dogs (Elad and Segal, 2018; Sarfati et al., 1996; Tell, 2005). The infection is characterized by granulomas in many organs, especially in the spleen, kidney, and bones. The occurrence of acute aspergillosis in chicks and young turkeys occasionally cause significant losses. The diseases characterized by Yellow granulomas in the lung and development of plaques in the air sacs (Seyedmousavi et al., 2018).

Aspergillosis in human

Aspergillosis occurs in patients with chronic disease (such as tuberculosis, diabetes, cancer), immunosuppressive disease, as well as in patients who are treated with antimetabolites, antibiotics, and corticosteroids for a long period. Aspergillosis has two differentiated clinical Manifestations, which include: invasive and localized. Aspergillosis is essentially characterized as infection of the respiratory system, which is acquired through inhalation of fungus conidia (Elad and Segal, 2018). In children who inhale a lot of conidia may manifest fever, and military infiltration, dyspnea. Allergic bronchopulmonary aspergillosis might develop in a patient who suffering from asthma with intermittent bronchial obstruction and eosinophilia. Another form of infection is aspergilloma, which developing by fungus colonization in respiratory cavities of a patient with the preexisting disease (bronchiectasis, bronchitis, tuberculosis). However,

aspergilloma is relatively benign but sometimes produces hemoptysis. Otomycosis and invasion of fungus to the paranasal sinuses are other forms of the infection. The cutaneous Aspergillosis may develop in immunodeficient patients. In an invasive form of infection, which is usually very serious, fungemia occurred, and fungus spared throughout the body through the bloodstream. The invasive form of aspergillosis occurs merely in patients with neutropenia (Latgé and Chamilos, 2019; Segal, 2009).

Reservoirs of infection and transmission mode

Soil is the reservoir of microorganism. The infective particle of fungus is conidia (exospore), which is transmitted to animals and humans through the air. Regarding the natural resistance to the infection, the occurrence of disease in humans is not frequent. The factors that could cause impairment of the immune system or immunosuppressant medications would decrease the natural resistance to the disease. One of the most important sources of infection is bedding and fodder, which is contaminated by the microorganism in birds, domestic animals, and people who work with them. Apparently, exposure should be massive or prolonged for the establishment of the infection (Sarfati et al., 1996; Segal, 2009).

3. Protozoal agent

Toxoplasma

Toxoplasma gondii is the infective agent. *T.gondii* completes its life cycle in the intestine of felines. *T.gondii* takes advantage of any 200 species vertebrates as intermediated hosts. The human can be an intermediate host for this microorganism, which makes this parasite medically important (Dubey and Beattie, 1988). By ingestion of parasite by felines, they invade enterocytes and multiply asexually and sexually, respectively and produce immature oocytes that cause the enterocytes to rapture. Then the oocysts are eliminated in the feces. Depends on the humidity and the temperature of the environment, maturation of oocyte occurs in 1 to 5 days. By the entrance of mature oocyte in the human or cat as an intermediate host, the parasite would release in the small intestine and invades the enterocytes where they proliferated until rupture the enterocytes, then disseminated through the bloodstream or lymphatic system. In the active phase of infection, the cycle of invasion and multiplication of tachyzoites continue for 1 to 2 weeks until developing of a degree of immunity in the host body. Following that, parasites as bradyzoites begin to replace in the tissues and form cyst, especially in nerve and muscle tissue in the latent phase. By ingestion of cystic tissue by felines, the evolutionary cycle starts again (Dubey and Beattie, 1988; Tenter et al., 2000).

Toxoplasmosis in animal

Disease in animals is prevalent, but the clinical manifestation is infrequent. Toxoplasmosis is particularly important in goat and sheep because it causes illness in newborn animals and abortion of the fetus. Lambs with congenital infections are physically weak with a lack of muscular coordination and are unable to feed themselves. Congenital infection of lambs occurred only when the dam is infected during gestation. If the infection of conceptus occurs in the range of 45 to 55 days of pregnancy, it usually results in death. The occurrence of conceptus infection during the third month of gestation results in the delivery of alive but sick lambs. With the occurrence of infection after four months, newborn lambs may be infected but asymptomatic. In adult sheep, disease is rare (Dubey and Beattie, 1988; Hill and Dubey, 2002). The rate of infection is high in dogs and cats. Clinical signs of toxoplasmosis in the dog can resemble distemper. The rate of infection is also high in cats. Both systemic and intestinal infections are asymptomatic in cats. Toxoplasmosis in birds is frequent but symptomatic infection is rare (Tenter et al., 2000).

Toxoplasmosis in human

Postnatal infection with *T. gondii* usually causes a mild disease. Most of the infections are asymptomatic, about 90% of symptomatic infections produce mild fever, asthenia, and persistent lymphadenopathy. Toxoplasmosis should be differentiated from influenza and infectious mononucleosis because of the similarity of symptoms. Patients with symptomatic infection would spontaneously recover in a few weeks or months. Neurological symptoms, such as cephalalgia, facial paralysis, lethargy, hemiplegia, coma, and severe reflex alterations are observed in 4% of symptomatic patients. A small percentage of symptomatic patients may have muscular signs such as weakness and myositis. It has been reported that toxoplasmosis can result in myocarditis and pneumonitis, but such these cases are not common (Navia et al., 1986). An ocular form of toxoplasmosis whit subsequent uveitis may be occurred in adolescents either as a delayed manifestation of postnatal infection. Encephalitis following infection with *T.gondii* in Immunodeficient patients is common. Pneumonitis and Retinitis following infection with *T.gondii* in acquired immune deficiency syndrome (AIDS) patients are also frequent. Congenital toxoplasmosis can result in severe disease and sequelae, but it is not frequent (Hill and Dubey, 2002; Navia et al., 1986; Tenter et al., 2000). Fetal infection occurs when a mother acquires a primary or acute infection during gestation, which results in parasitemia and transplacental transmission. Since infection causes generation of long-life

immunity, the intrauterine transmission of parasite would not occur in the next pregnancies unless the mother is intensively immunocompromised. By early transmission, in the gestation period, few cases of fetal infection would occur, but the risk of severe disease of the fetus is great. Early infection may result in prior or after born death or intense damage to the fetus. Late infection can result in generalized illness in utero, followed by the invasion of the nervous system, and birth of babies with sequelae such as chorioretinitis, cerebral calcifications and hydrocephaly (Tenter et al., 2000).

Reservoirs of infection and transmission mode

The human can infect in utero or postnatally. It has been estimated that less than 0.1% of adult patients infect congenitally. After birth, humans as an intermediate host, can acquire infection by ingestion raw or undercooked meat, particularly lamb or pork, or by ingestion of mature oocytes from the earth, food or water, which is contaminated with the feces of infected felines, especially the cat. Sheep, as one of the most important sources of infection for humans, acquired infection only by the ingestion of oocytes. So apparently, cat and other felines have a significant role in the contamination of pastures. It appears the main source of infection for felines are birds and rodent, which have bradyzoite cysts in their tissues (Hill and Dubey, 2002; Tenter et al., 2000).

4. Rickettsia agent

Q fever

Also known as pneumorickettsiosis, coxiellosis, Balkan influenza, abattoir fever, and nine-mile fever. The causative agent is *Coxiella burnetii* (*Rickettsia burnetii*), which is a strict intracellular microorganism. The presence of eukaryotic cells is necessary for its development. Gimenez staining is useful to identify *C. burnetii*. Its distribution is worldwide (Angelakis and Raoult, 2010b; Maurin and Raoult, 1999).

Q fever in animal

Infection in domestic animals has no clinical manifestation. In ruminant, *C.brunetti* becomes localized in the placenta, supramammary lymph nodes, and mammary glands following its invading to the bloodstream. Infection eliminates in many cows after a few months, but others may become carriers and shedding the microorganism through the lactation period. Shedding of large quantities of microorganism through the placenta and to a lesser extent, the amniotic fluid, feces, and urine during parturition occur. *C.brunetti* causes abortion and stillbirth in the final stage of gestation and ranges from 3 to 80%. Strong resistance of

C.brunetti causes its survival in the environment as well as the occurrence of infection in new susceptible humans or animals (Angelakis and Raoult, 2010b; Marrie, 2007).

Q fever in human

The incubation period is ranging from 14 to 39 days. The onset of illness is sudden with fever, profuse sweating, chills, anorexia, myalgia, malaise, nausea, and vomiting. Severe cephalalgia is a prominent symptom of illness and the occurrence of retro-orbital pain is frequent. About 50% of the patient's radiography findings reveal pneumonitis. Nearly half of the cases have alimentary tract disturbances such as diarrhea, nausea, and vomiting. Infection can cause acute hepatitis. Unlike other rickettsioses, Q fever does not cause a cutaneous rash. The severity of the disease varies over a range, but often is mild. A large number of human infections are unapparent and go unnoticed. In humans, Q fever can lead to abortions and stillbirth in pregnant women (Angelakis and Raoult, 2010a; Guatteo et al., 2011). The occurrence of Q fever in children under age of eight is rare. The illness is more severe in adults over 40 years of age. In the chronic form of Q fever, the cardiovascular system is affected. The case fatality rate of chronic form is 65%. In a retrospective study, which designed in France, 259 out of 313 cases of chronic Q fever had endocarditis. Endocarditis is the most dangerous complication of disease because it often is fatal. Most patients with an acute form of illness heal spontaneously. However, because of the possibility that it can become chronic, treatment is necessary. Administration of tetracycline or its derivatives, especially doxycycline, for 2 or 3 weeks is recommended. For the treatment of chronic form, several regimes such as a combination of doxycycline and rifampicin or tetracycline, and trimethoprim-sulfamethoxazole have been proposed (Angelakis and Raoult, 2010b; Berri et al., 2007).

Reservoirs of infection and transmission mode

There are two cycles of the infection in nature, one in natural foci, where the circulation of agent occurs between ectoparasites, particularly ticks and wild animals, and the other in domestic animals, mainly sheep, goat, and cattle. The relationship between these two cycles is not well studied. But it has been proposed infection could be transmitted to domestic animals through infected ticks which come from natural foci. The most frequent mode for transmission of infection between domestic animals is the inhalation of aerosols from contaminated afterbirth materials. Domestic animals and their contaminated

products, such as wool and leather are the main source of infection for humans. Handling of placentas, fetuses, uteruses, and wool causes generation of aerosols, which is the main mode for transmission of microorganism. So people who are in contact with infected animals and/or their contaminated products because of their occupation (such as veterinarians and workers of abattoirs) are most likely to acquire the infection (Guatteo et al., 2011; Marrie, 2007).

Conclusion

Beside economic loss of abortion in the herd, its zoonotic implications regard to human consumption of farm animal products or keeping pets must be considered. The recognition and diagnosis of zoonotic abortive pathogens can help reduce the economic loss in farm animals and the risk of the increasing of zoonotic disease.

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Conflict of interest statement

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Ethical approval

No applicable

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