

AVAILABLE CONTROL MEASURES FOR Q FEVER IN SHEEP

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Review paper

Abstract: Q fever is a worldwide zoonosis caused by Gram-negative bacteria, *Coxiella burnetii*. This antropozoonosis is characterized by a wide spectrum of hosts and vectors. Primary role of domestic animals as reservoirs of human infections emphasizes the accurate prompt detection of Q fever in domestic animals. This microbe can survive for months and even years in dust or soil. Sanitation of endemic foci of Q fever is practically pretty close to impossible because of the high resistance of the causative agent, small infectious dose and various epidemiologies. Within the group of zoonoses, Q fever takes a leading position in the region of Vojvodina. This is why Q-fever is considered a specific problem of this province. Control programs against Q fever in sheep and cattle, most frequently recommend serological examination and vaccination of animals. In animals, the most effective vaccines are those composed of inactivated whole phase I bacteria. Bacterial shedding in placental tissue and milk was reduced in experimental infection or in natural *C.burnetii* infection of sheep and cows vaccinated by phase I vaccines. One of the recommended measures is excluding positive reactors from the flock followed by continuous monitoring and separation of seropositive animals. Milk from seropositive cows must be pasteurized. The aim of the vaccination after lambing season, is to prevent new infections until next lambing of young animals, which were not pregnant. Well-timed sequential vaccination before pregnancy reduces the risk of *C.burnetii* infection, highly prevents the abortions decreases the shedding rate of *C.burnetii* after the abortion.

Key words: Q-fever, sheep, epidemiology, control

Introduction

Q fever is a worldwide zoonosis caused by Gram-negative bacteria, *Coxiella burnetii*. This antropozoonosis is characterized by a wide spectrum of hosts and vectors (Savić *et al.*, 2013). Animals such as cattle, sheep, and goats can

carry the Q fever microbe in tissues involved in birth--the uterus, placenta, and birth fluids. Infected animals also release the microbe in milk and manure. These particles are infected with a major route of infection for humans and animals. This microbe can survive for months and even years in dust or soil. *C. burnetii* is one of the most resistant of all non-sporulating bacteria. Sanitation of endemic foci of Q fever is practically pretty close to impossible because of the high resistance of the causative agent, small infectious dose and various epidemiologies. As regards disease transmission, agent inhalation in the dust is of much more importance than a vector-born disease spread by ticks.

Primary role of domestic animals as reservoirs of human infections emphasizes the accurate and prompt detection of Q fever in domestic animals (*Schliesser and Schmid, 1970; Biberstin et al., 1974; Rašeta and Mihajlović, 1983; Beaudeau, 2010*). Positive reactors are found in sheep, cattle, goats, swine, horses, poultry and cats (*Macellaro et al., 1993; Vidić et al., 1990; EFSA J., 2010*). From clinical point of view, Q-fever is not a negligible issue in veterinary medicine. The miscarriages have been registered primarily in sheep, cattle and goats, as well as some other reproductive disorders such as mastitis, poorly viable offspring, etc. (*Biberstin et al., 1974; Vidić et al., 1990b; Vidić et al., 1999; Boboš et al., 2011*;) which might lead to non-negligible economic losses infected herds (*Vidić et al., 2013b*).

Successful suppression and prevention of Q fever infections cannot be accomplished using common general preventive measures, and adequate specific prevention is not yet available worldwide. Control programs against Q fever in sheep and cattle, most frequently recommend serological examination and vaccination of animals (*Vidić et al., 1990; EFSA J., 2010; Hogerwerf et al., 2011*).

The main problem in Q fever prevention is the lack of adequate and specific protection measures as well as poor efficiency of general preventive measures. High rate of positive reactors among sheep, nomadic pastoralism and grazing system in sheep farming are major factors that negatively influence the epidemiological situation of Q-fever in Vojvodina (*Šeguljev et al., 1988; Vidić et al., 1996*). Seroepizootiological investigation in Vojvodina revealed higher prevalence of Q fever in sheep than in cattle (*Šeguljev et al., 1988; Vidić et al., 1996*). In Vojvodina Q fever persists in an endemic-epidemic form (*Šeguljev et al., 1997*).

Within the group of zoonoses, Q fever takes a leading position in the region of Vojvodina (*Šeguljev et al., 1993; Vidić et al., 1996*). This is why Q-fever is considered a specific problem of this province. Up to the beginning of 90s, Q-fever was a leading zoonosis in Vojvodina. Large epidemics of Q fever followed the line of nomadic sheep flocks movement. Since sheep are the main reservoir of the disease, Q fever demonstrated pronounced seasonal incidence with about 90% of affected patients at the end of winter and beginning of the spring, during the lambing season (*Šeguljev et al., 1993*). Since 1991, the number of

patients with Q fever has significantly decreased, therefore, during the last ten years, the average incidence is 0.82/100000 (*Vidić et al., 2012*). Q fever can now be seen as small family epidemics among owners of domestic animals and without pronounced seasonal character (*Vidić et al., 2013*).

Control measures

Successful suppression and prevention of Q fever infections cannot be accomplished using common general preventive measures, and adequate specific prevention is not yet available worldwide. High resistance of *C.burnetii* in the environment and various epidemiologies makes the sanitation of endemic foci almost impossible. In animals, the most effective vaccines are those composed of inactivated whole phase I bacteria. Bacterial shedding in placental tissue and milk was reduced in experimental infection or in natural *C.burnetii* infection of sheep and cows vaccinated by phase I vaccines (*Behumer et al., 1975; Brooks et al., 1986*). The phase I vaccine prevented abortion and reduced the shedding of *C.burnetii*, thereby reducing both environmental contamination and the risk of transmission to human (*Behumer et al., 1975; Vidić et al., 1990a; Arricau-Bouvery et al., 2005*).

Control programs against Q fever in sheep and cattle, most frequently recommend serological examination and vaccination of animals (*Guatteo et al., 2008; Gidding et al., 2010; van der Hoek et al., 2010; Vidić et al., 2013a*). One of the recommended measures is excluding positive reactors from the flock followed by continuous monitoring and separation of seropositive animals. Milk from seropositive cows must be pasteurized.

Vaccination

In everyday practice, vaccination is recommended in infected herds and flocks; however, efficiency of different vaccination protocols has not yet been fully investigated, particularly with regard to the duration of vaccination program, animal categories to be vaccinated and time of vaccination. The latest research showed good results at the level of individual animal and at herd / flock level. Vaccination resulted in an apparent significant decrease in infection rate during the first years upon application of vaccination program, strongly suggesting the prolongation of this period. Reduction of clinical symptoms (abortions, infertility) is noticeable in the first year after vaccination; however, vaccination period of 3-4 years is required to stop and prevent shedding of bacteria. Efficiency of the application of all control measures including vaccination should be monitored using serology tests and PCR methods by systematic sampling of blood, milk, vaginal mucus and faeces. Vaccination offers a new conception of suppression and

eradication of this zoonosis, not only in a view of public health safety but also in creating Q fever free regions in endemic areas (*Behumer et al., 1975; EFSA J., 2010*).

At present, several vaccines for cattle and sheep are available in the market, such as bivalent vaccine *C.burnetti* and *Ch.psittacci* for sheep. Vaccine phase I *C.burnetii*, virulent one (encoding a complete LPS) demonstrated much higher efficiency than the phase II vaccine made of non-virulent strains (*Behumer et al., 1975; Arricau-Bouvery et al., 2005*). Universal animal vaccination program is not feasible; vaccination practices are adjusted to the epidemiological situations in particular regions. Vaccination of dairy goats against Q fever with Coxevac was analysed in a study and it was shown that the percentage of animals in which bacteria were detected in uterine fluid, vaginal swabs, and milk was reduced. The biggest change was observed in prevalence in uterine fluid and in young animals. Vaccination may reduce environmental contamination, because shedding of bacteria is highest during parturition, abortion, and subsequent periods. This of course, contributes to reduction of risk for human exposure to Q fever (*Arricau-Bouvery et al., 2005*.)

There are other studies with similar results. *Guatteo et al., (2009)*, performed a clinical trial and demonstrated that vaccine was effective in reduction of a chance for the appearance of bacterial shedding in animal, if it is given to uninfected animals before pregnancy. *Arricau-Bouvery et al. (2005)* showed that vaccination of 17 goats in a clinical trial decreased excretion of *C. burnetii*. On the other hand, *Rousset et al., (2008)*, conducted a field study of a goat herd infected with *C. burnetii* where vaccination did not prevent shedding, but there was a reduction of bacterial load in vaginal swabs of primiparous animals. A definite association between vaccination and bacterial shedding is still to be looked into. It depends if the vaccination is done before first or subsequent pregnancy, or before, or after natural exposure.

With the aim of reducing the number of human cases of Q fever in some of the countries goats and sheep were vaccinated, and in other countries humans at risk are vaccinated against Q fever (*Hogerwerf et al., 2011*). In France, cattle are vaccinated to prevent economic losses caused by abortions (*Rousset et al., 2009*). In any of these countries, not one human case of Q fever has been reported (*EFSA J., 2010*). After vaccination of the animals, it has been found that the total number of human cases of Q fever has dropped within one year, what can be related to the intervention measures. For sure there is a relationship between the shedding of causative agent, environmental contamination, and number of human cases, but further analysis is needed. It can be assumed that vaccination in dairy sheep and goats can lead to the lower shedding of *C. burnetii*. This could mean a lower risk for the human population.

In Australia, vaccination is applied as a preventive measure in sheep and humans potentially exposed to risk (*Gidding et al., 2010*). In Russian Federation,

vaccination is conducted in certain regions where Q fever occurs endemically or where infection foci are widespread in the nature. In France and Slovakia, depending on the epidemiological situation, vaccination is applied in cows and sheep (EFSA J., 2010).

Vaccination is a measure that prevents shedding of *Coxiella* and significantly reduces the risk of spreading Rickettsia, thus significantly reducing the risk of human infections (Hogerwerf et al., 2011). This does not necessarily mean that the infection will not occur in humans during the next year - this disease can be eliminated but not completely eradicated (EFSA J., 2010). The aim of the vaccination after lambing season, is to prevent new infections until next lambing of young animals, which were not pregnant. Well-timed sequential vaccination before pregnancy reduces the risk of *C.burnetii* infection, highly prevents the abortions decreases the shedding rate of *C.burnetii* after the abortion.

Antibiotic treatment

Antibiotic treatment is used effectively in humans to reduce clinical symptoms associated with Q fever. Antibiotic treatment was not demonstrated to be effective in preventing the shedding of bacteria in sheep and also it is not effective in influencing the epidemiology of infection in domestic ruminant populations (Astobiza et al., 2010). According to data from the literature, application of chemotherapy in infected animals was investigated. Administration of tetracycline to sheep, at a dose 8mg/1kg in drinking water, several weeks before lambing, was recommended as a possible prevention protocol (Berri et al, 2005; Blain, 2007).

Preventive measures

Q fever is an occupational concern for workers who have contact with animals, animal products, or animal waste. Immuno-compromised persons, pregnant women, and persons with cardiovascular problems (with evident valve failure) should avoid close contact with animals, particularly during the labouring season. Such individuals should seriously consider avoiding contact with sheep and goats, particularly during lambing or kidding time. Consult with your health care provider to determine if you are at high risk for contracting Q fever. Consuming pasteurized milk and use of pasteurized milk for dairy products (cheese) is highly recommended.

Furthermore, access to facilities or space at high risk of Q fever should be restricted, i.e. allowed only to vaccinated persons. Immunization of humans exposed to high rate of professional risk is a primary preventive step against Q fever (EFSA J., 2010). As an adverse effect of the vaccines, severe local reactions may occur in humans who were previously exposed to the infection or were

vaccinated – immune compromised persons. Having in mind the importance of this zoonosis, good communication on local and regional level and cooperation between human and veterinary medicine is indispensable.

Suppression of Q fever in domestic animals and prevention of environment contamination with *C.burnetii* are the most important measures in protection of humans from infection (EFSA J., 2010). Other measures that can significantly reduce the risk from infection include education of residents in rural regions about infection route, possible risks and precautions, education of farmers and other professionally exposed categories with an aim of establishing good agricultural practice. These actions can influence the reduction of risk of Q fever.

Good farm practice is always in use of reduction of human and animal health risks. Measures of self- protection and zoo hygienic measures are many that are incorporated into good farm practice. Personal hygiene during and after working with animals in addition with regular cleaning and disinfection during lambing or calving is one of the most important measures. Then, wearing protective clothing and shoes, using protective gloves when removing postpartum products and also with safe disposal of placenta, aborted and stillbirth animals are essential. Investigation of farm abortion and stillbirth outbreaks with determination of the causes of abortion and still birth and isolation of aborted animals until discharges cease is also important. Usage of additional equipment for self-protection (mask, goggles) when in contact with hazardous materials (after abortions, during Q fever epidemics, when cleaning the facilities for keeping sheep, goat and cattle) is essential when working on farms. One of the measures is certainly control of ticks, rodents and other parasites of livestock. The dust has to be reduced and quarantine used when purchasing new animals. Entrance has to be restricted for people and other animals (including dogs and cats) whenever possible.

Prevention of Q fever in animals is difficult, since infected animals may show no signs of infection with the organism. Isolation of any newly purchased animals from pregnant ewes or does is advised until all pregnant animals have birthed. Isolate any animals that abort from the remainder of the herd, and consult a veterinarian to discuss diagnostic testing. Dispose of bedding and equipment contaminated with tissues and fluids from an abortion in a sealed trash bag bury or burn. Individuals handling these materials should take protective precautions. Clean contaminated equipment and facility surfaces with soap and water and disinfect with a phenol disinfectant. More precautions for people are described below.

Experience from the Netherlands

The public was informed about the massive Q fever epidemic in humans Holland (Karagiannis et al, 2009; EFSA J., 2010). The outbreak begun in 2005,

and in the period 2007-2009, the number of patients in one region reached even 3523 persons. Investigation of epizootiological background of the epidemics revealed numerous abortions in goats in the region, which were identified as the source of infection. The following procedures were applied: all pregnant animals were culled from all infected farms; all animals were examined three times using serological ELISA; bulk samples of milk were examined two times applying PCR method; infected animals were eliminated; animals were vaccinated according to the age and herd size; access to farm was prohibited for visitors; use of milk was prohibited and appropriate biosafety measures were applied (Karagiannis *et al*, 2009). During this period, 35000 pregnant animals were killed, and costs were estimated to 6 million Euros. In the same period, Q-fever was identified in humans and animals in neighbouring countries - Germany and Belgium (EFSA J., 2010).

After the epidemic in Holland, data collected in Europe showed great variability with respect to laboratory diagnostic methods used and criteria for interpretation of the results depending on diagnostic goals (herd screening, identification of Rickettsia-shedding animal, epidemiological research or routine diagnostics). One of the conclusions of this Symposium was that professional knowledge is still insufficient, especially concerning epidemiology, identification of infection routes and potential reservoirs. Regular veterinary surveillance of the herd is indispensable for monitoring the infection and setting an accurate and timely diagnosis. Based on the current knowledge, a cornerstone of Q fever control is the vaccination of the animals with phase I *C.burnetii* vaccine.

The importance of particular domestic animals in the epidemiology of Q fever is differs among regions depending on their number, infection level, herd size, breeding system and zoo-hygiene. The epidemic course of Q fever Q fever disease is influenced by the range of factors such as airflow, rainfall, density of the population and geological characteristics of the terrain (Šeguljev *et al*, 1997; Vidić *et al*. 2003).

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Mere kontrole Q groznice kod ovaca

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Rezime

Q groznica je oboljenje poznato širom sveta, a izaziva ga gram-negativna bakterija *Coxiella burnetii*. Ova antropozoonoza je poznata po širokoj paleti domaćina i vektora. Domaće životinje imaju primarnu ulogu kao rezervoari uzročnika i oboljenja za ljude i zbog toga je vrlo važna tačna i pravovremena dijagnostika Q groznice kod domaćih životinja. Uzročnik može dapeživi više meseci, čak i godina u prašini ili u zemlji. Sanitacija endamskih žarišta Q groznice je praktično skoro nemoguća, zbog visoke rezistencije uzročnika, male infektivne doze i raznovrsnosti epidemiologije. U grupi antropozoonoza, Q groznica zauzima vodeću poziciju na regionu Vojvodine. Zbog toga se Q groznica smatra specifičnim problemom ove pokrajine.

U programima kontrole Q groznice kod ovaca i goveda, uglavnom se preporučuju serološka ispitivanja životinja i vakcinacija. Najefikasnije vaccine kod životinja su one sa inaktivisanom fazom i bakterije. Izlučivanje bakterija u tkivo placente i mlekom je smanjeno prilikom eksperimentalne ili prirodne infekcije sa *C.burnetii* kod ovca i goveda vakcinisanih sa vakcinama koje sadrže fazu I. Jedna od preporučenih mera kontrole je isključivanje pozitivnih grla iz stada, kontinuirani monitoring i izdvajanje seropozitivnih životinja. Mleko seropozitivnih krava se mora pasterizovati. Cilj vakcinacije životinja nakon sezone jagnjenja je prevencija novih infekcija do sledećeg jagnjenja mladih životinja koje još nisu gravidne. Dobro planiranom vakcinacijom pre graviditeta se smanjuje rizik od infekcije sa *C.burnetii*, preveniraju se pobačaji i smanjuje izlučivanje *C.burnetii* nakon pobačaja.

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