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SCIENTIFIC EVALUATION OF THE EFFECTIVENESS OF VACCINATION OF TARGET ANIMALS (CATTLE, SHEEP AND GOATS) AS A MEASURE TO CONTROL AND ERADICATE Q FEVER DISEASE

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ABSTRACT

Q fever is a natural focal disease (ticks are one of the main reservoirs of *C. burnetii* in nature and play an important role in maintaining outbreaks in farm animals), which belongs to the group of zooanthroponoses, i.e. affects not only animals but also humans. The causative agent is the obligatory intracellular bacterium *Coxiella burnetii*, which has significant resistance in the external environment and high temperatures. Carriage of *Coxiella* has been demonstrated in 62 species of ticks of the families *Ixodidae*, *Argasidae* and *Gamasidae*. Among the most common vectors of *C. burnetii* are *Rh. sanguineus, H. plumbeum, Rh. turanicum, I. ricinus, H. marginatum, H. punctata*, etc.). From the public health point of view and economic consequences, Q fever is a zoonotic disease of high public importance, the etiological agent of which, *Coxiella burnetii*, is included in Group B of the OIE list of potential weapons.

After the scientific assessment of the possibilities for application of vaccine against *Coxiella burnetii* for control and eradication of Q fever, found in a number of areas of Bulgaria in humans (among which farm owners, veterinarians and staff) and established positive herds of large and small ruminants, it can be concluded that the most effective strategy for controlling Q fever is considered to be the long-term vaccination strategy and vaccination of the whole herd – vaccination in already infected herds of ruminants or in healthy herds.

Key words: Q fever, vaccination of target animals, eradication.

Introduction

The Q fever disease, first described among staff at slaughterhouses in Australia, is now recognized as endemic worldwide, with the exception of New Zealand. Although Q fever in humans is asymptomatic in more than 60% of cases, in some cases it can manifest as an acute or chronic disease and can lead to severe complications such as pneumonia or hepatitis, endocarditis, premature birth or abortion in pregnant women. Deaths in humans are rare – less than 2%, and after illness the body builds long-term immunity.

Ruminants (especially cattle, sheep and goats) are recognized as a major source of infection for humans Georgiev et al. (2020) emphasizes that the transmission of the infection can take place horizontally from animal to animal and without the mediation of ticks. In ruminants, *C. burnetii* infection mainly leads to reproductive disorders such as abortion, stillbirth, birth of weak calves, metritis and infertility, with associated negative economic impacts on farms. Of great importance for the maintenance of outbreaks is animal carriage and shedding, in which at certain intervals and under the influence of certain factors the infection is exacerbated and infected animals begin shedding ofthe infectious agent in large quantities into the environment, mainly at birth or abortion with amniotic fluid, placenta, uterine discharge, vaginal mucus, milk, faeces, urine and semen. Additionally, under the impact of delivery, the infection is activated and the pathogen is excreted in saliva and nasal secretions in large quantities and for a long time. *C. burnetii* survives very well in the

environment and contaminates aerosols and dust. These contaminated particles are the main route of infection for both animals and humans.

Humans become infected mainly by inhaling aerosols contaminated with extracellular forms of *C. burnetii* or dust containing *C. burnetii* shedded by infected animals.

Today, medical measures consist of the use of antibiotics (reduce the frequency of abortions but do not prevent the shedding of *C. burnetii* from animals) and/or vaccines to control the spill overof the bacterium in farm animals and, in infected herds of cattle – environmental measures such as destruction of placentas or disinfection of birth places.

Purpose of the study

The present study aims to make a scientific assessment of the possibilities for application of a vaccine in animals for control and eradication of Q fever, found in a number of areas of Bulgaria in humans (among which, farm owners, veterinarians and staff) and found positive herds of large and small ruminants.

Materials and methods

A review of the scientific literature, the experience of other countries and expert opinion were used to prepare the assessment on the feasibility of vaccination of domestic ruminants (cattle, sheep and goats) against *Coxiella burnetii* for the control and eradication of Q fever.

Results

Currently, two vaccines against *C. burnetii* are available on the world market – Coxevac, phase I, CEVA Santé Animale and Chlamyvax FQ, phase II, MERIAL.

In current scientific studies, vaccines prepared with phase I *C. burnetii* (virulent phase with complete lipopolysaccharide (LPS) are recognized as more effective to build protection than those prepared with phase II (avirulent phase with incomplete LPS). In order to protect at-risk groups such as slaughterhouse workers, veterinarians or farmers, a phase I vaccine is currently being used in Australia.

Vaccination of cattle

In scientific study Guatteo et al. (2008) found that non-pregnant cows/heifers vaccinated with a monovalent inactivated vaccine containing phase I *C. burnetii* were five times less likely to become shedders than placebo-treated animals. The likelihood for animals vaccinated during pregnancy of becoming shedders is similar to that of animals receiving placebo. Pregnancy has an adverse effect on the immune response after vaccination. These results underscore the value of vaccination, if possible, in uninfected herds. In infected herds, vaccination should be given to almost all presumably susceptible animals, i.e. at least heifers. Vaccination of dairy cows should be carried out when the seroprevalence inside the herd is low, i.e. in herds where the infection has not yet spread widely. However, there was no significant effect of vaccination compared to placebo control on the shedded bacterial load, regardless of the initial status of the animals. Vaccination has a high protective effect against the risk of spill over to susceptible animals and thus reduces the associated zoonotic risk. Due to the lack of reduction of the shredded bacterial load from infected animals during vaccination,

as well as the high resistance of *C. burnetii* in the environment, a combination of hygiene and medical measures is needed to further reduce the infectious load in infected herds (Raphaël et al. 2008). Indeed, a phase I vaccine has been shown to prevent abortions and drastically reduce the incidence of bacterial excretion in milk, vaginal secretions and faeces. In addition, according to Guatteo R. et al. 2008, susceptible cattle that were vaccinated when they were not pregnant were five times less likely to become shreddersthan placebo-treated animal. Thus, vaccination in infected herds after the onset of abortion due to Q fever is often recommended on farms.

Vaccination, which is widely used in this field, has been identified as a long-term option for controlling *C. burnetii* infections by the European Food Safety Authority (EFSA, AHAW, 2010). Indeed, phase I vaccination in cattle has been shown to inhibit the shedding of the causative agent in milk, placenta, uterine fluid, vagina and colostrum.

Rousset et al. (2011), believe that the vaccine is not able to prevent infection in kids, nor to clear the infection in infected goats, but effectively reduces the level of shedding in a highly infected goat herds. Bontje at al. (2016) also found that both the spread of shedders and the shedded bacterial load through uterine secretions, vaginal discharge and milk were reduced in vaccinated dairy goats.

Different vaccination strategies could be appliedin dairy herds, based on the duration of the vaccination program, as well as the category of vaccinated animals (e.g. the whole herd or only the heifers). The long-term effectiveness of these various strategies to reduce the shedding of infection in already infected dairy herds, to reduce the number of abortions and the bacterial load in the environment and the extent of infection disappearance was assessed by mathematical modelling. The vaccination strategies studied were: (1) vaccination of the whole herd for 10 years – all cows and all heifers, with revaccination every year; (2) vaccination of the entire herd for 3 years; (3) vaccination of heifers only for 10 years with revaccination each year.

Scenario 1 – Vaccination of the whole herd for 10 years is considered the most effective control strategy. All three vaccination strategies reduce the spread of shedders, the emitted bacterial load in the environment and the number of abortions, but with different effectiveness. As the infection is rarely eradicated during the first years of vaccination, early discontinuation of vaccination (scenario 2) would be ineffective in the long run. In this context, the increase in the spread of shedders, the shedded bacterial load in the environment and the number of abortions should be monitored in the first months after vaccination is stopped. Before stopping a farm vaccination program, it is important to determine the presence or absence of *C. burnetii* in the herd. Herd-level diagnostic tests (e.g. PCR in milk) may be useful, although they are imperfect.

Therefore, if the vaccine is to be used to eradicate *C. burnetii* in infected farms, both the susceptibility and the infectivity of the vaccinated animals must be determined precisely. According to Rousset et al. (2011), it has been shown that the lowest level of *C. burnetii* secretion in vaginal tampons is more common in vaccinated than in unvaccinated goats. The way the demographics are presented in the model must be adapted when representing the prevalence of *C. burnetii* in small ruminants. In addition, shedding characteristics and clinical manifestations may be different in different species: sheep have been found to shed the bacterium mainly in faeces and vaginal mucus, while goats shed mainly in milk; high abortions were rare, with the exception of some goat herds (Arricau-Bouvery et al. 2005).

In conclusion, although further cost-benefit analysis taking into account the economic aspects of control programs is needed to create an optimal control strategy, the modelling approach has shown that long-term annual vaccination will reduce the risk of infection in vaccinated cattle herds (Courcoul at al. 2011).

Vaccination of sheep and goats

Research examines the public health relevance of vaccination against *C. burnetii* from ovine and caprine animals through systematic review and meta-analysis to provide evidence for policy-making to prevent the potential spread of zoonoses. From the pooled analysis, the researchers concluded that an inactivated phase I vaccine significantly reduced the shedded bacterial load with uterine secretions, milk, vaginal secretions and faeces from naive goats. The shedding through all other routes from vaccinated goats does not differ significantly from the control goats. (O'Neill at al. 2011). Vaccination of **goats** two months before mating with a phase I vaccine shows that it is effective and drastically reduces abortions, in contrast to the phase II vaccine mixed with *Chlamydophila abortus*, which does not affect the course of the disease or shedding. (Arricau-Bouvery et al. 2005)

Vaccination of dairy **sheep** herds is considered one of the best options to control *Coxiella burnetii* infection. The efficacy of a phase I vaccine was studied for 4 years in sheep herds with confirmed *C. burnetii* infection. No shedding has been found in sheep and one-year-old lambs in the last 2 years, but *C. burnetii* is still present in the environment. (Astobiza at al. 2011)

Conclusion and recommendation

Due to its importance for both animal health and public health, control of this infection is crucial. Therefore, any control measure leading to a reduction in the spread of animal shedders and shedded environmental bacterial load is a key point in limiting both the spread of infection in ruminants and the zoonotic risk.

The high prevalence of *C. burnetii* infection in dairy herds reported in recent studies (Netherlands) and the long survival of this bacterium in the environment require the application of control measures aimed at reducing the level of exposure at the herd level. Control measures based on antibiotic treatment and the use of vaccinations have been implemented. A recent study showed that antibiotics administered to dairy cattle significantly prevented the shedding of *C. burnetii* during and after calving. Thus, when infection is detected in cattle herds and there is environmental contamination through faeces or vaginal excretions, the implementation of a vaccine program is not only useful but also necessary to reduce the shedding of *C. burnetii* from infected animals. This is mainly related to reducing the risks to human health, but not to production and economic benefits.

In cattle

1. A cost-benefit analysis is needed, taking into account the economic aspects of control and vaccination programs, in order to create an optimal strategy for control and eradication of Q fever. Research shows that long-term vaccination reduces the risk of infection in vaccinated cattle herds. Phase I vaccination in cattle has been shown to inhibit the shedding of *C. burnetii* in milk, placenta, uterine and vaginal fluid and colostrum.

2. Vaccination, which is widely used in bovine animals, has been identified as a long-term option for the control of *C. burnetii* infections proposed in a specific scientific opinion of the 2010 (EFSA, 2010).

3. The results of this opinion underline the value of vaccination in uninfected herds as well. In infected herds, vaccination should be given to all presumably susceptible animals, or at least to heifers. Vaccination of dairy cows should be carried out when the seroprevalence inside the herd is low, i.e. when the infection has not yet spread widely.

4. The well-organized and structured laboratory diagnostic system of the competent veterinary authority (CVA) should have an approved and funded plan for active and passive surveillance of Q fever in the country by farms and real data on the spread of Q fever. The CVA should work closely with the Regional Health Inspectorates (RHIs) in planning and implementing public health activities and exchanging data on the actual prevalence and status of Q feverin animals and humans.

In small ruminants– sheep and goats

Vaccination is effective in rapidly reducing the prevalence of *C. burnetii* in a dairy herd and is able to prevent and control outbreaks of Q fever in farms.

5. The vaccine is not able to prevent *C. burnetii* infection in kids, nor to clear the infection in infected adult goats, but it effectively reduces the level of shedding, both the number of shedders and the shedded bacterial load through uterine secretions, vaginal discharge and the milk of vaccinated goats in a highly infected herd.

6. Preventive vaccination should therefore be considered as a permanent control measure supported by annual re-vaccination, followed by reactive vaccination strategies – "Vaccination after abortion wave" and "Vaccination after a positive test of whole milk samples", to preserve herds from Q fever and to prevent indirect risks to human health. It is necessary to determine in advance the state of infection in the herd, individually and for all animals and to compare the collected individual data on the age and reproductive status of goats.

7. Vaccination causes an overall reduction in shedding levels and the greatest reduction is found in ewes and does (animals did not give birth). In practice, this means that young animals must be vaccinated before becoming pregnant. Vaccination of adult sheep is considered to be one of the best options for controlling *Coxiella burnetii* infection.

8. The most effective strategy for controlling Qfever by vaccination in already infected ruminant herds or in healthy herds is considered to be the long-term vaccination strategy and vaccination of the whole herd. This strategy most effectively reduces the spread of shedders, the shedded bacterial load into the environment and the number of abortions. As the infection is rarely eradicated during the first years of vaccination, early discontinuation of vaccination would be ineffective in the long run.

Discontinuation of vaccination (exit strategy)

9. Before stopping a vaccination program on a farm, it is important to determine the presence or absence of *C. burnetii* in the herd (diagnostic tests at herd level (e.g. PCR in milk) may be useful), as in the first months after discontinuation of vaccination to monitor the increase in the spread of shedders, the shedded bacterial load in the environment and the number of abortions.

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