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Review article

Acclimation strategies in gilts to control *Mycoplasma hyopneumoniae* infection

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ABSTRACT

Mycoplasma hyopneumoniae (M. hyopneumoniae) is the primary causative agent of enzootic pneumonia (EP), one of the most economically important infectious disease for the swine industry worldwide. *M. hyopneumoniae* transmission occurs mainly by direct contact (nose-to-nose) between infected to susceptible pigs as well as from infected dams to their offspring (sow-to-piglet). Since disease severity has been correlated with *M. hyopneumoniae* prevalence at weaning in some studies, and gilts are considered the main bacterial shedders, an effective gilt acclimation program should help controlling *M. hyopneumoniae* in swine farms. The present review summarizes the different *M. hyopneumoniae* monitoring strategies of incoming gilts and recipient herd and proposes a farm classification according to their health statuses. The medication and vaccination programs against *M. hyopneumoniae* most used in replacement gilts are reviewed as well. Gilt replacement acclimation against *M. hyopneumoniae* in Europe and North America indicates that vaccination is the main strategy used, but there is a current trend in US to deliberately expose gilts to the pathogen.

1. Introduction

Mycoplasma hyopneumoniae (M. hyopneumoniae) is the causative agent of *Mycoplasmal pneumonia* (MP), an important porcine respiratory disease. This infectious process is frequently complicated by other respiratory bacteria (such as *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and others) causing a more severe chronic and economically important disease known as enzootic pneumonia (EP). In addition to bacterial complication, viral pathogens like *Porcine reproductive and respiratory syndrome virus*, *Porcine circovirus 2* and *Swine influenza virus* can aggravate the disease scenario; this viral-bacteria complex is clinically referred as porcine respiratory disease complex (PRDC) (Thacker and Minion, 2012). Despite all efforts implemented to reduce the economic impact caused by *M. hyopneumoniae* (vaccination and antimicrobial treatments together with improvement of management practices), EP and PRDC still cause great concern in the swine industry worldwide.

EP mainly affects growing and finishing pigs and it is characterized by dry, non-productive cough, reduction in growth rate, and increased feed conversion ratio. The severity of the disease is dependent on the presence of co-infections and environmental conditions (Maes et al., 1996) and on the virulence and number of *M. hyopneumoniae* strains involved (Vicca et al., 2003; Woolley et al., 2012; Michiels et al., 2017). *M. hyopneumoniae* is mostly transmitted by direct contact (nose-to-nose) between pigs, horizontally from infected to susceptible/naïve pigs (Morris et al., 1995) as well as from dam to their offspring (Sibila et al., 2008; Nathues et al., 2014; Pieters et al., 2014). Other putative indirect transmission routes are aerosol and fomites. Whereas the aerosol transmission has been experimentally proved (Fano et al., 2005; Otake et al., 2010), transmission by fomites has not been clearly demonstrated and it can be potentially prevented by basic biosecurity practices (Batista et al., 2004; Pitkin et al., 2011).

Different studies showed that disease severity in growing pigs is correlated with *M. hyopneumoniae* prevalence of piglet colonization at weaning (Fano et al., 2007; Sibila et al., 2008). However, other studies could not show this association (Vranckx et al., 2012b). This prevalence can be influenced by different factors such as housing and management conditions of the production system as well as dam parity, piglet's age

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at weaning and replacement rate (Nathues et al., 2013, 2014). Since newborn piglets are *M. hyopneumoniae* free, the most logical source of infection is the dam at the time of farrowing or during the lactation period (Sibila et al., 2007). Some authors suggested this transmission could be influenced by the dam's parity (Calsamiglia and Pijoan, 2000; Fano et al., 2006). Indeed, bacterial shedding of gilts or young sows seems to be higher than that of older parity sows (Boonsoongnern et al., 2012). Therefore, the first farrowing is considered a critical moment at which *M. hyopneumoniae* excretion should have ceased (Pieters and Fano, 2016). These latter data together with a low transmission rate (reproduction ratio [R_n] varies among 1.16–1.28 and 0.56–0.71 under experimental and field conditions, respectively) (Meyns et al., 2006; Villarreal et al., 2009; Roos et al., 2016) and the persistence of infection in pigs (up to 214 days post infection, dpi) (Pieters et al., 2009) imply the need of performing an effective gilt acclimation process. This effective acclimatization protocol would reduce *M. hyopneumoniae* shedding at first farrowing (Pieters and Fano, 2016) and, consequently, would decrease pre-weaning prevalence, subsequent spread of the pathogen to growing pigs, and putative respiratory problems in fattening animals (Fano et al., 2007; Sibila et al., 2008). Therefore, assuming that gilt population are crucial in the spread of the infection, the purpose of this review was to summarize different management practices, antimicrobial treatments and vaccination protocols in replacement gilts to control *M. hyopneumoniae* infections in pig herds.

2. *M. hyopneumoniae* health status

2.1. Monitoring and diagnosis

One of the main risks for *M. hyopneumoniae* colonization in piglets at weaning is a high gilt replacement rate (Nathues et al., 2013). Therefore, the first step to perform an appropriate adaptation of future replacements to *M. hyopneumoniae* is monitoring the health status of the recipient breeding herd, as well as incoming gilts to detect potential disease/infection indicators. In case of *M. hyopneumoniae* infection suspicion, a definitive diagnosis should be performed.

Monitoring of *M. hyopneumoniae* associated disease is sometimes challenging as the infection can take a clinical or subclinical course (Table 1). In clinical cases, the observation of signs (dry, non-productive coughing) and lung lesions (pulmonary craneo-ventral consolidation) are indicative, but not exclusive of *M. hyopneumoniae*. In subclinical infections, animals can display *M. hyopneumoniae*-like lung lesions without any evidence of coughing (Maes et al., 1996). Therefore, clinical diagnosis should be confirmed by additional laboratory tests (Table 1).

The most commonly used herd monitoring method is *M. hyopneumoniae* antibody detection by ELISA. It provides evidence of exposure to *M. hyopneumoniae* without differentiating maternally derived antibodies, or antibodies elicited by infection, and/or vaccination (Bandrick et al., 2011; Thacker and Minion, 2012). Moreover, absence of antibodies (seronegative animals) may not be equivalent to a *M. hyopneumoniae* free status in early infection scenarios, suggesting that antibody and pathogen detection combined is the main goal for *M. hyopneumoniae* final diagnosis.

Different laboratory techniques have been described to confirm the presence of *M. hyopneumoniae* (Table 1). The most useful technique to detect *M. hyopneumoniae* is polymerase chain reaction (PCR), as it can be performed using different respiratory tract samples. Up to now, there is no consensus on which type of sample from the porcine respiratory tract is the most suitable to detect bacterial DNA in live pigs. To confirm *M. hyopneumoniae* free status of live animals or to determine the involvement of such pathogen in an outbreak, the desired sample should be collected from the lower respiratory tract (*i.e.* laryngeal or tracheo-bronchial swabs or tracheo-bronchial lavage fluids), where *M. hyopneumoniae* colonization of respiratory cilia occurs (Fablet et al., 2010; Pieters et al., 2017). In dead animals, the sample of preference is lung tissue or bronchial swab.

2.2. Recipient herd and incoming replacement classification regarding *M. hyopneumoniae* health status

Once the *M. hyopneumoniae* health status of the recipient herds and the incoming gilts has been assessed, farms and incoming replacement could be classified into negative, provisional negative and positive according the following criteria (summarized in Table 2):

2.2.1. Negative herds/replacement

Clinical signs and lung lesions associated with *M. hyopneumoniae* are not present and serology and detection of pathogen in lung by PCR are negative. This type of breeding and fattening farms is the less frequent one in the current swine production in Europe (Garza-Moreno et al., 2017). Nevertheless, *M. hyopneumoniae* negative farms are increasingly common among gilt producers, genetic companies, high health farms and in certain countries such as United States (US), where a trend for *M. hyopneumoniae* elimination is growing (Maria Pieters, personal communication).

2.2.2. Provisional negative herds/replacement

M. hyopneumoniae-like clinical signs and lung lesions are not observed but animals are seropositive and PCR negative. The presence of antibodies against *M. hyopneumoniae* provides evidence of exposure to the pathogen by prior infections and/or vaccination against it. This type of farms (PCR negative and seropositive) is frequently found in US since they are applying vaccination against *M. hyopneumoniae* (Maria Pieters, personal communication).

2.2.3. Positive herds/replacement

These farms can be classified into subclinical infected or clinical affected. Subclinical infected farms can be differentiated in two different categories (I and II) according to the presence of ELISA antibodies against *M. hyopneumoniae*, the detection of the pathogen by PCR and the presence of lung lesions attributed to *M. hyopneumoniae* (Table 2). In category I, lung lesions associated to *M. hyopneumoniae* are not observed, the detection of antibodies depends on the disease phase (in early stages might not be detected) but the presence of the pathogen is confirmed. Animals from herds included in category II do not show clinical signs compatible with *M. hyopneumoniae* but have *M. hyopneumoniae*-like lung lesions, antibodies against the pathogen might be detected and the presence of *M. hyopneumoniae* is confirmed by PCR. Finally, in clinical affected farms, infected pigs also display signs and lung lesions associated to *M. hyopneumoniae*.

3. Prevention and control

3.1. Vaccination

Vaccination against *M. hyopneumoniae* is the most commonly used strategy to control its associated diseases in worldwide swine production systems (Maes et al., 2017). Most commercial vaccines against *M. hyopneumoniae* are inactivated whole-cell preparations or bacterins, combined with an adjuvant to induce a stronger immune response (Haesebrouck et al., 2004). Administration route of these commercial vaccines is mainly intramuscular and the volume per dose can vary according to the vaccine used (Table 3). Besides bacterins, attenuated vaccines against *M. hyopneumoniae* are also available in Mexico and China (Feng et al., 2013).

An alternative to commercial vaccines may be autogenous vaccines, based on isolated strains from the affected farm. These vaccines are not frequently used because of the difficulty to isolate *M. hyopneumoniae* strains and the apparent lack of vaccine safety and efficacy data. Although information is limited, a single study has compared the efficacy of immunization with homologous and heterologous strains