MYCOPLASMA HYOPNEUMONIAE VACCINATION STRATEGIES IN PIGLETS AND SOWS, AND THE EFFECTS ON LUNG LESIONS

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Control of *M. hyopneumoniae* infections in pig herds can be accomplished by optimizing management and biosecurity practices and housing conditions (Maes *et al.,* 2008). However, these measures might not always provide the desired improvements and/or it might be difficult to implement changes because of financial, logistic and practical constraints. In that case, **vaccination against *M. hyopneumoniae* is a very useful tool to control *M. hyopneumoniae* infections. In infected herds, vaccination improves the health and performance of the animals and reduces the use of antimicrobials.** Vaccination is frequently practiced worldwide, and different *M. hyopneumoniae* vaccines are available. Commercial vaccines are mostly bacterins that are licensed either for single or double vaccination in piglets. Some vaccines are also licensed for use in breeding animals. Most bacterin vaccines should be administered intramuscularly, but some of them are licensed for intradermal administration (Maes *et al.,* 2020).

Effects of vaccination

The advantages of piglet vaccination are a decrease of the performance losses due to *M. hyopneumoniae* infections: improvement of average daily gain (ADG) (2-8%), feed conversion ratio (2-5%) and sometimes mortality rate (Del Pozo Sacristan, 2014).

Additionally, shorter time to reach slaughter weight, less variation in slaughter weight (more homogeneous carcasses), reduced clinical signs (coughing), lower prevalence and severity of *Mycoplasma*-like lung lesions and lower treatment costs are observed (Maes *et al.,* 1998, 1999; Jensen *et al.,* 2002). Although *M. hyopneumoniae* infections do not cause pleurisy lesions, infections gained early during the rearing of fatteners have been shown to predispose for pleurisy recorded at slaughter (Holmgren *et al.,* 1999). Correspondingly, studies showed that M. hyopneumoniae vaccination may lead to a decrease in pleurisy in slaughter pigs (Maes *et al.,* 1999; del Pozo *et al.,* 2014), probably due to a lower number of secondary bacterial infections such as those with Pasteurella multocida and/or Actinobacillus pleuropneumoniae (Marois *et al.,* 2009). The currently used vaccines also reduce the number of *M. hyopneumoniae* organisms in the respiratory tract (Meyns *et al.,* 2006; Vranckx *et al.,* 2012) and decrease the infection level in a herd (Sibila *et al.,* 2007).

However, the protection against clinical signs and Mycoplasma-like lung lesions is often incomplete and vaccination does not prevent colonization. Transmission models under experimental (Meyns *et al.,* 2006) and field conditions (Pieters *et al.,* 2010; Villarreal *et al.,* 2011) showed that vaccination conferred only a limited and non-significant reduction of the transmission ratio of *M. hyopneumoniae*. Therefore, these authors concluded that vaccination as only control measure will not eliminate M. hyopneumoniae from infected pig herds. The effects of vaccination may also be variable between herds. This may be caused by non-compliance with the basic principles of good vaccination practices e.g. improper storage conditions and administration of the vaccine, poor hygiene at vaccination, and not following the guidelines mentioned in the leaflet.

However, also other factors such as stress at vaccination, infections with other pathogens at the moment of vaccination, co-infections involved in porcine respiratory disease complex (PRDC), diversity of *M. hyopneumoniae* strains, and maternal immunity might influence vaccination efficacy (Maes *et al.,* 2020).

Vaccination strategies

In *M. hyopneumoniae*-free herds or in herds with very low infection levels, vaccination may not be recommended since under these conditions, the benefits of vaccination may not outweigh the costs. In other farms, different vaccination strategies have been adopted, depending on the type of herd, production system and management practices, infection pattern and preferences of the pig producer.

Piglet vaccination

Since infections with *M. hyopneumoniae* may already occur during the first weeks of life (Villarreal *et al.,* 2010), vaccination of piglets is the most common vaccination strategy.

Its efficacy has been demonstrated in numerous experimental and field studies (Jensen *et al.,* 2002). Vaccination of suckling piglets (early vaccination; < 4 weeks of age) is most common, especially in single-site herds, whereas vaccination of nursery/early fattening pigs (late vaccination; between 4 and 10 weeks) is sometimes practiced, especially in three-site systems where late infections are more common. Originally, double vaccination was the most frequent practice.

Currently, one-dose vaccination is more frequently used, mainly because it requires less labor and it can be implemented more easily in routine management practices at the farm (Baccaro *et al.,* 2006).

With one-dose vaccines, the skill of the pig producer or employee to vaccinate properly might be more critical for vaccine compliance since only one injection is administered. Single vaccination at either 7 or 21 days of age was efficacious (performance, lung lesions) in a pig herd with clinical respiratory disease during the second half of the fattening period (Del Pozo Sacristan *et al.,* 2014). Experimental (Arsenakis *et al.,* 2016) and field studies (Arsenakis *et al.,* 2017) have shown that vaccinating piglets three days prior to weaning conferred slightly better results (performance, lung lesions) than vaccination at weaning. An overview of the effect of piglet vaccination obtained in different studies on lung lesions and other parameters have been published by Del Pozo Sacristan (2014). Reductions of 5% to more than 50% in the prevalence of pneumonia lesions were obtained, along with a significant reduction in the severity of the lesions. A meta-analysis, based on 63 *M. hyopneumoniae* vaccination studies showed that vaccinated animals on average had 22 gram higher ADG than non-vaccinated animals (Jensen *et al.,* 2002).

As a general rule, vaccination needs to be administered before animals become infected. Vaccination of suckling piglets has the advantage that immunity can be induced before pigs become infected with *M. hyopneumoniae*, and that less infections with other pathogens are present that can interfere with the immune response.

Nursery pigs have a lower level of maternal immunity but may already be infected with *M. hyopneumoniae* (Villarreal *et al.,* 2010). In addition, the age-window in which piglets become infected may vary between successive groups within a herd (Sibila *et al.,* 2004). Vaccination strategies tailored to specific farm infection patterns e.g. vaccination of piglets at least two weeks prior to seroconversion have been successful in decreasing the impact of *M. hyopneumoniae* infection (Wallgren *et al.,* 2000). Some pathogenic infections e.g. with porcine reproductive and respiratory syndrome virus (PRRSV), porcine circovirus type 2 (PCV-2) or S. suis mainly take place after weaning and may affect the general health status of the pigs, and consequently interfere with proper immune responses after vaccination. Also, in case of intramuscular administration, iatrogenic transmission of these pathogens may take place during vaccination.

Breeding gilt vaccination

Vaccination of breeding gilts during gilt acclimation or quarantine unit is commonly practiced (Garza-Moreno *et al.,* 2018). Vaccination is recommended in case negative gilts or gilts with unknown infection status will enter a herd that is infected with *M. hyopneumoniae*.

The aim is to stimulate and homogenize the immunity of the replacement gilt population and to avoid destabilization of the breeding stock immunity. Vaccination of gilts twice (at 2 and 6 weeks post entry) in the gilt acclimation unit significantly reduced the proportion of PCR positive gilts at 14 weeks post entry in a farm that was clinically infected with M. *hyopneumoniae* (Garza-Moreno *et al.,* 2019).

Vaccination also increased the antibody levels of the gilts and their offspring. Although vaccination did not provide full protection, the infection level within the gilt population of the studied herd was significantly reduced compared to a group of gilts that was not vaccinated.

Sow vaccination

Vaccination of sows at the end of gestation is less commonly practiced. It aims to both reduce the shedding of *M. hyopneumoniae* from the sow to the offspring and to confer protection to the piglets via maternally-derived immunity.

Wallgren et al. (1998) showed that serum antibodies in the sow start declining during the last month of gestation and therefore, the authors recommended to vaccinate sows at least four weeks prior to expected farrowing. Maternally derived immunity in piglets provides partial protection against infection of *M. hyopneumoniae* and reduce the severity of clinical signs and Mycoplasma-like lung lesions upon challenge infection of piglets. The initial antibody titers in newborn piglets depend on the immune status of the sow and the amount of colostrum ingested by the piglets (Wallgren *et al.,* 1998). As maternally derived immunity decreases with age of the piglets, also the protection may decrease with age.

Field studies showed that vaccination of sows at the end of gestation resulted in a lower number of *M. hyopneumoniae* colonized piglets at and shortly after weaning, both in farrow-to-finish operations (Arsenakis *et al.,* 2019) and in multi-site production systems (Ruiz *et al.,* 2003; Sibila et al., 2008).

In addition, it was shown that pigs from vaccinated sows also had a lower number of Mycoplasma-like lung lesions at slaughter, compared to pigs from non-vaccinated sows (Arsenakis *et al.,* 2019).

Since piglets from vaccinated sows can still be infected, additional measures to control *M. hyopneumoniae* during the nursery and finishing phases may be warranted. In farms with high levels of *M. hyopneumoniae* infections or in case of clinical symptoms in the sow population, vaccination of all breeding animals at the same moment may be practiced in order to stabilize and homogenize the breeding stock immunity.

Administration routes

Intramuscular injection is the most frequently used route of administration of *M. hyopneumoniae* vaccination. Intradermal vaccination is also possible with some vaccines. This administration route directly targets epidermal Langerhans cells and dermal dendritic cells, which are essential for efficient T and B cell priming.

In this sense, intradermal vaccination against *M. hyopneumoniae* can be an asset, as more of these specialized antigen presenting cells are present in the skin compared to muscle tissue (Fu *et al.,* 1997).

In addition, no needles are used as the vaccine is administered intradermally via pressure, which may reduce the risk for iatrogenic infections.

The higher dispersion of the antigen at the site of injection may also reduce injection site reactions (Del Pozo Sacristán, 2014).

Beffort et al. (2017) observed less injection site reactions and better efficacy of intradermal compared to intramuscular vaccination in terms of the reduction of clinical signs and macroscopic Mycoplasma-like lung lesions.

Martelli *et al.* (2014) showed that intradermal vaccination with a bacterin induced a systemic humoral and cell-mediated immune response as well as local humoral immunity, which was comparable to that obtained by the intramuscular administration of a bacterin. Good results (performance, lung lesions) with intradermal vaccination against M. hyopneumoniae have also been obtained in other studies (Jones *et al.,* 2005; Ferrari *et al.,* 2011; Tassis *et al.,* 2012).

Take home messages:

1. Vaccination against *M. hyopneumoniae* is a very useful tool to control *M. hyopneumoniae* infections. In infected herds, vaccination improves the health and performance of the animals and reduces the use of antimicrobials.

2. Factors such as stress at vaccination, infections with other pathogens at the moment of vaccination, co-infections involved in porcine respiratory disease complex (PRDC), diversity of *M. hyopneumoniae* strains, and maternal immunity might influence vaccination efficacy.

3. One-dose vaccination is more frequently used, mainly because it requires less labor and it can be implemented more easily in routine management practices at the farm.

4. Intradermal vaccination against *M. hyopneumoniae* can be an asset, as more of these specialized antigen presenting cells are present in the skin compared to muscle tissue. Besides, better efficacy of intradermal compared to intramuscular vaccination in terms of the reduction of clinical signs and macroscopic Mycoplasma-like lung lesions.

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