M. hyopneumoniae and vaccine efficacy

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Mycoplasma hyopneumoniae, the cause of enzootic pneumonia, is one of the most serious pathogens for pig farmers worldwide.

This is not only due to the cost of the enzootic pneumonia but the additional extra expenses due to either synergistic pathogenic interactions, antibiotic treatment, vaccination or slaughterhouse condemnations, as well as other several direct and indirect costs.

The procedures and methods to control M. hyopneumoniae have already been widely established as have the different strategies to lessen its damaging effects.

These involve management, antibiotic treatment, vaccination and, most of the time, combinations of two or more of these.

Eradication is possible

M. hyopneumoniae eradication is certainly possible, but often not feasible for most farmers in the leading pig producing countries (Germany, Spain, Denmark, Netherlands, United Kingdom, USA, China).

One of the most common eradication drawbacks is its consistency over time.

We may be able to become M. hyopneumoniae free, but this necessitates keeping a M. hyopneumoniae negative status for a long time.

Many farms have failed and after very strict procedures they returned to positive status due to a newly purchased infected batch of gilts, or air transmission from a neighbouring farm (air transmission over 3.2km is possible).

Successful on isolated farms

In fact, M. hyopneumoniae eradication programmes are most likely to be successful for a longer time on very isolated farms that have very strict biosecurity conditions.

In the case of farms located in not so isolated conditions, a M. hyopneumoniae eradication scheme should include all the farms in the area.

Group	M. hyo MDA D0	Vaccination D0 and D21	Challenge D70	Lung lesion scoring D98
A	+	Two doses	YES	2.3
B	-	Two doses	YES	2.8
C	-	-	YES	16.5

Table 1. Design and lung lesions scoring results in an experimental challenge with three different groups of piglets. MDA was not a factor that decreased vaccine efficacy. D0 (seven days of age), D21 (28 days of age).

So, coordination between farmers and farmers' associations is essential for success.

It would be useless to invest in such goals individually in pig dense areas.

So, obviously, for most farmers worldwide it is more cost effective to learn how to cope with the pathogen than to think about its total elimination from their farms.

But, not having eradication as a goal does not mean that we should not use all the tools we already have available to control and minimise the disease.

Tools, which aim to lessen as much as possible the negative financial effects of M. hyopneumoniae.

Thus, in this article we are going to mainly discuss how to take the greatest benefits from one of the best tools available for many years – M. hyopneumoniae vaccination.

Unfortunately, the total beneficial potential of mycoplasma vaccines can be variable and may be reduced or totally impaired by different factors.

The list of influencing factors is quite extensive but we will focus on the most important ones according to their ability to influence M. hyopneumoniae vaccine efficacy.

Vaccination programme

Due to farmer convenience there are more established vaccination programmes than there really should be.

The decision as to which protocol is the most suitable should be decided after a serious study based on growth performances, lung lesion scoring and cost profitability values for the individual farm. In order to decide which protocol would fit better within your operation you should at least establish the moment of highest M. hyopneumoniae infection in your pigs, the immunity status of the sows that will be directly related with the MDA (maternally derived antibodies) in colostrum, and the degree and prevalence of M. hyopneumoniae lung lesions at slaughter.

Once we have an idea about all of this we have a better argument to defend a one or two shot vaccination programme on our farm.

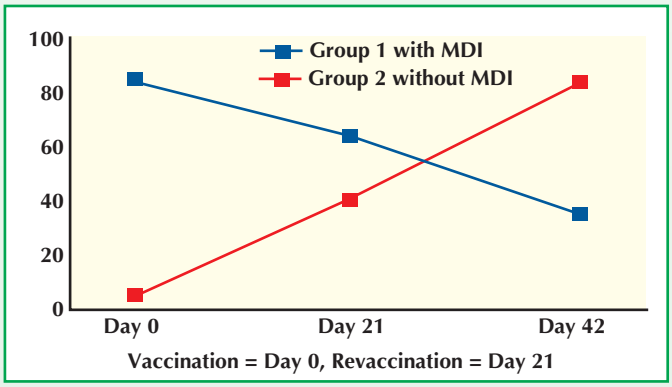
Of course, we are almost obliged to use appropriate tools to determine the most probable moment of infection.

Undoubtedly, the most used one is serum screening, which is based on serology analysis from different pigs from different ages, and sows from different parities.

This technique may tell us the moment of serum conversion and, thereby, indirectly, the moment at which most of the animals became infected as well as the general serological status of the sows.

In other words, it will give us information about the epidemiology of the disease within the farm. So, this technique will help us to also decide about both vaccination timings and vaccination dosage regimes (one or two dose protocols).

Fig. 1. Average antibody levels after two dose of vaccine at day 0 (seven days of age) and day 21 (28 days of age) in the presence of maternally derived immune globulins MDI (Group 1) and without (Group 2).



Better protection

As a general rule, a two shot protocol in field conditions induces a better protection and has the capability to greatly reduce the severity of lung lesions due to M. hyopneumoniae. This lung lesion reduction equates to better growth performance.

Naturally, each dose of vaccine has a cost and for this reason some farms that suffer from low infection pressure and delayed M. hyopneumoniae infections in the fattening period could have better cost profitability results when they use a one dose protocol.

This is because the advantage of a two dose protocol is not big enough to cost effectively allow a second dose vaccine investment.

Logically, with either earlier infections or with more secondary pathogen involvement, a two dose protocol is a more reliable choice.

As we will see later, MDA may

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also have a damaging effect on vaccine efficacy. This is even greater with a one dose protocol.

As we will also see MDA interference can probably be overcome, although serological results from piglets do show a depressed MDA after a very early vaccine application.

So, there must be other components besides serum conversion to define vaccine efficacy, for example, cellular immunity.

Mycoplasma epidemiology

As we have previously mentioned the time of infection, the sow's immune status, MDA levels and infection pressure are all factors that should be considered when designing the most appropriate vaccination programme for a specific farm.

There are some general rules in relation to the challenge moment and the infection pressure that are totally linked with the production system.

Thus, within a farrowing to finish system pigs are used to being challenged by M. hyopneumoniae and other porcine respiratory disease complex (PRDC) pathogens earlier than in multi-site systems.

In fact, originally, one of the most important objectives in all-in/all-out systems was, and currently still is, to avoid back tracking infection from older to younger animals in order to ease infection pressure or just control disease.

The production system is the main, indirect, decisive factor to consider when establishing a vaccination protocol. In Asia, as in other countries, farrowing to finish systems are designed in such a way that fatteners (in which M. hyopneumoniae is more active) are not far from nursery pigs or even from breeders.

Thus, re-infection can occur either by mouth to mouth or by aerosol transmission.

In addition, most of the fattening units contain pigs of different ages.

Therefore, if we know that recenly M. hyopneumoniae infected pigs can infect other pigs and we know that shedding of the new infected pigs will last for at least 15 days, it is easy to see why fattener units can become a huge source of infection and why this frequently occurs.

Clearly, such infection pressure ensures that younger, new pig batches will be automatically exposed to M. hyopneumoniae very quickly.

As a result we would obtain a new batch of shedding pigs and, thus, increase even more infection pressure within the barn.

In this case, a two shot vaccination protocol has more chance of being effective.

Benefits of multi-site systems

Multi-site systems (contrary to farrowing to finish systems) are already designed to cut off such back tracking of infections between different aged batches and, at the same time, to avoid the effects of over stocking dense areas.

Thus, as a general rule, multi-site systems use a philosophy of separation between batches according to age in such a way that M. hyopneumoniae epidemiology is limited mainly to fattening units.

Isolated fattener units are spreading around a theoretically much lower infection pressure since new, younger animals susceptible to be infected are not included in the multi-site systems anymore.

So, only in these privileged conditions may a one shot vaccination protocol be worthy of consideration.

Pathogen interaction

M. hyopneumoniae is one of the main components of PRDC in pigs. M. hyopneumoniae's pathogenic effects are produced by different pathogenic actions that weaken by themselves either specific or non-specific immunity barriers.

Thus, pathogenic effects from M. hyopneumoniae and other respiratory pathogens can be synergistic or complementary when they are infecting at the same time.

Then, M. hyopneumoniae can magnify the pathogenic effect of a bacterium as Pasteurella multocida. It has been observed that with the presence of M. hyopneumoniae lungs were more susceptible to suffer from P. multocida colonisation and infection but P. multocida on its own was not able to induce pathogenic effects when pigs had been previously vaccinated against M. hyopneumoniae.

Therefore, M. hyopneumoniae seemed to make P. multocida infection easier to control by pigs once M. hyopneumoniae was under better control due to the use of a vaccine.

In fact, some years before it had been concluded that P. multocida was just aggravating the effects of M. hyopneumoniae (animals double infected had consumed 60% more feed) but P. multocida by its own was not pathogenic.

Actinobacillus pleuropneumoniae and M. hyopneumoniae are also often present. Their interactions are well known.

For instance, it was observed that previously M. hyopneumoniae infected pigs after being exposed to A. pleuropneumoniae had alveolar macrophages with marked reductions in percentage of phagocytosis compared with alveolar macrophages from controls or single inoculated animals.

Later on, a much worse growth performance in pigs was seen when A. pleuropneumoniae and M. hyopneumoniae were infecting pigs simultaneously than when either pathogen was acting alone.

PRRSV interaction

A more widely studied pathogen interaction has been the one between porcine reproductive respiratory syndrome virus (PRRSV) and M. hyopneumoniae.

Both pathogens affect the normal macrophage function. PRRSV provokes a local immune suppression and obviously it may allow M. hyopneumoniae to be theoretically more damaging.

Relating to this interaction, it was shown that coinciding infection of M. hyopneumoniae and PRRSV was enhancing the pneu-

moniae lesions provoked by PRRSV.

Thus, both PRRSV and M. hyopneumoniae appear to alter the direction of the immune response in the lungs, making control of pathogens difficult. Ultimately, there has also been a lot of speculation about the relation between Circovirus type 2 (PCV-2) and M. hyopneumoniae.

Although this PCV-2 virus is more related to PMWS (post-weaning multi-systemic wasting syndrome), it seems that it could also play a role in PRDC.

According to some authors stimulation in the immune system could increase replication of PCV-2.

Thus, researchers concluded that the activation of the immune system is the pivotal event for PCV-2 replication. Obviously, any vaccine is an immune stimulating factor.

But, it is also obvious that any natural infection can potentially be a stronger or better immune stimulator than any vaccine.

Thus, for instance we should think more about the interaction between PCV-2 and PRRSV than PCV-2 and mycoplasma vaccines. Clearly pathogenic relationships exist with PRRSV and PCV-2.

It was observed that dual infection with PRRSV and PCV-2 increased PCV-2 replication and distribution when compared with PRRSV or PCV-2 alone.

A marked increasing severity with PRRSV-PCV-2 infected pigs was also demonstrated. In fact, 91% of three week old doubled infected pigs died (only 21% in the ones only infected with PCV-2). Therefore, the control of M. hyopneumoniae may indirectly reduce the increasing PRRSV replication.

Maternally derived antibodies

Certainly MDA protects piglets against M. hyopneumoniae damage but it can contribute to spare the effect of the vaccine. There is some controversy about the real MDA capability to reduce vaccine efficacy.

The first question we should ask is does MDA interference really exist and, secondly, can it be either observed in the laboratory (serologically) or even more importantly can it be observed in the tissues (lung lesions)?

The ordinary ways to measure the efficacy of a M. hyopneumoniae vaccine is by checking growth parameters as well as lung lesion scoring.

Although MDA interference can be checked easily with the use of serology (Fig. 1), serology is not a proper tool to define vaccine efficacy. Generally speaking, serologically observance of MDA interference is usually seen but serology results are just a part of the whole picture!

Other aspects, such as cellular immunity (probably the more important immunity type in order to control M. hyopneumoniae), have not been caught at all when serology is the only tool used.

Surely, if MDA is present it is a inconvenient to apply an early vaccine, but maybe this negative factor is amplified by the weak immune system situation of the piglet at that delicate age.

At the early time of seven days of age and until five weeks of age, the piglet's cellular immune system is not totally functional. In other words, piglets at this age could be considered the immune deficient animals.

So, it is logical to conclude that MDA interference is an added drawback to the already poor response that piglets can give after a very early vaccination.

Naturally, in farrowing to finish systems mycoplasma challenges are very early and, so, if we would like to apply a mycoplasma vaccine, early vaccination is the most suitable protocol if pigs are to be protected as soon as possible.

Some companies are already aware of this inconvenience and have developed vaccines which contain immune stimulating substances in their adjuvants to jump start the weak piglet's immune system as well as the MDA barrier in order to improve their response to the vaccine.

The most modern components in this respect are carbomer and levamisol.

Carbomer, already used in vaccines, is known to release the antigen of the vaccine slower in such a way that the piglet's immune system has longer to respond to the antigens. Levamisol is already a well known immune modulator component that improves cellular immunity.

In fact, levamisol has already been widely used in human medicine to improve immunity in immune depressed patients due to immunological disorders or cancer diseases.

It was also seen that levamisol could overcome the immune depression provoked by corticosteroids that are so frequently administered in piglets at early ages for lameness or nervous signs.

Therefore, new adjuvants need to overcome both drawbacks (MDA and weak immune system) and develop a proper vaccine response or at least a reduction in lung lesions due to mycoplasma.

Previous experiments in sheep demonstrated a higher increase of the immune response with a vaccine containing levamisol in comparison with the same vaccine type without levamisol.

It seems that this can also occur in pig vaccines. In a recent experimental challenge carried out in Hipra laboratory facilities, piglets with MDA and vaccinated twice at a very early age (seven and 28 days of age) had less lung lesions and better growth parameters, even with the MDA presence when compared with non-vaccinated piglets when they were challenged against a field M. hyopneumoniae strain at 70 days after the first dose of vaccine (77 days of age).

So, vaccinated piglets had more positive results independent of their previous MDA status (see Table 1 and Fig. 2).

So, early vaccination can still be an option even in the presence of MDA.

Therefore, clinical response, lung scoring and growth parameters show a better picture that foresees the important role of cellular immunity in M. hyopneumoniae control than does blood testing. There has also been the controversy about the real advantage of sow vaccination. It is observed that sow vaccination may reduce the transfer of the M. hyopneumoniae load from sows to piglets as well as increasing the MDA.

Both advantages are positive for controlling the transmission from the very beginning.

Therefore, sow vaccination may not be contrary to an early piglet vaccination protocol with the use of new technology vaccines.

Of course, in order to apply the most suitable vaccination protocol serology (in the form of serum screening) it is still the most suitable and practical tool to check MDA as well as M. hyopneumoniae.

Serum screening plus field observations will help you to decide the best vaccination timings in each specific case.

Naturally, other pathogens could also be analysed serologically in such a way that we may observe a better picture of the relationship between M. hyopneumoniae with other PRDC pathogens.

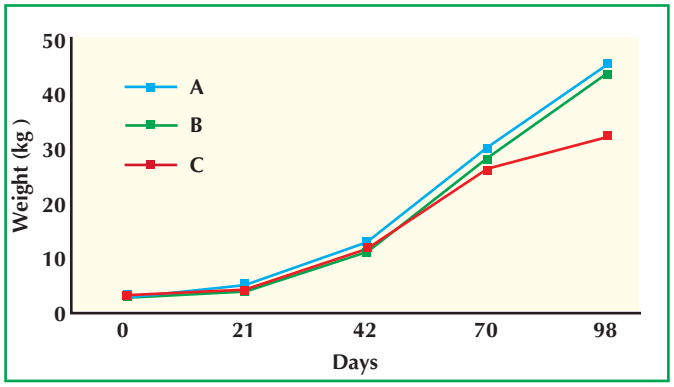

Fig. 2. Weight evolution in groups A, B, and C described in Table 1. Groups vaccinated independently their MDA status had a better performance after challenge than unvaccinated group C.

Implications

M. hyopneumoniae is a pathogen that should be approached from different angles. Vaccines and antibiotics must be considered and for its control other factors, such as production system, ventilation, stock density may also considerably influence the severity of this pathogen.

Serology is an appropriate tool to deduce the specific epidemiology of one pathogen on a farm and it is very helpful in designing vaccination protocols with better timings.

New vaccines with new adjuvants can overcome MDA interference in such a way that early vaccination may be the most suitable vaccination protocol in farrowing to finish systems, even with the presence of MDA.

Then sow vaccination is not contra-indicated to an early vaccination protocol in piglets.

Obviously, standard vaccination timings may not fit specific farms. So, we should design one specific vaccination protocol for such farms.

In order to design such a specific protocol, serum screening or serum profiling seems to be the most practical method, either for M. hyopneumoniae or for other PRDC pathogens. ■

References are available from the author on request