

Vaccination against PRRS: a matter of protection

Porcine reproductive and respiratory syndrome virus (PRRSV), a RNA virus member of the Arteriviridae, widespread among the swine population, causing reproductive failure in sows and respiratory and systemic disorders in pigs of all ages, continues to be a major problem in most pig-keeping countries. The economic impact of PRRS to US swine producers has been projected to be more than 600 million US dollars/year.

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This estimate is highly conservative, as it only accounts for direct losses due to the disease (mortality and reduced performance) and does not include cost of vaccination, medication, diagnostic testing and biosecurity measures incurred following onset of the disease. Other estimations exist also from Europe accounting for different types of production systems and country.

Questions still to answer

Despite years of intensive study, PRRS still poses numerous questions for which answers, once available, are often complex and difficult to interpret with regards to practical application. Part of the problem is that PRRS virus (PRRSV) is not a 'typical infectious agent'.

Moreover, its interaction (pathogenesis and immunity) with its only known natural host (swine) is not fully understood. As a consequence, the control, prevention and sometimes elimination of PRRS still present a formidable, sometimes frustrating, challenge for researchers, practitioners, and producers.

Severe reproductive failure, or respiratory disease, or both, are clinical features of PRRS during an epidemic in a fully susceptible herd. The respiratory disease is typically seen in nursery and/or early finish-

ing periods. In a continuous flow system, there are sometimes recurrent episodes of disease that are the result of viral shedding from infected older pigs to younger ones, or from persistently (often congenitally) infected pigs to age-matched cohorts that may have previously been immune. The presence of susceptible pigs (naïve subpopulations) because of only partial spread of PRRSV during the acute phase of an epidemic, and the introduction of naïve pigs or breeding stock (replacement gilts), provide additional means by which PRRSV is able to continue to circulate in endemic-infected herds.

Marked differences in infection rates between groups, pens or rooms of animals may occur. It is accepted that the clinical manifestations of PRRSV infection vary from subclinical to severe reproductive failure and/or respiratory/systemic disease.

Severity of PRRS may result from interactions among factors involving differences in virulence among PRRSV isolates (highly pathogenic – HP isolates exist), differences in concurrent infections (co-infection with other viruses, mycoplasma and bacteria), genetically-based differences in pig susceptibility, environmental factors, varying management conditions among herds (weaning age, pig flow, gilt acclimatisation strategies), level of PRRSV herd immunity, and other factors or circumstances.

PRRSV undergoes consistent genetic change, reducing the ability of conventional intervention strategies such as animal flow and vaccination to consistently control all cases. Therefore, attempts to eliminate the infection and the correlated diseases have been done with strategies such as depopulation and repopulation, herd closure and test and removal. While highly successful at eliminating the resident virus from the population, these strategies often fail and infection returns, because of the re-introduction of an unrelated/diverse PRRSV strain.

A clear and complete understanding of the nature of PRRSV (virulence, genetic and antigenic diversity), characteristics of the



Piglet vaccination reduces the viral load of PRRSV within the susceptible population in the nursery, partially protecting from clinical signs, and reducing the associated diseases and also the related costs (www.msdd-animal-health.com).

host-virus interaction (immune response, virus persistence) and current methods of swine production (often large, continuous-flow systems, typically with an outside source of replacement gilts) is essential in designing an effective strategy for PRRS control.

Genetic diversity

Genetic divergence and presumably at least some antigenic diversity among PRRSV strains raise questions about immunity and particularly cross-protection.

High nucleotide diversity (heterogeneity) in both North American and European genotypes has already been shown for a long time.

Extensive genetic variations have been observed among different PRRSV strains. It appears that accumulation of both random mutations and recombination drives variation of the PRRSV genome.

Despite all of the existing information about recombination and mutation of viruses, the factors which are primarily responsible for the high prevalence of variability among currently circulating PRRSV field isolates is unknown. In the field, co-existence of more than one isolate at the same time in a swine herd has already been docu-

mented for a long time.

Broad genetic variation is a major concern in the development of effective PRRS diagnostic tools, vaccines, and control strategies. The existence of antigenic variation was demonstrated between European and North American PRRSV with the immunoperoxidase monolayer assay (IPMA) very soon after the discovery of the virus.

Biologically, such an antigenic difference between European and American types of PRRSV is of concern with respect to cross-protection.

Cross-protection/vaccine efficacy

The relative effectiveness of a vaccine against heterologous PRRSV field isolates may largely depend on the antigenic relatedness of the virus strain to which the vaccinated animals are exposed. Antigenic relatedness is not correlated with the genetic similarity we are used to measure today for epidemiological purposes.

In fact, it is already well known and largely accepted that the genetic similarity (the degree of genetic homology of ORFs) between the MLV and the chal-

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lence/naturally exposed isolate is not a good predictor of vaccine efficacy.

Heterologous protection against PRRSV ranges from fact to myth and everything in between. The reasons for such disparate views vary due to differences in outcome measures, expectations, experimental designs, and economic considerations.

The ability of each strain to induce a strong cell-mediated immune response also seems to be more important than the genetic similarity.

In pigs vaccinated with a European MLV (DV strain-Lelystad cluster) subsequently challenged with a virulent heterologous PRRSV (Italian-like cluster) characterised by a high degree of ORF5 divergence compared with the vaccine strain, clinical and virological protection (100 fold reduction of the load and duration of viraemia, and reduced presence of the virus into BAL fluid) was demonstrated.

Field trial results

In a field trial based on the natural exposure/infection to PRRSV, it was calculated that in vaccinated growers the overall clinical protection (respiratory and systemic clinical signs) was 70%. This means that vaccinated pigs had only 30% of the clinical signs observed in the non-vaccinated controls.

Measures of disease, consisting primarily of lung lesion scores, were also significantly reduced.

Moreover, the results are independent of nucleotide sequence similarity between immunising and challenge viruses.

More recently, the partial protection induced by MLV based on PRRS-1 (DV strain) was demonstrated following challenge with Highly Pathogenic (HP)-PRRSV belonging either to the subtype 1 or subtype 3-Lena. This is a further clear and robust confirmation of the partial protection conferred by 'traditional' MLV. The efficacy of MLV on the infection is also supported by a reduced Basic Reproduction Ratio (number) (R_0), defined as the number of cases one case generates on average over the course of its infectious period, in an otherwise uninfected population.

The estimated transmission rate of PRRSV was 10-times lower in MLV vaccinated than in non-vaccinated piglets and the duration of infectiousness was reduced, leading to a significantly lower reproduction ratio R (0.30 [0.05-0.96] versus 5.42 [2.94-9.04] non-vaccinated piglets). Hence, vaccination was able to considerably decrease PRRSV spread.

This feature makes MLV a tool for control of PRRSV propagation and even for eradication of the infec-

tion at herd level. Moreover, this evidence supports the fact that continued vaccination of a dynamic population (weaners) tends to reduce the level of infection over time (months) as well as the clinical signs.

All PRRS attenuated vaccines provide partial protection because the isolates from which they were derived are presumed to no longer exist in the environment, so that the field isolates naturally infecting the vaccinated pigs are divergent and heterologous in respect of the priming virus, the vaccine strain.

The results obtained in laboratory trials with heterologous challenge can be easily measured by the investigators (rectal temperature, clinical scores, viraemia, viral excretion, pathological lesions).

Conversely, in field conditions, the partial protection obtained in vaccinated/infected animals is difficult to be measured as reductions in infection level and disease severity may be judged as failures if protection is not absolute or if the residual disease still results in economic losses. This is a matter of observer's perception!

Maternally derived antibodies

The influence of maternally derived antibodies (MDAs) on the post-vaccination humoral and cellular immune responses in piglets vaccinated against PRRS has not been investigated in detail. PRRSV-specific neutralising antibodies (PRRSV-NAs) transferred from the sow to the piglets by the colostrum can delay their infection by PRRSV. The passive transfer of sufficient amounts of PRRSV-NAs can also prevent PRRSV infection in piglets.

On this very interesting subject, more recently, Fablet et al (2016) investigated the potential interference of MDA on piglets' humoral and cellular immunity induced by PRRSV vaccination. Unfortunately, that interesting paper is not conclusive because of the experimental conditions do not mimic the real world. Overall, before drawing conclusions, further studies are absolutely needed to assess the impact of MDAs on PRRSV vaccine efficacy (clinical and virological) following a PRRSV natural or experimental challenge and its ability to reduce viral transmission.

PRRS control and sow vaccination

Substantial effort toward successfully controlling and eradicating PRRS has been placed on reducing negative production and economic effects of the disease in swine production systems. The first step in

PRRSV control is based on stopping the virus circulation in the sows in an attempt to prevent vertical (sow to foetuses) and horizontal transmission (sow to newborn) before weaning.

This condition is well known as stabilisation. So, a herd is stable when sows do not transmit the infection to the foetuses/newborn. In fact, infected weaned piglets that enter the nursery propagate the virus throughout the population by infecting the eventually non-infected weaners in the nursery.

In order to control PRRSV, critical issues that maintain PRRSV circulation within herds include co-existence of genetically diverse isolates, the existence of naïve breeding herd subpopulations, and improper management of gilt replacement pools.

Proper development of replacement gilts, an important component of PRRS control, involves exposing incoming naïve animals to the farm-specific resident PRRSV isolate before entering a positive breeding herd in order to reduce seronegative subpopulations.

Exposure can be done by vaccination, live virus inoculation (LVI), and contact with infected animals such as nursery piglets with clinical symptoms.

A minimum time following exposure is required for animals to recover clinically and establish immunity. Whole herd depopulation/repopulation has been used for the elimination of multiple swine pathogens including PRRSV.

Several methods of eradication have been shown effective in eliminating PRRSV from positive herds, including whole herd depopulation/repopulation, test and removal and herd closure.

Test and removal methods have also resulted in the successful elimination of PRRSV from positive populations.

The most frequently applied strategy to control and eliminate PRRSV from breeding herds is called load-close-expose (also called herd closure) which consists of interrupting replacement pig introduction for several months and exposing the pigs to a replicating PRRSV resulting in the reduction in viral shedding and elimination of carrier animals.

Attempts to expose the pig populations can be initiated through MLV vaccines. Although live-resident virus inoculation (LVI) is another way to expose the population to the virus and to induce population immunity, this method does not come without risk.

A recent paper by Linares et al compares successful application of both MLV vaccination and LVI. In this study, treatment groups (load-close-expose with MLV or LVI) were compared for:

- Time-to-PRRSV stability (TTS),

defined as time in weeks to produce PRRSV negative pigs at weaning.

● Time-to-baseline production (TTBP), defined using statistical process control methods that represent time to recover to the number of weekly weaned pigs prior to PRRSv-detection.

● The total production loss in terms of number of pigs weaned per week.

Herds in the MLV group recovered production sooner and had less total loss than herds in the LVI group. TTBP and TTS were significantly shorter and the total loss was significantly less in herds assisted by a specific veterinary clinic and herds that were infected with PRRSV in the three years prior to the study.

This study provided new metrics to assist veterinarians to decide between methods of exposure to control and eliminate PRRSV from breeding herds and mass vaccination with a MLV had an overall better performance as compared to LVI.

Although herd closure allows for the preservation of genetics and retains minimal diagnostic costs, it can be costly and can result in the production of an improper parity distribution within the breeding herd, effects that can be minimised through off-site breeding projects for replacement gilts.

Conclusions

The ability of PRRSV to escape or modulate the immune system of the host and the complexity of the immune response to PRRSV makes it difficult to develop a vaccine characterised by complete protection and universality, safety and desirable ability to differentiate vaccinated pigs from the infected (DIVA).

Even if live vaccines currently available on the market confer only partial protection, they are however a useful tool in PRRS control. In fact, in association with other necessary measures, sow vaccination contributes to the stabilisation of the herd, the key point towards the control/eradication of the infection. In that context of an integrated approach to PRRSV infection, piglet vaccination reduces the viral load of PRRSV within the susceptible population in the nursery, partially protecting from clinical signs, and reducing the associated diseases and the related costs.

The interference of maternal derived antibody on the active immunisation by vaccination is not completely understood and data available are contradictory so that accurate, further investigations are needed.

References are available from the author on request