Porcine circovirus diseases: A special focus on sub clinical forms

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Initially, porcine circovirus type 2 (PCV2) commercial vaccines were used to counteract outbreaks of overt PCV2-systemic disease (PCV2-SD, known formerly as postweaning multisystemic wasting syndrome, PMWS), through the administration to sows, piglets or both. More recently, they have been used on farms without overt signs of PCV2-SD. Their positive effect (improved average daily gain, percentage of runts, body condition and carcase weight) under these conditions confirmed PCV2 as the main culprit behind the decreased performance of pigs – even in the absence of obvious clinical signs. Currently, it is widely accepted that vaccination counteracts the subclinical impact of PCV2.

How often?

While it is assumed that PCV2 infection is ubiquitous and present worldwide, the prevalence of clinical disease linked to PCV2 is much lower. According to published data on PCV2-SD situations in the absence of PCV2 vaccination, morbidity is overall estimated at 4-30%. However, the proportion of infected animals within these herds was found to be close to 100% during the nursery and fattening periods. Also, since the first evidence of PCV2 infection can be traced back to 1962 (in Germany), and the oldest diagnosis of PMWS dates from the mid 1980s, it is safe to assume that the most common form of PCV2 manifestation is and has been the subclinical infection.

Diagnosis

A diagnostic approach, using specific ancillary post-mortem tests, has been validated for PCV2-SD and other PCV2-associated diseases (PCVDs). Alternative, non-lethal diagnostic methods have been suggested, relying on real-time quantitative PCR (qPCR) thresholds in serum, as suggestive of PCVDs. A similar approach would be relatively easy to propose for PCV2 subclinical infections. It would based on the absence of specific gross lesions, or a mild lymphocytic depletion with granulomatous inflammation of lymphoid tissues, and a qPCR result below 10^5-10^6 DNA copies per ml of serum with an absence (or low levels) of PCV2 antigen (immunohistochemistry) or DNA (in situ hybridisation) in the lymphoid tissues. But would swine practitioners use such a diagnostic procedure if the probability of occurrence of subclinical infection in a non-clinically affected, non-vaccinated farm is close to 100%? Probably not.

PCV2 vaccination

The cost of subclinical infection still needs to be quantified, and the use of PCV2 vaccines seems to be the most obvious tool for this. The return on investment of PCV2 vaccination in all subclinical scenarios remains to be fully explored, but unpublished data from large swine producing systems around the world suggest that, as a whole, it is positive. Furthermore, since PCV2 is ubiquitous and virtually global, systematic vaccination of all pigs against PCV2 would make sense. The present extensive use of PCV2 vaccines in a number of countries seems to confirm this hypothesis. At individual farm level, producers and veterinarians should assess whether PCV2 vaccination is a cost effective investment.

Conclusions

The past six years have shown that PCV2 vaccines have greatly contributed to pig health worldwide, and are considered by veterinarians and farmers as one of the most beneficial types of vaccines. However, the prevention and control of known risk factors for PCVDs are still a 'life insurance' for the full efficacy of the vaccine at farm level. This huge success contrasts with the fact that 15 years of intensive research on PCV2 and PCVDs have failed to answer certain fundamental questions, such as certain aspects of the pathogenesis of the disease, the specific interaction of PCV2 with the immune system and the lack of a reproducible and repeatable model of disease.

PCV2 piglet vaccination provides long lasting protection, which favours batch homogeneity

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Several field trials demonstrate that piglet vaccination with Circovac provides protection against PCV2-associated diseases up to slaughter, even in countries where pigs are fattened over 220 days of age. This reflects an improved FCR, higher homogeneity of body weights at slaughter and increased economic gain.

Since 2007, Circovac has also been registered for piglet vaccination in the EU and in other regions, and has been widely used. Numerous trials and studies have consistently confirmed the efficacy and the safety of Circovac use in piglets, in diverse country situations, management systems, health statuses and performance levels. Not only do piglets vaccinated with Circovac have a reduced mortality risk during both post-weaning and finishing, but they also have significantly increased growth performances (ADWG) in the different age groups, including the finishing stage. Also, the proportion of underweight pigs is reduced in vaccinates, compared to placebo-injected controls. Three recent trials further underline the positive impact of piglet Circovac vaccination on the production flow.

On two sites of a Spanish farrow-to-finish operation affected by PCVD, a controlled, randomised, blinded trial was performed under good clinical practices. Piglets were either vaccinated with Circovac (n=619) or injected with a placebo (n=620) at weaning, and were followed up to the slaughterhouse, in order to record the individual carcase weight (first departure to slaughter was 168 days of age in site 1 and 189 days in site 2). Individual prices were calculated with the standard Spanish 2011 slaughterhouse paying grid. The average prices between treatment groups were compared for each site. The economic benefit of carcase weight improvement and the impact of bodyweight homogenisation in vaccinated pigs was assessed by statistic simulation and equalising means, respectively. On average, Circovac vaccination produced a €2.55 gain per carcase in one site, and a €4.34 gain per carcase in the other. The gain ascribed to the homogenisation of bodyweights is €0.29-0.32 per carcase on average; it can reach €1.47 per carcase. Under the conditions of this study, up to €4.3 gain per pig was observed, following piglet vaccination with Circovac at weaning.

Furthermore, in site 1 the liveweight range of the pigs was significantly narrower in the vaccinated than in the placebo group (p=0.008), and the proportion of underweight pigs (< 80kg liveweight) was significantly reduced in the vaccinated group (-10.5%; p=0.006).

These clear-cut results can be further substantiated by another field study from Spain, which included 44 consecutive batches of fatteners in a 1,200-sow farrow-to-finish operation. The records of the 23 batches fattened before Circovac vaccination of piglets was implemented were compared to those of the 21 batches subsequently fattened. Over the vaccine use period, FCR improved significantly, from 3.13 to 2.88 ($p<0.001$), which is a further component of the farm's profitability.

Finally, a controlled, blinded and randomised field study was performed on an Italian 420-sow farrow-to-finish farm. At weaning, piglets were either vaccinated with Circovac or were injected with a placebo; 1,050 piglets were included, from five consecutive batches. Control and vaccinated piglets remained intermingled throughout the study. They were individually weighed at 25, 105 and 220 days of age (Parma ham production imposes the fattening of heavy pigs). Over the three considered periods (25-105d, 105-220d and 25-220d), the ADWG of the vaccinated groups were significantly higher than those of the control groups ($p<0.01$, $p<0.05$ and $p<0.01$, respectively). Also, the incidence of underweight pigs was statistically lower in the vaccinated groups.

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A review from Europe: profitable piglet vaccination with Circovac

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A review of the impact of Circovac piglet vaccination in Europe was presented in early March at the AASV 2013 congress in San Diego. Laboratory and field data concur that Circovac is efficacious and safe in piglets.

Long lasting protection

Laboratory studies with both SPF and conventional piglets demonstrated that neutralising anti-PCV2 antibodies are produced following vaccination with 0.5ml Circovac. This causes a significant reduction in PCV2 viraemia in vaccinated piglets challenged with a field PCV2 strain two weeks later. Piglets vaccinated at three weeks of age and challenged at 17 weeks of age and monitored up to 21 weeks of age were also protected against PCV2-associated clinical signs and lymphoid lesions, and had an average of +2.4kg individual live-weight compared to unvaccinated challenged controls. No adverse reaction was observed in any of these studies. The high level of protection was also observed in an Italian field study, where piglets vaccinated at three weeks of age had an improved growth performance over the 25-220 day (Parma ham production) period ($p<0.05$).

Improved growth and FCR

A similar impact of Circovac vaccination was observed for growth performance: the post-weaning ADWG was significantly improved on all farms ($p<0.05$) except one subclinical Bulgarian farm (which still showed +24g/d among vaccinated pigs). In all finishing stages, vaccinates performed significantly better; even in the Bulgarian farm, where ADWG improved from 980 to 1,050 g/d ($p<0.05$).

On a Spanish 1,200-sow operation, a trial compared 23 batches of fatteners produced before Circovac vaccination of piglets was implemented to 21 batches of fatteners produced after the start of vaccination. The feed conversion ratio improved in a highly significant manner among vaccinated batches (3.13 to 2.88, $p<0.001$).

In another study, on a Polish farm with a clear PMWS clinical condition, vaccination not only allowed mortality rates to drop to levels prior to the outbreak, but also led to a significant improvement in FCR and ADWG compared to pre-outbreak levels. In another Spanish trial, vaccinates also had a highly significant improved homogeneity at slaughter ($p=0.008$).

Reduced mortality

Compiled data from published field trials included results of 86 European farms in Spain, Germany, Austria, the Czech Republic, Bulgaria and France, with a total of 519,530 piglets. In farms where post-weaning mortality was over 4% in control pigs, the mortality rate was consistently significantly lower in vaccinated piglets ($p<0.05$). Interestingly, in farms with a post-weaning mortality below 4.0% vaccinated groups also had significantly lower mortality rates ($p<0.05$), except for the two showing the lowest initial mortality rate (2.9 to 2% and 2.6 to 2.3%, respectively).

In the finishing stage, a significant drop in mortality was found – with the exception of one German farm (4.1 to 3.1%, $p=0.066$) and one Spanish farm (4.8 to 3.8%, $p>0.05$) but in which however the proportion of runts was significantly reduced from 7.7 to 1% ($p<0.05$).

Highly profitable

These data further confirm the efficacy and safety of the use of Circovac in piglets, and underline a significant return on investment for this vaccination strategy: not only improved health and growth performances, but also improved economic parameters, including FCR, the percentage of underweight pigs and homogeneity at slaughter.

At a time of high feed prices and incentives for improved homogeneity, a full control of PCV2 is a major asset for high profitability, even in subclinical PCV2 infections.

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PCV2 piglet vaccination allows a reduction of antibiotic use at the growing stages

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A number of field trials have demonstrated that, among the effects of the consistent use of Circovac vaccination of piglets, there is a measurable reduction in the number and/or cost of treatments. Several independent scientific publications have also stressed, over the last months, that in swine herds which aim at reducing the quantity of antibiotics needed, the implementation of PCV2 vaccination helps to maintain a low medication level, together with a well managed herd health status.

The global implementation of PCV2 vaccination in swine herds and the observed results have lifted all doubts about the importance of this virus as a primary swine pathogen. It is also being recognised that this vaccination has an impact beyond reducing the clinical signs of PCV2 infection. By restoring the overall herd health, it allows a different approach to disease control, leading to a lower use of antimicrobials. A welcome finding in a global context of decreased exposure of farm animals to antibiotics.

For instance, a field trial in a 1,200-sow Spanish conventional farm had already evidenced that piglet Circovac vaccination has an impact on antimicrobial treatments. The results of 23 batches of pigs (n=13,892) before vaccine implementation were compared to those of 21 batches (n=15,800 piglets) afterwards. Not only did the production parameters improve significantly, but the cost of medication also decreased from 4.86 to 1.82 Euro cents/kg liveweight ($p<0.01$).

Also, a field trial in a 2,250-sow PMWS-affected Polish farm also showed that PCV2 vaccination of piglets with Circovac not only significantly improved health and growth performance of piglets, but led to a reduction in antibiotic consumption by a third.

On the other hand, recently published independent data show that, where the main objective is to reduce antibiotic consumption, PCV2 piglet vaccination is consistently part of the solution. This is reflected in a preliminary study of the implementation of the yellow card system in Denmark, published by experts from the Danish Agriculture & Food Council earlier this year. This system, which aims at lowering the amount of antibiotics used in the Danish swine industry by targeting herds with high antibiotic consumption, was found to increase the use of vaccines against respiratory, digestive and PCV2-associated diseases. Over a 12-month period, PCV2 vaccines were those with the most marked increase (+31% in number of doses), although there was also an increase in the use of other vaccines. Also in Denmark, another study focused on the management of post-weaning diarrhoea on two organic farms (no use of antibiotics).

Hygiene and nutritional measures increased the proportion of piglets with normal faeces in both herds. Although vaccination against PCV2 and Lawsonia did not lead to a further increase of the health status, it proved beneficial through the improvement of FCR, leading to an additional profit of €2.75/pig.

So far, no international standard exists for the assessment of alternatives to antimicrobials. It therefore seems reasonable to advocate PCV2 vaccination of piglets at herd level, not only because of the widespread subclinical PCV2 infection, but also for an optimal resilience of the production flow by lowering the degree of exposure to antimicrobial agents. And a timely published British economic modelling study evaluated the cost of subclinical PCV2 infection at £8 (€9.4) per pig. This underlines the cost-effectiveness of the strategy based on piglet PCV2 vaccination, when aiming both at improving the production flow and limiting the antibiotic exposure.

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Profitability of PCV2 piglet vaccination: a positive return on investment is proved

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The return on investment of PCV2 vaccination of piglets has to be considered in the context of the herd health status, i.e. whether there is an on-going PCVD clinical presentation or not. In the latter case, the situation is of a subclinical PCV2 infection, since the virus is present in swine worldwide.

In a published Polish field study, implementation of PCV2 vaccination of piglets with Circovac in a farm with an on-going acute outbreak of PMWS resulted in the significant improvement of all health and production parameters: ADWG (+80g/d as compared to the non-vaccinated groups), FCR (-0.3 points), total mortality
(-12 points), slaughter weight (+4.6kg).

In a field trial conducted on two Spanish farrow-to-finish farms affected with PMWS, the benefit of vaccination with Circovac was significant on the ADWG on both farms, of +10 and +40g/d, respectively.

Also, homogeneity of the pig bodyweights at slaughter was improved (p=0.008) and the proportion of light pigs (<80kg) at slaughter was reduced by 10.5%.

The profitability of vaccination was based on the paying scheme used in Spain, including the bonus/penalties applied to ranges of weights.

Circovac vaccination induced an average gain of +€2.55 per carcase in one farm, and of +€4.34 per carcase in the other.

The extra gain due to homogenisation of the bodyweights was estimated to an average of €0.29-0.32.

Taken together, these calculations estimate the economic benefit of vaccination to about €4 per pig, which outweighs the cost of the vaccine.

On a 1,200-sow Spanish farm that was diagnosed with PCVD (respiratory symptoms and delayed growth), the results of PCV2 vaccination of piglets with Circovac was evaluated on the 21 batches that had been vaccinated, compared to the previous 23 batches. Again, ADWG, corrected FCR and mortality were significantly improved (+41g/d, -0.27 points, -9.6%, respectively).

In addition, medication costs were strongly reduced (-€3.04 per kg live weight, p<0.001), the only latter being sufficient to observe that the margin increase with piglet vaccination with Circovac will at least be as important as in the previous study, over €4 per pig.

Regarding PCV2 vaccination in the context of subclinical infection, Prof. Joaquim Segalés (CReSA, Spain) wrote, at the occasion of the Merial Swine Forum that was held in Budapest (Hungary) last April, that "recent papers show that PCV2 vaccination is worthwhile in case of subclinical infection. Although more studies are needed in different subclinical scenarios, large integrators in Europe and North America have decided to vaccinate virtually all their produced pigs. These big companies are the ones that control their finances and revenues in the tightest way. They probably calculated that, in their production systems, PCV2 vaccination is also of value in subclinical scenarios. I believe that PCV2 vaccination is certainly cost effective."

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Comparison of immune response between different methods of PRRS vaccination

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Successful control of PRRS often involves strategies for immunising gilts and maintaining immunity in sows. In Spain, an approach was tested in which gilts are firstly immunised by using live virus vaccine and then booster vaccination of sows is performed using Progressis. This may avoid the use of live vaccine in gestating sows.

Material and methods

32 high health pigs were selected at weaning in a PRRSV-antibody-free farm by ELISA. At six weeks of age, piglets were randomly allocated in four separated groups: A, B, C and D and vaccinated with an adjuvanted modified-live PRRSV vaccine (MLV) or a placebo. Three months later, piglets were revaccinated with Progressis (once or twice) or with a MLV as shown in Table 1. At 6.5 months of age, all pigs were intranasally challenged with $1x10^6$ $TCID_{50}$ (2ml) of a Lelystad-like PRRSV strain and were followed for 21 days. Humoral response was evaluated by ELISA and viral neutralisation test (VNT) for the presence of neutralising antibodies (NA). The frequency of PRRSV specific IFN-γ cells in blood was measured by ELISPOT assay. After challenge, viraemia was examined by RT-PCR at days 0, +3, +7, +10, +14, +21 post inoculation (dpi).

	Months of age				
Group	1.5	4.5	5.5	6.5	7.5
A	MLV	Progressis	Placebo	Challenge	End
B	MLV	MLV	Placebo	Challenge	End
C	MLV	Progressis	Progressis	Challenge	End
D	Placebo	Placebo	Placebo	Challenge	End

Table 1. Design of the experiment.

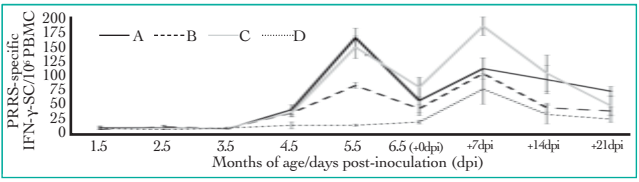

Fig. 1. IFN-γ response (ELISPOT) after vaccination.

Results

No reaction after vaccination was observed, showing safety of these treatments. Initial vaccination with the MLV produced seroconversion and raised the PRRSV specific cell mediated response. Following booster vaccination, no difference was seen in the ELISA humoral response between the vaccinated groups, but the use of Progressis as a booster antigen (groups A, C) induced a better PRRSV-specific IFN-γ response (Fig. 1) than the use of a repeated MLV administration (group B) immediately following the first booster injection ($p<0.05$), which lasted longer thanks to the second booster injection (group C) ($p<0.05$). Following challenge, seroconversion was observed in the unvaccinated pigs, while ELISA titres remained high in the vaccinated groups. At 14 dpi, all pigs in groups B and C had NA, while in the groups B and D some pigs had no detectable NA.
Furthermore, the highest booster effect in IFN-γ response was seen in group C ($p<0.05$ at 7 dpi) and the most sustainable one in group A ($p<0.05$ at 21 dpi). RT-PCR results confirmed viraemia in all unvaccinated pigs following challenge, while in groups A, B and C only one or two pigs became infected by 3 dpi.

Conclusion

Under the conditions of the study, combined protocols (MLV + Progressis) reached similar levels of antibodies, similar virological protection but even superior levels of neutralising antibodies response and cell-mediated immunity as compared to a repeated vaccination protocol with MLV only. ■

Ref: I. Diaz et al, The Veterinary Journal, 197 (2013) 438-444

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Mortality reduction following vaccination of piglets against PCV2

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Total mortality can be due to specific pathogens, for instance PCV2, PRRSV, PRV, CSFV, M. hyo, APP, etc but also due to many different causes, for instance lameness, intestinal occlusion, abscess, etc as well as infection with numerous opportunistic agents.

When implementing a control measure to reduce mortality targeted on a specific cause, it is of interest to separate what is its true contribution compared to other causes of mortality.

A new method has been established, using linear regression between total mortality before (without) vaccination and decrease of mortality following vaccination that enables producers to calculate an expected predictive mortality reduction.

It is based on the collection of results gathered in the literature and reporting mortality reduction after piglet vaccination with Circovac from weaning onward. These studies are of many different types: controlled trial, historical studies or even field data collection.

They have been performed in many different countries (Italy, Japan, Poland, Germany, Austria, France, Spain, the Czech Republic, Mexico, Thailand, etc) and in farms of different production systems: birth-to-finish, weaning-to-finish, post-weaning or finishing herds.

Initial or control group mortality were as diverse as from 37.7% to 2.34%. Farms were of all kind of health status, experiencing infections with many co-factors, such as PRRSV, M. hyo, APP, etc. Mortality data was collected: birth-to-finish, weaning-to-finish, post-weaning or finishing.

The predictive mortality reduction (PMR) is obtained after linear regression between mortality reduction following vaccination and mortality rate in unvaccinated pigs.

In this case, the R^2 coefficient is = 0.935, indicating that the linear model is well adapted for the calculation. Fig. 1 shows the plotting of the values, the regression line and the confidence interval.

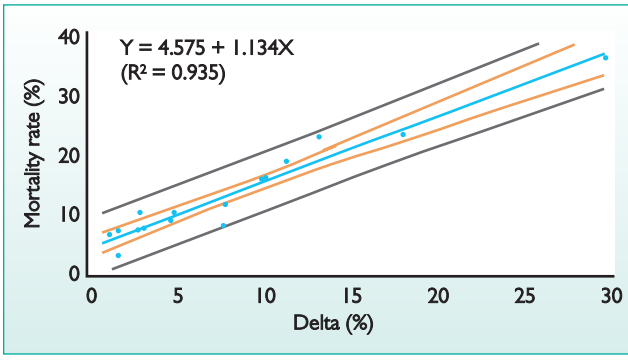

Fig. 1. Regression line between mortality reduction following vaccination and mortality rate in unvaccinated pigs.

The basic mortality i.e. due to other causes than PCV2 was evaluated on average as 4.57% and vaccination reduces specific mortality on average by 88%.

In conclusion, based on all published studies (n=17), in a wide array of different types of farms and situations, vaccination of piglets with Circovac is expected to bring an 88% reduction of specific mortality, which represents an approach of the real contribution of PCV2 vaccination of pigs on the damages actually provoked by PCV2. ■

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