PIGLETs WITH MATERNALLY DERIVED ANTIBODIES CAN BE VACCINATED AT 2 WEEKS OF AGE

G. Chénard¹*, P. Selman¹, P. Eblé², N. Stockhofe² and A. Dekker²

¹Products Division, Animal Sciences Group of Wageningen University and Research Centre
P.O. Box 65, 8200 AB Lelystad, The Netherlands
²Central Veterinary Institute of Wageningen University and Research Centre,
P.O. Box 65, 8200 AB Lelystad, The Netherlands

ABSTRACT

We investigated to what extent maternally derived antibodies (MDA) interfere with FMD vaccination in order to determine when piglets should be vaccinated in emergency situations. Groups of piglets with MDA were vaccinated at different time points following birth and the antibody titres to FMD virus were measured using virus neutralisation tests (VNT).

We used 50 piglets from 5 sows that had been vaccinated three times intramuscularly in the neck during pregnancy using a high potency trivalent Cedivac-FMD vaccine containing strains of FMD virus serotypes O, A and Asia1. Four groups of 10 piglets were vaccinated intramuscularly in the neck at 2, 4, 6 or 8 weeks of age using a 6 PD₅₀ monovalent Cedivac-FMD vaccine (serotype A). One group of 10 piglets with MDA was not vaccinated and another group of 10 piglets without MDA was vaccinated at 2 weeks of age. Sera samples were collected and (serotype A) antibody titres were determined using VNT.

The antibody responses of piglets with MDA vaccinated at 6 or 8 weeks of age were similar to the responses of piglets without MDA vaccinated at 2 weeks of age and reached the level corresponding with 6 PD₅₀ at 3-4 weeks post vaccination. The antibody responses of piglets with MDA vaccinated at 2 or 4 weeks of age were lower compared to the responses of piglets without MDA. Nevertheless, a partial immune response is better than a further decline in antibody levels in an emergency situation.

2. INTRODUCTION

Vaccination and revaccination are effective intervention tools in combating Foot-and-Mouth Disease (FMD). Revaccination is especially relevant for the pig industry given the relatively short gestation period of the species. Passive immunization by maternally derived antibodies (MDA) interferes to a varying degree with active immunization against FMD. It has been shown that the degree of suppression of the immune response is directly proportional to the MDA titre at the moment of vaccination (3). Factors such as the vaccination regimen of the sow, the antigenic payload of the vaccine, the type of vaccine adjuvant, the amount of colostrum uptake and the general health status and number of the piglets in a litter affect the quantity of MDA that are ultimately transferred to individual animals. Given the high turnover of animals in the porcine population, it has been suggested that the immaturity of the immune response of piglets makes vaccination of the sow during pregnancy a more effective method to protect the litter (4).

In the knowledge that MDA interferes with the immune response of young animals, it has been suggested that effective immunization can only be achieved in the absence of MDA (1). In piglets, the MDA levels drop to about 1-3% of their initial value after about 60 days (5). It is important to realize that the observed drop of MDA levels in piglets is largely due to the rapid increase in blood volume. Vaccination of piglets with MDA has generally been recommended to be performed only after levels are very low. Indeed, in order to circumvent interference of the immune response due to MDA, vaccination of piglets born from vaccinated sows can be delayed until approximately 8-10 weeks of age. Such a strategy however is more suited to increasing the herd protection levels in a number of months and is less suited to emergency or other situations with imminent threat of
exposure to live virus. In an emergency situation, it is of paramount importance to maintain the highest possible levels of herd protection. Any delay in vaccination of piglets with MDA results in a further drop in herd protection levels. However, vaccination in the presence of high levels of MDA may be ineffective. The optimal vaccination moment is likely dependent on a number of factors including the quality and potency of the vaccine being administered. For this reason, it is advisable to generate data to support the decision-making process in an emergency situation.

2. MATERIALS AND METHODS

2.1 Vaccines
The vaccines administered were manufactured by the Products Division of the Animal Sciences Group (ASG), Lelystad, The Netherlands and contained inactivated, purified FMD virus antigens using a mineral oil as adjuvant in a double oil emulsion formulation. The pregnant sows were vaccinated with a trivalent Cedivac-FMD vaccine formulated to contain a high antigen payload. This payload corresponded with approximately 15 times the antigen required for one 50% protective dose (PD$_{50}$) for each of the strains: A Turkey 14/98 (A Iran96 analogue), Asia1 Shamir and O1 Manisa. A monovalent Cedivac-FMD vaccine containing the strain A Turkey 14/98 was used to vaccinate the piglets. The antigen payload of this monovalent vaccine corresponded with a potency of at least 6 PD$_{50}$.

2.2 Animals and husbandry
The 5 pregnant sows in this study were primipari and purchased (at day 21 of gestation) from Van Beek SPF Varkens BV (Putten, The Netherlands). The sows were individually housed in farrowing boxes with tenderfoot floor in the animal experimental facilities of ASG and were fed rationed portions appropriate for their age. Each of the 5 vaccinated sows had between 11 and 13 piglets; 10 piglets of each litter were used in this study. The piglets were allowed colostrum uptake and distributed evenly over 5 groups so that each group had 2 piglets from each sow.

2.3 Vaccination regime
The sows were subject of a vaccine safety study in pregnant animals following the European Pharmacopoeia monograph for FMD vaccines (2). The animals were vaccinated intramuscularly in the neck in each trimester of pregnancy using a double dose (first trimester) or regular dose (second and third trimesters) of the trivalent vaccine described earlier. Four groups of 10 piglets were vaccinated intramuscularly in the neck at 2, 4, 6 or 8 weeks of age using a dose volume of 2 ml of monovalent A Turkey Cedivac-FMD vaccine described earlier. In addition, one group of 10 piglets with MDA was not vaccinated. Another group of 10 piglets without MDA was vaccinated at 2 weeks of age. Both groups served as a control group.

2.4 Virus neutralization tests
Blood samples were collected from all piglets periodically and antibody titres in the resulting sera were assessed against homologous FMD virus (A Turkey) by virus neutralisation tests (VNT) performed as described in the OIE manual (6) using secondary porcine kidney cells. Blood samples were collected until 6 weeks post vaccination.

2.5 Antibody titre expected for 6 PD$_{50}$ vaccines
Using the virus neutralization test described above, a mean antibody titre of log$_{10}$ 1.50 for FMD virus strain A Turkey has previously been observed 28 days post vaccination in adult pigs vaccinated with a 6 PD$_{50}$ vaccine.

3. RESULTS
All sows had normal pregnancies and normal size litters. Following colostrum uptake, the piglets born from the immunized sows had MDA against A Turkey with a mean antibody titre of log$_{10}$ 1.73, which is above the VNT titre expected for a 6 PD$_{50}$ vaccine. The rate of decline of the MDA was similar in all the groups (Figure 1). MDA titres declined to below the detection level of the VNT (log$_{10}$ 0.30) at approximately 7 weeks of age. The half-life of antibodies was approximately 16 days when corrected for increase in body weight.

The antibody profiles are shown again in Figure 2 but shifted to the same moment of vaccination to facilitate comparison of immune responses. Piglets without MDA vaccinated at two weeks of age showed a normal immune response and antibody levels reached the 6 PD$_{50}$ level at 4 weeks. The
neutralising antibody responses of piglets with MDA vaccinated at 6 or 8 weeks of age were similar to the responses of piglets without MDA vaccinated at 2 weeks of age and reached the 6 PD<sub>50</sub> level 3-4 weeks post vaccination. The neutralising antibody responses of piglets with MDA vaccinated at 2 or 4 weeks of age were suppressed compared to the responses of piglets without MDA. The levels of MDA continued to decline at the same rate for 2 more weeks after vaccination and by 3 weeks post vaccination, the mean VNT titre had stabilized or increased marginally. The neutralising antibody response of piglets vaccinated at 4 weeks of age was reasonable and the mean titre approached the 6 PD<sub>50</sub> level at 6 weeks post vaccination. In the case of piglets vaccinated at 2 weeks of age, the immune response resulted in antibody levels that remained below the 6 PD<sub>50</sub> level.

All vaccinated piglets had mild to moderate injection site reactions, transient temperature increases and histology of vaccination sites revealed no unusual findings.

4. DISCUSSION

The objective of this study was to determine when piglets with MDA should be vaccinated in an emergency situation. The main obstacle to effective vaccination is undoubtedly the presence of maternally derived antibodies. The results presented here confirm that MDA levels at the time of vaccination are directly proportional to the degree of interference to active immunization.

In this study, the MDA titres in piglets declined to below the detection level of the VNT after approximately 7 weeks, which is in agreement with earlier findings. This explains why groups of piglets (with MDA) that were vaccinated at either six or eight weeks of age had very good immune responses. It is therefore tempting to designate this time point as the “best” moment to vaccinate. However, delaying the vaccination of piglets until protective antibody levels are very low allows the herd protection level to drop to undesirable levels. This is due to the sheer numbers of piglets born and the dilution effect this has on the herd. The optimal vaccination moment it seems, is at the trade-off point where levels of maternally derived antibodies still offer a reasonable level of protection but still allow a reasonable immune response following vaccination. When observing the antibody level profiles of piglets vaccinated at two weeks of age, it is interesting to note that following vaccination, protective antibody levels declined for a further two to three weeks before reversing. This time gap is important as any further delay in vaccination of piglets allows an undesirable window of susceptibility to open.

In order to maintain the highest herd immunity levels possible in the farrowing period, it is necessary to prevent drops in levels of protective antibodies in piglets. This means vaccinating as early as possible and brings us back to the problem of vaccination in the presence of antibodies of maternal origin. In fact, it is not the vaccination that is the problem, but rather achieving an effective immune response. There is only limited experimental evidence available of effective vaccination in the presence of maternally derived antibodies. However, it is reasonable to expect that vaccines of good quality can, to a certain limit, overcome maternally derived antibodies to induce a good immune response. FMD vaccines using an oil emulsion adjuvant, such as Cedivac-FMD, are known to be effective in pigs. This study shows that piglets respond to vaccination at 2 weeks of age and that the decline in levels of protective antibodies in piglets can be stopped by vaccination using Cedivac-FMD at 2 weeks of age.

5. CONCLUSIONS

The immune system of piglets is capable of responding to vaccination at 2 weeks of age.

The immune response following vaccination of 2 week old piglets was partially suppressed by the presence of MDA.

The decline in levels of protective antibodies (and the corresponding decline in herd protection levels) can be stopped by vaccination of piglets at 2 weeks of age.

6. REFERENCES


**Figure 1:** Antibody profiles (FMD strain A Turkey 14/98) in piglets with MDA vaccinated at 2, 4, 6, 8 weeks of age. Profiles are shown real time.

**Figure 2:** Antibody profiles (FMD strain A Turkey 14/98) in piglets with MDA vaccinated at 2, 4, 6, 8 weeks of age. Profiles are shifted to allow comparison of responses.