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Herd Profiling as a strategy for the diagnosis of PRRS virus infections.

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ABSTRACT

The frequent use of PRRS vaccines in the United States swine industry has added difficulty in the interpretation of serology of any type since there is not assay that can differentiate natural from vaccine response. A considerable effort has been made to develop and assess a strategy using the IDEXX PRRS ELISA as a quantitative tool to assay herd samples over time. Software, xCHEK, has been developed to assist the user in capturing, analyzing, reporting and graphing individual herd sampling times and comparing the results to previous test points.

Diagnostically significant findings were determined by testing samples from detailed vaccine animal trials obtained from two commercial firms: NOBL/BI Laboratories and Schering-Plough Animal Health (SPAH).

Examples of herd profiling strategies are reported here showing the benefits of the xCHEK software. The significance of proper sampling techniques are described showing the impact on decision making.

The strategies described here are being successfully used in small, medium and large production units around the world.

INTRODUCTION

The advances in our understanding of the virology of PRRS, the many variants, and the pathology and immunology of the disease have reached critical mass. Within the next year research will probably provide answers that clarify the role of cell mediated immunity and it's relationship to the measured humoral response and protective immunity.

The ability of the PRRS virus to respond to genetic pressure through altering its genetic make-up gives testimony to the success of the virus in surviving efforts to control and even eradicate the disease in some countries. This ability has also contributed to the decision that the development of a differential diagnostic test and companion biomarker deleted vaccine would be risky from the standpoint of the previously demonstrated ability
to spontaneously delete genes from the virus'genome. Therefore, other strategies were examined in an effort to maximize the utility of the PRRS ELISA in diagnosis and herd management decision making are discussed herein.

MATERIALS and METHODS

IDEXX Laboratories Temporal Study: Five (5) Duroc pigs approximately 60 pounds were exposed to an Iowa isolate of the PRRS virus (3798) via the intra-nasal and pharyngeal routes

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using approximately 1 x 10^3 fluorescent antibody infectious units (FAIU). Serum was obtained from samples obtained using a daily detailed protocol through post infection day (PID) 14, and then weekly through PID 308. Serum was stored at -20C until tested

NOBL/BI Vaccine Animal Trials: Four (4) primary studies were conducted and evaluated using the IDEXX PRRS ELISA: Onset of Immunity Study, Mature Pig Study using a heterologous challenge (Lelystad Strain of PRRS Virus), and a Mature Pig Study using a homologous challenge (Vaccine parent strain, 2332).

Onset of Immunity: Four groups of mature swine were established:

- Group 1: Ten (10) pigs were vaccinated 14 day prior to challenge (V14/C).
- Group 2: Ten (10) pigs were vaccinated 7 days prior to challenge (v7/C).
- Group 3: Ten (10) pigs unvaccinated were used as the challenge controls
- Group 4: Five (5) pigs were unvaccinated and unchallenged which served as the untreated control group

Mature Pig Study: Heterologous Challenge Study: Fourteen (14) pigs were separated into three groups

- Group 1: Seven (7) pigs were administered vaccine on PVD 0 and challenged on PVD 118.
- Group 2: Five (5) pigs were unvaccinated but were challenged on PVD 118 and served as the challenge control group.
- Group 3: Two (2) pigs were maintained as a non-treatment control group.

Mature Pig Study: Homologous Challenge Study: A similar study using 20 pigs was conducted as described for the Lelystad strain challenge group, except the homologous PRRS(US) 2332 parent strain was used to challenge the swine, again on PVD 118.

SPAH Vaccine Animal Trials: Two complex studies were conducted and evaluated using the IDEXX PRRS ELISA: Vaccination using PrimePac™ followed by homologous strain challenge, and a second study followed by heterologous strain challenge.

PrimePac Vaccination with Homologous Challenge: Three (3) Groups of gilts were established. Serum samples for virology and serology were collected at the time of vaccination and at monthly intervals until the time of challenge. Gilts were challenged at approximately 85 days of gestation using approximately 6.3 $\log_{10}$ ($TCID_{50}$)/ml using the Neb-1 strain of the PRRS virus.

- Group A: Each gilt was inoculated with 2 mls of vaccine intramuscularly and subsequently challenged as previously described.
- Group B: Each gilt in the control group was allowed to co-mingle with gilts of Group A and were challenged in the same manner.
- Group C: Gilts in this group served as challenge controls and were maintained separately throughout the course of the study. The gilts were not vaccinated, or exposed to vaccinated animals prior to challenge.

PrimePac Vaccination with Heterologous Challenge: Two (2) Groups of gilts were established. Serum samples for virus and serology were collected at time of vaccination and at monthly intervals until the time of challenge. Gilts were challenged at approximately 75 days of gestation using approximately 5.4 $\log_{10}$ ($TCID_{50}$)/ml using the Lelystad strain of the PRRS virus.

- Group A: Each gilt was inoculated with 2 mls of vaccine intramuscularly and subsequently challenged as previously described.
- Group B: Each gilt in the control group was allowed to co-mingle with gilts of Group A and were challenged in the same manner.

Pigs farrowed from gilts of each group were studied for viremia using MARC 145 cells and serologic response using the IDEXX PRRS ELISA and a SPAH virus neutralization test.

Herd Studies: A grow/Finish Respiratory Disease Investigation. [2]

This herd study was selected from 12 similar studies to illustrate the importance of sampling and understanding the changing sero-profile over time.

This group of pigs were moved from the nursery to another separate finishing complex. Pigs were sampled at placement, then every two weeks following through slaughter. Each sampling of 35 pigs represented the entire test group of 1000 pigs. The goal was to have a minimum of 30 of the original 35 pigs sampled through the course of the study. This sample size provided the ability to detect one or more positive animals/changes in sero-status at a true prevalence of ≥ 10% with a confidence of 95%. Several other parameters were measured during the study as detailed in the full article sighted below.

RESULTS

IDEXX Laboratories Temporal Study: Figure 1 illustrates the complete profile of the 5 pigs and the mean plot of the study as calculated S/P (Sample to Positive) Ratios. Figure 2 illustrates the temporal profile for 6 selected profile periods: PID 0, 10, 28, 98, 182, and 242. Each point was selected to illustrate a specific event and how it would be displayed using herd profiling. During actual herd profiling, one would usually use set intervals for sampling, every 3 weeks as an example. The profiling shows several events and can be interpreted in the following way with the knowledge the pigs were not vaccinated.

1. Negative herd status
2. Early response to a recent infection
3. Peak immune response
4. Decaying immune response
5. Decaying, but stabilizing antibody level
6. Secondary response in a positive herd.

PRRS Onset of Immunity: This study demonstrated that serologic response to the MLV vaccine was not detected on PVD 7, but was detected by PVD 14. The non-vaccinated challenge group pigs showed the same response to challenge where seroconversion occurred on, or before day 14. These data showed general agreement with the IDEXX temporal study where the 5 pigs seroconverted from PID 9 through 14. Pigs vaccinated 7 days prior to challenge did not response as rapidly as those vaccinated 14 days prior to challenge.

Mature Pig Study: The mature pig studies illustrate two important points:

1. The IDEXX ELISA detects response to the two strains of PRRS used in these studies: PRRS(US, 2332) and the Lelystad strain
2. A heterologous challenge produces a higher and therefore, anemnestic response which is not observed where homologous challenge exists.

[2] John R. Kolb DVM, et. al.: Quantitative PRRS ELISA: A decision making tool. IDEXX Laboratories Compendium. March 1997 edition. Section 8.

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SPAH Homologous and Heterologous Gilt/piglet Studies

Homologous Challenge Study: Vaccination induced ELISA and virus neutralizing antibodies in Group A gilts. The ELISA and VN did not detect an anemnestic response following homologous strain challenge. Passive antibodies were detected by the ELISA and VN in pigs from the vaccinated and challenged gilts. Piglet ELISA and VN serology results demonstrated that all groups of piglets had antibody titers in the day of age sera, which steadily decreased during the post parturition sampling period.

Piglets born from Vaccinated and Challenged Gilts: Antibodies decayed to baseline in a linear and predictable fashion expected of passively acquired antibodies.

Piglets born from Non-Vaccinated/Challenged Gilts: Antibody level was constant to increasing indicating a response to vertical congenital infection.

Piglets from from Contact Controls: Antibodies decayed, then increased as a response to horizontally transmitted virus.

Heterologous Challenge Study: The ELISA and VN detected anemnestic response in the vaccinates by post challenge day (PCD) 7 and primary response in the challenge controls by PCD 10 to 14. The ELISA and VN detected antibodies during the two week viremia in the control group. Passive antibodies were detected by the ELISA and VN in pigs from the vaccinated and challenged gilts. Piglet ELISA and VN seroconversion results demonstrate that Group A and B piglets had antibody titers in the day of age (0 week) sera which steadily decreased during the post parturition sampling period. Unique serologic profiles for piglets of both groups were observed.

Piglets born from Vaccinated and Challenged Control Gilts: A high level of antibodies decayed to an antibody titer of about 1500 then sharply increased, indicating response to infection.

Piglets born from Challenge Control Gilts: A lower level of antibodies decreased to an antibody titer of about 1500 and then increased sharply. Twenty of 21 pigs died in this group and was probably the result of congenital infection with the PRRS virus.

Herd Study (Herd 3, Midwest): A peak or elevation in S/P ratio was noted following clinical disease at 19 weeks post placement. Ratio increases were noted of greater than 0.5 for the mean of these groups. A temporal association of rising HI titers to swine influenza virus accompany these rises in PRRS S/P ratios. It could be speculated that pigs in this group completing seroconversion to PRRS infection, were initially exposed to Mycoplasma hyopneumonia at that time while pulmonary function may still have been impaired from PRRS virus infection.

DISCUSSION and CONCLUSIONS

These studies representing both experimental and production herds in character, support the useful application of quantitative herd profiling. Without this tool, one would fail to obtain in most cases decision supporting data and conclusions.

This approach appears to us to have similar applications in assessing the potential role of the collective diseases contributing to what now is globally referred to as porcine respiratory disease complex, or PRDC.

Numerous data and charts will be presented to illustrate the many points described herein.