RESEARCH REPORT

SWINE HEALTH

Title: RespPRRS^{R} vaccinated and nonvaccinated gilts challenged in late-gestation with a neurovirulent strain of porcine reproductive and respiratory syndrome virus. – **NPB #97-1985**

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Abstract:

Despite the use of modified-live porcine reproductive and respiratory syndrome virus (PRRSV) vaccines, PRRSV isolates have been recovered from vaccinated animals experiencing clinical disease. A PRRSV isolate from a vaccinated swine herd experiencing unusually severe PRRSV-induced neurologic disease was used to challenge PRRSV vaccinated gilts. Five gilts from a PRRSV seronegative and naïve farm were vaccinated twice prebreeding (30 days apart) with RespPRRS^{R}, synchronized 3 weeks later and artificially inseminated. The vaccinated gilts were infected intranasally with a neurovirulent strain of PRRSV at 90 days of gestation. Fetal survival in vaccinated gilts was compared to fetal survival in a group of 5 nonvaccinated, PRRSV naive gilts.

Two prebreeding vaccinations with RespPRRSR vaccine virus did not prevent fetal infection and death in gilts challenged with a neurovirulent strain of PRRSV. The number of fetal deaths in the RespPRRS^{R} vaccinated gilts was similar to the number of fetal deaths in the PRRSV nonvaccinated, naïve challenged gilts. These findings demonstrate that PRRSV strains existing in or introduced into PRRSV vaccinated herds are capable of causing reproductive loss.

Introduction:

Porcine reproductive and respiratory syndrome virus (PRRSV) infection is characterized by late term reproductive failure, interstitial pneumonia complicated by concurrent bacterial or viral infections and persistent infections (Collins 1992, Rossow 1995, Benfield 1996). PRRSV infection infrequently causes mild encephalitis and the clinical signs of PRRSV induced encephalitis are commonly subclinical (Collins 1992, Rossow 1995).

Swine herds vaccinated with RespPRRS^{R} are protected from many of the clinical effects of PRRSV infection; however, some vaccinated herds experience PRRSV induced encephalitis in neonatal pigs (Rossow 1997). Infected pigs are lethargic, fail to nurse and may exhibit head tremors. Mortality in affected litters ranges from 50-100%.

Severe encephalitis caused by the neurovirulent PRRSV (PRRSV-NV) isolates have not been previously described. The reason(s) for the severity of the brain lesions has not been determined but may be influenced by PRRSV strain variation or the route of PRRSV exposure (i.e. transplacental or post-farrowing). Differences in the severity of neurologic disease have been related to the route of inoculation (Lane 1996). Therefore, to characterize a PRRSV-NV isolate the route of pig infection needs to be evaluated.

We plan to evaluate a PRRSV-NV isolate to determine if the brain lesion can be reproduced by the PRRSV isolate alone and if the route of virus exposure influences the development and severity of PRRSV induced encephalitis.

OBJECTIVES:

The primary objective of this experiment is to determine if prebreeding vaccination with RespPRRS^{R} will prevent fetal death in pregnant gilts challenged with a neurovirulent PRRSV isolate. Secondary objectives include the reproduction of brain lesions with the neurovirulent PRRSV and a comparison of the polymerase chain reaction (PCR) to virus isolation to diagnosis fetal PRRSV infection.

PROCEDURES:

Gilts from a PRRSV seronegative, naive herd were purchased, housed in isolation facilities and separated into three groups. Group 1 contained 5 gilts vaccinated intramuscularly with RespPRRS^{R} vaccine virus twice prebreeding, 30 days apart. Group 2 contained 5 nonvaccinated positive control gilts and group 3, three nonvaccinated negative control gilts. Twenty one days after the second RespPRRSR vaccination in the group 1 gilts, all gilts were synchronized with Regu-mate^{R} at a dose of 15mg orally, once a day for 18 days. Gilts were bred by artificial insemination with semen from a PRRSV seronegative and naïve boar stud. Purchased semen was also negative for PRRSV by PCR technique. Gilts in groups 1 and 2 were challenged by nasal instillation of 10^{3} $TCID_{50}$ of a first passage, neurovirulent PRRSV isolate cultured in MARC-145 cells. Group 3 gilts were sham inoculated intranasally with MARC-145 cell culture supernate. Gilts were monitored daily for abortion. Gilt sera were collected for virus isolation and antibody testing (IDEXX Elisa) at days 0, 5, 14 and 21 after PRRSV infection. Tissues (lung, brain, spleen, tonsil, lymph node, heart and kidney) and thoracic fluid from each fetus were collected for PRRSV PCR testing, virus isolation (porcine alveolar macrophages) and histopathology. Live pigs were allowed to nurse and were euthanized when clinical signs of CNS disease developed or at 14 days post farrowing. Serum from live-born pigs was tested for PRRSV by PCR and virus isolation.

Results:

Fetal Survival

The number of fetal deaths in group 1 and 2 gilts was similar. Thirty-six of 54 (68%) of group 1 fetuses were born dead and 34 of 45 (75%) of group 2 fetuses were born dead. Two of the 18 live-born group 1 pigs died within 4 days of birth; the remaining 16 pigs survived to 14 days after farrowing. None of the live-born group 1 pigs developed clinical signs of CNS disease. One group 1 sow died 7 days after PRRSV infection. The uterus of the dead sow contained 8 markedly autolyzed fetuses. The 11 live-born group 2 pigs were euthanized within the first week after to birth due to poor viability associated with clinical signs of pneumonia and lethargy. Twenty-three of 24 group 3 pigs were live-born and viable; there was 1 stillborn, partially mummified fetus.

Serology, polymerase chain reaction, virology, and virus sequencing

Each group 1 gilt vaccinated with RespPRRSR was seropositive for PRRSV antibodies (S/P ratio > .39) at the time of breeding and each group 2 and 3 gilt was seronegative. Three of 5 group 1 gilts had PRRSV S/P ratios less than .39 at days 0 and 5 post PRRSV infection. The four surviving group 1 gilts each had a PRRSV S/P ratio greater than .39 at 14 and 21 days post infection. Group 2 gilts had PRRSV S/P ratios less than .39 at days 0 and 5 post exposure and ratios greater than .39 at 14 and 21 days post exposure. Group 3 gilts had PRRSV S/P ratios less than .39 at all test days post exposure. One of 31 thoracic fluid samples available from group 1 fetuses had a PRRSV S/P ratio greater than .39. Three of 36 thoracic fluid samples from group 2 fetuses had a PRRSV S/P ratio greater than .39. All group 1 and 2 live born pigs nursed and serum had a PRRSV S/P ratio greater than .39. Each of the live-born group 3 pigs was PRRSV seronegative.

In group 1 pigs, PRRSV nucleic acid was detected in thoracic fluid from 6 of 31 fetuses, tissue homogenate from 10 of 54 fetuses and serum from 1 of 18 live-born pigs by PCR technique. In group 2 pigs, 29 of 36 fetal thoracic fluid samples, 23 of 45 fetal tissue homogenate samples and 7 of 11 sera from live-born pigs had PRRSV nucleic acid by PCR technique. No PRRSV was identified in serum or tissues of each group 3 pig.

PRRSV was isolated from 5 of 31 group 1 fetal thoracic fluid samples and 1 of 18 live-born pig serum. In group 2 pigs, PRRSV was isolated from 1 of 45 fetal tissue homogenate samples and 4 of 11 live-born pig sera. PRRSV was isolated from 3 of 5 group 1gilt sera on day 5 post PRRSV infection. PRRSV was isolated from 4 of 5 day 5 post exposure sera and 3 of 5 day 14 post exposure sera of group 2 gilts. No PRRSV was isolated from any of the remaining group 1 or 2 sera or from any of the group 3 gilt sera.

The genetic sequence of open reading frame 5 and a portion of open reading frame 6 of the neurovirulent PRRSV challenge isolate was identical to the PRRSV recovered from one of the group1 pigs and one of the group 2 pigs.

Histopathology

Lesions in tissues from both group 1 and 2 fetuses were similar and were characterized by lymphoplasmacytic arteritis. Artery lesions were most common in the lung and also found in the kidney. Two group 1 fetuses had mild encephalitis and 7 group 2 fetuses had mild to moderately severe encephalitis. Only one live-born group 1 pig had mild encephalitis. Two live-born group 2 pigs had moderately severe encephalitis and pneumonia. Tissues from group 3 pigs did not have lesions.

Summary:

Two prebreeding vaccinations with RespPRRS^{R} did not prevent fetal infection and death in late-term pregnant gilts challenged with a field strain of PRRSV. The number of fetal deaths in the RespPRRS^{R} vaccinated gilts was similar to number of fetal deaths compared to PRRSV naïve, infected control gilts. The PRRSV used in this project was obtained from pigs in a RespPRRSR vaccinated swine herd experiencing PRRSV induced encephalitis in neonatal pigs. The clinical findings in the affected herd and the experimental findings of this experiment demonstrate that PRRSV strains can either develop within a PRRSV positive herd or be introduced into a herd resulting in reproductive and neonatal pig loss. Lack of protection from clinical signs of disease may be affected by differences in strains of PRRSV or duration of immunity. The live-born pigs from RespPRRS^{R} vaccinated gilts were viable through 14 days post farrowing when compared to pigs from the non-vaccinated infected gilts. The findings indicate that the pregnant sow model is a sensitive test for evaluating immune cross protection between PRRSV isolates. The experiment also helps demonstrate that PRRSV

induced reproductive loss can occur in swine with some degree of previous PRRSV exposure; a finding that corresponds with field observations of PRRSV infection.

Severe encephalitis lesions were reproduced in some fetal and live-born pigs similar to lesions described in the case report. In addition, this PRRSV isolate commonly crossed the placenta in naïve gilts and less commonly in the vaccinated gilts. The original case history for this PRRSV infection did not report reproductive loss as a part of the clinical problem indicating immunity to the circulating field virus(es) on the farm may have been important for protection from reproductive loss. The variations in clinical and microscopic presentations of PRRSV infections correspond to the increasing genetic heterogeneity of PRRSV strains within the United States. Continued evolution of PRRSV strains will likely frustrate many control procedures.

In this experiment, more PRRSV infections were identified in fetuses from vaccinated and nonvacinnated gilts by PCR compared to virus isolation. This is due to the sensitivity of the PCR test and independence from the need for viable virus that limits virus isolation. Over the past several years PCR testing has increased the number of diagnoses of PRRSV induced abortion from fetal tissues; however, it has not been successful in diagnosing most cases of PRRSV reproductive failure (personal observation). Currently, PRRSV induced reproductive failure is better diagnosed from weak-born pigs or sera of acutely infected sows. Identification of portions of the PRRSV involved in the pathogenesis of abortion would strongly influence future vaccine design and selection.

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* This trial was conducted at the Animal Disease Research and Diagnostic Laboratory, South Dakota State University.