**Title:** PED virus re-infection rate of sow herds, associated risk factors, production impact and time to achieve stability – NPB #14-271

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**Industry Summary**

The purpose of this study was to quantify the rate of sow herds re-breaking with PED virus and evaluate the impact on performance. The study involved participants’ data from an existing program called the Swine Health Monitoring Project (SHMP). In this program, veterinarians enroll sow farms and report weekly change in health status for PEDv. Performance records were requested for those herds that experienced an outbreak before July 1, 2014.

From May 1/2013 through July 1, 2014, 474 / 1027 (46%) herds broke with PEDv. After July 1, 2014 through June 30, 2016, a herd that had a previous outbreak was approximately three times as likely to re-break as herds in our database that have never had an outbreak (23.8% vs 7.8%). This difference was statistically significant (p<0.001).

Prior to July 1, 2014, 474 herds were infected with PEDV. Of the 474 herds, 429 herds achieved the stable state of weaning PEDV PCR negative pigs, the median time was 28 weeks, ranging from 7 to 64 weeks. Performance data were made available from 190 herds to estimate the time required for the herd to recover back to the production level before the outbreak. A median of 2.7 piglets/invented sow were not weaned and the average time required to recover to baseline production was 10 weeks in 183 herds. Herd infected in quarters 3 or 4 of the year had approximately twice the negative impact. These data are valuable for veterinarians in advising clients on the anticipated impact and time to re-achieve a stable state with regards to PEDV.

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**Keywords:**
Swine PEDV Production Mortality Stability

**Scientific Abstract:**

PEDV was first detected in United States in May, 2013. The virus spread through the swine industry and was reported in 30 US states by June, 2014. This study involved participants and data from an existing program called the Swine Health Monitoring Project (SHMP). The SHMP registered an incidence of 57%, 9% and 8% in 2013/14, 2014/15 and 2015/16, respectively. From July 1, 2014 – June 30, 2016, a herd that had a previous outbreak was approximately three times as likely to re-break as herds in our database that have never had an outbreak (23.8% vs 7.8%). This difference was statistically significant (p<0.001).
There are limited data describing the impact on production in sow farms. Veterinarians attempt to control the virus in sow herds with a program that stimulates herd immunity. There are no data on how long it takes with this control program to achieve a stable state of consistently produce weaned pigs that are not infected with the virus. Veterinarians were invited to share production data from 429 herds infected with PEDV. These data, in conjunction with diagnostic reports, were used to estimate the time required for the herd to produce PEDV PCR negative pigs and the production loss. Of the 429 infected herds that achieved the stable state of weaning PEDV PCR negative pigs, the median time was 28 weeks, ranging from 7 to 64 weeks. Of the 429 herds, 190 supplied production records. A median of 2.7 piglets / inventoried sow were not weaned and the average time required to recover to baseline production was 10 weeks in 183 herds. Herd infected in quarters 3 or 4 of the year had approximately twice the negative impact. These data are valuable for veterinarians in advising clients on the anticipated impact and time to re-achieve a stable state with regards to PEDV.

**Introduction:**

New cases of PEDV have spread extensively within the United States since the first diagnosed farm was confirmed in April, 2013. The virus spread through the country being detected in 30 states and approximately 50% of the US swine breeding herds by June30, 2014.

The original US PEDV strain can cause up to100% suckling piglet mortality. PEDV is an enveloped, single stranded, positive sense RNA virus of the genus Alpha coronaviridae in the family Coronaviridae similar to transmissible gastroenteritis virus (TGEV). The two viruses infect swine of all ages with identical clinical effects of watery diarrhea and vomiting, but can be differentiated via RT-PCR testing of fecal material and environmental samples. Aside from the identified US strains of PEDV with reported similarly severe clinical impact, a variant of PEDV characterized by a large deletion in the spike gene(S-INDEL variant) has been detected.

Cases of infection with the S-INDEL variant of PEDV (also identified as OH851) have resulted in apparent milder clinical impact and faster return to baseline production than original US PEDV clades. The S-INDEL variant was initially identified by whole-genome sequencing due to the unexpected observation of low mortality and rapid time to stability in some herds diagnosed with PEDV by RT-PCR.

Efforts to control the virus after infection include a whole-herd exposure program inspired by the same feedback exposure methods used to eliminate TGE virus from breeding herds. This program includes “loading” the breeding herd with as many gilts as capacity allows, closing the herd to any more introductions and then exposing all present through the feedback program in an attempt to infect all sows at the same time. The goal is to stimulate sufficient herd immunity, such that in conjunction with aggressive environmental cleaning and restricted movement of sows and pigs, the virus is eliminated from the premises. After whole herd exposure to PEDV via feedback of intestinal and fecal material, the sows’ immunity reduces the 100% morbidity of watery diarrhea and 50–100% pre-weaning mortality that is seen during an acute outbreak in naïve herds. While the long term goal at a sow herd might be to eliminate the virus, a shorter term goal in all herds is to wean pigs that are not infected. Holtkamp et al. attributed the term “stable” to herds infected with Porcine Reproductive and Respiratory Syndrome virus (PRRSV) where pigs are PCR negative at weaning but there is insufficient diagnostic evidence to indicate that the herd is free of the virus. Linares et al. (2014) proposed the term “time to stability” (TTS) as being the time from last known exposure of the sow herd to PRRSV until there was 4 consecutive samples of at least 30 weaned pigs that tested PCR negative. This same goal of stability has been adopted for PEDV. After clinical signs subside, veterinarians typically test piglets’ feces for the presence of PEDV by PCR with the goal being to wean PEDV negative pigs as soon as possible after the herd is infected. Whereas the programs have been anecdotally successful at controlling clinical signs, these methods and their success as measured by time to stability have not been reported.

Similarly, Linares et al. (2014) measured time for herds to recover performance back to the level achieved before PRRSV infected the herd. They quantified the loss as pigs not weaned and described the parameter as “time to baseline performance” (TTBP). This has not been reported for PEDV. Also, given the identical clinical signs between original PEDV strains and the S-INDEL variant, it is important to compare TTS and TTBP between the S-INDEL variant PEDV and the original strain.
Stated Objectives

Objective 1. Determine the reinfection rate of PEDv.

Objective 2. Identify risk factors associated with reinfection of PEDv.

Objective 3. Evaluate production impact and management strategies for stability.

Materials & Methods:

All herds enrolled in the Swine Health Monitoring Project (SHMP) that were infected with PEDV after April 2013 when the virus was detected in United States through July 2016 were eligible to participate in this study. Briefly, this SHMP project represented a convenience sample of sow herds including a total of approximately 2.3 million sows. Veterinarians represent each herd and voluntarily report diagnostic status for PRRSV and PEDV on a weekly basis (Tousignant et al., 2015). The number of herds sharing diagnostic results for PEDV before 7/2/2014 was 1,027 farms.

For Objective 3, 474 of the 1,027 herds had been infected before July 1, 2014 and were included in the assessment of TTS. Following the guidelines for PRRSV, herds were declared “stable” by the veterinarian after finding 4 consecutive samples of at least 30 litters to be PCR negative for PEDV. Time to achieve stability was determined as the number of weeks from reported initial infection until the last week of achieving 4 consecutive negative samples.

To evaluate production impact, all veterinarians were invited to share production records and 190 herds participated. Pigs weaned per week was the key outcome compared before and after PEDV infection was detected. Briefly, 26 weeks of performance data prior to the onset of clinical signs of PEDV were collected as the control period to determine baseline production for each farm (“in control” level of production). Baseline was estimated by calculating the arithmetic mean of weekly number of piglets weaned throughout the control period. Two methods were used to determine TTBP. The time for the exponentially-weighted moving average (EWMA) of weaned pigs/week (λ = 0.40) to return to 100% of previous production was used to accurately describe herds exhibiting lengthy return to baseline after initial rapid response. Comparatively, the time for the EWMA to return to within 99% confidence limits (3a) of the baseline production was used as a standard method to evaluate return to an acceptable baseline range of production.

Net loss of weaned pigs was calculated as a measure of production impact for each TTBP calculation method. Net loss was defined as the baseline expected production minus the area under the curve of weekly piglet weaning numbers from week 0 post- diagnosis to re-achieving baseline production plus the number of piglets weaned off in the first week of infection. Early weaning of piglets immediately after detection of the PEDv outbreak in farrowing became typical practice shortly into the nationwide epidemic in an attempt to save as many piglets as possible through weaning onto solid food and into a clean environment. This early weaning is thought to prevent exacerbation of diarrhea by milk product maldigestion and by removing piglets from rapidly-increasing viral challenge in the environment. This net loss was then standardized by herd size to “piglets lost per 1000 sows” for comparison among herds.

There were only 5 herds in the SHMP database confirmed to be infected with S-INDEL variant. To increase the sample size for comparing production impact with herds infected with the Original strain, 5 other sow herds confirmed to be infected with S-INDEL variant were recruited through contacts with veterinarians involved in the study. All remaining 185 herds were assumed to have been infected with original strain of US PEDV. Veterinarians reporting sample sequences and by considering the timing of early infections in the US epidemic participating in the study before sequencing was widely available, lead us to believe that approximately 5% of these herds could have potentially been S-INDEL cases. Risk factors potentially associated with TTS and production loss included herd inventory, quarter of the year when the herd was infected with PEDV and PRRS infection status when the herd was infected with PEDV. PRRSV infection status was analyzed as infected (status 1) vs pooled herd statuses of stable, provisionally negative or negative (status 2, 2v, 3, 4). Herds confirmed to be infected with S-INDEL variant were compared to herds presumed to be infected with the original PEDV strain.

Standard testing guidelines were recommended to participating veterinarians highlighting that 4 negative sampling rounds including 30+ litters sampled would be used to determine stability. Few production companies tested differently than the
recommended sampling. One company used 3 negative sampling rounds to determine stability and 2 others that we are aware of, sampled variable numbers of litters, but never less than 15.

Descriptive and analytic statistics were conducted using Statistix v10.0 software (Analytical Software, Tallahassee, FL). Frequency distributions of TTBP, net piglet loss and TTS were tested for normality with Shapiro–Wilk test. Testing for association between TTBP, net loss and TTS and respective risk factors were conducted using Spearman rank correlations and Kruskal–Wallis ANOVA.

Results:

Objective 1 – From May 1/2013 through July 1, 2014, 474 / 1027 (46%) herds broke with PEDv. Of these 474, 113 (23.8%) re-broke after 7/2/2014 and up to June 30, 2016.

From May 1/2013 through July 1, 2014, 553 / 1027 herds did NOT break with PEDv. Of these 553, 43 (7.8%) re-broke after 7/2/2014 and up to June 30, 2016.

Comparing these two risks suggest that a herd that has had a previous outbreak was approximately three times as likely to re-break as herds in our database that have never had an outbreak. This difference was statistically significant (2 tailed Chi square p<0.001).

Objective 2 – There was a dramatic reduction in incidence from 46% in 2013 /’14 to 9% in 2014 /’15 and 8% in 2015/’16. Two significant risk factors were identified. First, “System” was significantly associated with incidence of breaks (P<0.0101) and re-breaks (p<0.001). Second, of the herds that re-broke, herd status for PEDv was significantly associated with incidence of re-breaks (p=0.005). Status 2 herds had substantially fewer re-breaks than expected. One inference is that herd immunity from the previous break is providing some protection.

<table>
<thead>
<tr>
<th>Status at re-break</th>
<th>did NOT re-break</th>
<th>DID re-break</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>2fvi</td>
<td>105</td>
<td>31</td>
</tr>
<tr>
<td>3 or 4</td>
<td>203</td>
<td>89</td>
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Objective 3 - Of the 454 herds that were infected with PEDV, 429 achieved stability. The average and median TTS were 29.5 and 28.0 weeks, respectively and values ranged from 7 to 64 weeks.

There was no correlation between TTS and total inventory at the site (r = 0.04, p = 0.45) or sow inventory alone (r = −0.05, p = 0.31). Similarly there was no association between TTS and S-INDEL variant vs Original strain, or PRRSV status of the sow herd at the time when PEDV infection was detected. Herds infected in quarters 3 or 4 of the year had approximately 12 weeks longer TTS than herds infected in quarters 1 or 2.

For the 195 herds that shared production records, 183 (94%) returned to baseline production as defined by the 99% confidence interval. The median TTBP was 10 weeks and median net loss of piglets was 2.3/inventoried sow. Only 148 (76%) of the sow herds returned to baseline as defined by getting back to 100% of that achieved before PEDV. In these herds, the median TTBP was 21 weeks and net loss was 2.7 piglets/sow.

For the 173 herds that were presumed to be infected with the original strain of PEDV, and using the 99% confidence interval as indication of achieving “in control” baseline production, the median TTBP was 10 weeks and net loss was 2.3 pigs/sow. All 10 herds confirmed to be infected with the S-INDEL variant achieved baseline by 52 weeks using the same 99% confidence interval and TTBP and net loss were 8.0 weeks and 1.5 piglets, respectively. Net loss and TTBP were significantly shorter in herds infected with S-INDEL variant.
There was no association between any measure of production loss and herd inventory. Median net loss of pigs sow in sow herds that were PRRS unstable at the time of PEDV infection was significantly higher compared to herds with other PRRS status.

Herd descriptive information suggests that both TTS and TTBP herd samples were representative of the three major geographic regions where swine are raised in the US with the majority being in the Midwest. There is bias in the dataset towards farms larger than 500 sows due to the selection process of larger production companies for the Swine Health Monitoring Project from which much of the data was collected. In the 2012 US agricultural census data for sow herds with more than 500 head, only 28.8% were farrow to wean indicating that the TTBP analysis over-represents farrow to wean herds and under-represents farrow to finish herds in the US.

Before a sow herd is stable, it presents an ongoing source of virus through known routes of transmission such as weaned pigs, transportation, personnel, fomites and pests.

The median TTS of 28 weeks is very similar to the 26.6 weeks estimated by Linhares et al. (2014) for PRRSV. It should be noted that this time to stability was calculated as being reached after confirmation of the required number of tests as opposed to stability defined by Linhares et al., 2014 where stability was reported as time to the first negative sample of a series of testing. While Linhares et al. (2014) are probably correct that the virus was at extremely low or even 0% prevalence at the first time of sampling, the veterinarian cannot have confidence that a herd is stable until the series of consecutive negative samples are achieved.

On average, herds experience a “rapid recovery” to approximately 80% of previous production within 12 weeks and then a gradual continued recovery to 100% of previous production. Of equal importance is that approximately 6% of our cohort of 185 herds had not recovered to 100% of baseline production by 52 weeks after the herd was infected. This observation, in conjunction with the lack of correlation between TTS and TTBP, indicates that PEDV infection causes or is associated...
with long term reduction of productivity in some herds. This may be due to effects of the virus on reproductive performance as has been reported in one herd (Olanratmanee et al., 2010), effects on morale of staff, reduced inventory associated with herd closure, or other management interventions.

The higher TTS and production impact observed in herds infected in quarters 3 or 4 is an important observation. After the first 3 months, approximately 80% of production has recovered and aggressive efforts are being directed to clean and disinfect facilities. These data suggest that colder weather will make this process more difficult and lengthy. This is consistent with what is known about virus survival outside the pig. The veterinarian can use this information to stress the importance of cleaning, especially at this time of year. Both lower TTS and production impact data from Q2 2013 and Q1/Q2 2014 were used for this assessment indicating that this seasonality may have been more of a factor than improving education regarding methods of management and hygiene throughout the first year of the epidemic. Estimates of seasonal changes in production including the number of piglets born alive, number of litters per sow per year produced, and percent change in preweaning mortality lead us to believe that at most, a 4–6% change in production may occur from winter to summer months (Stalder 2013). The quarterly differences that were observed overwhelm this influence and emphasize the apparent effect of season on virus survival.

Comparison of S-INDEL variant infected herds’ production data to original severe PEDV-infected herds’ production data is consistent with anecdotal reports of S-INDEL variant infection resulting in milder impact. This finding may be particularly useful for herds that detect and sequence S-INDEL variant infection given its ability to induce cross-protective lactogenic immunity to other PEDV strains. One limitation of this observation is that while S-INDEL variant was confirmed in the 10 herds sharing production records, the Original strain was not confirmed in all the remaining herds. Some of these remaining herds may have been infected with S-INDEL variant thereby diluting the observed difference. A second limitation is that not all herds infected with S-INDEL variant were part of the SHMP. Therefore, TTS was not available and however unlikely it seems, the herds may differ in other, undefined ways from SHMP herds.

In conclusion, this study provides a valuable estimate of time required and the variability that seems to exist for a herd to eliminate PEDV from weaned pigs. This is important to know for planning a virus elimination program from the herd that is based on herd closure. Secondly, this study provides estimates of the impact on production and time required for a herd to recover back to levels of production achieved before the virus infected the herd. Such estimates are important for budgeting financial performance of herds. Lastly, lack of correlation between time to stability and production loss suggest that the virus may persist in a herd long after the majority of the clinical impact has been experienced. One consequence of this may be farm managers being tempted to relax their cleaning and disinfection efforts which could in turn perpetuate virus in the farm.

Figure 1. Quarterly incidence of PEDV virus infection by history of previous infection, beginning May 2013.