**Production impact & time to stability in sow herds infected with
Porcine Epidemic Diarrhea virus (PEDV)**

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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 (Morrison 2014). 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. This study involved participants and data from an existing program called the Swine Health Monitoring Project. 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 – 64 weeks. 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.

Keywords: Swine, PEDV, Production, Mortality, Stability

Introduction

New cases of PEDV have spread extensively within the United States since the first diagnosed farm was confirmed in April, 2013 (Stevenson et al, 2013). The virus infected approximately 50% of the US swine breeding herds from July 2013 through June 30, 2014 as

estimated by the Swine Health Monitoring Project (Morrison 2015). The original US PEDV strain can cause up to 100% suckling piglet mortality (Pensaert et al 2006, Waters 2014).

PEDV is an enveloped, single stranded, positive sense RNA virus of the genus *Alphacoronaviridae* in the family *Coronaviridae* similar to transmissible gastroenteritis virus (TGEV) (Hofmann et al 1989, Stevenson et al, 2013). 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 (Oka et al 2014, Vlasova et al 2014). 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 (Goede et al 2015). 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 (Geiger et al 2013). 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 (Gerber et al 2014) reduces the 100% morbidity of watery diarrhea and 50-100% pre-weaning mortality that is seen during an acute outbreak in naïve herds (Pensaert et al 2006). 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 (2011) attribute 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. Linhares 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 (Chen et al 2013) 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, Linhares 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.

The objectives of this study were to determine TTS and TTBP in a sample of sow herds infected with PEDV.

Materials and 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 2014 were eligible to participate in this study and were included in analysis regardless of vaccine product use. Briefly, this SHMP project represents a convenience sample of 910 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). Of the 910 herds in SHMP, 863, 538 and 491 participate in sharing diagnostic results for PEDV, PRRSV or both, respectively.

Diagnostic records were not audited and veterinarians' reports were assumed to be accurate. This included the diagnosis of PEDV, monitoring the requested sample size after PEDV infection and characterizing the sow herd status for PRRSV.

Of the 863 sow herds enrolled in the Swine Health Monitoring Project for PEDV, 454 (53%) had been infected and were included in the assessment of TTS. Following the guidelines for PRRSV (Holtkamp et al 2011), 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. Statistical process control methods were used as described by Linhares et al. (2014). 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 ($\lambda = 0.40$) 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 (3σ) of the baseline production was used as a standard method to evaluate return to an acceptable baseline range of production. (De Vries 2010).

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

Of the 454 herds that were infected with PEDV, 429 achieved stability. The TTS distribution differed significantly from normal ($p < 0.001$, figure 1). The average and median TTS were 29.5 and 28.0 weeks, respectively and values ranged from 7 to 64 weeks.

The 429 herds had an average inventory of 3,025 sows ranging from 500 to 12,410 sows. Of these sow herds, 80.9% were farrow to wean commercial sow units, 3.5% were farrow to feeder commercial sow units, 12.8% had finishing pigs on site, 2.6% were multiplier sow herds, and 0.2% were genetic nucleus farms. Geographically, 47.1% of the herds are in Southeast region, 38.9% are in the Midwest region, and 14.0% are in the Southern panhandle region.

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 (table 1). Herds infected in quarters 3 or 4 of the year had approximately 12 weeks longer TTS than herds infected in quarters 1 or 2 (table 1).

The distribution of values for TTBP was significantly different from normal ($p < 0.001$, figure 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.

These herds had an average sow inventory of 3,609 ranging from 516 to 13,200 sows. Geographically, 53% of these herds are in the Midwest region, 32% are in the Southern panhandle region, and 21% are in the Southeast region.

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 (figure 3). 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 (figure 4). 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. Herds that were infected in 3rd or 4th quarter of the year had almost twice the production impact in TTBP and net loss of piglets compared to herds infected in first 2 quarters of the year (table 1).

There was no correlation between TTS and TTBP or net loss by either measurement method for establishing return to baseline ($r = 0.10$, $p = 0.22$).

Discussion

It is imperative for producers and veterinarians to understand the expected production impact and duration of shedding after a sow herd becomes infected with PEDV. The expected time required to achieve stability is important for planning the gilt needs and associated herd closure. Unfortunately, capacity limitations at some herds may prohibit sufficient closure time and the herd may need to live with the virus or experience a reduced inventory of sows.

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.

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. Average herd inventory nationwide of herds larger than 500 head in 2012 was 3,362; a similar figure to our herd samples (USDA 2012). It is the opinion of the authors that the analyses presented here may not represent the experiences of all small herds undergoing a PEDV outbreak, but that the analyses represent the majority of the hog production industry's breeding herds and largest sources of finishing pigs going to the food supply chain.

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 can't 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 (Pensaert et al 2006). 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 (Goede et al 2015). 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.

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Table 1. Median values for production loss and time to achieve stability in sow herds infected with PED virus.

	99% CI			100% baseline				
	No herds	TTBP	Net loss	No herds	TTBP	Net loss	No herds	TTS
All data	183	10.0	2.3	148	21.0	2.7	429	28
Quarter of year								
1	58	9.0 a	2.0 a	54	16.0 a	2.3 a	163	24.0 a
2	45	9.0 a	1.9 a	35	14.0 a	1.8 a	75	22.0 a
3	17	18.0 b	3.3 b	6	18.5 ab	3.0 ab	46	36.0 b
4	63	15.0 b	3.4 b	53	26.0 b	3.8 b	145	33.0 b
PEDv strain								
Original US PEDv	173	10.0 a	2.3 a	138	21.0 a	2.7 a	424	28.0 a
S-INDEL variant	10	8.5 b	1.5 b	10	18.0 a	2.0 b	5	28.0 a
PRRS status at PED break								
1	23	9.0 a	2.6 a	22	23.0 a	3.3 a	40	24.5 a
2, 2v, 3, 4	111	10.0 a	2.0 b	103	21.0 a	2.5 a	172	26.4 a

ab median values within same risk factor column were significantly different at $p \leq 0.05$

Figure 1. Time to stability in 429 sow herds infected with PED virus

	<i>Bin</i>	<i>Frequency</i>	<i>cumulative %</i>
5	5	0	0.00%
10	10	5	1.17%
15	15	34	9.09%
20	20	53	21.45%
25	25	87	41.72%
30	30	76	59.44%
35	35	53	71.79%
40	40	49	83.22%
45	45	28	89.74%
50	50	24	95.34%
55	55	15	98.83%
60	60	2	99.30%
65	65	3	100.00%

	<i>Bin</i>	<i>Frequency</i>	<i>umulative %</i>
5	5	2	1.08%
10	10	91	50.27%
15	15	33	68.11%
20	20	19	78.38%
25	25	17	87.57%
30	30	7	91.35%
35	35	3	92.97%
40	40	0	92.97%
45	45	0	92.97%
50	50	1	93.51%
		173	
		12 never reached	
		185 total	
		93.5% TTBP (99% CI)	

Figure

Figure 2. Time to achieve baseline production in 185 sow herds infected with original strain of PEDv

Figure 3

Figure 4