Epidemiology and economic impact of PED

Bob Morrison, DVM, MBA, PhD; Dane Goede, DVM
College of Veterinary Medicine, University of Minnesota

Porcine epidemic diarrhea (PED) virus and transmissible gastroenteritis (TGE) virus belong to the Coronaviridae family. As such, they have a large, single-stranded, positive-sense RNA genome. These viruses are important causes of enteric disease in swine and replicate in the differentiated enterocytes covering the villi of the small intestine leading to villous atrophy and malabsorption.

Dick Hesse (2013) performed a study to determine tissue localization, shedding pattern, virus carriage, antibody response, and aerosol transmission of virus following inoculation of 23, 4-week-old pigs with intestinal mucosal scrapings containing PED virus. Preliminary results are:

- All samples were negative for the virus at 24 hours post inoculation.
- Fecal and nasal shedding of the inoculated group was first observed at 48 hours post inoculation.
- Nasal shedding was detected in the contact control pigs 48 hours post inoculation and fecal shedding occurred 24 hours later.
- Peak fecal shedding occurred 5 to 6 days post challenge and was significantly higher than nasal shedding.
- 3 pigs in the inoculated group and 1 contact control pig were still shedding virus at 21 days post inoculation and 1 pig was positive at 28 days post inoculation.
- Oral Fluids were PCR positive at 48 hours post inoculation and remained positive until day 28 post inoculation.
- PEDV viremia was detected in 3/5 contact pigs and 9/22 inoculated pigs.
- Only tissues from the GI tract tested positive for the presence of viral antigen.
- Geometric mean indirect fluorescent antibody titers from the day 43 sera for inoculated pigs averaged 350. Contact pigs had GMT of 200. GMT for pigs in aerosol contact was negative.
- Aerosol transmission was not detected in this study.
- Room environmental samples were collected at 14 days post inoculation and viral nucleic acid was abundant on the walls, pens and food bins on both the inoculated and aerosol control areas in the challenge room.

The virus is highly infectious and as little as $10^{-8}$ dilution of mucosal scraping caused infection when 10 day old pigs were intra-gastrically inoculated. That means approximately 1 pencil eraser of diarrhea diluted into 130 cubic yards can still cause diarrhea.

PED virus is very stable in the environment. Infectious virus has been reported to still be alive after:
- > 28 days in fecal slurry at -20°C,
- > 28 days in wet feed mixture at room temperature,
- < 2 weeks in dry feed at room temperature,
- > 14 days and < 28 days in fecal slurry at room temperature,
- > 28 days in 40°C fecal slurry at three relative humidity levels,
- No effect of relative humidity (30%, 50%, and 70%) on virus survival was detected.

Production impact

Clinical signs are characterized by acute vomiting, anorexia, and watery diarrhea, with high mortality in pigs less than 10 days old. PED virus is highly contagious disease and diarrhea can be observed in all age groups of pigs. We analyzed production records from 18 farrow to wean farms that were infected with PED and acutely affected. Productivity was summarized as number of pigs weaned per week and compared after the outbreak to 26 weeks before. It took approximately 5.9 weeks (95% CI 4.2-7.6) to return to baseline productivity. The average number of pigs not weaned was 1,688 / 1,000 sows (95% CI 1,077-2,299).

These pigs not weaned were primarily composed of pigs that died in the suckling phase due to diarrhea and dehydration. PED virus infection may also have contributed to an increase in reproductive failure including decreased born alive and increased abortions particularly in gilts (Olanratmanee et al.). Specifically, they reported:

- Pregnant females infected with PEDV during the first 30 days of gestation had a 12.6% decrease of farrow rate (91.1% vs. 78.5%, P = 0.003),
- Decrease born alive by 2.2 (10.7 vs. 8.5 piglets/litter, P < 0.001) in gilts’ litters if infected during the first 30 days of gestation, and
- Impact of PEDV infection on subsequent reproductive performance was more severe in the pregnant gilts than the pregnant sows.

Diarrhea in growing pigs may also have an impact on growth performance although this has not been
quantified. Moon et al reported that three week old pigs replace villous absorptive cells in the small intestine about three times more rapidly than do newborn pigs (Moon et al). The implication is that the older the pig, the less severe is the clinical impact.

**Immune response**

Much remains to be learned on immunity to PED. In particular, how should we measure it, how long does it last and how can we most effectively stimulate it? Paraphrasing from a PED review article by Song et al (2012):

PEDV antibodies, detected by the ELISA-blocking and IF-blocking tests have been reported to persist for at least 1 year. Piglets can be protected until approximately 2 weeks of age against PEDV by specific IgG antibodies from the colostrum and milk of immune sows. However, the length of immunity depends on the titer of the dam. Also, due to the special features of the porcine mucosal immune system, the presence of serum antibodies against gastroenteric pathogens is not always correlated with protection. Rather, detection of these antibodies only proves that individuals had contact with infectious microorganisms.

Colostrum IgA concentration is a better marker of protection from PEDV infection than serum neutralizing (SN) titer from serum samples. Pigs that regularly suckle immune dams are constantly inoculating their intestinal lumens with milk-bound IgA antibodies, a process that confers passive immunity. So while IgG accounts for more than 60% of colostrum immunoglobulin content, IgA is more effective at neutralizing orally infectious pathogens than either IgG or IgM because it is more resistant to proteolytic degradation in the intestinal tract and has a higher virus neutralizing ability than IgG and IgM. Therefore, only passive transfer of IgA from an immunized dam effectively induces immune responses in suckling piglets. However, these antibodies do not protect against intestinal infection with PEDV.

**Transmission among farms**

Fecal-oral is clearly the predominant means of spread among pigs. And given the high concentration of virus shed in feces and the profound stability of the virus, it appears that fecal contamination of farms via contaminated equipment, fomites, or personnel is a likely method of spread. Two studies at collection points have highlighted the risk. First, Lowe et al assessed 669 trailers @ 7 plants sampled before/after unloading. They took 89-102 samples over 2-3 days in June 14-20, 2013 and reported 17.3% (range 2.0-69.7%) of trailers to be positive at arrival. Furthermore, 11.4% of the trailers negative on arrival tested positive before leaving the plant. Matthew Turner took the initiative to collect swabs at 4 cull buying stations on June 27, 28 2013. He found 3/4 loading chutes were PED positive and 6/10 swabs from pigs with loose stool were positive. These data promoted NPB to develop and make available transportation protocols to reduce risk of contaminating vehicles. [http://aasv.org/aasv20website/Resources/Diseases/PorcineEpidemicDiarrhea.php](http://aasv.org/aasv20website/Resources/Diseases/PorcineEpidemicDiarrhea.php)

We are conducting an epidemiologic study to identify risk factors for lateral transmission among farms. Several analyses are being conducted and preliminary results are as follows. Note that these results are preliminary and WILL change as more data is analyzed.

OK cluster of farms:

- Proximity to positive sites increased the risk of becoming PEDv positive
- A 5 day delay between the first case and subsequent cases indicated infection from the earliest case by a mechanism that may depend on geographic proximity.
- Week 3 of the epidemic showed a case appearing far from other cases which may indicate transmission via truck movement.

North Carolina cluster of farms:

- Cases immediately following previous infections occurred directionally at 20 degrees NE on average.
- Odds of being infected given distance to nearest known positive neighboring site:
  - within 1 mile = 8.4×
  - within 2 miles = 6.3×
  - Within 3 miles = no increase
- Sites with sows and grow/finish pigs had highest incidence of PEDv
- Site capacity was not significantly associated with PEDv

Analysis of questionnaires: Preliminary data from the first 26 / 47 questionnaires including 11 positive and 15 negative sites were reported. These results WILL change as more data are available and analyzed.

- Positive sites had average herd size of 4610 vs. 2644 for negative sites ($P < 0.05$). This significantly larger herd size may explain why positive sites had more frequent occurrences as described below. That is, the observations below may have nothing to do with higher risk for PED virus.
- There was approximately double the frequency of feed truck deliveries to positive sites compared to negative sites.
- There was approximately half the frequency of company service person visits to positive sites compared to negative sites.
• There were approximately double the frequency of
  trucks visiting to remove pigs of any age from posi-
  tive sites compared to negative sites.
• There was approximately 5 times the frequency of
  trash pickups from positive sites compared to nega-
  tive sites.
• There was approximately twice more positive sites
  that had culls removed from the site in the two
  weeks preceding infection.
• Approximately 30% more positive sites had dead
  haul vehicles visit the site in the two weeks preceding
  infection.
• There were approximately 3 times more positive sites
  that had staff / family members working off farm in
  an abattoir or other swine farm.

Elimination vs control
After a herd is infected, one must decide whether to try
and eliminate the virus or live in a state of perpetual con-
tral. One might choose control if it seems highly unlikely
to eliminate PED virus from the herd or keep it out of
the herd for very long. The disadvantage of not eliminat-
ing the virus is the possibility of living with endemic
PED. Furthermore, if efforts are not made to promote
ongoing herd immunity, one might expect repeated epi-
demics of clinical disease.

With control, one tries to stimulate herd immunity in an
ongoing fashion. Given that vaccines are largely ineffec-
tive, purposeful exposure of gilts in acclimation to live
PED virus is part of the effort to minimize long term
clinical impact. Our personal opinion as of today is that
intensive effort to inhibit spread of the virus should be
implemented if endemic disease occurs. Strategic use of
feedback may be applied in the sows when efforts to con-
trol sporadic outbreaks of PED fail.

As of today, we have no data on incidence of endemic
infection in sow herds that attempt elimination of the
virus vs long term control.

Barry Wiseman and colleagues (1988) first described a
protocol for eliminating TGE virus from sow farms. Jer
Geiger (2004) reviewed this paper as follows: The strategy
focuses on stabilizing the immunity of an entire popula-
sion simultaneously (best achieved in an acute outbreak),
allowing the virus to “burn-out.” The strategy is used today
world-wide, with such success that TGE is no longer the
feared disaster it once was. The process involves:
  • Addition of 4-6 months of replacements. The herd is
    “closed” at that point.
  • Feedback (forced exposure) of the entire herd. Feces,
infects, and intestinal contents from acute farrow-
ing/nursery cases are used.
  • Strict all-in/all-out (AI/AO) and one-directional
    flows, after clinical signs have subsided.
  • Introduction of sentinels >30d days after secession
    of clinical signs. This is to verify virus is not circulating.
  • Strict enforcement of uni-directional flow (both pigs
    and people) and AI/AO strategies allow the producer to
    “walk” the virus off the farm and out of the system even
    in one-site systems. TGE-negative replacements can be
    added after the flow is verified negative.

More recently, Geiger (2013) described using this tech-
nique to successfully eliminate PED virus from a sow herd.
Connor (2013) summarized a feedback protocol for ac-
complishing widespread herd immunity (Appendix 1).

In both control and elimination efforts, the veterinarian
attempts to minimize clinical impact and eliminate the
virus from the sow herd as soon as possible. The elimina-
tion protocol described above suggests that 90 days clo-
sure is adequate to eliminate the virus. We have initiated
a study to measure time to “stability” as defined by failing
to detect PED virus in 30 litters over 4 consecutive weeks
described below.

To date, we have 14 sow farms enrolled in a study to
determine time to achieve stability. Three of the farms
have achieved stability at an average of approximately 18
weeks post-infection. All other farms are in process.

Before a herd achieves “stability,” there will be a critical
dynamic in effect between waning herd immunity and
remaining PED virus in the environment. This is similar
to PRRS where we can watch prevalence of PCR posi-
tive pools gradually decline as a herd gradually becomes
“stable.” The major factors that dictate whether we can
eliminate a pathogen or not include:

• stability of pathogen outside pig
• persistence (or latency) in the pig
• how hard we practice bio-containment (cleaning etc)
• herd immunity
• propensity for transmission (infectiousness of the
  pathogen); called Ro
• Closed vs open population (and population size)
• Milk production by sows (off feed sows will milk
  less).

For PRRS, apparently the combination of rigorous bio-
containment (McRebel etc) efforts in conjunction with
herd immunity can win over the prolonged potential
infection time of the pig (can be months) and propensity
for transmission (Ro) to occur among pigs. Otherwise,
we could not achieve stability and eventually even nega-
tive status.
Site classification guideline for PED virus

Bob Morrison (P.I. Swine Health Monitoring Project), Matt Ackerman, Joe Connor

Sow farms

I – Infected and shedding virus

II – Stable – weaned pigs are negative for PED

- Herd is free of clinical signs of PED
- At least 4 consecutive samples of piglet feces collected as often as weekly from farrowing are PCR negative.
  - Each sample must represent 30 litters between 7 days of age and weaning (95/10).
  - Collect 1 Swiffer sample per litter. Bias the litters towards younger parity sows and/or have any diarrhea. Swab diarrhea when evident.
  - You may pool up to 5 swabs (litters) together for PCR testing.

III – Provisionally negative

- Herd is free of clinical signs of PED and at least 60 gilts have been introduced and have remained free of clinical signs of PED for at least 60 days.
- These sentinel gilts should have no known history of prior PED infection.
- Serum test is negative on at least 30 gilts present in sow herd for at least 60 days
- Ongoing monthly testing of gilt litters is encouraged

IV – Negative

- Herd has no clinical history of PED virus
  Or
- Herd was provisionally negative, has had no clinical evidence of PED virus for at least 6 months and gilts entering herd have no history of PED infection and have remained free of clinical signs.

Growing pig sites

Infected (positive) sites – have a presumed positive shedding status.

- Status I source and/or positive PCR status. It is the default category when history and diagnostic information is inadequate to classify a site as negative.

Not infected (negative) sites - have a presumed negative shedding status. Note that slurry at this site may be contaminated.

- Absence of clinical signs and at least 5 PCR negative, pen-level oral fluid samples (5 samples/40 pens). Negative serum test on at least 30 head / contiguous population (may have maternal immunity).
- Continued absence of clinical signs and a second negative test (as above) 30 days later.
Comparing PED to PRRSv, the propensity for transmission (Ro) seems higher with PED, stability of PED virus in environment is higher and sow immunity is lower. That is, these 3 parameters are working against us compared to PRRS. However, one factor works in our favor - pigs are infected for dramatically shorter time. Only a few of the above factors are in our control. Rigorous bio-containment is a must if we hope to have a chance. Occasional litters and sows will have clinical signs. Rigorous containment and sanitation are our only hope in the critical phase as sow immunity wanes. The herd is a time bomb in this phase.

Conclusion
Unfortunately, at the time of this writing, sow herds are becoming infected at a disturbing rate despite best attempts at biosecurity. Much has been learned in a very short period of time. And much remains to be learned such that we have minimum incidence and successful control programs.

References
Appendix 1

Protocol and procedures for PEDV elimination

Joseph F. Connor, DVM, MS

Porcine epidemic diarrhea virus (PEDv) has been successfully eliminated in many of the first cluster of cases. This paper summarizes the present situation and clarifies the success factors.

Sow herds are experiencing 3 clinical presentations:

1. Explosion and then after exposure program weaning negative pigs.

2. Explosion and then after exposure program endemic circulation with 10-20 percent of piglets exhibiting diarrhea > 10 days of age.

3. Explosion and then after exposure and reduction in clinical signs, a re-break 45-60 days later.

These re-breaks may occur because of incomplete exposure, limited protective immunity, non-responders, prolonged shedding, high environmental contamination, concurrent enteric infections, and strain mutation. In a survey of the first cluster of cases, the success rate of weaning negative pigs is 65%. Generally the herds are weaning negative pigs between 60 and 90 days post exposure indicating that herd closure needs to target at least 90 days. In all of these cases feedback was used to expose the sow and gilt populations. Sow herd size may be a factor in success and thus as herd size increases more discipline feedback, clinical monitoring, and environmental reduction may be required.

A review of the successes by veterinarians within the United States indicates that these steps are helpful for successful elimination.

1. Natural exposure will already be occurring during the diagnostic confirmation.

2. Immediately mark animals that are exhibiting signs to ascertain a clinical prevalence. Individual animals that have not exhibited clinical signs should have a statistical population sampled and submitted for IFA or ELISA to determine exposure. Herds frequently only identify 40-50 sows diarrhea and 70-80% when identifying diarrhea and off feed. Collect serum for IFA and/or Elisa from 30 gilts or sows that are non-responders (no diarrhea or off feed) and submit for antibody detection.

3. Start feedback on day 2-3 after the initial sows are coming back on to feed. Feedback daily until clinical signs disappear in the population. Be aggressive and relentless with the feedback procedure. Feedback needs to continue until greater than 90% of the sows have exhibited clinical signs.

4. The herd must be closed for at least 90 days. Replacement gilts need to be exposed and the herd needs to be closed (no introduction of additional gilts at this point). Replacement gilts can either be exposed as part of this population or in a separate facility.

5. Feedback material should consist of fecal material and/or the intestinal tracts (viscera) from infected freshly scouring piglets. For maximum viral concentration, sacrifice the piglet within the first six hours of its clinical signs. Samples should be submitted to the diagnostic lab for confirmation and CT values.

6. Feedback one piglet intestinal tract per ten head of developing gilts or gestating sows. Process the viscera through a garbage disposal, food processor, or fan tip pressure washer to macerate thoroughly. Dilute collected material with cold water to extend the material to ten head. The virus is temperature and disinfectant sensitive thus do not use warm, hot, or chlorinated water.

7. Distribute the feedback material (mixed with feed) at the beginning of a feed drop. Herds utilizing pen gestation should have the feedback material distributed down the trough or feed pad similar to a maternal pen facility.

8. Freeze this raw, undiluted visceral material in an at least -20 centigrade freezer to preserve material in case feedback needs to be reinitiated.
9. Sows that are lactating will have lost 100 percent of their piglets and may be off feed for several days during the drying up period.

10. Early wean pigs as soon as clinical signs in piglets appear or clinical signs appear in lactating sows. Sows quickly become agalactic. After the initial early weaning, mortality of suckling piglets is frequently 100% and early weaning 3 weeks after the initial episode may or may not be beneficial.

11. High concentration of the virus and long environmental survivability can result in facility contamination. Procedures that can be helpful in reducing this exposure:

11.1 Completely wash the gestation barn.

11.2 Disinfect the gestation barn.

11.3 Whenever possible, make sure environment dries well. Consider force drying it with heat.

11.4 Initiate strict McRebel for 4 weeks after the suckling pigs < 7 days of age have ceased scouring and tests are negative.

11.5 Reduce weaning age to 18 days, initiating 6 weeks after feedback is completed.

11.6 Wash and disinfect hallways and holding areas post weaning prior to loading the farrowing rooms.

11.7 Euthanize any sick or poor body conditioned pigs. Eliminate very thin starve outs, lames, lightweight pigs, or chronically scouring pigs as soon as they are found.

11.8 Use the litter as the all-in, all-out population.

11.9 Change needles between every litter.

11.10 Wear gloves and change gloves immediately in between each litter.

11.11 Discard tails and testicles in a container during processing.

11.12 Avoid stepping in the crates.

12. If some animals fail to show clinical signs within the first few days, repeat the exposure/feedback process. At some point, infective material may run short, so target those animals that have not already shown clinical signs.

**Precautions**

Elimination will succeed with a disciplined program under the direction of a veterinarian. Careful discussion in herds that are PRRS active need to be conducted before feedback is initiated.