Porcine Epidemic Diarrhea is Here... Ready or Not

K-State Swine Day 2013

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Kansas State Veterinary Diagnostic Laboratory
Abilene Animal Hospital PA
21 November 2013
Porcine Epidemic Diarrhea Virus

- Vomiting and occasionally diarrhea in sows and gilts and severe diarrhea and vomiting in nursing and recently weaned pigs.

- Mortality of ~100% in nursing pigs initially

- Diarrhea with occasional vomiting in growing pigs, low mortality

- Clinical signs of PED are indistinguishable from the epidemic form of the disease caused by a different porcine coronavirus, Transmissible Gastroenteritis Virus (TGE).

- There is no cross-protection between these two coronaviruses.
Porcine Epidemic Diarrhea Virus

- PED is a pig-only disease which does not affect other species or humans and is not a food safety concern.

- PED has been in Europe since 1971, Asian variants are more virulent & traditional vaccine doesn’t work anymore.

- Incubation time is typically less than 36 hours and virus is shed in feces for up to 11 days.

- Laboratory diagnosis is required for definitive confirmation—Especially in Older Pigs
The Disease

Courtesy of Dr. Matt Ackerman
What is PEDV?

“Porcine Epidemic Diarrhea Virus”

- Corona-virus
- Villous atrophy
- Malabsorptive diarrhea – death from dehydration

- Clinically Indistinguishable from TGE
  - Fecal-Oral Pathogen
  - ↑ Morality rates approaching 100% in naïve neonate populations
  - ↓ Mortality and severity of clinical disease in growing-finishing pigs

- Not a Zoonotic Disease or Food Safety Concern
PEDV Historical Distribution

- TGE-like outbreaks → England → 1971
  - Multiple European Countries
    » Most often in nursery/grow finish pigs

- More recently an issue in Asia
  » China
  » Japan
  » Korea
  - Severe epizootic outbreaks
  - Persists as endemic disease

- Not Confirmed in North America Prior to May 2013
PEDV in the US--Initial Events

- PEDV was confirmed in the US on May 17th, 2013 by diagnostic tests at the USDA National Veterinary Services Laboratory (NVSL) in Ames, IA

- Coordinated effort by all key stakeholders to understand where PEDV was/is occurring and how to best manage it:
  - United States Department of Agriculture (multiple divisions)
  - National Pork Board
  - National Pork Producers Council
  - American Association of Swine Veterinarians

- Diagnostic laboratories and researchers - awesome!
New (red) & Cumulative (blue) Lab Accessions in Sow / Boar Herds

chart courtesy of Dr. Matt Ackerman, compiled by D Goede
PEDV – how is it spreading?

• Rapidly Spread Across Broad Regions
  – Role of Transport Vehicles, Lairage at Collection Points, & Animal Movement
  – Lowe et al..... PEDV negative trucks returning from plant positive (amplifier)
  – Turner, Battrell et al.....PEDV positive sow collection stations prior to PEDV in NC

• Ability “Break-Through” Conventional Biosecurity Measures

• Area Spread – Clear & Present Danger
  – Most apparent in areas of high breeding herd concentration
    • Concentrated areas of sow farms in panhandle OK/TX and SE NC
University of Minnesota’s Swine Health Monitoring Project
Where the Pigs Are Located in US

“Industry on wheels”.....about 500,000 pigs per week move into Iowa alone
November 11th, 2013

Swine Health Monitoring Project

Porcine Epidemic Diarrhea Virus Reporting
Collated by APHIS, VS, NVSL, National Animal Health Laboratory Network & Univ of MN VDL.
Reporting Laboratories include: ISU, KSU, OH Department of Agriculture ADDL, SDSU, Univ of
MN. Date Reported 11/06/2013, data through 11/02/2013

Updated Number of Positive Lab Accessions by State

Number of Cases
- 0
- 1 - 4
- 5 - 16
- 17 - 26
- 27 - 46
- 47 - 85
- 86 +

MAP DETAIL:
- IA
- OK
- MN
- IN
- CO
- KS
- OH
- NY
- WI
- MD

CASES:
- PA
- MI
- KY
- IL
- MO
- SD
- NC
- TX
- TN

176 3 2 1 10 1 1 1 4 3
PEDV Diagnostics
Diagnostic Specimens

• Intestine (Fresh & Fixed)
• Feces
• Fecal Swabs
• Oral Fluids
• Serum (PEDV Antibody)
Immunohistochemistry (IHC)

1. Normal neonatal pig: Healthy, long intestinal villi

2. Early PEDv infection (~8 hrs PI): Infected cells (brown stain) line the villi

3. Late PEDv infection (~36 hrs PI): Severe villus atrophy & loss of absorptive epithelium

4. Late PEDv infection (~36 hrs PI): Few infected cells remain (brown stain) & absorptive cells destroyed

(Source: Schwartz, Madson, Magstad et al.)
TISSUE LOCALIZATION, SHTIDDING, VIRUS CARRIAGE, ANTIBODY RESPONSE, AND AEROSOL TRANSMISSION OF PORCINE EPIDEMIC DIARRHEA VIRUS (PEDV) FOLLOWING INOCULATION OF 4 WEEK OLD FEEDER PIGS.

Preliminary Results

K-State
KSVDL PEDV Team Members

Dick Hesse, Andrew Suddith, Barb Breazeale, Alex Fuller, Curtis Concannon, Joe Anderson, Jerome Nietfeld

Jianfa Bai, Baoyan An, Lalitha Peddireddi, Richard Oberst

Maureen Kerrigan, Megan Niederwerder, Ranjni Chand, Bob Rowland

Ying Fang, Russell Ransburgh, Lonjchao Zhu
Housed in BSL3 Ag isolation rooms at the Biosecurity Research Institute (BRI) at Kansas State University.

33 PEDV naive 3-week-old feeder pigs, obtained from a high health commercial source.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th># of Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>PEDV oronasal inoculated</td>
<td>23</td>
</tr>
<tr>
<td>B</td>
<td>None—Contact Control</td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>None—aerosol transmission controls</td>
<td>5</td>
</tr>
</tbody>
</table>
**Challenge:** Pool of gut derived intestinal content that was used as “feedback” inocula for controlled exposure of a sow herd in a commercial swine production unit.

The inocula had a PEDV nucleic acid “CT titer” of 22 in a real-time PCR assay.

Pigs challenged at 4 weeks of age via intranasal and oral routes with 5 ml of inocula per route.
Fig. 1: Fecal and Nasal Shedding following PEDV Inoculation of 4-Week old Pigs

- **Group Average CT**
  - Y-axis: 0 to 40
  - X-axis: -3 to 43 days

- **Legend**
  - "C" Aero Con Fecal
  - "B" Contact Con Fecal
  - "A" Inoc Fecal
  - "C" Aero Con Nasal
  - "B" Contact Con Nasal
  - "A" Inoc Nasal

- **Neg Cutoff**

- Data points show a trend of shedding with a peak around Day 0 and a decrease thereafter.
Surprisingly, all samples were negative for the virus at 24 hours post inoculation.

Fecal and nasal shedding of the inoculated group (A) was first observed at 48 hours post inoculation.

Nasal shedding was detected in the Contact Control group (B) at 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.
In Groups A and B, the majority of the animals were negative for fecal shedding at 21 days post inoculation. However, 3 of 11 animals in the inoculated group and 1 of 5 animals in the contact control group were still shedding virus at 21 days post inoculation and 1 of 11 was positive at 28 days post inoculation.

Most inoculated (A) and contact control (B) animals were not shedding intranasal virus at 21 days post inoculation.
- Oral Fluids from the pen housing Inoculated animals (Group A) and Contact Controls (Group B) were PCR positive at 48 hours post inoculation and remained positive until day 28 post inoculation.

- Oral fluids from the aerosol control group appeared to be positive at the time of the first successful collection point (D-4) and they remained positive through day 28 post inoculation.
• Room environmental samples were collected at 14 days post inoculation—the data demonstrate that viral nucleic acid was abundant on the walls, pens and food bins on both the inoculated and aerosol control areas in the challenge room.

• Due to the possibility of a false positive PCR reaction, questionable samples were retested and the reaction products were sequenced to determine if the product was PEDV specific. All questionable reactions demonstrated the presence of PEDV viral nucleic acid.
Experimental results demonstrate that aerosol transmission did not occur in this study.

Seem to be in conflict with reports from the field that implicate aerosol transmission, but lack confirmation via bioassay.

Water transmission—water fowl??

Factors like disinfectant and ultraviolet inactivation of PEDV sensitivity of the indicator animal (nursing pigs vs. weaned pigs) and infectious dose as a function of route of exposure need to be investigated in order to gain insight into modes of transmission of PEDV.
Histopathology
Virus Localization

- Histological lesions of the GI tract were minimal.

- PEDV was demonstrated via IHC in the villi tips of the small intestine.
IFA Antibody Response Following PEDV Inoculation of 4-week-old Pigs
Antibody titers were higher than expected in some of the samples; the mid-point of the next higher dilution was used as the value to calculate geometric mean titers.

There is no evidence of seroconversion in the aerosol control group in spite of the clear demonstration of PEDV nucleic acid in nasal and oral fluid samples.
The IFA data was in complete agreement with an E. coli expressed NP ELISA (96 well format) that is being developed.

Additional serological assays currently under development and optimization include a multiplex Luminex assay and a serum neutralization assay.
The Common Good--Sharing

- Complete sets of serum samples have been provided to 4 laboratories (~800 samples) for assay development/standardization.

- Two complete sets of oral fluid samples have been provided to a requesting lab.

- More to come.
Thanks To:

- Matt Ackerman—Swine Veterinarian, providing feedback on inocula used as challenge material.

- ISU—Kent Swartz, providing convalescent serum for virus detection. Darin Madson, sharing challenge results—blow by blow.

- NVSL—Sabrina Swenson, providing cell culture adapted PED virus, culturing methods and sharing challenge results.
Thanks To:

- SDSU—Eric Nelson, providing Vero cells and sharing VI frustrations/experience.

- Stephen Higgs, Biosecurity Research Institute, providing challenge rooms free of charge ($33,000) for timely initiation of the project.

- National Pork Board for providing Funding for the project.
Easy to Isolate, Difficult to Grow
PEDV Knowledge Gaps???

- **Understand Transmission**
  - Biological and Physical Routes

- **Define Age Differences in PED**
  - Duration of Shedding
  - Persistence

- **Develop Good Cell Culture Methods**

- **Develop Serological Assays**
  - National and Regional Prevalence

- **Develop Efficacious Vaccine**
“Oh no! PEDv has arrived!”

**Perspective**

**IF:** 10% of **ALL** US suckling piglets die of PEDv annually, losses are ~$440 million
One of PEDV’s “Little Friends”—it has many--BEWARE.
“You never let a serious crisis go to waste. And what I mean by that, it's an opportunity to do things you think you could not do before.”

Rahm Emanuel
Preventing introduction of PEDv
- it’s really about feces of the species! -

- Packing house information, cull markets
Slaughter truck contamination and biosecurity study

• Why? Know this is issue with dysentery and TGE – what about PEDv?
• Mid-June, EARLY in outbreak, veterinarians sampled 7 plants
• 100 trailers at each plant, swabbed before unloading and after using Swiffer pads
• 17% of trailers were PEDv positive on arrival
• 11% of trailers, arriving negative, were positive on departure from the plan

J. Lowe, etal, In Press
P. Yeske, ISU Swine Disease Conf, Nov 15, 2013
Delivery to plants – what was learned?

All truck drivers enter the plants!

• Bills of lading to the scale
• Off load pigs and pen in holding area
• Break down load into multiple lots
• Take pigs to the scale
• If mortalities, drag dead pig off and out of flow
• If down, get sled from plant and move pig off of truck
• Minimum of 5 trips on/off truck and into plant

• Plants have working groups and changes are coming
Conclusion from Paul Yeske

“Currently, trucks that enter the slaughter plant are not only highly likely to be contaminated with PEDv, TGE, swine dysentery, and other diseases such as PRRS, but washing out the back compartment is likely a waste of time...since the truck has the opportunity to be contaminated all the way through by following the procedures at the plant.”

P. Yeske, ISU Swine Disease Conf, Nov 15, 2013
Preventing introduction of PEDv
- it’s really about feces of the species!

• Packing house information, cull markets
• People and vehicle traffic
  – Moving weaned pigs and culls
  – Maintenance and repair personnel, equipment
  – Feed deliveries, supplies
  – Showers, benches, barriers for outdoor footwear
  – Workers
  – Veterinarians
• AND survival is enhanced when cold and wet!
Fumigation chamber – tools, supplies, equipment, materials

Additionally, some now have UV light boxes for personal items and other material approved to enter the farm.
Preventing introduction of PEDv
- it’s really about feces of the species! -

• Packing house information, cull markets
• People and vehicle traffic
• Manure spreading and handling
www.aasv.org and www.pork.org
Preventing introduction of PEDv
- it’s really about feces of the species!

- Packing house information, cull markets
- People and vehicle traffic
- Manure spreading and handling
- Mortality disposal
Dead stock - compost? bury? render?

**KDHE understands** and their support is greatly appreciated!

Handling unexpected mortalities is a **biosecurity** and **environmental** issue.
Preventing introduction of PEDv
- it’s really about feces of the species! -

• Packing house information, cull markets
• People and vehicle traffic
• Manure spreading and handling
• Mortality disposal
• Disinfectants – what and how
<table>
<thead>
<tr>
<th>Disinfectant Category</th>
<th>Aldehydes</th>
<th>Biguanides</th>
<th>Hyopchlorite</th>
<th>Iodine</th>
<th>Oxidizing agents</th>
<th>Phenols</th>
<th>Quaternary ammonium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Trade Names</td>
<td>Synergize, DC&amp;R</td>
<td>Chlorhexadine, Nolvasan, Virosan</td>
<td>Bleach</td>
<td>Betadyne, Providone</td>
<td>Virkon S, Accel</td>
<td>Tek-Trol, One-Stoke</td>
<td>Roccal, DiQuat, D-256</td>
</tr>
<tr>
<td>PEDv and PRRSV viruses</td>
<td>Effective</td>
<td>Variable</td>
<td>Effective</td>
<td>Effective</td>
<td>Effective</td>
<td>Effective</td>
<td>Variable</td>
</tr>
<tr>
<td>Efficacy with organic matter</td>
<td>Reduced</td>
<td>?</td>
<td>Rapidly reduced</td>
<td>Rapidly reduced</td>
<td>Variable</td>
<td>Effective</td>
<td>Inactivated</td>
</tr>
<tr>
<td>Efficacy with Hard Water</td>
<td>Reduced</td>
<td>?</td>
<td>Effective</td>
<td>?</td>
<td>?</td>
<td>Effective</td>
<td>Inactivated</td>
</tr>
<tr>
<td>Efficacy with Soap, Detergents</td>
<td>Reduced</td>
<td>Inactivated</td>
<td>Inactivated</td>
<td>Effective</td>
<td>?</td>
<td>Effective</td>
<td>Inactivated</td>
</tr>
</tbody>
</table>
Clean and disinfected is powerful!

Trailers, chutes, load-out areas, boots, etc
- Contact time is important, >1 hour
- Drying improves effectiveness
- Propylene glycol (NOT antifreeze!) if frozen
Preventing introduction of PEDv
- it’s really about feces of the species! -

• Packing house information, cull markets
• People and vehicle traffic
• Manure spreading and handling
• Mortality disposal
• Disinfectants – what and how
• TADD systems
TADD – time and temperature

• “......it may be possible to inactivate PEDV in the presence of feces by heating trailers to 160F for 10 minutes or by maintaining them at room temperature (68F) for at least 7 days. The other combinations .......were not sufficient to kill the virus as at least one pig out of 4 was infected.”

<table>
<thead>
<tr>
<th>Group</th>
<th>Bioassay POS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neg Control</td>
<td>0% (0/4)</td>
</tr>
<tr>
<td>Pos Control</td>
<td>100% (4/4)</td>
</tr>
<tr>
<td>160° 10 min</td>
<td>0% (0/4)</td>
</tr>
<tr>
<td>145° 10 min</td>
<td>25% (1/4)</td>
</tr>
<tr>
<td>130° 10 min</td>
<td>25% (1/4)</td>
</tr>
<tr>
<td>100° 12 hours</td>
<td>50% (2/4)</td>
</tr>
<tr>
<td>68° 24 hours</td>
<td>25% (1/4)</td>
</tr>
<tr>
<td>68° 7 days</td>
<td>0% (0/4)</td>
</tr>
</tbody>
</table>

D Holtkamp and R Main, ISU – NPB 13-227 Evaluation of time and temperature to kill PEDv in feces on metal surfaces
“My farm has acute PEDv (or PRRS)!!!”

What intervention is next?
What are our goals?

• Contain the infection, don’t spread it.
• Wean negative pigs.
• Keep pigs negative for the rest of their lives.

“How do you do that, Doc?”
What happens when my herd is infected?

- Diagnosis – critical **first** step is CALL! Don’t panic! Sit tight! We don’t want to miss other agents!
  - Feces
  - Tissues – proper fixed and fresh from **acutely** affected
  - Oral fluid ‘rope testing’ – good, rapid, economical
- Sow herd – careful exposure to make all ill
  - Close for 120+ days, gilts needed
  - Details are **critical** to success; don’t want endemic result
- Nursery, growing pigs will be sick also
  - First 2 weeks post-weaning vulnerable
  - Nursing care and support = dry, warm, electrolytes
Acute sow herd PED infection
Acute sow herd PED infection

Intervention:
Intentionally infect the population with the pathogen. Now!!!
Acute sow herd PED infection

Intervention: Intentionally infect the population with the pathogen. Now!!!

Succeed! Wean negative pigs
Acute sow herd PED infection

Intervention:
Intentionally infect the population with the pathogen. Now!!

Succeed!
Wean negative pigs

Fail!
Endemic infection established
Success = details, details, details.....

- Prepared – must close herd for at least 120 days, gilts on site to expose?
- Timing is critical – must be early in outbreak to capture enough virus
  - Pigs shed virus until intestinal lining is lost – hours
  - Requires a lot of virus to expose all sows and gilts adequately
- Handle virus carefully – don’t kill it in process!
- Prompt and timely euthanasia for debilitated, chronically infected piglets (*do you have a euthanasia plan?*)
- Destroy and disinfect all materials – do not track from the farm!
Percent Survivability to Day 7

Week 1: 0%
Week 2: 0%
Week 3: 25%
Week 4: 70%
Week 5: 95%
Week 6: 100%

Dr. Matt Ackerman, Swine Veterinary Services, Greensburg IN
Losses and Impacts

• The individual infected sow farm
  – Will lose about 5 weeks of weaned pig production
    • Piglet acute death ~4 weeks
    • Sows farrowing 20 weeks later….low production
  – Growing pigs lose a week + growth
  – “52 weeks of expenses, 47 weeks of revenue”

• The industry – to be seen
  – Regional impact on slaughter pig supply?
  – Markets for weaned pigs?
  – Slaughter weights?
  – Cost of production?
PRRS

Still Here

$1,000,000,000,000 annually
Reset time – PRRS and PEDv

• **Good news:**
  – Every biosecurity improvement against PEDv counts against PRRS too. Promotes behavior and investment. “Two for one…”
  – Intervention discipline – similar concepts and implementation can succeed, industry understands
  – Will radically rework sanitation chain from farm to plant

• **Bad news:**
  – Failure rate i.e. endemic outcome is very real risk
  – Validated procedures and methods are lacking; living on TGE experience so far
  – “Boots on the ground” capacity is inadequate
Questions are welcomed!