Periweaning Failure-to-Thrive Syndrome

Terri O’Sullivan
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Presentation Outline
• PFTS introduction and background
• PFTS clinical presentation
• Hypotheses
• Diagnostic investigations
• Prevalence survey and awareness campaign
• Future research
• Questions and discussion
Emerging Disease...

World Health Organization

http://www.who.int/topics/emerging_diseases/en/

"An emerging disease is one that has appeared in a population for the first time, or that may have existed previously but is increasing in incidence or geographic range"

PFTS - Background

• PFTS considered an emerging/re-emerging clinical syndrome
• First reported case: Canadian 100 sow farrow-to-finish farm (Gauvreau & Harding, 2008)
• Subsequent reports of PFTS cases
  • Canada and USA 2009 to present (Moeser et al., 2012; Huang et al., 2011)
  • Spain (Segales et al., 2012)
  • Field reports

PFTS - Background

• Increased concern in Canada and USA
• Treatment and control strategies implemented have been unrewarding
• IPVS 2010 PFTS working group
  • Post-weaning catabolic/wasting syndrome
• North American collaborative research group
  • Prevalence unknown
  • Etiology and pathogenesis undetermined
PFTS - Clinical Presentation

- Characterized clinically
- Normal pigs at weaning
- Clinical condition develops
  - Within 60-72 hours post weaning
  - Anorexia, weight loss
  - Chomping, licking
  - Progresses to debilitation

PFTS - Clinical Presentation

- Variable morbidity
- High case fatality
- Poor to no response to therapies/interventions
- November to May

2011 Questions....

*Unknown*

- Case definition
- Etiology, pathogenesis
- Prevalence of PFTS in North America
- Prevalence of clinical signs being observed
  - What is the most common clinical sign?
- Proportionate mortality due to PFTS
- Economic significance
- On-farm risk factors
PFTS - Case Definition

“PFTS is characterized clinically by the **progressive debilitation of weanling (nursery) pigs in the absence of** discernible and detrimental infectious, nutritional, managerial, or environmental factors that can explain the clinical syndrome”

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**PFTS - Case Definition cont...**

- At weaning, affected pigs are of **average to above average body weight**
- neither affected pigs nor their cohorts show evidence of residual illnesses from the suckling phase
- **Within 7 days of weaning, affected pigs are anorexic and lethargic**

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**PFTS - Case Definition cont...**

- Deteriorate and within 2–3 weeks of weaning demonstrate marked muscle weakness and loss of body condition
- Some affected pigs in all affected farms show repetitive oral behavior such as **licking, chewing or chomping**
- In affected farms, batch morbidity and mortality varies over time, but case fatality is high

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Hypotheses....

**Hemagglutinating Encephalomyelitis Virus (HEV)**
(Rossow, 2011 Leman Conference)
- Increase in number of HEV positive pigs and tissues
- Histopathology
  - Peripheral neuritis, rhinitis, gastritis
  - +/- presence clinical signs of failure-to-thrive
- Increased detection sensitivity of PCR??
- Research ongoing....

Hypotheses....

**Vitamin D** (Henry et al., 2011 Leman Conference)
- PFTS affected pigs
  - Poorly mineralized ribs
  - Micro fractures on histopathology
- Vitamin D25-hydroxycholecalciferol
  - 25(OH)D below normal range for age group
  - Normal = 25-30ng/ml
- Supplemented piglets at processing with Vit D
  - Achieved Vit D levels in normal range
  - Increased weaning weights
- Research ongoing....
Hypotheses....

On-farm risk factors
• Diet/rations
  • Milk/whey sensitivity
• Gastritis lesions observed in many cases
  • IBD in canine, milk allergy in children

Other infectious agent
• +/- Porcine cytomegalovirus (PCMV)
• +/- Unknown agent

Other Metabolic condition

PFTS - Diagnostic Investigations

PFTS - Gross Lesions
• Empty gastrointestinal tract
• Thymic atrophy
• Bronchopneumonia

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Sick (%)</th>
<th>Healthy (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thymic Atrophy</td>
<td>15/17*</td>
<td>0/7</td>
<td>0/6</td>
</tr>
<tr>
<td>(88.2)</td>
<td>(0)</td>
<td>(0)</td>
<td></td>
</tr>
<tr>
<td>Broncho-pneumonia</td>
<td>7/18</td>
<td>0/7</td>
<td>0/8</td>
</tr>
<tr>
<td>(38.9)</td>
<td>(0)</td>
<td>(0)</td>
<td></td>
</tr>
</tbody>
</table>

* The findings in the thymus of one pig was not recorded
PFTS - Microscopic Lesions

- Superficial lymphocytic fundic gastritis
- Atrophic enteritis
- Superficial colitis
- Chronic active rhinitis
- Mild meningoencephalitis
- Thymic atrophy

Slide courtesy: Dr. Y Huang

<table>
<thead>
<tr>
<th>Group</th>
<th># fundic gastritis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sick</td>
<td>16/16* (100)</td>
</tr>
<tr>
<td>Healthy</td>
<td>0/6* (0)</td>
</tr>
<tr>
<td>Control</td>
<td>0/8 (0)</td>
</tr>
</tbody>
</table>

* Funds of 2 sick and 1 healthy pigs were not available

Gastritis - frequent observation

- Gastric lymphocytic periganglionitis
- Subjectively more severe in sick pigs

Gastritis with bacteria negative for Helicobacter sp.
Slide courtesy Dr. J Delay
### Meningioencephalitis

<table>
<thead>
<tr>
<th>Group</th>
<th># of meningioencephalitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sick</td>
<td>6/13 (46)</td>
</tr>
<tr>
<td>Healthy</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td>Control</td>
<td>0/8 (0)</td>
</tr>
</tbody>
</table>

- Significance?
- Mild
- Chomping – neurological sign??
- Found in “normal pigs” in subsequent investigations?
- Neurological exams – nystagmus in sick pigs

### PFTS - Testing for bacterial pathogens

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Sample</th>
<th>Assays</th>
<th># positive/# tested (positive%)</th>
<th>Sick</th>
<th>Healthy</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmonella</td>
<td>Colon, ileum</td>
<td>Culture</td>
<td>0/18 (0)</td>
<td>0/7 (0)</td>
<td>0/8 (0)</td>
<td></td>
</tr>
<tr>
<td>F4+ E. coli</td>
<td>Colon, ileum</td>
<td>Culture, agglutination</td>
<td>0/18 (0)</td>
<td>0/7* (0)</td>
<td>0/8 (0)</td>
<td></td>
</tr>
<tr>
<td>Brachyspira spp.</td>
<td>Colon</td>
<td>PCR</td>
<td>0/12 (0)</td>
<td>0/3* (0)</td>
<td>NT**</td>
<td></td>
</tr>
<tr>
<td>Campylobacter spp.</td>
<td>Stomach</td>
<td>PCR</td>
<td>0/3* (0)</td>
<td>NT</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>Helicobacter spp.</td>
<td>Stomach</td>
<td>PCR</td>
<td>0/3* (0)</td>
<td>NT</td>
<td>NT</td>
<td></td>
</tr>
</tbody>
</table>

* When the denominators are smaller than the total numbers in that group, the remaining samples were not tested.
** NT = Not tested.

### PFTS - Testing for bacterial pathogens

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<thead>
<tr>
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<th>Sample</th>
<th>Assays</th>
<th># positive/# tested (positive%)</th>
<th>Sick</th>
<th>Healthy</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic E. coli</td>
<td>Colon, ileum</td>
<td>PCR</td>
<td>8/12* (66.7)</td>
<td>2/3* (66.7)</td>
<td>4/7* (57.1)</td>
<td></td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>Colon, ileum</td>
<td>Culture</td>
<td>4/18 (22.2)</td>
<td>2/7 (28.6)</td>
<td>0/8 (0)</td>
<td></td>
</tr>
</tbody>
</table>

* When the denominators are smaller than the total numbers in that group, the remaining samples were not tested.
PFTS - Interpretation of bacterial testing

- *Clostridium perfringens* type A
  - Present in both sick and healthy pigs
- *E. coli*
  - Present in both sick and healthy pigs

PFTS - Testing for viral pathogens

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Samples Assays</th>
<th>Assays</th>
<th># positive/# tested (positive %)</th>
<th>Sick</th>
<th>Healthy</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRRSV</td>
<td>Lung</td>
<td>PCR</td>
<td>0/18 (0)</td>
<td>0/7 (0)</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>SIV</td>
<td>Lung</td>
<td>PCR</td>
<td>0/18 (0)</td>
<td>0/7 (0)</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>TGEV</td>
<td>GI</td>
<td>IHC</td>
<td>0/18 (0)</td>
<td>0/7 (0)</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>PCV2</td>
<td>Lymphoid GI</td>
<td>IHC</td>
<td>0/18 (33.3)</td>
<td>0/7 (0)</td>
<td>NT</td>
<td></td>
</tr>
</tbody>
</table>

Pathogens Samples Assays # positive/# tested (positive %) Sick Healthy Control
Enteric calicivirus Jejunum PCR 4/18 (22.2) 1/7 (14.3) 1/8 (12.5)
Cytomegalovirus Tonsil, lung, kidney, GI PCR 17/18 (94.4) 7/7 (100) 8/8 (100)
Rotavirus A GI IHC 4/18 (22.2) 0/7 (0) NT
HEV Tonsil PCR 6/18 (33.3) 0/7 (0) 0/8 (0)
HEV Lung, kidney, GI PCR 0/18 (0) 0/7 (0) 0/8 (0)
HEV Brain stem, stomach PCR 0/6 * (0) Not tested Not tested

*These 6 medulla oblongata are from the pigs that tested positive for HEV 1 in tonsils.*

Slide courtesy: Dr. Y Huang
PFTS - Interpretation of viral testing

- **Rotavirus A** – lack of consistent diarrhea; rotavirus B and C was not investigated at this time
- **Enteric calicivirus** – Causes atrophic enteritis in gnotobiotic neonatal pigs. (Guo, M., et al., 2001)
- **CMV** – Rarely causes severe disease. No histological evidence of systemic infection.
- **HEV** – Clinical signs not typical (Vomiting and wasting disease); only positive in tonsil; gastric ganglionitis/periganglionitis?

PFTS - Testing for parasitic pathogens

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Samples</th>
<th>Assays</th>
<th># positive/# tested (positive%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sick</td>
</tr>
<tr>
<td>Coccidia</td>
<td>Feces</td>
<td>Flotation</td>
<td>3/5* (60)</td>
</tr>
<tr>
<td>Coccidia</td>
<td>Jejunum and/or ileum</td>
<td>Histology</td>
<td>6/18 (33.3)</td>
</tr>
</tbody>
</table>

* Not tested in 13 sick pigs (feces not available) and 4 healthy pigs
** These pigs are different from those necropsied control pigs

No other parasitic oocysts found

PFTS - Interpretation of parasitic testing

- **Coccidia** – *Isospora suis*
  - but need to be confirmed
- **I. suis** – Usually causes diarrhea with high morbidity and moderate mortality, which does not match PFTS
- **I. suis/coccidia**
  - primary or secondary pathogen??
Diagnostics - Conclusions
• PFTS seen in the this farm is NOT caused by
  • Clostridium perfringens A
  • Brachyspira
  • TGEV
  • Rotavirus A
  • PRRS
  • PCV2
  • SIV

Diagnostics - Conclusions
• E. coli, CMV, enteric calicivirus, HEV and coccidia (probably I. suis) are present in the PFTS-affected farm.
• But PFTS doesn’t match the typical clinical presentations of the infections of these pathogens
  ......as we understand them today....

Diagnostics - Conclusions
• Potential roles of rotavirus, enteric calicivirus and HEV are not fully investigated at this time
  • Rotavirus B and C?
  • Genetic diversity of enteric calicivirus
  • Significance of gastric ganglionitis/ periganglionitis/meningoencephalitis and their association with HEV or other pathogens?
  • Efforts to search for uncommon or novel pathogens is warranted
Terri’s Diagnostic Thoughts

- Anorexia/thymic atrophy
- Chicken or the Egg?
- Anorexia/chomping
- Anorexia/gastritis
- Meningoencephalitis/chomping
- Sick pigs

Prevalence survey and awareness campaign

PFTS - Project Objectives

- Increase awareness of PFTS among swine veterinarians and producers
- Demonstrate clinical signs – video
  - Case definition
- Determine
  - Crude prevalence - Canada and USA
  - Proportion of affected pigs in affected nursery flows
  - Common clinical signs
PFTS - Awareness Campaign
• September – December 2011
• Oral presentations at major swine practitioner meetings in USA and Canada
• Demonstrated clinical signs
  • Instructional video and still photos
• Questionnaire – recruit respondents
• Discussion and collaboration

PFTS - Questionnaire
• Administered September – December 2011
• Questions
  • Open and closed, comment sections
• Beta tested
  • Question clarity, reliability
• Asked to view video prior to completing questionnaire
  • Case definition

PFTS - Questionnaire
• American Association of Swine Veterinarians (AASV)
  • Email list-serve announcements made to AASV membership every 2 weeks
• Alternate online access available for non-AASV members
• Questionnaires available at meetings during awareness campaign
PFTS - Video

- Access via AASV website
  - Anonymous, password protected
  - Number of “hits” unknown
- Video inquiries from outside North America
- Comments regarding video were very positive
  - “The video was very informative and will help me to identify possible PFTS cases in the future”
  - “Excellent initiative. The video is a very good way to raise awareness of the condition and the clinical signs”

Results

- 52 questionnaires completed
  - 30 AASV website
  - 18 attending conferences
  - 4 alternate on-line option
- 88% (46/52) were swine practitioners
  - Academia, diagnosticians, industry, government
- 85% reported that >50% of their practice time was devoted to swine practice

Results

- 1,927 nursery flows
- 12 US States
- 6 Canadian Provinces
- 3 survey respondents were from outside North America
PFTS - Crude Prevalence

- Nursery flow prevalence of PFTS
  - 4.0% (CI 3.3-5.0%)
- PFTS affected flows in
  - 10 States, 4 Provinces
- A nursery flow was defined as:
  - one flow if the source of pigs is from a single sow operation that supplies 1 or more nurseries
  - one flow if the source of pigs is from multiple sow operations supplying 1 or more nurseries

Proportion of nursery pigs reported to be affected with PFTS within affected flows

<table>
<thead>
<tr>
<th>PFTS-affected pigs within an affected flow (%)</th>
<th>Veterinarians reporting (n=24) (%)</th>
<th>95% CI (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>50.0</td>
<td>29.1 - 70.9</td>
</tr>
<tr>
<td>4-10</td>
<td>45.8</td>
<td>25.6 - 67.2</td>
</tr>
<tr>
<td>11-25</td>
<td>4.2</td>
<td>0.12 - 21.1</td>
</tr>
<tr>
<td>26-50</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>&gt;50</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

*Binomial exact

Reported clinical signs associated with PFTS affected pigs

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>% of Veterinarians Reporting (n=24)</th>
<th>95% CI (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>100</td>
<td>85.7 - 100</td>
</tr>
<tr>
<td>Loss of body condition</td>
<td>87.5</td>
<td>67.6 - 97.3</td>
</tr>
<tr>
<td>Prolonged standing</td>
<td>83.3</td>
<td>62.6 - 96.3</td>
</tr>
<tr>
<td>Oral behavior of licking and chomping</td>
<td>75.0</td>
<td>53.2 - 90.2</td>
</tr>
</tbody>
</table>

*Binomial exact
Conclusions - Survey

- First reported estimate of flow-prevalence of PFTS in US and Canadian nurseries
- Small questionnaire sample size
  - > 1900 nursery pig flows
- Convenience sample
- Reasonable to expect that reported prevalence may change as we further understand PFTS

2011 2012 Questions....

Unknown...
- Case definition - dynamic
- Etiology, pathogenesis - dynamic
- Prevalence of PFTS in North America - dynamic
- Prevalence of clinical signs being observed
  - What is the most common clinical sign?
- Proportionate mortality due to PFTS - dynamic
- Economic significance
- On-farm risk factors - unexplored

Future research....

- Diagnostic investigations continue
  - University of Saskatchewan
  - University of Guelph
- Behavioural study – chomping
  - Prevalence in normal pigs
- Metabolic disease studies
  - Vitamin D and others
Take Home Message

PFTS - Considered an emerging/re-emerging disease....

“An emerging disease is one that has appeared in a population for the first time, or that may have existed previously but is increasing in incidence or geographic range”
http://www.who.int/topics/emerging_diseases/en/

Take Home Message

• Pathogenesis and etiology unknown
• Prevalence in Canada and USA = 4.0%
  • Field reports other countries
• On-farm prevalence variable = 1-10%
• High quality video and emerging diseases
• Continued collaboration important!

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*peer-reviewed