An epidemiological investigation of porcine-origin feed ingredients and the occurrence of porcine epidemic diarrhea on Midwestern United States pork farms

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Roadmap

Background (brief)
  Bias
Objectives
Methods
Results
Discussion
• PED virus was confirmed for the first time in the U.S. on May 16, 2013 (Canada reported on January 22, 2014)
  – United States
    • Investigations into the route of introduction were industry-led and included feed analysis (negative samples from May, June 2013)
    • Other routes were hypothesized
    • Invited by Matt Ackerman to investigate risk pathways associated with feed manufacture and delivery
    • Awareness (vitamin, minerals, proteins) → trace-back problem → bioassay → on-going concerns prompted another level of commitment to work
  – Canada
    • Empirical association between feeding spray-dried porcine plasma (SDPP) and occurrence of a cluster of early outbreaks
• Have a consultancy role with JBS United
• JBS United is a large animal nutrition company
  – Like any other suppliers, if there is a problem with their product they want to be the first one to know.
  – They provided me with full access to their company information and management processes.
• Feed can be (cross-)contaminated and therefore can be a vector for PED virus (just like any other product)
  – Vaccine, AI rod, tube of semen, piece of equipment, people, pigs, birds, trucks, and the list goes on)
  – Pigs have to eat, what is your risk tolerance?
Anecdotal observations

- Unpublished data (non-peer-reviewed)
  - Bioassay studies
    - Minnesota (inoculated feed and contaminated feed)
    - Ohio (feed from an infected farm)
    - SDPP manufacturer (natural and inoculated product)
    - Canada (and USDA-NVSL) related to Canadian outbreak
  - General observations
    - SDPP was PCR(+), technically difficult to confirm by virus isolation
      - Oral exposure to PCR(+) SDPP = possible infection
    - Feed formulated with PCR(+) SDPP was PCR (+/-)
      - Oral exposure to feed = no infection
Published studies

- **Dee et al (2014).**
  
  An evaluation of contaminated complete feed as a vehicle for porcine epidemic diarrhea virus infection of naive pigs following consumption via natural feeding behavior: proof of concept. *BMC Vet Res*, 10(1), 176.  
  
  Feed can be a vector for PEDV, even when it has been formulated without something like SDPP.

- **Pasick et al (2014).**
  
  
  Confirmed that PCR(+) SDPP can contain infectious PED virus.

- **Opriessnig et al (2014).**
  
  
  Even when SDPP is intentionally spiked with PED, exposure doesn’t necessarily result in infection.

- **No analysis of field data on the risk of exposure!**
Objective

• Objective
  – To investigate the association between exposure to porcine-origin feed ingredients and the occurrence of PED

• Study design
  – Field-based, retrospective case-control study of Midwestern U.S. pork farms (May 2014)

• Null hypothesis
  – No association between exposure to porcine-origin feed ingredients and occurrence of PED.
• **Reference population**
  - The premises locations at which prepared feed (or feed ingredients) were delivered by a U.S. licensed manufacturer of feed between May 2013 and August 2014.
  - Included single-site pork production operations, premises within multi-site pork production enterprises, and in some instances secondary private feed milling facilities.
  - Two feed manufacturing plants equipped with ingredient tracking systems at both the ingredient- and final batch-levels.
  - Premises in Indiana, Illinois, Iowa, and Ohio.
Methods (2)

• Study population
  – Criteria for case premises
    • All premises in the reference population with PED outbreaks that had been confirmed by laboratory diagnosis (date of first appearance of clinical signs was also recorded); AND
    • Data on feed deliveries was available at an ‘ingredient lot level’ from the feed manufacturer’s computerized information system

• ASSUMPTION: If feed was the source of infection, then it must have been delivered in the two-weeks prior to the start of the outbreak.
Methods (3)

• ‘Risk-products’
  – SDPP
  – Spray-dried blood cells (SDBC)
  – Choice white grease (CWG)
  – Hydrolyzed porcine peptones (HPEP)

• Study population
  – Criteria for control premises
    • Risk-product ingredient lot numbers that were delivered to case premises were ‘back-traced’ to the mill.
    • These lot numbers were then ‘forward-traced’ to identify the complete list of premises in the reference population to which the lot numbers were delivered (but were not infected with PED).
• Statistical analysis
  – The **strength of association** between each of the animal protein ingredients and the occurrence of PED was determined.
    • Odds ratios (OR) were the basic statistical test used
  – Estimated through the construction of 2 x 2 contingency tables.
    • Lot numbers were nested within ingredients – managed through Mantel-Haenszel adjustment when determined to be necessary.
  – Also estimated through logistic regression.
    • Conducted using hierarchical mixed model logistic regression to account for the nesting of lot numbers within each ingredient.
Odds ratio de-mystified

Odds of the disease in an exposed group, divided by the odds of disease in a non-exposed group

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Disease</th>
<th>Simple math</th>
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Example data: 112 premises

\[ \text{OR} = \frac{1/10}{1/100} = 10 \]
The strength of association between four porcine-origin feed ingredients (SDPP, HPEP, SDBC, and CWG) and the occurrence of PED was estimated at both an ingredient- and lot-level basis.

- In addition, the strength of association between fish meal (FISH) and the occurrence of PED was determined as a reference value for the population.

There were 43 cases and 418 controls represented in the study population.
Results (2)
SDPP1 lot numbers

Unadjusted ORs for SDPP1 lots. Dot represents the OR estimate and length of the bar indicates 95% CI.
Unadjusted ORs for CWG lots. Dot represents the OR estimate and length of the bar indicates 95% CI.
Summary ORs for each ingredient. Dot represents the OR estimate and length of the bar indicates the 95% CI. The ORs for SDPP1 and CWG have been adjusted by Mantel-Haenszel technique.
Other epidemiologic work

- **Lowe et al (2014)**
  - 3x as likely for truck to become contaminated if slaughterhouse staff enter truck when unloading when selling pigs
  - 4x as likely if unload after a positive truck
- **Morrison et al (2014)**
  - 4x more likely to be positive if you are within 1 mile of PED positive farm
  - Being a sow farm = 8.8x more likely
  - Rendering pickup = 7.1x more likely
- **U of MN – Feed Risk Assessment project**
Discussion

• In some cases, more than one cohort of pigs was represented at a given delivery premises.
  – Identical situation for both cases and controls, should have minimized any bias

• Some premises received more than one lot number of an ingredient, or multiple deliveries of one lot number, or diets were not identical in each case or control – i.e. a ‘dose-effect’
  – Assessed, and no effect was detected. However, data was not well-suited to this analysis.

• Other risk factors were not assessed due to the retrospective nature of the study.
  – All outbreaks were included, no attempt to distinguish source of introduction

• Only evaluated ‘porcine-origin ingredients’
Conclusions

- Ingredients had negligible to very low association with PED in this study.
- Minor differences among lot numbers for some products – not a consistent issue.
- No compelling evidence in this study for recall.
- Work with reputable suppliers.
- Work to improve traceability from the ingredients to the pigs:
  - Tracking systems (pigs, product, feed) are available off-the-shelf.
- Educate clients and production staff, communicate, report:
  - Underpins all PED mitigation strategies.