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Porcine epidemic diarrhea virus introduction into the United States: Root cause investigation

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ABSTRACT

Porcine epidemic diarrhea (PED) was identified in the United States in the spring of 2013, and professionals from many parts of the U.S. swine industry responded rapidly to understand and control the newly emerging disease. In less than two months, the disease had spread to more than 200 herds in thirteen states. Experts from the US Department of Agriculture (USDA) engaged in laboratory diagnostics, analytic support, epidemiology expertise, and data management to facilitate the effort. By 2014, a great deal had been learned about the disease; however, the question of how it entered the United States remained unanswered. In 2014, USDA formed an investigative group to address the question and leverage current knowledge with resources and partnerships not readily available to non-federal investigators. The group formed collaborations with other government and non-government organizations and individuals, and followed many avenues of inquiry; ultimately arriving at a small number of scenarios that describe possible mechanisms for PED introduction. For a scenario to be plausible, it had to explain: contamination of a person or product in the source country, its transit and entry to the United States, rapid dispersal across a wide geographic area, and exposure/infection of pigs. It had to be compatible with findings of swine herd investigations and research studies. Potential products had to have been imported legally during the time prior to the beginning of the epidemic, or delivered to the United States through prohibited channels. Follow-up studies were initiated to gather more evidence for the most plausible scenarios. Of the scenarios, flexible intermediate bulk containers ("feed totes") used to transport bulk feed serving as fomites for movement of PED virus provided the simplest explanation for the accumulated findings of the investigation.

1. Introduction

Cases of porcine epidemic diarrhea (PED) were first diagnosed in the United States (U.S.) beginning in April 2013. The swine industry and associated professionals responded on many fronts with the Veterinary Services (VS) branch of U.S. Department of Agriculture (USDA), Animal and Plant Health Service (APHIS) initially engaging in laboratory diagnostics, analytic support, epidemiology expertise, and data management. Multiple investigations and studies were conducted in an attempt to answer questions about the epidemic; at the top of the list were how the virus arrived in the United States and if there was risk of another disease following the same path.

Feed was initially suspected by veterinarians in several of the first-detected cases, and became a focus for a case-control study. The study included multiple farms with 25 cases and 18 controls. It was completed by June, 2013 and summarized by Dr. Harry Snelson from AASV at the 2014 World Pork Expo (Snelson, 2014). This was conducted as a collaborative effort between the American Association of Swine Veterinarians (AASV), National Pork Board (NPB), National Pork Producers Council (NPPC), VS' Center for Epidemiology and Animal Health, VS' Chief Epidemiologist, and the National Center for Foreign Animal and Zoonotic Disease Defense (currently: Institute for Infectious Animal Diseases (IIAD), a DHS Center of Excellence at Texas A&M University). Univariate regression analysis on the probability of being a case (i.e., presence of PED virus RNA plus animals with clinical signs) revealed feed factors that were associated with statistically significant higher odds of having PED. Feed that was custom mixed off-farm, increased number of meal/mash rations fed to nursery or finisher pigs, and whether vitamins and minerals were in the same as opposed to separate

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premixes increased the odds of PED on a farm between 1.5 and 3.5 times. These variables suggest the potential for contamination of feed where complete feed mixed off-farm is related to an effect where more ration types could mean more chances to get a contaminated batch. Although the case-control study suggested that feed was associated with the outbreak, subsequent investigations and herd histories failed to show a common feed or ingredient among the farms.

In late spring 2014, the mechanisms by which PED arrived in the United States had not been determined. USDA formed an investigative group to research the root cause of the epidemic; that is, to find the initiating cause or causal chain where an intervention could reasonably be implemented. A Root Cause Investigation Group (RCG) was tasked with revisiting the mass of information that had accumulated following the initial outbreak, and to leverage resources and partnerships not readily available to non-federal investigators. The group's objective was to identify the mechanism or most likely mechanisms by which PED reached the United States and infected U.S. pigs. The RCG reviewed literature; evaluated data from research projects; consulted with swine industry and veterinary specialists familiar with the individual outbreaks; collaborated with U.S. Government partners; reviewed reports published on university, industry, and laboratory websites; examined U.S. Customs and Border Protection (CBP) data on imported products; evaluated data from prohibited product seizures at U.S. ports; and collated testing data from affected herds. Additionally, the RCG initiated new studies as indicated, analyzed data, and conducted follow-up investigations of early-affected farms, and also reached out to international partners that had experienced outbreaks of novel swine enteric coronavirus diseases.

In many instances, information gathering was complicated because records and recall were not available or not collected at the time of the initial veterinarian's herd examinations. Although many people were eager to help solve the problem, some had concerns about sharing intellectual property or individual information with the Federal Government.

1. In order to travel from another country-particularly from Asia, environmental and carrier matrix conditions must be must be adequate for virus stability.
2. The scenario should explain why the epidemic occurred in the United States and not Canada or the EU given their similar industries, travelers, and international imports.
3. The scenario must be compatible with the outbreak investigation data. That is, a product or person is not likely associated with the epidemic if never in contact or linked in some way to the index farms.
4. The scenario must explain virus transit through four segments of travel, all are necessary and none sufficient alone:
   a. How people/fomites became contaminated in the source country,
   b. How the virus entered the United States,
   c. How it was dispersed to separate geographic locations in a short time, and
   d. How pigs were exposed and infected.
5. If the scenario involves legal imports, the product must have record of being shipped to the United States in the time prior to the outbreaks (e.g., CBP data and APHIS import permits).

Fig. 1. Criteria to narrow the scope of the investigation.

2. Methods

2.1. Epidemiology approach

During 2014, APHIS-VS prepared a pathway entry risk assessment entitled, *Pathways Assessment: Entry Assessment for Exotic Viral Pathogens of Swine* as the first step towards determining whether significant gaps exist in import regulations that may result in infections of U.S. domestic swine with exotic viral pathogens (USDA-APHIS, 2014). The RCG used the conclusions of this report and results of published research studies as a baseline, and followed with an epidemiological approach to narrow the scope and more specifically address the entry of PED virus into the United States. The group applied basic concepts of host, agent, environment, and evaluation of transmission mechanisms to develop scenarios that could explain the epidemic. National epidemic curves and timelines were developed to plot the course of the disease spread. Individual herd data gathered by first-responding veterinarians, and later augmented by revisits by VS officers to farms provided vital information for limiting the number of likely disease introduction mechanisms. Host factors, such as a naïve swine population with an explosive spread of disease, helped to limit the probable time of first introduction. Data from genetic epidemiology, virus survival, and infectious dose studies further narrowed the possibilities. Fig. 1 describes five criteria the RCG considered essential for a scenario to explain PED virus entry to the country.

2.2. Collaborations

Collaborations were established with other government and non-government entities, including Food and Drug Administration (FDA), other APHIS units (Wildlife Services (WS) and Plant Protection and Quarantine (PPQ)), U.S. Department of Homeland Security National Biodefense Analysis and Countermeasures Center (NBACC), and CBP, as well as universities and industry organizations.

2.3. Interviews with swine veterinary consultants

U.S. veterinary consultants were interviewed for their front line perspective on the herd outbreaks and impressions about the disease introduction. Unlike the case control study which had detailed survey questions (Snelson, 2014), the interviews were structured as informal discussions. A framework for topics was formulated to guide the discussions (Figs. 2 and 3), but the experts were encouraged to brainstorm and speculate about potential scenarios.

2.4. Herd investigations

Eight infected herds were identified by the testing data or by swine consultants as having occurred in April and May 2013, and were believed to include the earliest affected farms. These were chosen for further investigation. Results from the case control survey (Snelson, 2014) that included the eight farms were evaluated, and the farms re-visited by VS veterinary officials during summer and fall 2014. The veterinarians originally attending the herds were interviewed as well as production managers or owners. In some cases, the follow-up visits extended to the feed mills that formulated rations for the farms.

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