Development and application of the effective vaccine and other strategies against recent porcine epidemic diarrhea outbreaks

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Received for publication, January 20, 2016

The goal of this presentation is to summarize the response of US pork producers to the recent emergence of porcine epidemic diarrhea virus (PEDV) in North America. Additional presentations at the 2016 International Symposium on PED and TGE vaccine and its application meeting will focus on the PEDV experience in other countries as well as the pathogenesis, epidemiology, and virology of PEDV; such information will not be discussed in this paper.

In April 2013, PEDV was detected for the first time in the US and within months it spread throughout all major swine producing regions of the country. The virus caused severe diarrhea in young piglets leading to high mortality. Within the first year of the epidemic about 50\% of the sows in the US became infected resulting in a 7–8\% loss in total pig production with most of these losses occurring during the winter of 2013/2014. During the second year of the epidemic, the incidence of new cases declined dramatically during the summer months with a slight increase during winter. This rapid decline in new cases raised hope this new disease would fade away and pork production would return to normal. At present, in the third year of the epidemic, there has been a low, but steady number of PEDV cases reported each month suggesting the disease has reached an endemic equilibrium. To date, PEDV-related disease has been mild in the winter of 2015/2016.

For the purposes of this report, sow herds in the US will be defined as negative, active, or stable.

**PEDV-negative herds** are herds that have never been infected.

**PEDV-active herds** have ongoing clinical disease and virus can be easily detected. In the third year of the epidemic, most of the PEDV-active herds are herds that have previously been infected. In such cases the clinical disease is usually not as extensive as when PEDV first entered the naïve herd. There are still occasional cases of a PEDV-negative herds becoming infected for the first time and experiencing dramatic losses as first reported in 2013.

**PEDV-stable herds** are herds that once experienced an epidemic, and now there is no clinical disease recognized. In addition, the herd is negative for virus based on PCR testing, but some or all sows are PEDV-antibody positive.

The different PEDV statuses described above...
may provide some insight into the spread of the disease and possible control strategies. However, it is difficult to make generalizations in the US because most pigs are raised using a multi-site practice, and the majority of pigs are derived from sow farms containing more than 1,000 sows, with many sites housing 2,000 or more sows under one roof. In addition, some sites may have a complex of large sow barns located close together. In contrast, there are more traditional farrow-to-finish farms located all on one site that contain relatively small numbers of sows. This diversity in swine husbandry does contribute to a complex epidemiology for most swine diseases, and this may especially be true for porcine epidemic diarrhea.

During the first year of the PEDV epidemic field observations reported the rapid spread of disease from farm-to-farm, especially in winter. Diagnostic tests confirmed the etiologic agent was PEDV. This unprecedented transmission of virus was attributed to movement of infected animals, movement of contaminated people or equipment, aerosolization of the virus, and use of PEDV-contaminated feed.

Experimental studies have demonstrated that dramatic amounts of virus can be shed in the feces of PEDV-affected pigs. Moreover, PEDV appears to be highly infectious requiring only a small amount of virus to infect a pig. It is likely that one small pig could shed enough virus to infect thousands, if not tens-of-thousands of pigs. Multiply this potential by how many pigs are in a 1,000 sow barn and it is easy to understand how efficiently the virus could move within a barn. Likewise, it is easy to imagine how a continuous “cloud” of virus might travel through the exhaust fans in a sow barn to infect a nearby sow farm, or how easily a transport vehicle could be contaminated. In addition, since pigs of all ages are susceptible to PEDV infection, it is reasonable to expect nursery and finisher sites to become infected. Since these sites are continuously restocked with new pigs, once infected, the nurseries and finishers could act as a sustained virus reservoir. In short, there is little surprise that PEDV could easily spread following traditional pathways for most pathogens. However, there is a potential route of transmission that is more novel.

There is good evidence that some farms became infected following the consumption of PEDV-contaminated feed. Although this route of transmission may only explain a few cases, it could explain how almost identical PEDV isolates ended up in different countries around the Pacific Rim at almost the same time. Understanding how the virus moves from farm-to-farm and is sustained in a population is very important when designing control strategies.

Initial attempts to control PED involved “feedback” or controlled oral exposure that involved exposing the entire sow herd to infectious material (feces collected from sick and infected piglets) in an attempt to stimulate active PEDV immunity in the sow herd. The goal was to develop PEDV immunity in the sow which would be transferred to her piglets through colostrum. This would protect young piglets when they were most vulnerable. In general, this strategy seems to have worked well since the incidence of clinical disease has declined dramatically, but feedback has not worked all of the time. The apparent failure of feedback practices to consistently reduce or eliminate clinical disease has raised questions about the duration and quality of sow immunity following a controlled infection. In addition, there are questions about the difficulty of trying to expose a large group of sows to virus, and the quality of the biologic material used for feedback, and how well staff actually performs the task.

Modifications to the feedback strategy have involved multiple feedback attempts to improve the chances that all sows were infected (expose all sows 2–3 times over a 2 week period) with the
goal of making sure that all sows had at least one exposure to infectious virus. This practice did improve conditions on some farms, but there are still field reports of farms that would have a chronic low level of clinical disease as if some of the sows were never immunized through the feedback program. Or, if the sows were actually immunized (infected with wild-type virus) but their piglets still were clinically affected, then the duration or magnitude of sow immunization was considered inadequate.

As the US epidemic nears the end of its third year, field case reports are beginning to be published and shared. One thing to learn from this growing body of work is that the feedback strategy did help many farms reduce losses during the acute phase of the outbreak, and it seems to have prevented future disease (PEDV-stable herd). However, there are farms that have initiated the feedback practice and have had a difficult time controlling the disease (PEDV-active herds). One consistent factor in the PEDV-active herd is the large size of the herds suggesting it is difficult to implement an efficacious feedback program when thousands of sows and pigs are housed together. The exact reasons for this are not clear, but may involve the difficult task of providing an adequate challenge dose to each sow and gilt. One deficit in the general knowledge about PEDV is a lack of understanding about the duration and magnitude of the protective PEDV immune response. Based on success in PEDV-stable herds, it appears the immune response induced by feedback programs is adequate since the sow and piglets are protected. The duration is long enough for any contaminating virus originally on the farm to become inactivated either through cleaning or just time.

A common factor for PEDV-negative farms is size, with such farms being relatively smaller than the PEDV-active herds. The smaller herds may relate to less movement of incoming pigs, but their negative status probably reflects less movement of potentially contaminated vehicles and clothing on workers. It may be that on smaller farms compliance of workers is easier to monitor than on larger farms. Also, smaller farms can be more geographically separated than larger systems that seem to be located more closely together.

It is assumed PEDV isolates are antigenically closely related resulting in one serovar, and immunity to one virus can cross-protect against other viruses. If this is true, then there is a place for commercially produced vaccines to induce, or enhance a protective immune response, especially in gilts and sows prior to farrowing. Currently, there are two vaccines commercially available in the US. One is a whole virus inactivated vaccine, and the second one is a non-replicating virus-vectored vaccine. To date, there is no refereed published data on the efficacy of these vaccines. Based on company data from the field, either vaccine when given to sows prior to farrowing helps reduce the clinical disease in neonatal piglets. Since available data on these vaccines is limited, there is a need for controlled experiments evaluating vaccine efficacy of these vaccines as well as potential attenuated or modified-live virus vaccines.

Currently, in the US there are swine herds that have never been infected with PEDV which probably reflects very good biosecurity practices in these herds. PEDV-stable herds demonstrate how a herd once infected can eliminate PEDV from the site, and then keep the virus out. The PEDV-active herds generally are large herds on a single site for which it has been difficult to eliminate the virus from the farm. This endemic PEDV infection probably reflects a lack of immunity in the sow herd more than the presence of a unique environmentally stable virus that can re-infect sows. Presumable, all of the PEDV isolates are physically similar and should have the same sensitivity to disinfectants, dessication,
etc. Thus, differences between farms are related to farm-specific activities and not some novel virus property. It may be that PEDV-stable herds are typically smaller, and thus more likely to be thoroughly disinfected than larger sites. In addition, there is experimental evidence for infectious PEDV to be detected in a fecal slurry for extended periods of time which could serve as a potential reservoir of infectious virus to re-infect a farm. Differences in how manure is handled on small and large farms might explain some of the differences between PEDV-stable and active sites.

In summary, PEDV control can be achieved through the use of feedback strategies that involve multiple exposures of the sow herd to infectious virus. Ideally, each sow and gilt is repetitively exposed which may induce a superior immune response compared to a single challenge. This immunity may be augmented through the use of inactivated or non-replicating vector vaccines. Attenuated or modified live virus vaccines may be an improvement, but such vaccines need evaluation as well as possible other types of PEDV vaccines. Lastly, once a herd has become stable, there is still the inherent risk of re-introducing a new virus into the herd through contaminated feed which indicates a critical need to understand and eliminate this novel route of transmission.