



Mathematical modeling of porcine epidemic diarrhea virus dynamics within a farrow-to-finish swine farm to investigate the effects of control measures

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ABSTRACT

Porcine epidemic diarrhea (PED) is a highly contagious enteric disease in swine that can cause devastating economic damage to pig producers. Japan was severely affected by PED epidemics from 2013 through 2015, with over 1000 farms were affected during this period. Although many studies have unraveled pathological and molecular characteristics of PED virus (PEDV), the mechanism for within-farm spread is largely unknown. Here, we constructed a deterministic compartmental model to quantitatively describe the infection dynamics in a farm setting and to investigate effective control measures. The model consisted of three separate houses and four swine populations framed in a standard commercial farrow-to-finish swine operation in Japan, with a special focus on the role of indirect transmission via the on-farm environment contaminated by feces of infected pigs. Some model parameters were estimated using the Japanese empirical outbreak data. Model outputs over a 90-day period showed that the number of infected sows in a dry sow house peaked within a week after disease introduction, and PEDV was retained on the farm. In the farrowing house, the number of infected sows also peaked within a week followed by a tentative disappearance of infected pigs, whereas the number of infected piglets in the farrowing house spiked and the number of neonatal deaths increased rapidly until around Day 21 followed by a continued increase at a slower pace. In the fattening house, the number of infected pigs reached an equilibrium at around Day 25 and approximately 15% of pigs continued to be infected thereafter. Herd size was not found to have a significant influence on the overall trend in our model output. Among the control measures examined using our model, the application of effective vaccination was considered to be the most promising. Activities such as performing more thorough cleanings to remove residual virus or implementing stricter on-farm biosecurity to cease between-house virus transfer demonstrated little effectiveness for the control of PED. These results may imply that preventing PEDV incursion on a swine farm by elevated farm biosecurity measures is critically important, and that further research is necessary to prepare for future outbreaks, particularly research related to development of an effective vaccine that can prevent infection, and/or reduction of piglet mortality.

1. Introduction

Porcine Epidemic Diarrhea Virus (PEDV) is the causative agent of porcine epidemic diarrhea (PED), a highly contagious enteric disease in swine that affects neonatal pigs most severely with a morbidity and mortality of up to 100% (OIE, 2014). PED epidemics have recently been reported in multiple countries such as the United States, Canada, China, South Korea and Japan, and have become a major challenge to the global swine industry (Song et al., 2015). In Japan, PED re-emerged in October 2013 after a 7-year period with no reported cases and caused nationwide outbreaks of unprecedented size (Suzuki et al., 2015). From

October 2013 to May 2015, over 1000 farms were affected throughout Japan according to the Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF). In Japan, this PED epidemic with high pre-weaning mortality caused significant decrease in the number of slaughtered finished pigs and the subsequent surge in pork price as a result of the tremendous piglet losses in swine industry. Pigs infected with PED, especially pre-weaning piglets, show severe, watery diarrhea containing large amounts of PEDV. Many virological and serological diagnostic methods have been developed and are currently available for the detection of PEDV (Diel et al., 2016). In the epidemic period in Japan, diagnosis based on clinical signs and real-time RT-PCR was

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common in the field.

Although some factors, including contaminated feed and transport vehicles, have been suspected as causes of PED spread (Bowman et al., 2015; Lowe et al., 2014), little is known about PEDV dynamics within a swine farm following virus introduction. Previous studies on survival of PEDV in outer environments have demonstrated that detectable amounts of PEDV continue to exist in the environment for a long time (e.g., in fecal slurry for at least 28 days at 4 °C) (Goyal, 2014) and that PEDV could survive up to 9 months in manure storage sites in the affected farms, indicating the persistence of PEDV in the on-farm environment and the necessity of continued and heightened biosecurity measures (Tun et al., 2016). Thus, the environment contaminated with fecal matter of infected pigs is believed to be the primary cause of PEDV spread in PED-affected farms.

In veterinary medicine, SIR (susceptible-infected-recovered) models have been used to simulate the transmission dynamics of different pathogens and investigate the role of the environment in the transmission (Breban et al., 2009; Gautam et al., 2014; Rueda et al., 2015). Although transmission of PEDV has been quantified in animal experiments (Crawford et al., 2015; Niederwerder et al., 2016; Ouyang et al., 2015), the contribution of the environment to the virus transmission has neither been quantified or modeled. To address such lack of evidence and improve the disease management and control, we examine the within-farm epidemiological dynamics of PEDV, while incorporating the role of on-farm environment contaminated with feces of infected pigs in the disease spread and persistency, using a mathematical modelling approach.

The aim of this study was therefore (a) to develop a deterministic compartmental model that describes PED infection dynamics through indirect transmission via a contaminated environment in a typical one-site farrow-to-finish swine operation; (b) to assess the effectiveness of some control measures, including vaccination, in the developed model.

2. Materials and methods

2.1. Structure of pig populations

An epidemiological model is constructed to describe the PEDV transmission dynamics in a farm setting, which represent a commercial one-site farrow-to-finish swine farm, which is typical and the most commonly seen in Japan in terms of swine demography and farm structure. The features of the demographic and spatial assumptions in our model are illustrated in Fig. 1.

This hypothetical farm encompasses sows, piglets and fattening pigs, but gilts or replacement stock are not explicitly incorporated into the model for the sake of simplicity. There are three separate buildings assumed on the farm, namely, a dry sow house, farrowing house and fattening house. Since we needed to take into account the spatial partitioning of the entire herd and the physical movement of pigs between houses in accordance with the normal production stage in our model framework, we built a population-based model, which consisted of four different populations, namely, i) gestating sows and sows awaiting service in the dry sow house, ii) lactating sows in the farrowing house, iii) pre-weaned piglets in the farrowing house and iv) fattening pigs (weaner, grower and finisher pigs) in the fattening house. The physical movement of pigs, which corresponds to the white arrows in Fig. 1, is incorporated into the model. In the dry sow house, sows are inseminated and kept until just before farrowing in the model. Pregnant sows give birth to 10.68 piglets per litter on average in the farrowing house. The newborn piglets are housed for 23 days before weaning in the farrowing house, after which they are moved to the fattening house. Weaner pigs are fattened to achieve market weight for 160 days in our model and the finished pigs are removed for slaughter at the age of 183 days. Many of these parameters regarding the rates of pig movement between houses, which link four different populations, were obtained from the publication (Koketsu et al., 2010) and the Japanese

swine production statistics (JLIA, 2010).

Furthermore, loss of pigs from all compartments of live pigs due to natural death was taken into account by considering the industry average mortality rate for each population (arrow s corresponding to natural death are omitted in Fig. 1). The number of lost sows was replenished to keep the number of sows constant during the modeling period.

2.2. Transmission of PEDV and infection states

To describe PEDV transmission in a pig house, we expanded the standard Susceptible-Exposed-Infectious-Recovered (SEIR) compartmental model to further include compartments for the interactions with the viable virus in the environment (En) and the pigs that died as a result of infection (D) (Fig. 2).

In our model, susceptible pigs (S) become exposed (E) via the fecal-oral route, which occurs through indirect contact between susceptible pigs and viable virus in the contaminated environment. Direct transmission can only occur if a susceptible pig ingests the PEDV in the fresh feces from the recto-anal region of an infectious pig, which was assumed negligible in this study. All other body parts of pigs are most likely contaminated by contact with the pen environment that is already contaminated with feces from other infected pigs. Therefore, ingesting viable virus from a contaminated pig hide was viewed as a kind of indirect transmission due to animal-to-animal contact (Gautam et al., 2014).

In addition, the transmission from infected sows to newborn piglets via sow milk (Jung and Saif, 2015) or contaminated pen environment was taken into account, and piglets born from infected sows were assumed to have E states at birth. We subdivided the Infectious (I) compartment to account for subclinical infectious state (I_{sub}) and clinical infectious state (I_{clin}). It is also assumed that recovered (R) pigs lose their immunity over time and eventually revert to full susceptibility at the rate of decay of protective immunity.

The infectious animal sheds virus in the environment, where the virus can continue to be viable for a certain period of time. The overall virus load in a pig house is assumed to increase by the feces excreted from infectious pigs, and to decrease by the natural decay of virus and removal of feces by cleaning. The mechanical transfer of fecal matter in/out of a house by physical movement of persons and fomites are also considered in the model.

2.3. Model assumptions

Our model assumed that new infection of pigs occurs as a result of indirect virus transmission via the contaminated environment because the source of infection is merely identifiable for horizontal infection of PED, whereas the extent of direct transmission was regarded as trivial.

It was also assumed that infection states do not change at the time of physical movements between different populations, which was set to occur based on the rates calculated from the published data (Koketsu et al., 2010).

Other assumptions for the model building include: (i) all but one infected sow in the entire pig farm population are immunologically naïve at start, and (ii) pigs are well mixed in the house environment and thus are all equally likely to contact viable PEDV.

2.4. Transition between infection states

The model comprises a series of ordinary differential equations that describe the intricate relationships among the four swine populations in the three contaminated house environments. For each population, a total of seven model equations are constructed to describe the development of infection states. The model equations are written and individually explained below. The parameters involved in these equations are given and notated in Table 1. These parameters were derived from

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