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A Review of Area Spread and Summary of Recent Studies

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The focus of this paper is aerosol transmission of porcine reproductive and respiratory syndrome virus (PRRSV). To begin this discussion we believe it is necessary to define a few terms that will be used and to provide a brief review of veterinary literature about aerosol virus transmission. For the purposes of this paper we will use the following definitions for these selected terms.

Horizontal transmission
Transmission of virus from one pig to another pig requiring close contact between them. In addition, we will include the use of PRRSV-contaminated semen collected from virus-positive boars.

Vertical transmission
Transmission of virus from one generation to the next, in the case of PRRSV from dam to pig.

Fomite
An object that can harbor a pathogen and serve as an agent of transmission.

Vector
A carrier of infectious agent from one host to another host, can be *mechanical*—i.e., just transmitting the agent—or *biological*—the vector replicates the agent before transmission to a susceptible host.

Area spread
Recognition of virus infection among swine herds in a selected geographical region at about the same time.

Direct area spread
Transmission of virus among herds in an area related to horizontal or vertical transmission.

Indirect area spread
Transmission of virus among herds in an area not related to direct area spread, assumed transmission owing to fomites, aerosol, or vectors.

Perhaps the most compelling evidence for aerosol virus transmission is the work describing the indirect area spread of foot-and-mouth disease virus (FMDV) over water, e.g., the English Channel or the Baltic Sea.[1] These papers report field investigations that suggested FMDV aerosol transmission did occur, the diagnostic investigations that indicated similar virus was involved in these cases, the experimental-infection studies that demonstrated FMDV can be transmitted by an aerosol route, and the epidemiologic models that were constructed to predict the aerosol spread of FMDV. Concerning swine-specific diseases, there is a growing body of work describing pseudorabies (PRV), classical swine fever virus (CSFV), and swine influenza virus (SIV) aerosol transmission.[2-5] Again, this area of study began with field observations suggesting aerosol transmission of each virus did occur. Diagnostic investigations followed with serologic and/or biochemical tests supporting the field observations, and experimental work has demonstrated that aerosol transmission is possible. FMDV-infected pigs shed significantly higher quantities of virus via the respiratory tract when compared to CSFV-infected pigs and this difference may account for the apparent higher incidence of FMDV aerosol transmission when compared to CSFV epidemics. The early field reports describing what is now known as PRRS suggested that there was indirect area spread and this may have been related to aerosol PRRSV transmission.[6] In fact, the reporting of clinical cases in some areas followed a pattern similar to prior PRV epidemics in which the spread of PRV was considered to be by way of aerosol transmission.

Following the discovery of PRRSV several laboratories initiated studies successfully demonstrating direct PRRSV transmission. The first report supporting indirect PRRSV transmission involved 3 groups of pigs housed on 3 raised decks in a row (identified as 1, 2, 3) with about 1m separating each deck.[7] A solid partition separated deck 1 from deck 2 and there was no partition between deck 2 and deck 3. Pigs in deck 2 were infected with PRRSV and, in 3 out of 5 trials, virus was transmitted between decks 2 and 3 and, in 2 out of 5 trials, between decks 1 and 2. Results from this study demonstrated indirect spread, but the route was not determined since it was possible that activity of the pigs could have transferred virus-contaminated material—feces, for example—from one deck to another. The first report of aerosol transmission involved housing PRRSV-infected pigs in a container that was connected to another container holding sentinel pigs by a 1m section of tubing that allowed the passage of air from the infected pig chamber into the sentinel pig chamber.[8] Virus was transmitted in one trial but not in a second trial using a different PRRSV strain. The authors speculated that the failure of virus transmission in the second trial may have been related to the virus strain. In this same study, 2 unsuccessful attempts to transmit *Actinobacillus pleuropneumoniae* were completed using the same methodology attempted previously for PRRSV.

Recently, two reports have confirmed the observation of aerosol PRRSV transmission. In the first, pigs were once again housed in isolation chambers, one containing virus infected pigs and the second containing sentinel pigs.[9] The isolation chambers were connected with a 1m length of tubing, and the amount of air forced from the infected chamber into the sentinel chamber could be regulated. This study evaluated the aerosol transfer of PRRSV and *A. pleuropneumoniae*, with PRRSV being transmitted when 70%, 10%, and 1% of the exhaust air was routed into the sentinel chamber and *A. pleuropneumoniae* being transmitted only when 70% of the exhaust air was routed into the sentinel chamber. The second report describes an experiment carried out under field conditions where PRRSV-infected pigs in a swine barn were separated from sentinels by about 2.5m.[10] These sentinel pigs did become infected; however, additional sentinel pigs placed outside the barn in 2 trailers were not infected. One trailer was located about 1m from an exhaust fan and the second trailer about 30m from an exhaust fan. The authors concluded that aerosol transmission could occur over short distances, within shared airspace, but that it would be unlikely for aerosol transmission to occur over long distances.

We have completed a study evaluating aerosol transmission of PRRSV and *Bordetella bronchiseptica*[11] using a PRRSV isolate recovered from an epidemic of reproductive failure in north-central Iowa that appeared to be the result of indirect area spread of PRRSV.[12] In early August 1998 we were contacted by a veterinarian that had an epidemic of PRRS-like reproductive failure spreading across his practice area in north-central Iowa. We collected or received samples from 7 farms in one county, most of them located relatively near one another. The samples were collected during the first 2 weeks of August; PRRSV was isolated from each of the farms. We analyzed isolates from each farm with a type of DNA fingerprinting test called restriction fragment length polymorphism (RFLP), a qualitative test that can group PRRSV isolates by specific patterns. Viral isolates from 6 of the farms (n = 19) had the same 1-4-1 RFLP pattern, while the 7th farm had 1-4-1 (n=4) and 1-7-1 (n=2) RFLP patterns. Based on our experience this frequency of the same RFLP pattern among a group of farms was unusual and the decision was made to sequence a gene from each of the isolates. The envelope protein (ORF 5) gene was selected for sequencing since it is considered to be the most variable PRRSV gene and, if there were to be any variation or differences between isolates, then it ought to be detected in this gene. Surprisingly, the ORF 5 nucleotide sequence for most of the isolates from the group of 6 farms with the 1-4-1 pattern had a 100% identical match and the remaining isolates matched at the 99.7%–99.8% level. The seventh farm had the most divergence, with those isolates matching the other farms at a 98.7%–99.5% level. Again, based on our previous experiences and the work of others, this was an unusual finding. So unusual, in fact, that we have hypothesized that the same virus was present on each of the farms, suggesting some common link. Interviews with the attending veterinarian and pork producers indicated there was no common link among the farms that would explain a direct route of transmission (pig-to-pig, semen, fomites) leaving one with the conclusion that there must be an indirect route of transmission (aerosol, biological, or mechanical vector) among the farms. Since we believed that indirect area spread did occur during this epidemic, we wanted to evaluate some of the possible indirect routes of transmission beginning first with the aerosol route.

We speculated that the occurrence of aerosol transmission of respiratory pathogens is related to the pathophysiology of the respective disease, that is, any physiologic response that would productively expel secretions containing the pathogen (coughing, sneezing, etc.) would increase the likelihood that the agent could transmit to susceptible animals, perhaps even miles away. This physiologic response would increase virus output, one of the factors that could contribute to aerosol transmission. Experimental PRRSV infections generally do not induce any physiologic response that would productively expel virus-containing respiratory secretions, a phenomenon that may contribute to inconsistent experimental aerosol transmission results. However, in the field an uncomplicated PRRSV field infection is a unique scenario and the multifactorial etiology of the porcine respiratory disease complex can produce many opportunities that might enhance the aerosolization of a respiratory pathogen.

A study was completed with the following objectives:

- Demonstrate aerosol transmission of a PRRSV field isolate that may have been transmitted among farms by aerosolization; and
- Evaluate if a dual infection with PRRSV and another respiratory pathogen has a synergistic effect on aerosol PRRSV transmission.

Two isolation chambers connected by three 8cm diameter tubes (1m in length) were used for this study with the following protocol. On day 0, 3 pigs were placed in chamber A and given 1 of 3 treatments—oronasal exposure to PRRSV, oronasal exposure to *B. bronchiseptica*, or oronasal exposure to both agents. On day 5, one direct contact pig was placed into chamber A, and 3 indirect contact pigs were placed into chamber B. On day 12, the 3 infected pigs in chamber A were euthanized, and the direct contact pig was removed and placed into an isolation room. At this time the 3 indirect contact pigs were also removed from chamber B and placed into a separate isolation room. On day 26, the direct and indirect contact pigs were euthanized. Blood samples were collected from all pigs on day 0, day 12, day 26, and from directly infected pigs on day 5. Nasal swabs were collected on days 12 and 26. Lung lavage and tonsil tissue were collected at the time of necropsy. Day 0 and necropsy sera were tested for PRRSV-specific antibody. Aerosol PRRSV transmission occurred in 4 of 5 trials in which PRRSV was the only agent and in 2 of 5 trials with coinfection. Aerosol *B. bronchiseptica* transmission occurred in 5 of 5 trials in which *B. bronchiseptica* was the only agent and in 3 of 5 times with coinfection. Under the conditions of this study aerosol transmission of both agents did occur, however there was no apparent synergistic effect in the co-infection.

It seems clear under experimental conditions that PRRSV can be transmitted via an aerosol route over short distances, and under field conditions PRRSV may be transmitted a few meters within shared airspace in a barn. It is not clear if PRRSV can be readily transmitted between barns or even farms. We believe aerosol transmission among barns and perhaps farms is a possibility, we are just not sure of the probability of such an occurence.

The probability of aerosol transmission may be dependent on the following conditions or factors that have been proposed as necessary to maximize the potential for aerosol FMDV transmission over a long distance:

- high virus output;
- low virus dispersion;
- high virus survival; and
- large numbers of susceptible livestock exposed to virus for many hours.[1]

With regard to PRRS, it is not clear how much virus may be shed by an individual pig, but the need for high virus output to enhance aerosol transmission should be met by housing thousands of pigs within a single barn. High virus output can be further enhanced in swine-dense regions where pig barns can be located relatively close together. Virus dispersion is a concept that may best be summed up by: steady atmospheric conditions are best for virus distribution from one location to another. Although the ideal conditions for aerosol PRRSV transmission may not be known, it seems probable that if one can "smell" pigs, then that plume of odor might contain virus. This is a simplistic response to a growing body of science that quantitates atmospheric conditions and their relationship to odor and, perhaps, virus transmission. In addition, conditions that might favor low virus dispersion (cool temperature, high humidity, low steady winds) might favor PRRSV survival. As mentioned previously, the density of swine farms can be high, providing large numbers of susceptible livestock, a necessary aspect of the aerosol transmission equation. Moreover, one fact that may increase the chance for aerosol transmission is susceptibility of swine to PRRSV, as pigs have been infected with as little as 20 $CCID_{50}$ of PRRSV following oronasal inoculation.

The direct route of virus transmission is the predominant form of transmission and we would suggest pig-to-pig and the use of PRRSV-contaminated semen probably account for the vast majority of virus transmission among herds. Luckily, these threats can be controlled by following strict biocontainment strategies. Likewise, biosecurity strategies can also mitigate the significance of fomite and vector modes of transmission. These are simple comments to make, but as everyone knows all too well it is a difficult task to maintain strict biocontainment protocols, especially with regard to protecting swine against the potential threat from biting insects. Alas, there seems to be little protection against the risk of aerosol PRRSV transmission, an occurence that we hope is rare as there is little one can do to prevent it.

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