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The effect of vaccination on transmission of flu virus in weaned pigs

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Influenza in swine is an acute respiratory disease caused by influenza A viruses within the *Orthomyxoviridae* family, first isolated and identified in North America in 1930 (Shope, Exp Med 1931). Orthomyxoviruses have negative stranded RNA genomes that are segmented, allowing for shuffling of the gene segments (reassortment) and production of novel viruses (reassortants). In addition to major antigenic shifts via reassortment, the influenza A virus polymerase complex has the propensity to make nucleotide errors during replication. It is through this mechanism that antigenic drift occurs. There are 2 major surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA), important for host range, antigenicity, pathogenesis, and diagnostic detection. The other proteins encoded by the viral RNA are: nucleoprotein (NP), matrix proteins (M1 and M2), non-structural (NS1 and NS2 or NEP), polymerase A (PA), polymerase B1 (PB1), and polymerase B2 (PB2). The tracheal epithelium in pigs expresses the receptors for avian viruses and human influenza viruses, suggesting the pig as a mixing vessel for the emergence of new isolates with human pandemic potential (Ito et al., J Virol 1998; Scholtissek et al., Arch Virol 1993).

It is because of the changing nature and complexity of the virus itself that influenza virus in pigs has become a major challenge today for the North American swine industry. Economic losses are significant, particularly in growing pigs, due to increased mortality, poorer productivity, increased susceptibility to secondary infections, and treatment costs (Kay et al., Vet Rec 1994; Torremorell et al., Vet Rec 2009; Reeth et al., Vet Microb 1996). More recently, swine influenza has captured the spotlight with the emergence of pandemic H1N1 (pH1N1) of swine related origin. The emergence of pH1N1 has raised concerns about the ubiquity of flu viruses in US swine herds and potential human health implications. The industry is under considerable pressure to demonstrate that its production systems do not adversely impact public health. In addition, pH1N1 has reminded us of the complexity of flu and the commonalities that humans and pigs share regarding the nature and origins of their influenza viruses.

The epidemiology of flu in pigs in North America is complex. For many decades and until 1998, flu had limited impact in pig production. Only one H1N1 subtype of SIV, also referred as "classical flu", was recognized in pigs in North America. Clinical presentation of "classical flu" was considered mild and its epidemiology fairly well understood. However, starting in 1998, a plethora of diverse subtypes and strains emerged in North American pigs (Webby et al., Virus Res 2004) representing a quantum shift in the epidemiology of flu. As a result, control strategies considered valid for "classical flu" in pigs are no longer applicable. Many herds are endemically infected, sometimes with multiple strains, and viruses can persist and evolve even when control strategies are implemented (Brown, Vet Microb 2000; Vincent et al., Adv Virus Res 2008).

Vaccination is among the most common strategies to control flu virus infection in pigs. Flu vaccines in pigs prevent flu clinical signs and lesions but not infection. Vaccinated pigs tend to have improved performance and are less susceptible to secondary infections. There is very limited information in understanding the effect of vaccination on flu virus transmission. In the US, both commercially available vaccines and vaccines prepared with isolates recovered from client herds (autogenous vaccines) are available. Commercially available vaccines have one or more viral isolates representatives of subtypes H1 and H3 that are considered cross-protective with current circulating strains.

Most common vaccine protocols in the US include vaccination of sows prior to farrowing with the aim to provide maternal immunity to the neonatal pigs and protect those pigs throughout the lactation stage and until they are able to mount an effective immune response. Vaccination of growing pigs is recommended but not frequently implemented due to cost and labor.

One key question that remains to be answered is how immunity, whether natural or by vaccination, affects transmission within pig populations. Active transmission even in the absence of clinical signs may contribute to the establishment of endemically infected populations which in turn represent a potential source for flu virus infection for other pigs, other species and also people. However, limited information is available on the effect of vaccination on transmission and this paper presents preliminary data on how vaccines may affect transmission in pig populations.

Montse Torremorell, Anna Romagosa, Matt Allerson

Transmission of flu virus in naïve and vaccinated pig populations

We recently completed a study to evaluate the transmission dynamics of flu virus in non-immune (naïve) populations and in immune populations of vaccinated pigs. Pigs were either not vaccinated or vaccinated with a commercially available multivalent vaccine or a vaccine prepared with the challenge strain later used in the study (autogenous vaccine). The basic reproduction ratio (Ro) is a measure to determine how fast, or slow, an infection will spread in a susceptible population and it is defined as the number of secondary infections caused by one infectious individual. Ro above 1 indicates than an infection will spread, while Ro below 1 indicates than an infection will die-out.

In our study, the pigs were divided in 3 groups and received a treatment according to their vaccination status or lack of. Pigs in the control group were naïve and non-vaccinated. Pigs in the group vaccinated with a multivalent commercially available vaccine were vaccinated twice two weeks apart. The commercially available vaccine contained two distinct H1N1 strains and one H3N2 isolates. The H1 isolates were genetically and phenotypically different from the challenge strain used later in the study (A/Sw/IA/00239/04 H1N1). The pigs vaccinated with the product produced using the challenge strain (autogenous vaccine) followed the same protocols than the groups vaccinated with the commercially available vaccine.

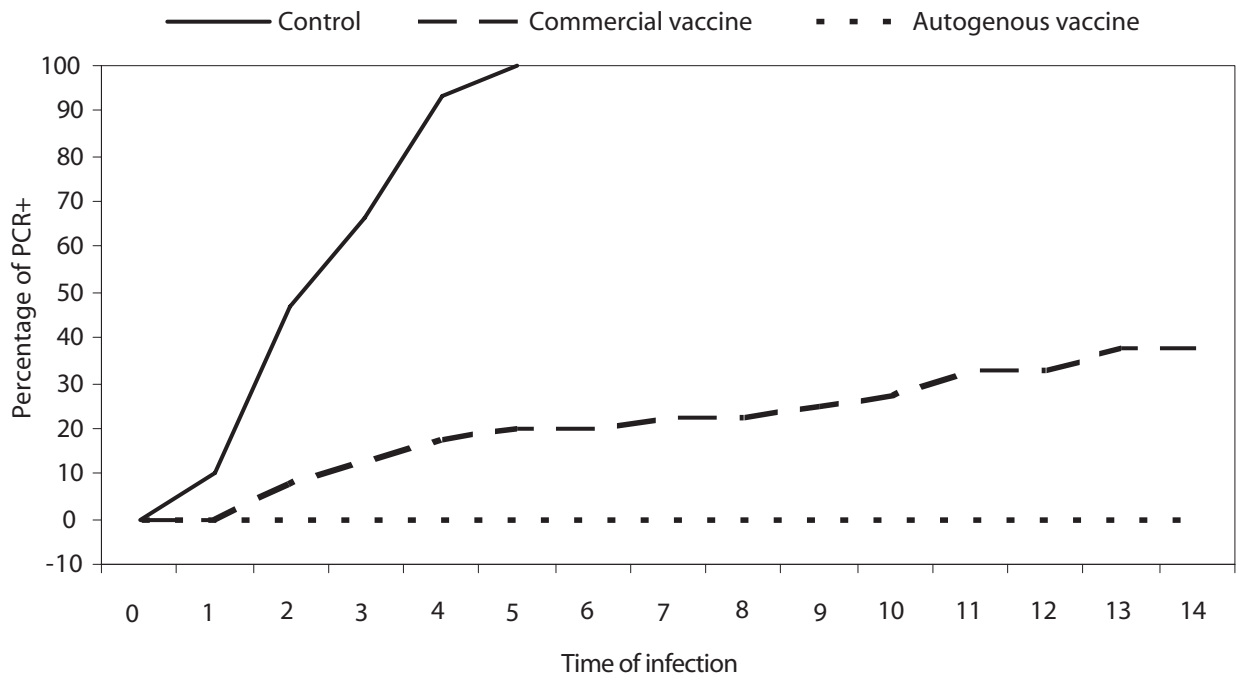
Two weeks after the last vaccination was completed, an infected pig shedding virus was commingled with the treatment groups and flu transmission assessed on a daily basis by collecting nasal swabs. Nasal swabs were then tested by flu RT-PCR.

Results from this study indicated that immunity induced by vaccination can have an effect in transmission of flu in pig populations. Results can be seen in Figure 1. As expected transmission in naïve pigs was fast and flu virus spread readily across all susceptible populations. On the other extreme, transmission in the autogenous vaccinated pigs could not be detected. Pigs vaccinated with the in house prepared autogenous vaccinated pigs did not become positive and infection could not be established in this group. Interestingly, transmission in the pigs vaccinated with a commercially available vaccine distinct from the challenge strain, was variable and although transmission was identified in all replicates, transmission was delayed in comparison to transmission in the control group. In addition, pigs vaccinated with the commercial vaccine had virus circulating when the study ended at a time when we had expected the virus to have died-out if compared to naïve populations.

Summary

In conclusion, vaccination can influence the dynamics of flu virus transmission and spread in pig populations. Managing immunity by means of vaccination can be a tool to mitigate or prevent transmission of flu virus in pig populations. However, although partial immunity induced by multivalent heterogenous commercially available vac-

Figure 1: Time course of infection for control and vaccinated groups.



cines may slow the spread of flu virus in populations, it may favor the establishment of endemically infected populations.

More studies are needed to better understand how vaccination may alter transmission of flu in populations, which protocols may contribute to it and whether vaccination can also be used to prevent within herd transmission and subsequent elimination. In addition, factors that contribute to the establishment of endemically infected populations need to be investigated further including understanding the role of immunity both, passive and active, as well as evaluating the effect of immune pressure on influenza virus mutations and the emergence of new strains.