Influenza A virus in swine – moving beyond 2009

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Pandemic H1N1 (2009). The pH1N1 possesses a unique genome with six gene segments (PB2, PB1, PA, HA, NP and NS) with the closest known genetic lineage being the triple-reassortant influenza viruses of the North American swine lineage and the M and NA genes derived from a Eurasian lineage of swine influenza viruses (17). The 2009 pandemic influenza became infamously known as “swine flu” due to the phylogenetic origin of the gene segments. However, the unique combination of gene segments had never before been recognized in swine and since the recognition of the pandemic, the epidemiology in humans has not been affected by the subsequent human to pig transmission and outbreaks in pigs (17).

The initial documented swine outbreaks were preceded by reported human influenza-like illness during the pandemic (18). The 2009 pH1N1 was shown to replicate efficiently in the lower and upper respiratory tract of experimentally infected pigs and to cause a clinical disease comparable to that typically observed during common enzootic influenza virus infection in swine (19-21).

Early reference to the 2009 pH1N1 as “swine flu” led to unnecessary alarm over the safety of pork meat products and culminated in the ban of exported pork from the U.S. by several countries, resulting in billions of dollars in lost revenue for the U.S. swine industry. However, contamination of fresh pork meat with the novel virus was experimentally excluded (22). Immediately after the onset in humans, cases of infection of pigs with the p2009 H1N1 were reported in different areas of the world. The first case was detected on April 28, 2009 in Canada in a farm with pigs that were not previously vaccinated against swine influenza (18, 23). Based on observations thus far, it is likely that the virus will continue to jump from humans to susceptible pigs with subsequent pig-to-pig transmission and establishment of yet another endemic virus in swine populations around the world. The 2009 pH1N1, a virus shared between people and pigs, has the potential to further change the epidemiology of influenza viruses in human and swine populations.

None of the 8 genes of the 2009 pH1N1 cluster tightly with the genes of SIV circulating in the U.S. prior to the outbreak in humans (3). In the phylogenetic analyses of each gene segment, the 2009 pH1N1 formed a distinct and independent branch from the U.S. swine lineage genes in viruses collected prior to 2009 and continues to do so. This suggests that neither the 2009 pH1N1 nor closely related progenitor viral genes were present in U.S. swine influenza viruses prior to 2009. A closely related progenitor virus with the same 8-gene constellation has yet to be identified in swine or other species, although a 2004 swine virus with 7/8 of the 2009 pH1N1 genome was identified in Hong Kong, China (3). The temporal
A recent study demonstrated an enhancement of disease and pathologic changes in the lungs of pigs vaccinated with a virus with the H1 HA derived from human seasonal influenza virus (ã-cluster SIV) and challenged with 2009 pH1N1 (24). These data suggest that non-neutralizing inactivated vaccine-induced immune response contributed to the enhanced disease. This phenomenon has the potential to be realized in the swine population due to the concurrent circulation of genetically diverse H1 SIV among swine vaccinated with inactivated virus vaccines that are potentially mismatched to the circulating strains. The vaccine associated enhanced respiratory disease (VAERD) underscores the need for improved surveillance, antigenic mapping and vaccine strain selection. Additionally, this phenomenon may have relevance in the human population with some vaccine formulations as suggested by the association between the 2008-09 seasonal human vaccine and pH1N1 illness during 2009 (25) and low avidity, complement fixing antibodies in the lungs of fatal cases of pH1N1 in humans (26). Additional studies are in progress to further evaluate the kinetics and mechanism of VAERD in pigs.

Relevance to human health. The trivalent human vaccine no longer contains the seasonal H1N1 that circulated in the human population from the mid-1970s until 2009 due to its recent replacement by the pH1N1. If this remains the case in the coming years, the youngest subset of the human population may not have immunity against viruses related to the swine ã-cluster. The pig population may now serve as a reservoir of influenza genes historically shown to be successful in humans, such as the ã-cluster HA and NA; the pH1N1 HA, NA, and M; as well as the TRIG genes of human and pH1N1 virus lineage. This combined with sporadic infections with avian-lineage viruses in pigs may provide the right opportunity for continued IAV reassortment and emergence in pigs. The potential for further zoonotic transmission events of novel viruses from pigs to people remains an unknown but possible risk that must be considered.

Conclusions

Surveillance and genetic characterization of influenza viruses associated with respiratory disease outbreaks in pigs are necessary for monitoring the evolution of viruses in the pig population to minimally aid in the development of sensitive and specific diagnostic tests. In addition, antigenic characterization is critical to fully understand the relevance of genetic changes for vaccine strain selection, and vaccine efficacy must be evaluated minimally by serologic activity when new variants arise. The 2009 pH1N1 underscores the potential risk to human and animal populations of influenza virus subtypes and genotypes that may evolve with the SIV TRIG backbone and/or other virus lineages. Increased surveillance for the pH1N1 as well as reassortants between pH1N1 and endemic SIV in the swine and human populations is essential to understand the dynamic ecology of influenza A viruses in susceptible host populations.

The World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) formed OFFLU in 2005, a network of laboratories formally organized to demonstrate
expertise in the animal health sector for surveillance, diagnostics, research, and control of highly pathogenic avian influenza H5N1. Influenza viruses circulating in swine and other animal hosts have recently been added to the OFFLU objectives and the potential for collaboration and exchange of information and resources between all influenza sectors is supported by OFFLU, with WHO also a contributing member. Although pigs may support the emergence of new viral reassortants, they may more often be the victim of cross-species transmission from people or birds than they are the source of new viruses. However, this cross-species transmission and the true directionality of virus movement cannot be fully understood without surveillance. A global surveillance system in pigs has not yet come to fruition, despite the existence of several successful local and regional programs.

A limitation of the regional approach is that the information is not always integrated and shared across species and regions, diminishing the effectiveness of surveillance efforts. Furthermore, unless a wide variety of pigs and geographical locations are sampled, the information may be biased and lead to inaccurate interpretation and/or decisions. The necessary global integration and sharing of data and resources for SIV will be addressed through the OFFLU network, but will require grass roots support from veterinarians and the swine industry.

Facing the swine and human health issues with influenza proactively with science, transparency, and cooperation is our challenge and opportunity now and in the coming years.

References


