

Influenza A Virus Diversity and Transmission in Exhibition Swine

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(See the major article by Nelson et al on pages 173–82.)

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Swine are permissive to infections with both avian and human influenza A viruses, facilitating genomic reassortment among viruses from multiple host species. As a result, swine have been identified as mixing vessels for influenza A viruses and a source of emergence for novel viruses, including those with pandemic potential [1, 2]. Since July 2011, human infections with influenza A virus of swine (IAV-S) subtype H3N2 (H3N2v to distinguish them from seasonal H3N2 influenza A viruses) have occurred throughout the United States with more than 340 cases and 1 death (as of July 2015) [3]. The main risk factor for infection with H3N2v was identified as direct contact with swine, primarily during agricultural fairs [4].

There are 3 major swine-human interfaces in the United States: domestic swine (commercial swine and exhibition swine), feral hogs (hunted for sport, food, and animal control), and abattoirs. It is estimated that some 150 million people visit

agricultural fairs in North America annually, allowing for considerable contact with live swine [5]. This is more than for any other interface in the United States. Furthermore, agricultural fairs allow for prolonged commingling of pigs from numerous breeders and multiple states. Collectively, these contacts create an environment conducive to zoonotic transmission, potential for viral reassortment with other strains, and geographic spread of influenza A viruses to new regions. Yet, surveillance, risk assessment, and evolutionary studies of IAV-S at the domestic swine-human interface have been conducted mainly in commercial swine [6–10], and little is known about the diversity of influenza A viruses circulating in exhibition swine. While control measures addressing activities before, during, and after swine exhibitions [11] reduced the infection risk (as demonstrated by the absence of human cases to date in 2015), H3N2v continues to circulate among North American swine and, as such, has high pandemic potential.

In this issue of *The Journal of Infectious Disease*, Nelson and colleagues [12] present results from the largest molecular epidemiology study of influenza A viruses in exhibition swine to date. They carried out large-scale comparative genomic and statistical phylogenetic analyses to provide a detailed picture of the evolution and spread of the IAV-S in exhibition swine in the United States during 2009–2013. They showed annual introductions of IAV-S to exhibition swine from commercial pigs. Yet, similar geno-

types circulate in exhibition swine in neighboring states, suggesting that viral transmission and genetic exchange among viruses are found exclusively in exhibition swine populations. Movement of exhibition swine, therefore, may create opportunities for IAV-S to transmit to naive populations and generate novel influenza variants through reassortment. Even though there is evidence of direct transmission of human IAV to exhibition swine, this occurred less often than swine-to-human transmission. The manners in which these H3N2v viruses have become established in exhibition swine suggest that exhibition swine should be considered a unique reservoir for influenza viruses with pandemic potential. This study provides a framework to generate testable hypotheses and insights into specific risk assessments for potentially pandemic influenza strains.

Even though the viruses in exhibition swine are ultimately derived from those circulating in commercial herds, the conditions at agricultural fairs, and the rearing behaviors of exhibition swine, allow those viruses to diversify from their common ancestors. Control efforts, such as pre-pandemic vaccine stockpiling, designed to target viruses circulating in commercial swine might not be effective against viruses circulating in exhibition swine. The fact that many more people have direct contact with exhibition swine than commercial swine means that risk mitigation must also account for the diversity of viruses circulating among exhibition swine. Therefore, large-scale comparative genetic

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studies need to be conducted to inform pre-pandemic planning and select viruses for virus-host characterization.

Although there is no shortage of influenza viruses with pandemic potential, it is critical to continue surveillance efforts in exhibition swine. Incorporating epidemiological information into molecular epidemiology studies could help us to understand the underlying ecological processes that generate the diversity of viruses we observe through surveillance. While our ability to predict future influenza pandemic viruses is poor, the separation of traditional virological characterization and statistical phylogenetic modeling limits our ability to make robust inferences. It is impossible to perform pandemic risk assessment analysis for each circulating influenza virus strain. While we may never predict which specific virus will trigger a pandemic, we need to understand the systems that generate potentially pandemic strains of influenza viruses and integrate virological characterizations (eg, replication, pathogenicity, transmissibility) to predict the behaviors of circulating viruses.

Focusing on mutations present in a few individual variants instead of the systems that generate those variants may be too narrow in scope to fully benefit pandemic preparedness efforts. Studies that investigate viral diversity at various transmission interfaces need to be integrated with efforts

to characterize viruses. If the influenza research community does not incorporate large-scale comparative genetic studies in generating their hypotheses, they risk inappropriately generalizing their results to all circulating viruses, even though their observations are based on a narrow scope of circulating variants. Focusing on individual variants instead of systems that generated the viruses with pandemic potential may, therefore, limit the effectiveness of pandemic mitigation plans.

Nelson et al [12] demonstrate that it is critical to continue surveillance efforts among exhibition swine. This reservoir may be contributing to the diversity of viruses that infect people. Those viruses need to be characterized by virological methods and placed side by side with detailed clinical, epidemiological, and genomic information to maximize the potential of phylogenetic approaches, in order to help us understand the biology of influenza viruses in exhibition swine and predict the next influenza pandemic.

Note

Potential conflict of interest. Both authors: No reported conflicts. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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