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Considerations in managing type A influenza virus in swine populations

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Introduction

Type A influenza virus has been a clinical problem in swine in North America (N. Am.) from as early as 1918 and has circulated continuously in the population since that time.[1] From 1930 until the late 1990's a single Type A viral subtype that remained genetically and antigengenitally stable was present.[2] Over the last 20 years several new subtypes of virus have emerged in North America and Europe that have been both genetically an antigengenitally less stable than the H1N virus present since at least 1930.[3] Control methods for influenza virus in swine to date have relied on the use of attenuated vaccines in either pigs and or breeding herds. There has been wide spread adoption of these vaccines in the N. Am. swine industry. Reports at scientific meetings and casual observation suggest that in spite of the introduction of these new tools influenza virus continues to be and in some cases is increasingly a problem. This paper will be a brief review of the epidemiology, immunology and vaccinology of type A influenza viruses that would be relevant to managing infection in swine herds.

Epidemiology of influenza in the north American swine herd

Until recently, the virus circulating in the N. Am. swine herd was a single sub-type (H1N1) that had undergone little change it is genetic make up or antigenicity.[2] In the late 1990's a second Type A virus type (H3N2) that contained genes from Type A viruses that were of avian or avian and human lineages emerged in the N. Am. swine herd.[4] At a similar time the emergence of H3N2 isolates in Europe were identified.[5] With in a few years, H1N1 isolates were found in Europe that had both internal and HA gene segments that were from avian linage.[6] In North America, there has been the emergence of H1N2 isolates that appear to be recombinants of H1N1 and H3N2 viruses that most likely were residing in the same host. More recently, there have been H1N1 isolates from swine in N. Am. that have HA and NA genes from other swine isolates but internal genes (PA, PB1, and PB2) that are from avian lineages.[2] The rate of genetic and antigenic change in the HA gene segment has increased dramatically since the emergence of these "swine-avian" recombinant H1N1 subtypes.[7]

Historically, influenza outbreaks were seen in swine seasonally in the fall but it has been suggested that this pattern was the result of continual sub-clinical transmission of influenza in the herd.[8] Cross sectional surveys have identified a large percentage of finishing pigs with antibodies to swine influenza virus where in most cases there have been no reports of clinical disease in these herds.[8] The pattern of influenza transmission between swine herds is different that what is seen in the human population. The source of infection in most herds appears to be other swine and not lateral transmission.[8] In addition, the infected animals that are introduced into the herd appear to be sub-clinical infections that have remained in a herd or pyramid of herds for an extended period of time.[8] These data suggest that influenza is circulating in the swine population continuously at a level that does not produce clinical disease.

Immunity to influenza in swine

Historically hemagglutination inhibition (HI) has been the measure of immunity to swine influenza virus.[9] This test detects antibodies to epitopes on HA protein that resides in the membrane of the virus.[5] The introduction of a commercial vaccine (Flusure(r), Pfizer Animal Heath, Kalamazoo, MI) that originated from a group of viruses that had H1 HA gene segments of a more recent linage resulted in the discovery that the HI test to the A/swine/IA/30 virus that NVSL uses as a standard was less reliable for the "new" H1N1 sub-types.[10] In addition, the HI cross reactivity to a virus in vitro has not been predictive of clinical protection.[11] Studies with monoclonal antibodies have demonstrated that recent H1N1 isolates can be grouped with very different cross reactivity patterns.[8] This suggests that using the HI test to determine the correct antigens to include in vaccines may not be adequate to accurately predict their protection in clinical cases. There is evidence that in birds, there is wide spread cross protection not only between variants with in a sub-type but even between sub-types . This cross protection seems to be provided by influenza specific cell mediated immunity (T cells).[12] In swine, there appears to be an increase in T cells in the lung even when there are low numbers of

circulating anti- influenza antibodies in response to infection with influenza virus.[11]

The development of active immunity, both cellular and humoral, can be influenced by the presence of maternally derived antibodies (MDA) in piglets. Piglets with MDA that are exposed to homologous SIV demonstrate a reduced level of serum IgM, serum IgG and nasal IgA in response to primary infection.[9] Interestingly, the MDA carrying piglets also have a altered CMI and humoral immune response after a second infection with autogenous virus eight weeks after the primary infection.[9] These data suggest that high levels of MDA may not be as beneficial as commonly believed and that reassessment of immunity management may be necessary. Even with high levels of MDA or active immunity, infection is not prevented as demonstrated by the ability to isolate virus from the respiratory tracts of pigs following exposure regardless of immune status. This fact alone brings into question the vaccination of dams prior to farrowing.

Vaccinology of influenza in swine herds

Control methods for influenza virus in swine to date have relied on the use of attenuated vaccines in either pigs and or breeding herds. Initially, monovalent vaccines for the H1N1 subtype virus that were closely related to the a/swine/IA/30 virus were produced by several manufactures for commercial use (Schering-Plough Animal Health, Union, NJ; Intervet Inc, Millsboro, DE). With the emergence of H3N2 isolates in N. Am., several companies began to produce commercially available bivalent vaccines with both H1N1 and H3N2 subtypes (Schering-Plough Animal Health, Union, NJ; Intervet Inc, Millsboro, DE; Pfizer Animal Health, Kalamazoo, MI; Fort Dodge Animal Health, Fort Dodge, IA). Recently a trivalent commercial vaccine was introduced that has both historical H1 antigens and H1 antigens that are more closely related to more recent H1 isolates (since the emergence of recombinant H1N1) (Schering-Plough Animal Health, Union, NJ). With the introduction vaccines, there has been widespread adoption. The commercial vaccines are universally licensed for use in both breeding swine and growing pigs (Schering-Plough Animal Health, Union, NJ; Intervet Inc, Millsboro, DE; Pfizer Animal Health, Kalamazoo, MI; Fort Dodge Animal Health, Fort Dodge, IA).

In addition some veterinarians have chosen to use vaccines that the antigen (virus) originates from the farm of origin (autogenous vaccines). These vaccines have been used to address the apparent failure of commercial vaccines in swine herds that have been perceived to be due to antigenic drift in viruses circulating on farms away from vaccine strains. Clinically there appear to be two strategies that are employed in selecting the antigens for these vaccines. The first strategy is to find a single isolate for each of the subtypes of interest and use that vaccine in place of commercial vaccine. The second, more active strategy, would employ continuous surveillance of the herd. If isolates are recovered from the herd they would be compared to the current isolate in the vaccine (typically through phylogenic analysis of the HA gene or though cross reactivity in an HI test) and if the new isolate is determined to be "different" then it is included in the vaccine.

Control of influenza infections in modern swine production systems

All of the above vaccination strategies are fraught with challenges. The biggest challenge in developing any vaccination strategy is that imperfect immunity is achieved following infection. The theory behind the autogenous antigen vaccines is that improved immunity would be achieved. While this does appear to be true, even this immunity is not sterilizing and would allow for the transmission of virus to other animals. The currently available information would suggest that with current inactivated vaccine technology elimination of influenza virus form swine herds may be impossible. There is also data to suggest that many herds are infected with influenza virus even if they do not exhibit clinical signs. The European data would suggest that control of source herds and minimizing the number of sources into a system or herd may be the most valuable tool in controlling infections. Unlike human influenza most transmission appears to be with in and not between herds unless there are pig movements between those herds.

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