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Relation of Protection and Serological Results: an Efficacy Study with MAXIVAC EXCELL Using a Heterologous Challenge Strain of Swine Influenza Virus, Subtype H1N1

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Introduction

Classical H1N1 SIV has been the predominant subtype circulating in swine since its isolation in 1930. Even after the appearance of H3N2 SIV in 1998, H1N1 has remained a significant subtype and still accounts for the majority of isolates¹. Antigenic drift has been documented in H1N1 SIV although not to the point where vaccine efficacy has become a concern.² In previous vaccination and challenge studies, a heterologous strain of H3N2 was used to demonstrate the efficacy of the H3N2 fraction of MaxiVac Excell, Schering-Plough Animal Health's bivalent swine influenza vaccine³. A vaccination and challenge study was conducted to verify the ability of MaxiVac Excell to provide protection against a heterologous challenge of SIV H1N1.

Materials and Methods

Vaccines and Vaccination: A commercial production serial of SPAH's bivalent H1N1 and H3N2 SIV vaccine, MaxiVac Excell was used. Swine, four to five weeks of age, from a high-health herd free of swine influenza, *Mycoplasma hyopneumoniae*, PRRS, and pseudorabies were placed in isolation facilities and vaccinated twice, 14 days apart, with 2 mL intramuscularly as follows:

Challenge and Post-challenge Procedures: Three weeks following revaccination, swine were inoculated intranasally with a virulent virus challenge of heterologous H1N1 SIV. On day 5 post-challenge, swine were euthanized and lungs were scored for gross lesions.

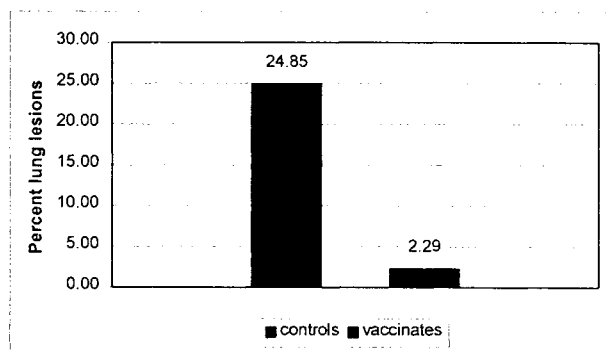
Hemagglutination Inhibition (HI) Antibodies: Sera were tested using the HI procedures supplied by the Center for Veterinary Biologics Laboratory (CVB-L), Ames, IA. Inactivated antigens were prepared to the homologous vaccine virus as well as to the heterologous challenge virus. Sera were also analyzed using the HerdCheck Swine Influenza (H1N1) Antibody Test Kit (IDEXX Laboratories, Inc., Westbrook, ME).

Statistical Analysis: Lesions Scores (%) were transformed by arcsine-square root transformation and analyzed by analysis of variance procedures. Pairwise comparisons were performed using least squares means.

Results

Lung Scores: The SIV challenges were severe, producing a median lung consolidation score in the nonvaccinated swine of 24.85 %. Vaccination resulted in a highly significant ($P < 0.0001$), reduction in lung lesions in vaccinated swine challenged with the heterologous SIV H1N1 strain. The median lung consolidation score for the vaccinates was 2.29%. This resulted in a 92% reduction in lung lesions in vaccinates versus controls.

Figure 1: Median lung consolidation scores of swine after challenge with virulent heterologous H1N1 SIV.



Antibody Titers: All swine were negative (titer < 10) to H1N1 prior to vaccination. Vaccinates developed significant H1N1 titers, while nonvaccinated pigs remained serologically negative prior to challenge. HI geometric mean titers three weeks after the second vaccination and the median lung score for the vaccinates are summarized in Table 3. Previous challenge trials have shown that a HI titer of 1:40 or greater results in significant reductions in lung lesions⁴. In this trial, there was an almost 2.5 fold difference in geometric mean HI titers between tests using heterologous vs. homologous viral antigen while producing a highly significant reduction in median lung lesion scores. Therefore, the use of heterologous viruses in HI tests may yield misleading results when used to predict the degree of reduction in lung lesions.

Table 3: Serological cross-reactions between SIV H1N1 isolates and lung lesion scores.

	SPAH HI	CVB-L HI	ELISA S/P	Median % Lesions
Geo mean	103.3	41.5	0.702	2.29

Conclusions

- ◆ Swine vaccinated with MaxiVac Excell exhibited statistically significant reductions in lung lesions when experimentally challenged with a heterologous H1N1 SIV isolate.
- ◆ Postvaccinal HI titers using heterologous challenge viral antigen were significantly lower than those obtained with homologous viral antigen. Use of heterologous viruses in HI tests for the purpose of predicting protection may be misleading.
- ◆ The IDEXX ELISA test called 18/19 pigs positive after vaccination, which closely matched results obtained with the homologous HI test (19/19 positive). The ELISA test may thus have potential to be a useful tool for vaccination monitoring.

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