Head at the University of Nevada at Reno. As Dean, Dr. Thawley had a strong commitment to outreach at the College and saw the Leman Conference as a great opportunity to help the swine industry. He encouraged faculty in their efforts to build a quality program each year and provided the staff to support a conference of this size. He will be remembered for his commitment to the growth and success of the Allen D. Leman Swine Conference.

Regardless of all the efforts previously mentioned, you, the individuals who attend the Leman Conference, are the most important reason for success. Without your presence, there would be no need for this meeting. Your commitment to your education brings you here. You have challenged yourself and others to be better. We want to meet that challenge.

Thank you for attending the 1998 Allen D. Leman Swine Conference. Please feel free to suggest ideas to improve future conferences.

— Charles H. Casey, DVM

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Comparative Pathogenesis of Severe Versus Mild Swine Influenza Virus Infections

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Introduction Swine influenza virus (SIV) can cause acute outbreaks of respiratory disease, with high fever and weight loss. Still, subclinical or mild SIV infections frequently occur, even in fully susceptible, seronegative pigs. The pathogenetic mechanisms that determine the severity of a SIV infection are not yet clear. Production of pro-inflammatory cytokines by an infected host can mediate lung inflammation, fever and anorexia1. Here, we have examined whether levels of interferon-(IFN-α), tumor necrosis factor- (TNF-α) and interleukin-1 (IL-1) correlate with disease severities during experimental SIV infection. To strengthen our case, we also examined pigs from natural SIV outbreaks.

Experimental design Four litters of 3-week-old gnotobiotic pigs were inoculated intratracheally with $10^{7.5}$ EID50 of the A/Sw/Belgium/1/83 (H1N1) strain (n=14) or with phosphate-buffered saline (PBS) (control pigs, n=4). Pigs of each group were killed between 18-72 hours post inoculation (h PI) with virus or 24 h PI with PBS. Four 6-week-old gnotobiotic pigs were inoculated by aerosol at the same virus dose and killed 2-6 days PI (DPI). One uninoculated control was included. We evaluated clinical signs, lung virus titers, and cytokine levels and % neutrophils in bronchoalveolar lavage (BAL) fluids.

Pigs from herds with acute respiratory disease suggestive of SIV were killed and, upon a positive virological diagnosis, further examined as in experimental studies.

Results Experimental studies: All 5 control pigs remained healthy, they had less than 1% neutrophils in their BAL fluids, and tested negative for virus and cytokines. Intratracheal SIV inoculation was followed by characteristic signs - tachypnoea, labored abdominal respiration, coughing, lethargy, shivering and anorexia - in all 4 groups of pigs. These developed within 18-24 h PI and were accompanied by a drastic neutrophil infiltration (24-77% of BAL cells). Peak disease signs and lung inflammation coincided with massive virus production ($10^{8.4-10.2}$ EID50/g lung) and unusually high levels of IFN-α, TNF-α and IL-1. Recovery already started between 18 and 24 h PI, when virus titers declined and cytokines became low or undetectable. There was a clear association between individual cytokine levels on the one hand, and the severity of disease and the extent of neutrophil infiltration on the other.

Aerosol inoculation produced only slightly increased respiration rates and occasional coughing between 2-5 DPI. Neutrophil percentages varied between 7 and 28%. Compared to the intratracheal inoculation, there was less extensive virus replication ($10^{6.2-7.2}$ EID50/g lung) and a strikingly different cytokine profile: IFN-α was about 100 times lower, and TNF-α and IL-1 were undetectable.

Field study: is in progress; results will be presented at the symposium.

Discussion These findings indicate that pro inflammatory cytokines are in part responsible for typical SI symptoms and pathology. The amount of virus that reaches the deeper airways and the resulting production of infectious virus in the lungs seem to determine the extent of cytokine production. We conclude that, in the case of SI, environmental measures reducing virus load in swine buildings (i.e. proper ventilation and stocking densities) are extremely important in disease control. These data further substantiate that SIV vaccination must confer only limited virological protection in order to protect against clinical outbreaks3.