

S 11-2

Exposure of cynomolgus macaques to aerosolized *Francisella tularensis* SchuS4

H. C. Gelhaus¹, D. Pak¹, A. Lindsay¹, J. Cross¹, J. Hyung¹, K. Battles¹, R. Krile¹, R. Barnewall¹, K. Van Zandt¹, H. A. Lockman¹

¹Battelle Biomedical Research Center, Columbus, United States

Objectives: *Francisella tularensis* is a highly virulent intracellular pathogen, the etiologic agent of tularemia, and is classified as a category A priority biodefense pathogen. Due to the low natural incidence of tularemia, FDA licensure of tularemia countermeasures will require well developed animal models of disease. To establish a non-human primate tularemia model, we defined several parameters of inhalational tularemia in cynomolgus macaques.

Methods: Mauritian origin cynomolgus macaques (*Macaca fascicularis*) were exposed to various dosages of aerosolized *F. tularensis* SchuS4. Macaques were exposed to a range of dosages to estimate the median lethal dose (LD₅₀). To document the progression of disease, animals were observed for clinical signs of disease as well as implanted with radiotelemetry transmitters to obtain temperature, activity, pulmonary and arterial pressures, and electrocardiograph parameters. Blood samples were drawn periodically to measure clinical laboratory parameters, bacteremia, and immune responses.

Results: The preliminary aerosol LD₅₀ for *F. tularensis* SchuS4 in cynomolgus macaques is 294 cfu/animal. Animals were commonly observed to be lethargic with hunched posture post exposure. All exposed animals experienced temperatures above 40°C between two and four days post exposure. Some animals experienced reduced temperatures (< 34 °C) prior to death. Animal activity was reduced beginning 1-2 days post exposure. Elevated heart rates and abnormal blood and pulmonary pressures were also observed. Bacteremia was observed in some animals prior to death. Animals were observed to have increases in numbers of neutrophils and large unstained cells and a decrease in numbers of eosinophils within one week post-exposure.

Conclusions: We have characterized a number of parameters for cynomolgus macaques infected with *F. tularensis* SchuS4 following aerosol exposure. The cynomolgus macaque is a good model of inhalational tularemia.

The research described herein was sponsored by the Defense Threat Reduction Agency, Department of Defense, contract number HDTRA1-08-C-0019. Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the United States Army.