

Development of a Model for Use in Pharmaceutical Trials: Induced *Pasteurella* Pneumonia and Body Temperature Telemetry in Weaned Beef Calves

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Introduction

The most common method for inducing pneumonic pasteurellosis in cattle for the study of therapeutic and immunologic interventions is to instill fresh live cultures of *Pasteurella haemolytica* into the trachea, into main stem bronchi, or into the thoracic cavity percutaneously (transthoracic). Evaluating therapeutic outcome may include comparisons of clinical recovery, mortality, weight gain, or other response variables.

Our initial efforts to induce pneumonia in beef calves utilizing a model previously validated in neonatal dairy calves produced inconsistent results. In order to use the model in pharmacotherapeutic trials, disease must be reliably produced. We were interested in developing a model for induction of pneumonia in weaned beef calves (approximately 400 lbs.) so that differences in body temperature, lung consolidation and neutrophil function could be used to compare antimicrobial therapies.

Materials and Methods

Our initial goal was to develop a method of inducing pneumonia in weaned beef heifers that consistently produced rectal temperatures of at least 104°F (40°C) at the time of treatment along with a clinical score of 1 or greater (see Table 1). Our first efforts, inoculating via intratracheal placement, were unsuccessful. Subsequent inoculation via bronchoalveolar lavage catheter¹ using a larger bacterial inoculum (20 cc, approximately 2 x 10⁸ cfu/ml) produced clinically apparent disease meeting our criteria. The live *Pasteurella* cultures were instilled at the level of the bifurcation of the trachea. The pneumo-

Table 1.

Score	Clinical signs
0	Normal, no signs of disease
1	Noticeable depression, signs of weakness are usually not apparent
2	Marked depression, moderate signs of weakness may be apparent but without significantly altered gait
3	Severe depression accompanied by signs of weakness such as altered gait or lowered head
4	Moribund, unable to rise

nia produced lung lesions of sufficient size and severity to allow comparisons between treatments to be made.

Radiotransmitters² were used to monitor body temperature. The radiotransmitters broadcast pulses proportional to temperature which were then saved to computer disk at programmed intervals. The radiotransmitters were placed intravaginally using minimally invasive procedures. No surgical fixation or other device to prevent expulsion was used, which makes the use of the transmitters in heifers more attractive since surgical placement is required in steers. The radiotransmitters remained in place for at least 1 week. Statistical models for analyzing the temperature data are being developed and will be discussed.

The third piece of this model was to determine the feasibility of collecting neutrophils from the lungs in live animals and performing function assays on the collected neutrophils. Neutrophils are implicated in some of the lung

¹ Bivona Equine Bronchoalveolar Catheter.

² Minimitter Company, Sunriver, Oregon; Datacol5[®] Large Animal Monitoring Software.

damage that occurs during pasteurilla pneumonia. Bronchoalveolar lavages and transtracheal washes were performed on animals exhibiting signs of disease. Relatively few neutrophils could be isolated from these lavages. Those neutrophils isolated were mostly degenerate and non-functional. The collection of neutrophils from the lungs was therefore eliminated from the model. In the subsequent trial, circulating neutrophils were evaluated as an indication of neutrophil function in the lungs.

Conclusion

The model was used successfully in a study comparing the efficacy of two antimicrobials in the treatment of respiratory disease. The majority of animals inoculated met the entrance criteria of temperature greater than or equal to 104°F (40°C) and clinical score of 1 or greater.