

# Effect of ampicillin trihydrate in preweaned Holstein calves after experimental bacterial challenge with *Pasteurella multocida*

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## Introduction

Respiratory disease in adult dairy cattle is reported infrequently by producers (< 3%) (USDA, 2018). Interestingly, nearly 40% of affected cows are removed from the herd despite antibiotic therapy in most cases (USDA, 2018). Treatment failure due to late detection or incorrect antibiotic dose, duration or spectrum, are potential reasons for poor outcomes after therapy. Ampicillin has bactericidal activity against organisms, such as *Pasteurella multocida*, and is indicated for the treatment of respiratory infections in cattle. The aim of this study was to improve our understanding of the bovine lung's response to antibiotic therapy after a bacterial respiratory infection by assessing lung consolidation via ultrasound. Ultrasound can evaluate the extent of lung consolidation in calves with or without clinical signs of BRD (Ollivett et al, 2016). A challenge model using calves could provide information regarding the lung's response to therapy more efficiently than a field trial in lactating cattle. Therefore, our first objective was to investigate the effect of ampicillin on ultrasonographic lung consolidation after experimental bacterial challenge in preweaned dairy calves. Our second objective was to determine if ampicillin affected the likelihood of detecting *P. multocida* in lung tissue.

## Materials and Methods

Holstein bull calves (n=39), obtained for this randomized, controlled challenge study, were transported from the source farm to the university isolation facility in southern Wisconsin at 52 ± 6 d of age. After a 7 d acclimation period, calves free from respiratory disease, determined by respiratory score and lung ultrasound, were eligible for challenge (n=30). Calves were sedated and inoculated intratracheally with 10<sup>10</sup>cfu of ampicillin-sensitive *P. multocida*. Lung ultrasound was performed 2, 6, 12, and 24 h post-challenge; then once daily until d 15. Calves were randomized 2:1 to receive ampicillin (TX: 3.0 mg/lb [6.6 mg/kg] IM once daily for 3 d) or placebo (CN: sterile saline, equal volume, IM once daily for 3 d) using a random number generator. Treat-

ment began when ≥ 1 cm<sup>2</sup> of consolidation was observed and ≥ 6 h had elapsed since challenge. Necropsy was performed after the last exam. For analyses, severe consolidation was defined as the presence of 1 or more completely consolidated lung lobes. Respiratory pathogens were assessed by culture and PCR of lung tissue at necropsy. Continuous variables were described using non-parametric methods (wilcoxon rank sum test). Contingency tables were created for analyses and fisher's exact test was used to evaluate the effect of treatment on the probability of developing severe lung consolidation and testing positive for *P. multocida*.

## Results

Twenty-eight (TX, n=17; CN, n=11) calves developed ≥ 1 cm<sup>2</sup> of lung consolidation and were eligible for treatment. All calves survived the study period. Severe consolidation developed at least once in 88% (15/17) and 82% (9/11) of TX and CN, respectively (*P*=1.00), and was detected numerically later in placebo calves (TX, median (IQR): 24 (12, 24) h vs CN, median (IQR): 12 (12, 12) h; *P*=0.21). At the midpoint of follow-up, severe consolidation was detected in 6% (1/17) of TX and 55% (6/11) of CN (*P*=0.01). On d 14, 36% (6/17) of TX and 46% (5/11) of CN had severe consolidation (*P*=0.59). Lung tissue culture was positive for *P. multocida* in 77% (13/17) of TX and 91% (10/11) of CN (*P*=0.62). Lung tissue PCR was positive for *P. multocida* in 82% (14/17) and 91% (10/11) of TX and CN, respectively (*P*=1.00).

## Significance

Lung health benefited from a 3 day ampicillin therapy, but benefits were short lived. These results, along with detection of live bacteria in lung tissue, suggest that treatment failures in cattle might be due to incomplete resolution of the initial lung infection. Future work is needed to determine if adjusting the antibiotic dose or duration could improve ultrasonographic and bacteriologic cures and lead to improved outcomes for affected cows.