# Effect of metaphylaxis on the temporal dynamics of *Mannheimia haemolytica, Mycoplasma bovis, Histophilus somni* and *Pasteurella multocida* in the upper respiratory tract of low-risk cattle

M. McClurg,[1] BS, MS; A. Olsen,[2] M. Scott,[3] BS, DVM, PhD; J. Richeson,[4] BS, MS, PhD; L. Pinnell,[3] BS, MS, PhD; P. Morley,[3] BS, DVM, PhD, DACVIM; R. Valeris-Chacin,[2] DVM, MS, PhD

[1]Veterinary Education, Research and Outreach, Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843
[2]Veterinary Education, Research and Outreach, Department of Veterinary Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843
[3]Veterinary Education, Research and Outreach, Department of Large Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843
[4]Department of Agricultural Sciences, Paul Engler College of Agriculture and Natural Sciences, West Texas A&M University, Canyon, TX 79016

## Introduction

Bovine respiratory disease (BRD) is the main cause of morbidity and mortality in beef cattle. Four bacterial species (*Mannheimia haemolytica, Histophilus somni, Pasteurella multocida* and *Mycoplasma bovis*) are considered key pathogens in the development of BRD. To minimize the risk of developing BRD, beef cattle are often administered antibiotics at the time of their arrival to a feedlot (also known as metaphylaxis). While metaphylaxis is a widely employed control strategy, little knowledge exists regarding its impact on the microbiome of cattle at low risk for developing BRD. This study aimed to identify the influence of different metaphylactic treatments on the temporal dynamics of BRD-associated bacterial pathogens in the upper respiratory tract of cattle at low risk for BRD development.

## Materials and methods

Upon arrival, 105 cattle at low risk for BRD development were stratified by weight, randomly allocated into 1 of 7 treatment groups (tulathromycin, tildipirosin, enrofloxacin, florfenicol, ceftiofur, oxytetracycline, or negative control group), and housed in 1 pen per treatment group. Each pen consisted of 10 animals that received treatment according to the pharmaceutical label, and 5 animals that received no treatment and served as sentinel animals within the pen. Treatment pens were not allowed nose-to-nose contact at any time during the trial. Nasopharyngeal swabs were collected at 6 timepoints throughout the study (Days 0, 3, 7, 14, 21 and 56). DNA was extracted from the swabs using DNeasy PowerSoil Pro Kit (QIAGEN). Absolute abundance of the 4 bacterial agents was quantified using digital dPCR in a microfluidic platform (QuantStudio Absolute Q digital PCR system, Applied Biosystems). Generalized linear mixed models (binomial distribution, complementary log-log link, animal ID as random intercept, and $P < 0.05$) were used to compare the pathogens' absolute abundance between treatment groups and time points.

## Results

The prevalence of *M. haemolytica* followed a general downward trend across all treatment groups except ceftiofur through day 56. *M. bovis* prevalence remained stable across all treatment groups until day 21, where the tulathromycin group demonstrated a sharp decline, and the enrofloxacin and tildipirosin group showed a steady decrease in prevalence. The tulathromycin group is the only group in which there was any decrease in prevalence in the *P. multocida* group over time, and the *H. somni* group had the lowest prevalence overall, with very few notable changes. The absolute abundance of *M. haemolytica* fluctuated in each treatment group until day 21, where each group then decreased steadily until day 56. Notably, the tulathromycin group was the only one in which *M. bovis* absolute abundance was equivalent or lower than the negative control group from day 7 to day 56. Interestingly, in the *P. multocida* group, the tulathromycin and ceftiofur treatment groups were significantly lower than the negative control. Ceftiofur was lower throughout the study, and the tulathromycin group was lower at days 0, 7 and 56. The absolute abundance of *H. somni* was too low across treatment groups to make a statistical inference.

## Significance

Metaphylaxis exhibited an anticipated short-term impact on the targeted pathogens within the microbiome, aligning with the half-life of the treatments. Remarkably, a sustained influence on the targeted pathogens in the microbiome, surpassing the anticipated half-life of the treatments, was also observed. These findings suggest that metaphylaxis imparts a lasting effect on key bacterial pathogens that play a critical role in the development of bovine respiratory disease.