Understanding contagious transmission of *Mannheimia haemolytica* in feedlot calves by leveraging whole genome sequencing of a unique isolate collection

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Introduction

The goal of this project is to evaluate the contagious spread of *Mannheimia haemolytica* (*Mh*) between cattle in a feedlot setting, by utilizing whole-genome sequencing to analyze genetic relationships of *Mh* between contiguous pens of cattle. The overall objective for this research is to inform best practices for management of respiratory disease in high-risk feedlot calves by better understanding the relative contribution of changes in respiratory bacteria and antimicrobial effectiveness in individual calves following metaphylaxis as compared to evidence for contagious transmission of respiratory bacteria and antimicrobial resistance within and between pens of calves.

Materials and methods

Deep nasopharyngeal swabs were collected at arrival from fall placed, auction-mart-derived steer calves entering a Saskatchewan feedlot in fall of 2020. The calves were purchased at approximately 1-week intervals in groups of 100 from pre-sort sales through a local auction mart and placed in adjacent research pens constructed to reflect a commercial feedlot. Calves were processed and vaccinated according to industry standards and received a metaphylactic dose of the antimicrobial tulathromycin at arrival. In this study, swabs from a total of 400 calves in 4 adjacent pens of 100 head were analyzed. Water sources were shared between the first 2 pens, 2045A and 2045B, and 2046A and 2046B. Deep nasopharyngeal swabs were collected at 3 timepoints; arrival, 13 and 36 days on feed (DOF). At 36 DOF only 10 calves per pen were sampled. The swabs were cultured for *Mh* and submitted for whole genome sequencing. A total of 485 individual *Mh* isolates were identified. Genetic analysis was performed on the isolates to understand how they were related to each other and to identify antimicrobial resistance genes.

Results

Results of the phylogenetic analysis showed that at arrival, the *Mh* isolates had a high level of genetic diversity, which decreased at 13 DOF, with one or 2 genetic isolate clusters becoming dominant in each pen. Isolates representing dominant clusters were additionally present in each pen at arrival, except for pen 2046B. At 36 DOF, isolates representing the dominant clusters were still present. There was evidence of contagious spread of one dominant cluster from pen 2046A to 2046B between arrival and 13 DOF. There were 7 different antimicrobial resistance genes identified in the isolates. All dominant genetic clusters carried resistance genes; most carried only 3 genes, while some carried 5. The clusters containing 3 genes carried genes causing resistance to tulathromycin, while those with 5 genes did not.

Significance

This study provided additional evidence to show that selection for and expansion of a dominant strain of *Mh* appears to be a not uncommon occurrence in cattle entering feeding operations. We were able to reveal genetic shifts and loss of diversity in the *Mh* population over the study period and found evidence of contagious spread between neighboring pens of cattle. What was surprising was the ubiquity of isolates at arrival that would go on to become dominant at later sampling times in all 4 pens, which suggests a common point source of "contamination" that occurred prior to feedlot placement. In addition, resistance genes conveying resistance to tulathromycin were present in most of the dominant isolates, suggesting that there could be a potential role for this antimicrobial in the selection of dominant strains within pens.

