"A cross-sectional survey of cattle on entry to Alberta feedlots to measure prevalence and factors associated with antimicrobial resistance in respiratory isolates"

ANTIMICROBIAL RESISTANCE ON ARRIVAL

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Background: Bovine respiratory disease (BRD) is a complex and multifactorial issue that is the leading cause of morbidity and mortality in the feedlot. Involving bacteria (*Mannheimia haemolytica, Histophilus somni, Pasteurella multocida and Mycoplasma bovis*) as well as viruses, individual animal characteristics and environmental influences, treatment, and prevention of BRD continues to rely heavily on antimicrobials. Given increasing public scrutiny on beef production, including antimicrobial use (AMU), and the documented emergence of multi-drug resistant respiratory pathogens, more information on the patterns and associations of antimicrobial resistant (AMR) BRD pathogens in cattle on arrival to the feedlot is necessary.

While previous research has identified patterns of AMR in BRD pathogens, generally those bacteria are isolated from cattle with BRD symptoms that have likely been treated at least once. This increases the probability that AMR bacteria will be discovered. In addition, anecdotal reports have indicated that initial treatment protocols at the feedlot level are becoming less effective, but little published data on the subject exists. It is also unknown if these reports are due to cattle already carrying AMR pathogens prior to any antimicrobial treatment at the feedlot, what factors may play a role in the development of resistance, or if there is another issue potentially reducing treatment efficacy.

Objectives: The objectives of this study were to:

1. Describe patterns and prevalence of BRD pathogens in cattle on entry to the feedlot prior to any antimicrobial treatment.
2. Describe patterns and prevalence of AMR in those pathogens.
3. Investigate potential factors contributing to BRD and AMR in cattle on arrival (e.g., weight, source, geographic location, predicted BRD risk category, transport time, weather, etc.).
4. Investigate associations between the characteristics of the BRD pathogens on arrival and the BRD status of the animal during the feeding period.

What they did: Upon feedlot arrival and before antimicrobials were administered at the feedlot, nasal swabs were collected from 2,824 feedlot cattle from ten different feedlots in southern and central Alberta over 19 months. During off-loading, animals were randomly selected from each load as they passed through the chute for sampling. Data on the date of feedlot arrival, cattle type (beef or dairy), sex (heifer, bull, steer), weight, age class (calf, yearling), source (ranch direct, auction barn, backgrounding operations), BRD risk (high, low), and weather conditions at arrival were

recorded. In addition, morbidity and mortality data were recorded for all the cattle enrolled in the study for up to 120 days post-arrival.

BRD pathogens (*Mannheimia haemolytica, Histophilus somni, Pasteurella multocida* and *Mycoplasma bovis*) were isolated from the nasal swabs and sent for antimicrobial susceptibility testing. Whole genome sequencing was also completed on a subset of isolates to determine AMR genes.

What they learned: Six feedlots provided samples only from beef cattle, two from only dairy cattle, and two provided a mixture from both types of cattle. Beef cattle tended to be heavier, older, and of Canadian origin compared to dairy cattle. Beef cattle were also more likely to be auction derived and classified as low BRD risk.

Over the follow-up period, 12% (338/2,824) of the study cattle were clinically diagnosed with BRD, with 5.6% (29) of those dying. Among the mortalities, 65.5% (19) had been previously treated for BRD at least once.

Almost 60% of the nasal swabs were positive for at least one of the bacterial pathogens commonly associated with BRD. *Pasteurella multocida* was most commonly found (41% of positive samples), followed by *Mannheimia haemolytica* (17%), *Mycoplasma bovis* (16.1%), and *Histophilus somni* (8.5%). The prevalence of *P. multocid*a and H. somni in beef cattle was higher compared to previous studies that collected feedlot on-arrival samples.

Overall, the proportion of AMR isolates of *P. multocida, M. haemolytica* and *H. somni* in dairy type feeder cattle tended to be higher than those from beef feeders. For *M. haemolytica* the most frequently observed resistance was to oxytetracycline (i.e., Bio-Mycin), tilmicosin (i.e., Micotil), and ampicillin (i.e., Polyflex) for beef type cattle, and oxytetracycline, tilmicosin, tulathromycin (e.g., Draxxin) for dairy type.

P. multocida isolates from beef cattle were most commonly resistant to oxytetracycline, spectinomycin and ampicillin, while the dairy isolates were most commonly resistant to oxytetracycline, tilmicosin and danofloxacin (i.e., A180).

Beef cattle *H. somni* isolates were most frequently resistant to ampicillin while dairy isolates were more commonly resistant to oxytetracycline, spectinomycin, and penicillin.

M. bovis showed decreased susceptibility to the macrolide class of drugs (i.e., Draxxin, Tylosin, Micotil, Zactran, Zuprevo, etc.) regardless of cattle type. Beef cattle from backgrounding operations tended to have bacteria more resistant to antimicrobials like oxytetracycline, spectinomycin, and tulathromycin compared to auction-derived calves.

Multidrug resistance was most common in *P. multocida* isolates (34%), followed by *M. haemolytica* (12%), and *H. somni* (1.25%)

These results were corroborated by the presence of known AMR genes discovered during whole genome sequencing.

What it Means: This study was initiated as a result of concerns raised at the feedlot level of decreasing antimicrobial effectiveness, particularly for macrolide drugs like Draxxin. While some information on the history of the calves arriving to the feedlot was available, this study could not determine if there was previous antimicrobial use prior to feedlot arrival, which would be reflective of the information most feedlot operators and veterinarians have when designing treatment or prevention options for BRD. While AMR tended to be higher in dairy type cattle and cattle derived from backgrounding operations, these cattle will often be mixed with others in a feedlot situation, possibly promoting transfer of AMR bacteria amongst animals. This study also confirmed previous reports that AMR in cattle pathogens to the drugs of most importance to human health remains low, but did report a slight increase of *M. haemolytica* resistance to macrolides, and suggests that macrolides may not be an effective treatment option against *M. bovis*.

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