



“Assessment of feedlot cattle respiratory pathogens’ antibiotic sensitivity and development of a screening management tool for industry implementation.”

TESTING FOR ANTIMICROBIAL RESISTANCE IN THE FEEDLOT

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Background: Bovine respiratory disease (BRD) is a major cause of morbidity and mortality among feedlot cattle in North America. In western Canada approximately 10 to 30% of auction market calves are treated for BRD with mortality in treated animals ranging from 5-10%. Management of BRD includes the use of vaccines and antimicrobial drugs, and exposure of bacteria to antimicrobial drugs has the potential to exert pressure for selection of resistant organisms.

Traditionally, antimicrobial surveillance has centred on pathogens that may cause disease in humans, such as campylobacter or using indicator bacteria such as *E. coli*. Programs such as the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) regularly monitors bacterial resistance at abattoirs and retail outlets, and a new system called FoodNet is currently expanding

surveillance to include on-farm pathogen data. However, very few studies monitor the changes in the susceptibility of pathogens that cause illness in cattle, and if resistance builds over time, the standard treatment options become less effective.

The increasing societal pressure about the use of antimicrobials in agriculture provides an opportunity to improve practices and investigate alternatives, but continued access to effective products is extremely important in managing cattle health and welfare.

Objectives: To establish a cost effective antimicrobial susceptibility management tool to allow for the periodic testing of pathogen susceptibility, and to reduce antibiotic use by ensuring the antibiotics used are those which will be effective in treating illness.

What They Did: Seven veterinary practices were recruited to submit samples from clinical BRD cases on farm. Samples included nasal swabs, tissue samples (primarily lung tissue), and joint fluid. Approximately 750 samples were received, containing 1045 isolates of bacteria that play a role in BRD (*Mannheimia haemolytica* (Mh), *Mycoplasma bovis* (Mb), *Pasteurella multocida* (Pm), *Histophilus somni* (Hs) and *Trueperilla pyogenes* (Tp)). The isolates then underwent antimicrobial susceptibilities testing (AST) to 18 different antibiotics.

All participating veterinary clinics were provided with an AST report for the samples they provided, and one on one contact was established with each clinic to introduce them to AST as a tool they could potentially use with their clients to monitor and manage the development of antimicrobial resistance (AMR).

Feedlot-associated samples such as feed, catchment basin, and feces were submitted for metagenomic sequencing to aid in the identification of bacterial diversity throughout the feedlot.

What They Learned: AST results were provided back to veterinary clinics for most isolates within 72 hours. The exception to this turnaround time is Mb, which takes about a week to culture. This project allowed for the development of a more robust isolation protocol for Mb, so this new protocol will be of use to other laboratory groups as well. Infrastructure improvements to the Alberta Veterinary Surveillance Network mean that clinics will be able to enter AST results into the system once the upgrade is complete.

As samples were taken from clinically ill or deceased animals, antimicrobial resistance rates would be expected to be higher than those in a healthy population.

Mh was the most frequently (22.5% of all isolates, 26.2% of lung isolates) isolated microbial agent and was commonly resistant to antimicrobial agents of high importance (Category II) to human health. Considerable (54.7%) proportions were resistant to four or more antimicrobial classes.

There was generally a low frequency of resistance to antimicrobials of very high importance (Category I) in human health. Mb was most frequently resistant to Category I antimicrobials. Mb does not have a cell wall, so is intrinsically resistant to beta-lactams including ceftiofur (e.g. Excenel). Previous literature indicates that Mb is potentially susceptible to the fluoroquinolones (e.g. Baytril), and these results support that, indicating that 18% of *M. bovis* isolates were resistant. Resistance to Category I antimicrobials ranged from 0.8-3.8% (Mh), 0.0-1.7% (Pm), 0.0- 0.7% (Hs), and 0.0-91.5% (Tp). The high level of resistance in Tp isolates

to danofloxacin could be linked to the use of enrofloxacin (in the same drug family), as Tp isolates were neither wholly susceptible nor wholly resistant to enrofloxacin.

Resistance of the various pathogens to florfenicol (Category III; trade names Nuflor or Resflor), a common treatment option for BRD, ranged from 1.3% to 30.9%, indicating that it remains a viable treatment option.

Potentially concerning was that each pathogen contained isolates resistant to up to 6-7 antimicrobial classes. Mb was most frequently resistant to four or more classes of antimicrobial. However, a few isolates of Mh were resistant to 8-9 antimicrobial classes. Previous to this study, Mh isolates displaying resistance to that many classes of antimicrobials had not been identified in Canada (Klima et al. 2014).

Table 1. Multiclass Resistance

Number of antimicrobial classes in resistance patterns for important BRD pathogens

Isolate	Number of isolates ¹	Number of isolates by number of antimicrobial classes in the resistance pattern					
		0	1	2-3	4-5	6-7	8-9
<i>M. hemolytica</i>	223	0	13	84	106	16	4
<i>M. bovis</i>	211	0	1	3	69	121	17
<i>P. multocida</i>	113	0	0	24	42	47	0
<i>T. pyogenes</i>	82	0	0	14	45	23	0
<i>H. somni</i>	72	7	13	26	18	8	0

¹An animal is represented only once for any one microbial agent. Where the same microbial agent was recovered from different samples/tissues from the same animal, only one sample (the lung sample if available) was retained.

What It Means: Results show a wide variance in resistance to individual antimicrobials, but are generally consistent with previous research demonstrating a low level of resistance to Category I antimicrobials. There is likely an opportunity to both decrease the usage of Category I and II antimicrobials, while still retaining some antimicrobials that are effective in combating BRD.

Unfortunately, while treatment protocols were requested from the participating clinics, some clinics elected not to provide any treatment data, or provided incomplete information, so no conclusions can be drawn regarding arrival or treatment protocols and AMR patterns among the participating practices.

Much like herbicide resistance and rotating herbicide treatments, rotating antimicrobial drug classes may be effective in reducing AMR

in some cases. By knowing the AMR status, it is possible to derive much more targeted and effective treatment options. Some participating clinics utilized the data as part of their herd health management programs during the course of the study. Anecdotally, those clinics used their AST reports to make real-time treatment and protocol changes based upon judicious antimicrobial use and effectiveness.

A current limitation of Canada's antimicrobial surveillance program is a lack of on-farm data in cattle, and having AST diagnostic capabilities in Alberta would be a valuable addition to the province's currently limited diagnostic capacity. There is a need to expand and promote this type of surveillance among vet clinics and feedlots so that data is collected and utilized on a routine basis, and integrated into a national system. This project was only one year in duration, but lays an excellent foundation for expansion.

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