Biosecurity and bovine respiratory disease on beef operations in western Canada

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Abstract

Biosecurity practices of beef cow-calf herds in western Canada have not been studied extensively, and the impacts these practices have on animal health with the herd. The association between not implementing good biosecurity practices and herd health in cow-calf herds is not well understood. This study used a survey of 103 cow-calf producers who were part of the Western Canadian Cow-Calf Surveillance Network. Eighty-one questionnaires were returned. The questionnaire asked about current cattle inventory, other animals on the farm (dairy cattle and other species), purchased animals, source of purchased cattle, procedures done to purchased cattle (i.e. disease testing and vaccinations), commingling with other herds, management of people and equipment, and biosecurity within the herd. There were also questions about the incidence of diseases within the herd to determine the impact of biosecurity practices on animal health. During the study period of 2014-2017, all the herds purchased bulls, 54% of herds purchased heifers, and 42% purchased cows. The use of standard biosecurity practices was generally low with 30% of producers keeping purchased animals separate and 30% vaccinating new additions. Logistic regression models found that none of the biosecurity practices were significantly associated with having Johne's disease. The purchase of 10 bulls or more over the four years, and the purchase of any cows from other farms or private sales was associated with a higher risk of reporting an outbreak of Bovine Respiratory Disease (BRD) in the herd. Not vaccinating animals purchased into the herd and use of community pasture also was associated with the risk of a BRD outbreak. Outbreaks of calf diarrhea were similarly significantly associated with the purchase of over 10 bulls and use of community pasture, as well as leasing and sharing bulls. Biosecurity is not emphasized on cow-calf farms in

western Canada and the purchase of adult cattle and using community pasture are risk factors for BRD and calf diarrhea.

Next, was a study to describe the prevalence and antimicrobial sensitivity of 3 major BRD bacterial pathogens from auction market derived vs single ranch source calves, at arrival and later in the feeding period. The animals enrolled were 299 calves of various beef-type breeds derived from multiple auction markets (AUCT) and 300 similar breed-type-calves sourced directly from a single ranch (RANCH). All calves were sampled using a deep nasal pharyngeal swab at the time of entry to the feedlot and again at 64 to 168 days after arrival. The swabs were cultured within 24 hours of sampling and sensitivity testing of isolates for *Mannheimia haemolytica* (MH), *Pasteurella multocida* (PM) and *Histophilus somni* (HS) was performed. In the AUCT calves, the prevalence of MH decreased significantly from 38% to 20% (P <0.001), and the prevalence of HS increased significantly from 17% to 30% (P = 0.001) between sampling events. In the AUCT calves there was an increase in calves with MH isolates not sensitive to tulathromycin from 1% in the first sample to 7% in the second. There was also a significant increase in calves with PM isolates not sensitive to florfenicol (from 0% to 3%), oxytetracycline (from 1% to 4%) and tulathromycin (from 0% to 3%). Finally, in the AUCT calves there was a significant increase in calves with HS isolates not sensitive to oxytetracycline (from 0% to 12%), tilmicosin (from 0% to 10%) and tulathromycin (from 0% to 9%). In the RANCH calves, prevalence of all pathogens decreased significantly throughout the study. From 30% to 20% (P = 0.01) for MH, from 60% to 43% (P <0.001) for PM and from 40% to 6% (P <0.001) for HS. In the RANCH calves there was a significant decrease in calves with MH isolates that were not sensitive to oxytetracycline (from 6% to 0%), tilmicosin (from 5% to 0%), and tulathromycin

(from 5% to 0%). There was also a significant increase in calves with PM isolates not sensitive to florfenicol (from 0% to 9%), oxytetracycline (from 0% to 10%), tilmicosin (from 2% to 14%) and tulathromycin (from 0% to 10%). There were few or no isolates not sensitive to ceftiofur or enrofloxacin. Antimicrobial resistance of BRD pathogens and prevalence of bacterial pathogens can vary over the feeding period differently in calves sourced either from auction markets and directly from a single source.

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List of Abbreviations

AMR	Antimicrobial Resistance
AST	Antimicrobial Sensitivity Test
AUCT	Auction market derived calves
BHV1	Bovine Herpes Virus Type 1
BRD	Bovine Respiratory Disease
BSE	Bovine Spongiform Encephalopathy
BVDV	Bovine Viral Diarrhea Virus
CLSI	Clinical Laboratory and Standards Institute
DD	Digital Dermatitis
DNS	Deep Nasopharyngeal Swab
DOF	Days on Feed
HCCA	α-cyano-4- hydroxycinnamic acid
HS	*Histophilus somni*
ICE	Integrative Conjugative Element
IQR	Interquartile Range
IBR	Infectious Bovine Rhinotracheitis
MALDI-TOI	Matrix Assisted Laser Desorption and Ionization Time of Flight
MAP	Mycobacterium avium subspecies paratuberculosis
MDR	Multi-Drug Resistance
MH	*Mannheimia haemolytica*
MIC	Minimum Inhibitory Concentration
NAHMS	National Animal Health Monitoring System
OR	Odds Ratio
Pi3	Bovine Parainfluenza-3
PM	*Pasteurella multocida*
RANCH	Ranch Raised calves

WCCSN	Western Canadian Cow Calf Surveillance Network

Chapter One

Literature Review

1.1.1 Biosecurity Introduction

Biosecurity in animal agriculture is the outcome of all activities undertaken by a farm, ranch, or feedlot personnel to preclude the introduction of disease agents into an area that one is trying to protect [1]. Herd biosecurity as a concept has existed in North America since the eradication of Contagious Bovine Pleuropneumonia from the United States in the late 19th Century [1]. Most formal biosecurity programs that cattle producers and veterinarians have become involved in up to the present time have been organized or mandated by government agencies[1]. Two of the earliest examples in Canada were the tuberculosis and brucellosis control programs. In these early cases, biosecurity was mandated at a national level, not the farm or individual herd level. However, for both programs, there was conviction that producers' and public's needs were best served by control of these diseases. In 1951-1952, Foot and Mouth Disease spread rapidly in Saskatchewan[2], and in 2003 the first case of Bovine Spongiform Encephalopathy was diagnosed in a cow that was born in Canada[3]. More recently bovine tuberculosis was diagnosed in 6 cows from a farm in Alberta requiring the testing of 34 000 cows[4]. All these examples have highlighted the needed for greater biosecurity measures at both the national and farm level.

In Canada, the number of farms with cattle and calves has steadily dropped from over 225 000 in 1976 to just over 73 000 today[5]. However, the number of cattle in Canada has increased slightly over that same time and is now close to 13 million[6]. With those changes come increased purchases of animals, herd consolidation of smaller herds into larger herds, and a

greater risk of introducing disease into those herds. The average cow-calf herd in Canada increased in size from 74 head in 2011 to 84 in 2016[7]. This trend appears to be accelerating as a recent Canadian study showed that the average age of cattle producers is increasing, with an increasing rate of retirement[8]. However, in comparison to the feedlot industry, the average cow-calf herd size is quite small. Over the same period, feedlot operations grew on average from 185 head of beef cattle in 2011 to 212 head in 2016 [7]. When we look at where most of the feeding capacity for cattle is, 69% of Canada's fed cattle production is concentrated in Alberta[9]. In Alberta, there are 149 feedlots with an average annual capacity of 1000 head or higher, and together they feed 1.6 million head of cattle[9]. In Canada, the cow-calf industry is characterized by a large number of relatively small cow-calf operations sending cattle through auction markets for sale, which are then consolidated into large feedlots to be fed to slaughter.

As a result of the structure of the beef industry, there is significant mixing of cattle that promotes the spread of disease and makes effective biosecurity measures very difficult. There have been many efforts to reduce this mixing by directly marketing of cattle from the ranch to feedlots; however, most cattle are still sold through the auction market where they are co-mingled into groups for shipment to the feedlot.

It has been previously reported that 75% of emerging diseases originate from domestic or wild animals and 60% of existing human infectious diseases are zoonotic[10]. The risk to human health from diseases that originated in animals in substantial. Biosecurity is therefore not only important for the health of beef cattle, but also for the population as a whole.

1.2.1 Current Biosecurity Practices in Beef Cattle Herds

The current study investigated the biosecurity practices of beef cattle herds in western Canada. This has not been studied in detail to the knowledge of the author, and the information that exists is mostly in other areas of the world, such as the European Union, and in other areas of animal agriculture, such as the swine and poultry industries.

There has been a number of studies investigating biosecurity practices on beef cattle farms in other countries, particularly in the European Union[11–15]. This type of research is lacking in North America. Biosecurity in beef cattle can be very different than biosecurity practices that are common in other areas of animal agriculture. Exclusion biosecurity is a strategy aimed at preventing the introduction of disease agents by not allowing contact between the animals you are trying to protect and other animals. Typically, this is achieved using a barn or fences and not allowing new additions to be introduced until they have been quarantined and tested. In beef cow-calf herds, it is not possible to practice total exclusion biosecurity, due to the extensive nature of how beef cattle are raised and exclusion from other cattle and wildlife in open ranges is often not feasible. As well, the segmented nature of beef production in Canada necessitates that cattle are often bought and sold between herds and moved from cow-calf herds through auction markets to backgrounding lots and finally to finishing feedlots prior to slaughter. Within the backgrounding lots and finishing feedlots, almost all cattle are sourced from other farms and mixed either prior to or at the time of arrival. As a result, exclusion biosecurity is usually not possible, and this creates multiple opportunities for disease introduction and transmission.

This is very different from the situation in poultry and pig farms, where the movement of people and animals into and out of a barn is often more tightly controlled[12,16].

In general, cattle farmers' knowledge about biosecurity is low[16]. In a survey of Belgian cattle farmers, only 2.1% were able to give a fully correct definition of biosecurity compared to 8.2% of pig and poultry farmers. Over 15% of cattle farmers could only give a partially-correct definition of biosecurity and 83% could not give a correct definition at all[16]. Despite not being able to give a definition of biosecurity in the same survey, 85% of cattle farmers felt their own knowledge of biosecurity was average or above average. This disconnect between cattle producers' perceived knowledge and actual knowledge may create an environment where learning about biosecurity seems unnecessary.

In any animal facility, biosecurity relies on five stages[17] (i) Bio-exclusion: limiting the risk of introduction; (ii) Biocompartmentation: limiting the spread within the same facility; (iii) Biocontainment: limiting the spread to other animal facilities (inter-herd transmission); (iv) Bioprevention: preventing human contamination; and (v) Biopreservation: preventing environmental contamination with potential pathogens. Other terminology is sometimes used such as biocontainment instead of biocompartmentation and biosecurity instead of bio-exclusion[18]; but the meaning is the same. In current beef production systems in North America the utilization of these stages is limited. The following paragraphs will describe in more detail bio-exclusion and biocompartmentation.

1.2.2 Bio-exclusion: limiting the risk of introduction

Bio-exclusion is often referred to as external biosecurity. In the U.S. Department of Agriculture's National Animal Health Monitoring System (NAHMS) study conducted in 2007–08, 67.8% of all beef cow-calf operations had added new cattle to the herd in the previous 3 years[19]. In the same study, 30.7% of herds purchased, leased, or borrowed bulls for the previous breeding season. As well, 29.4% of operations had more than 10 visits per month from visitors (employees, neighbors, veterinarians, etc.) and only 17.9% of operations had no visits. Animal movement and human movement into beef cow-calf herds is a very common event and presents a very real risk for disease introduction.

As mentioned before, by nature, beef feedlots cannot exclude disease as the cattle are not born on site. In the U.S., 58% of feedlots source over half of the cattle in the feedlot from auction marts and not directly from farms[18]. This increases the number of sources from which the cattle are coming and increases the potential for disease introduction. In the same study only 14% of feedlots required trailers to be cleaned prior to loading incoming cattle and only 2% of visitors were required to wear clean boots or foot coverings when visiting the feedlot.

1.2.3 Biocompartmentation: limiting the spread within the herd

Biocompartmentation is also often known as internal biosecurity. In the U.S. Department of Agriculture's National Animal Health Monitoring System (NAHMS) study conducted in 2007–08, 66.3% of cow-calf operations did not quarantine new arrivals to the herd, exposing the rest of the herd to any diseases the new arrivals might carry[19]. Another strategy to reduce the spread

of disease from new arrivals is to test them for any diseases they may be carrying. In the NAHMS study only 4.5% of herds tested for Bovine Viral Diarrhea Virus (BVDV) and 5.4% tested for Bovine Tuberculosis.

The situation is similar in other parts of the world. A survey in the United Kingdom found that 59% of cattle farmers had recently brought cattle onto the farm, and although 70% did ask about previous disease history, 73% either never or only sometimes isolated cattle arriving onto the farm[11]. Less than 30% of farmers took preventative measures with newly introduced cattle such as vaccinations, anthelminthic protocols, or testing for diseases such as tuberculosis. Other studies show similar results in Australia[20], Finland[12], Belgium[15] and Ireland[21].

Personal hygiene (cleaning and disinfecting of boots and clothing) is also not routinely practiced. In the UK study mentioned above, only 7% of farmers carried out personal hygiene such as boot washing or changing coveralls when moving from one management group to the next[11].

A survey of feedlots in the U.S found that 37% of the feedlots allowed fence-line contact between sick animals and healthy animals[18]. Also, 25% of feedlots used the same equipment to handle dead cattle, manure, and feedstuffs, with only 14% of those feedlots cleaning the equipment between uses. Transmission of agents with a fecal-oral route of spread such as BVDV, Escherichia coli O157, and Salmonella spp. may be facilitated by this practice[18]. Less than half of feedlots cleaned processing and treatment facilities on a daily basis[18].

1.3.1 Biosecurity Practices in Other areas of Animal Agriculture.

As mentioned previously, other areas of animal agriculture use much different biosecurity methods than beef cattle herds. Dairy cattle would have the most similar practices, with the key difference being that dairy is more vertically integrated; replacements and production animals more often exist in the same herd. However, in one study, 44% of dairy producers had purchased new cattle and introduced them to the herd in the previous 3 years[22]. In the same study, the most common type of cattle purchased were lactating cows, which would have the highest disease risk to a dairy herd due to opportunity for exposure to disease pathogens such as those that cause mastitis[22].

Hygiene appears to be better on dairy farms, but still low with 43% of dairy producers changing boots and 39% wearing gloves when working with sick calves in one study[23]. Testing of new arrivals for diseases such as Johne's disease (*Mycobacterium paratuberculosis*) is higher in dairy herds as well at 18%[22].

In swine production, practices such as not allowing visitors to enter the barn freely and requiring visitors to wear clothing specific to that barn are commonplace – over 85% of barns in one study[24]. Very similar results are seen in Swedish[25] and Finnish[12] studies. Entry rooms to allow for the changing of clothes are common as well[26]. In almost every study comparing biosecurity measures on pig farms to beef cattle farms, swine producers have more stringent standards in controlling disease entry and spread[12,25]. Swine producers also commonly use a practice known as all in/all out where a section or the entirety of the barn is emptied of animals

then cleaned and disinfected before a new groups of pigs is introduced[26]. This practice is virtually nonexistent in cattle farms.

1.3.2 Motivators for Improved Biosecurity

It is important to look at what motivates producers to implement improved biosecurity practices on their farms. In one study, the top 3 reasons for implementing biosecurity practices by cattle producers were to improve profit due to higher productivity, to have farm stability (the absence of disease outbreaks), and to improve animal welfare[16]. However, research in Denmark has demonstrated that even legislation on biosecurity plans does not lead to implementation if there is no perception of benefits[27]. Farmers seem to be strongly motivated by what is their standard practices, and generally only implement those measures that they understand and know the most about[28]. Biosecurity practices that are based on local knowledge of disease are more likely to change farmers behaviors than standardized practices[29]. In a study of pig farmers looking at both endemic and epidemic diseases, farmers valued on-farm biosecurity measures as a significantly more effective risk management strategy than animal health programs[30]. When looking at the risk of actual diseases, the majority of the farmers (68.9%) implemented biosecurity measures to manage animal disease risks on their farms whereas only 35.6% farmers participated in animal health programs with the same purpose[30]. The animal health programs in that study involved the producers learning more information about the diseases.

In a questionnaire to Belgian cattle farmers 46.5% of the farmers were convinced of the positive effect of biosecurity. Very few farmers (0.9% of the cattle farmers) indicated that they

thought biosecurity had no influence at all on the reduction of diseases[16]. Another concept is the idea of being a "good farmer". Farmers take pride in their work and a strong motivator for having good biosecurity was to appear to others that they were doing a good job[31,32]. Farmers tend to be very independent and this trait seemed to come out in the research as well. A Danish study on the control of Johne's disease showed that motivation to participate in a voluntary control program came primarily from not only hoping to improve animal health but also a wish to be certified free of Johne's disease[33]. However when biosecurity controls are imposed on farmers by government, there seems to be much less willingness to cooperate[34].

A study by Cardwell et al. looked at the impact of tailored biosecurity advice given to farmers by their veterinarians versus more generic advice about biosecurity, and how that impacted their behavior related to biosecurity. In both cases, biosecurity practices on the farms improved, but there was a trend towards even greater biosecurity improvements when the advice was tailored to a specific farm[35].

1.4.1 Barriers to implementing biosecurity measures

Many studies have asked the question – "What is holding farmers back from instituting biosecurity measures?" A Belgian study found that the most important reason for not implementing more biosecurity measures was that it is too expensive and too much work. However, the second most common response was that there was nothing holding them back from implementing greater biosecurity[16]. A lack of knowledge or understanding of biosecurity principles among farm employees and visitors has already been proposed as another reason for

poor biosecurity[36]. Poor biosecurity compliance may also be related to an unwillingness to comply and intentional errors seem to be related to beliefs and attitudes[36].

There is wide variations in recommendations for biosecurity practices and some producers may not comply due to confusion[37]. The cost of implementing biosecurity measures has a strong influence on farmers willingness to implement them[38]. Economics are also an influence[38] with farmers needing evidence of effectiveness before implementation[39]. There is also a need to build trust amongst stakeholders[20,39,40]. There seems to be a feeling that responsibility for biosecurity and the costs of it should be shared by government and industry. However, government involvement can have the opposite effect to that which is desired. In the United Kingdom where there have been recent outbreaks of Foot and Mouth Disease (FMD) and Bovine Spongiform Encephalopathy (BSE), 58% of cattle and sheep farmers felt that the most desirable biosecurity measures were having none at all. They also felt that the least useful measures were those imposed on them by the government during the FMD outbreak[34].

1.5.1 Sources of Information on Biosecurity

Many studies have looked at where farmers get their information on biosecurity. The number one source in a number of studies is the herd veterinarian[34,41,42]. The other most common sources include other farmers and publications targeted towards farmers.

1.6.1 Biosecurity and Prevention of Disease

Purchase of new livestock when the incoming animals remain in contact with the recipient herd for an extended period of time presents the highest risk for introducing infectious hazards[43]. Bringing in new livestock as infrequently as possible and taking appropriate precautions – quarantine, vaccination, disinfection, etc. – is the most effective way to use biosecurity to prevent disease. In a study of Dutch dairy farms, farms that purchased cattle and/or shared pasture (termed as 'open' farms) differed in performance from farms that did not ('closed' farms). The results showed that the 'closed' farms incurred lower costs for veterinary services, and had a lower average age at first calving and a higher birth rate per 100 dairy cows. Being 'closed' was found to increase the net profit by approximately £25 per cow per year at the time of the study or 5 per cent of the typical net return to labor and management[44].

Much of the current literature describes the current practices that exist in various agriculture industries when it comes to biosecurity. However, there is much less relevant research on the role of biosecurity in preventing disease – especially when it comes to beef cattle. The most relevant research to the current study was done by Waldner et al. on over 200 beef cow-calf herds in 2001 and 2002. Their research looked at different management aspects of cow-calf production, with some of these related to biosecurity. They found that cows bred on community pastures were more likely to be pregnant and less likely to have an abortion if they had been previously vaccinated for BVDV and BHV1. Cows bred on community pastures that were not vaccinated were less likely to be pregnant and more likely to abort than those that

were not bred on community pastures regardless of vaccination status[45,46]. Aspects of biosecurity such as mixing from communal grazing seems to play a role in abortion and non-pregnancy.

1.6.2 Biosecurity and Bovine Tuberculosis.

A study in England and Ireland on the spread of bovine tuberculosis found that increasing the contact time with potentially infected cattle increased risk of contracting bovine tuberculosis. In Ireland, up to 25% of bovine tuberculosis cases were attributed to spread from herds on adjacent farms. Farms with a neighboring infected herd were almost four times as likely to have a bovine tuberculosis case[47]. Bringing new animals into the herd is also a significant risk factor for bovine tuberculosis in a number of studies[47–49]. Introduction of bovine tuberculosis to a herd is strongly associated with cattle movements[48]. Gopal et al. found that purchased animals were the most likely source of bovine tuberculosis in 30 out of 31 herds[49].

1.6.3 Biosecurity and Bovine Viral Diarrhea Virus (BVDV)

A well-documented way to introduce BVDV into a herd is through the purchase of transiently or persistently infected cattle[50]. Other risk factors for having BVDV seropositive animals in a herd are herd-to-herd contact across pasture fences, using common pastures, and acquiring insufficient information about BVDV status in purchased animals[50]. Another study demonstrated that importing pregnant animals and youngstock have the greatest impact on increasing the financial risks from BVDV, while strategic testing and vaccination programs have the most impact on decreasing the risk of herd outbreak of BVDV[51]. In a Scottish study, for every $\log_{10}$ increase in number of beef cattle moved onto a farm, the odds of being seropositive

for BVDV increased by a factor of 3.21[52]. Cattle movements (purchasing of cattle onto the farm) have 3 times greater explanatory power for BVDV seropositivity than local spread risk factors (disinfection, double fencing, shared pastures, visitors on farm)[52]. Tailored biosecurity advice to individual farmers has been shown to have a significant impact in decreasing BVDV seropositivity in beef herds[35].

1.6.4 Biosecurity and Bovine Herpes Virus - 1 (BHV-1)

A study on Dutch dairy farms showed that direct animal contacts with other cattle (i.e. allowing cattle to return to the farm when not successfully sold and grazing cattle at other farms) increased the risk of BHV-1. As well, professional visitors such as the herd veterinarian should be required to wear protective clothing provided by the farmer before they handle cattle, as this was also a risk factor for BHV-1 infection[53]. Implementation of general biosecurity practices in beef herds in England and Wales decreased the seropositivity to BHV-1 after 2 years[14]. Finally, Dias et al. found that buying in cattle, renting pasture from other farmers and use of a bull were risk factors for BHV-1 infection[54].

1.6.5 Biosecurity and *Mycobacterium avium* subspecies *paratuberculosis* (MAP)

In dairy herds with greater than 25% of replacement females purchased and brought into the herd, the risk of having a cow test positive for MAP in the herd increased by an odds of 2.1[55]. If a producer purchased cattle in the last 5 years the odds of having MAP was 3.1 times higher[56]. In dairies, allowing calves to be exposed to the feces of adult cattle increased the odds of MAP in a herd by over 30 times[55]. In a western Canadian study, purchased replacement beef heifers

had a 2.3 times higher odds of being MAP positive[57]. Restocking after herd depopulation and importation of animals have also been associated with MAP infection[58,59].

1.6.6 Biosecurity and Digital Dermatitis (DD)

In a study on digital dermatitis in dairy cattle, poor external biosecurity measures associated with higher prevalence of DD were recent animal purchase, access to pasture, lack of boots available for visitors, farm staff working at other dairy farms, hoof trimming without a professional attending, and animal transporters having access to cattle area[60]. For biosecurity within the herd, digital dermatitis was more prevalent in herds with infrequent foot bathing, manure scraping less than 8 times a day, manure removal direction from cows to heifers, the exits from animal pens not being equipped with water hoses, manure-handling vehicle used in other activities, and water troughs contaminated with manure[60].

1.6.7 Biosecurity and Disease Prevention in Other Species

There has been some interesting research in the prevention of disease using biosecurity in other species. In pigs, Laanen et al. showed that improved external (measures to keep disease out of the herd) and internal (measures to prevent the spread of disease in the herd) biosecurity resulted in improvements in daily weight gain and feed conversion[61]. They also found that as biosecurity improved there was a decreased use of antibiotics for prophylaxis[61]. A case control study conducted during the outbreak of Classical Swine Fever in the Netherlands in 1997 showed increased risk of infection in herds that had commercial poultry on the farm, did not require visitors to wear boots and coveralls provided by the farm, and where truck drivers

did not wear boots from the farm[62]. Elbers et al. demonstrated that hygiene precautions such as changing boots and coveralls in between farms are very important in the transmission of Classical Swine Fever[62].

Firestone et al. found in the equine influenza outbreak in Australia in 2007 that having a footbath in place, improved hygiene precautions such as hand washing and changing clothes and shoes, and the farm being located greater than 5km from an infected premises helped to prevent influenza infection[63,64].

1.7.1 Bovine Respiratory Disease (BRD)

Bovine Respiratory Disease is the most significant disease of beef cattle in North America and the most common cause of morbidity and mortality in cattle feedlots[65]. The primary bacterial pathogens associated with BRD are *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni*. As well, viral pathogens discussed earlier such as BVDV and BHV-1 are often associated with BRD. Overall, an estimated 21 percent of cattle placed in feedlots show signs of respiratory disease at some point during the feeding period and 4 percent of these die as a result[65]. Bovine Respiratory Disease accounts for 70-80% of all morbidity in feedlots and 40-50% of the mortalities[66]. As well, despite numerous advances in vaccine use, newer antimicrobials and other advances, the incidence of BRD has not declined since the 1990's[66]. Cattle with respiratory disease have reduced feed intake, require treatment with antimicrobials, and as noted above, can die as a result of the disease, making respiratory disease very costly to the feedlot industry. Annual global losses due to respiratory disease are

estimated to be around $3 billion[67]. Surveys of cow-calf producers indicate that bovine respiratory disease in preweaned beef calves is recognized on approximately 20% of operations and in the US, BRD is reported to be the leading cause of death in calves 3 weeks of age up to weaning[68].

The pathogens associated with BRD are enzootic in the general cattle population so attempts to eliminate the pathogens are impractical[69]. Biosecurity in the feedlot is especially difficult as cattle are sourced and mixed from many farms[18]. Instead, feedlots attempt to limit the spread of BRD through practices such as metaphylaxis (treating entire groups of cattle with antimicrobials on arrival), vaccination, separating sick animals and placing them in hospital pens, controlling the spread of diseases that potentiate the effects of BRD pathogens such as BVD virus, and reducing commingling of cattle by sourcing cattle from a limited number of farms[69].

1.8.1 Cattle source and impact on bovine respiratory disease

There have been many attempts to reduce morbidity and mortality due to BRD by changing the risk factors in calves arriving at the feedlot. The management term “preconditioning”, which has been around since the mid-1960’s, has been proposed as a method to reduce morbidity due to BRD. Preconditioned calves are typically vaccinated, weaned, dehorned, dewormed, castrated, and trained to eat from a bunk prior to entry into the feedlot[70]. Multiple studies have shown that preconditioning reduces morbidity and mortality due to BRD in the feedlot[70–72]. Preconditioning implies some knowledge on the source and management history of the calves

prior to being moved into the feedlot. The source of calves also influences morbidity and mortality due to BRD in the feedlot. Step et al. showed that ranch-origin calves were less likely to be treated for BRD than auction market-derived calves, and calves that were weaned 45 days prior to feedlot entry also were less likely to be treated[71]. Richeson et al. showed markedly greater morbidity for auction market (86%) versus preconditioned (4%) calves during a 14-d study period[73]. In that study, the auction market calves also required a second treatment with antibiotics more often (33% versus 4% for the preconditioned calves)[73].

1.9.1 Antimicrobial treatment of BRD

Antimicrobials are commonly used to help control and treat BRD in high-risk feedlot cattle. The term high-risk can have many definitions but generally these calves are light weight, recently weaned, highly commingled, of auction market origin, or a combination of these things[66]. Additionally, they generally have experienced an extended duration of transport and have an unknown health and vaccination history[74]. Since 1988, a number of new antimicrobial agents have been approved to treat BRD[67]. These include ceftiofur, tilmicosin, tulathromycin, florfenicol, enrofloxacin, danofloxacin, gamithromycin, and tildipirosin. This new suite of antimicrobials has transformed the treatment of BRD in feedlots by offering both superior efficacy to previous drugs, as well as greater ease of use due to the extended duration of action of many of them.

Many of these drugs have label claims for metaphylaxis to prevent and treat early cases of BRD in feedlot cattle. Metaphylaxis is the treatment of an entire group of cattle with an

antimicrobial intended to control BRD in highly stressed, newly received calves[75]. Metaphylaxis has been shown to consistently reduce morbidity and mortality in feedlot cattle through a number of studies[75–78], and for that reason, its use is widespread in the feedlot industry[75,78]. A recent meta-analysis of 58 publications showed a combined relative risk of 0.49, indicating a substantial reduction in morbidity from metaphylaxis[78].

1.10.1 Measures of Antimicrobial Resistance

Antimicrobial resistance of BRD pathogens can result in treatment failures and losses associated with increased treatment costs, the need to retreat calves, and mortalities. In a recent review article looking at 16 publications, the authors stated "there appears to be a clear trend of a decrease in susceptibility of the three major BRD pathogens to the antimicrobials used commonly for treatment and control of BRD"[79]. There is also the concern that antimicrobial resistant genes could be transmitted to people[80–84]. Resistance genes to antimicrobials not used in humans have been found in bacteria that are zoonotic to humans such as salmonellae, and in pathogens only found in humans such as shigellae[83]. This would suggest there is a risk that genes that are resistant to antimicrobials used to treat BRD could transfer to humans.

Antimicrobial Sensitivity Tests (AST) are the most used method to determine the sensitivity of a particular pathogen to an antimicrobial drug. The Clinical Laboratory and Standards Institute (CLSI) provides the most commonly used standards to determine if an organism is susceptible to a particular antimicrobial drug. Minimum Inhibitory Concentrations (MIC) provide the most

used standard for determining if an antimicrobial is active against a pathogen *in vitro.* The MIC is the lowest dose of an antimicrobial drug that prevents visible growth of a bacteria. The two most commonly used systems to determine MIC are agar dilution and broth microdilution, with broth microdilution being the most popular due to the availability of commercial kits[67]. Agar dilution involves combining 2-fold dilutions of an antimicrobial drug with agar media and then plating a standard concentration of bacteria onto each plate, followed by observing the lowest concentration of antimicrobial where bacterial growth still occurs[85]. This is a labour-intensive process which is why the more automated broth microdilution process is more commonly used. The microdilution system contains doubling dilutions of the antimicrobial agent in broth. Each dilution is inoculated with a standardized bacterial suspension and incubated for 18 to 24 hours[85]. The first dilution with no visible growth is considered the MIC for that bacteria.

It can be very challenging to extrapolate the MIC of an antimicrobial drug determined using this process to the clinical efficacy that would be observed in the field. Factors such as how advanced disease was at the time of treatment, health status of the animal, as well as pharmacokinetic and pharmacodynamic parameters need to be considered[67]. For example, certain antimicrobials such as florfenicol and tulathromycin achieve higher concentrations in lung tissue than in plasma, which could affect the clinical efficacy[86].

The MIC values can be used for individual cases to help determine if an antibiotic is likely to be effective against a particular BRD pathogen. However, an MIC value for an individual case of BRD can take many days to obtain, so it is necessary to choose an antimicrobial for treatment prior to having this information. Often the MIC_{50} and MIC_{90} values are used to guide empirical

therapy. These values represent the levels at which 50% and 90% of strains in a bacterial population are inhibited[67]. If the MIC_{50} and MIC_{90} are low for an antimicrobial against a particular BRD pathogen, one can be relatively certain that there is not significant resistance and that the therapy is likely to be effective.

1.10.2 Determination of Clinical Efficacy

To determine if an antimicrobial will be effective in a clinical setting, information about microbiologic distribution, pharmacokinetic and pharmacodynamics, and outcome data from clinical efficacy trials needs to be examined[85,87]. In North America, this is done by the CLSI to establish breakpoints for a bacterial isolate. A CLSI-approved veterinary breakpoint is established by looking at a number of factors such as the disease being treated, type of bacteria, animal, and antimicrobial treatment. In this way, a BRD isolate can be classified as susceptible, intermediate or resistant. A susceptible isolate would be expected to be affected by treatment with the chosen antimicrobial, and a resistant isolate would be expected to be unaffected, resulting in treatment failure. Intermediate is a transitional zone where the treatment may work or fail depending on factors such as dosage and local drug concentrations. The actual response is, of course, dependent on a number of other factors such as immune status of the animal, stage and severity of the disease when the animal is treated, and actual antimicrobial concentration in the lung, among others.

1.11.1 Current Antimicrobial Resistance in Bovine Respiratory Disease Pathogens

The following section looks at the known resistance to each class of antimicrobial used to treat BRD in bacterial pathogens that are commonly associated with BRD.

1.11.2 Tetracycline Resistance

The first report of tetracycline resistance in *Pasteurella multocida and Mannheimia haemolytica* is from a study done by Chang and Carter in 1976[79]. They used susceptibility criteria that predate current CLSI standards are therefore difficult to compare to current studies.

The first study published using CLSI standards and microdilution methods to look at MIC distributions consistent with the methods used today was published by Watts et al. in 1994[88]. They looked at isolates from animals that had died of acute BRD over a four-year period from 1988 to 1992. There were high levels of resistance to tetracycline in the *P. haemolytica* isolates tested with a MIC_{90} of 32.0 μg/ml (the breakpoint used was 4 μg/ml) for all 4 years and only 57% of the isolates were susceptible. There was significant resistance found in *P. multocida* as well with only 71.1% of isolates being susceptible. The compound was more active against *H. somni* with 98.2 % of isolates susceptible. Welsh et al. looked at antimicrobial resistance in BRD pathogens isolated from lung samples collected during necropsy of calves with pneumonia submitted from 1994-2002. They found a significant decline in susceptibility to tetracycline in *P. multocida* isolates over that time period[89]. Portis et al. conducted a 10-year study from 2000-2009 looking at the major BRD pathogens collected from diagnostic laboratories across the United States and Canada. The samples were all from diseased and deceased calves, but there was not any information on age or previous treatment history. All of the antimicrobial

susceptibility testing was done according to current CLSI standards at only 2 laboratories, to keep results consistent. They found high resistance rates to tetracyclines among *M. haemolytica* isolates with only 48-53% being susceptible over the 10 years[90]. Similar results were found with *P. multocida* with around 54-67% of isolates being susceptible. Interestingly, the susceptibility of *H. somni* appeared to change over the course of the study with over 80% of isolates susceptible in 2000 and 2001, dropping to 47% in 2009.

Tetracycline has the highest levels of resistance from BRD pathogens of any of the antimicrobials. It is not entirely clear why this is, although it may be due to the fact that it has been in continuous use for the longest time, as well as the fact that it has highest frequency of use by a significant margin[91]. The United States Food and Drug Administration reported in 2015 that tetracycline drugs account for two-thirds of the antimicrobials used for the prevention of BRD[91].

1.11.3 Macrolide Resistance

The macrolide class of antimicrobials are used extensively in the treatment of BRD, particularly for metaphylaxis[92]. Currently approved macrolides used commonly for metaphylaxis include tilmicosin, tulathromycin, gamithromycin and tildipirosin. Two of the earliest available macrolides used for BRD treatment were erythromycin and tilmicosin and they were first examined for antimicrobial resistance from 1988 - 1992 by Watts et al. Tilmicosin has been an important drug for metaphylaxis since 1990 in Canada and surprisingly they encountered significant resistance in that early study to the BRD pathogens. Only 69.1% of *M. haemolytica*

isolates obtained from the lungs of cattle that died of BRD were susceptible to tilmicosin over the four years and only 58.9% of *P. multocida* were susceptible[93]. Interestingly, in the same study isolates from Canada were much more susceptible, in the 90-100% range for BRD pathogens[93]. It was speculated whether these results were due to extensive use of erythromycin in the United States and not Canada, thus conferring cross resistance in the more affected population. Other Canadian based studies have shown similar results. Several Canadian studies have shown almost no resistance to tulathromycin in *M. haemolytica* isolates[94–96]. However, Timsit et al. found resistance to tulathromycin (71.8%) and tilmicosin (79.5%) to be high[97] in research done in western Canada. A project from 2015 had similar findings suggesting that the Canadian resistance patterns may be changing to match those in the United States[98].

1.11.4 Fluoroquinolone Resistance

Currently, there are three fluoroquinolones that are approved for use in the treatment of BRD: enrofloxacin, danofloxacin, and marbofloxacin. In the United States, fluoroquinolones are prohibited for extra-label use[99]. In Canada, the label for Baytril 100 (enrofloxacin) states the following,

> "To limit the development of antimicrobial resistance: Baytril 100 should not be used as a mass medication for cattle and swine. Baytril 100 should only be used for treating individual cases of bovine and swine respiratory disease after first choice treatment has failed. The choice of Baytril 100 as the most appropriate treatment should be confirmed by clinical experience supported, where possible,

by pathogen culture and drug susceptibility testing. Do not use in an extra-label manner in cattle, swine or any other species[100]."

In Canada, this label is unique in its restrictions on extra-label use and recommendation for use only when a first treatment has failed.

One of the earlier studies looking at susceptibility of BRD to the fluoroquinolones was done by Welsh et al. and showed high susceptibility to enrofloxacin in both *M. haemolytica* (89–98% susceptible) and *P. multocida* (96-100% susceptible) isolated from the lungs of calves that died of BRD[89]. The Portis et al. 10-year study ending in 2009 found that the number of *M. haemolytica* isolates from BRD cases susceptible to enrofloxacin decreased from 95% to 80%[90]. Similarly, susceptibility of *P. multocida* to enrofloxacin dropped from 100% to 91% and *H. somni* from 100% to 86%[90]. The Portis et al. study concluded that while a "majority of BRD isolates that were tested between 2000 and 2009 demonstrated susceptibility to danofloxacin and enrofloxacin, there was a slow decline in the percentage of isolates that were susceptible[90]."

1.11.5 Phenicol Resistance

The only antimicrobial approved for the treatment of BRD from this family is florfenicol. Chloramphenicol was used extensively in the treatment of BRD up until the early 1980's when it was banned due to human safety concerns[67]. Florfenicol has been ~~for~~ approved for the treatment of BRD since the mid 1990's. Florfenicol achieves high concentrations in the pulmonary fluids, with levels at 200% of plasma levels reported[86]. The earliest survey reporting antimicrobial resistance to florfenicol was published by Welsh et al. (2004). Their research

showed a significant decline in antimicrobial sensitivity to florfenicol in *M. haemolytica* and *P. multocida* but no change in *H. somni* in the period from 1994 to 2002[89]. Portis et al. found there was close to a 10% decrease in susceptible isolates from 2000 to 2009, from 100% down to around 90% for all three major BRD pathogens[90].

This increasing level of resistance to florfenicol in the major BRD pathogens is supported by recent studies in the United States. Lubbers and Hanzlicek found an increase in *M. haemolytica* resistant isolates from 5% to 35% in the years 2009 to 2011 to 5 or more antimicrobials, with florfenicol being one of those antimicrobials. Snyder et al. found high levels of resistance (69.4%) to florfenicol in nasal swabs taken from calves after 10-14 days on feed[101].
In southern Alberta, the area of Canada where the highest number of feedlot cattle are located, florfenicol resistance is still low. Anholt et al. found only 4.3% of samples from cattle sick or dead from BRD positive with *M. haemolytica* were resistant to florfenicol[98]. The levels of resistance were below 2% for *P. multocida* and *H. somni.* Very low levels of resistance to florfenicol were also found by Timsit et al. in the same area of Alberta[97].

1.11.6 Beta-Lactam Resistance

Penicillin and ampicillin have been used for the treatment of BRD for decades; however, today with the newer antimicrobials their use has greatly decreased[92]. Penicillin still accounts for 10% of all antimicrobial drugs sold in the United States for all food producing animals, second only to tetracycline[91]. Beta-lactamases produced by *M. haemolytica* and *P. multocida* degrade penicillin and ampicillin, making them less effective[67]. Prior to the use of current CLSI criteria,

both Chang and Carter[102] as well as Post et al.[103] found resistance to penicillin and/or ampicillin. Watts et al. in 1994 demonstrated high levels of resistance to ampicillin by *M. haemolytica* isolated from calves that died of BRD with only 60% of samples taken over a 4-year period being susceptible[93]. In the same study, for both *P. multocida* and *H. somni* there were higher rates of susceptibility, around 90%. Interestingly, the survey study over 10 years by Portis et al. ending in 2009 showed almost identical rates of susceptibility for penicillin to the 3 major BRD pathogens[90].

Today, the most commonly used beta-lactam antimicrobial agent for the treatment of BRD in North America is ceftiofur. This agent is a third-generation cephalosporin that is unaffected by the beta-lactamases produced by *M. haemolytica* or *P. multocida*[67]. Ceftiofur was first introduced in the United States in 1988 and was included in the survey by Watts et al. starting in 1988. For all 4 years of the study, the 3 major BRD pathogens remained 100% susceptible, with a MIC_{90} of <0.06 µg/ml[93]. The ten year survey by Portis et al. showed identical results[90]. In fact, ceftiofur is unique in that almost every study of BRD pathogens up to and including the present day have a very low MIC_{90} of less than or equal to 0.06 µg/ml for ceftiofur and susceptibilities at or very near 100%[67,97,98,101,104]. Ceftiofur stands alone as the only antimicrobial that has not shown any appreciable increase in resistance since its introduction. Health Canada has categorized ceftiofur as a Category 2 antimicrobial of high importance to human medicine[105], therefore this lack of resistance is positive.

1.12.1 Multi-drug resistance

Perhaps the most concerning development in the last few years in the area of antimicrobial resistance is multi-drug resistance (MDR). MDR can be of major concern in feedlot cattle, as it makes it more difficult to find effective antimicrobials to treat BRD. In some areas of the United States BRD isolates are being found that are resistant to multiple classes of antimicrobials[104,95]. This is also starting to occur in Canada[98]. Most of the available research would suggest that there is substantial MDR in the tetracycline and macrolide classes of antimicrobials. Lubbers et al. found that *P. haemolytica* isolates from clinical cases of BRD that were resistant to oxytetracycline were 3.52 times more likely to be resistant to 1 or more additional antimicrobials compared to non-oxytetracycline resistant isolates[104]. Timsit et al. in a 2016 western Canadian study found high levels of resistance (>70%) against oxytetracycline in *M. haemolytica* and *P. multocida* isolated from cattle with BRD and high levels of resistance against oxytetracycline (67%) in *H. somni* isolates[97]. When looking at the macrolide class, Lubbers et al. showed that isolates from clinical cases of BRD that were resistant to tilmicosin were 2.64 times more likely to be resistant to another antimicrobial. Many studies have shown that MDR is common with macrolides, and there does appear to be evidence that the level of resistance is increasing, particularly in cattle that have already been treated with a macrolide such as in the case of metaphylaxis[97,98,101,104,106].

Most research does not implicate the fluoroquinolones as having a significant role in multi-drug resistance. A 2017 study by Anholt et al. in Alberta, Canada showed high levels of multidrug resistance with 47% of the BRD isolates from dead and diseased calves being resistant to 4 to 5 antimicrobial classes. However, the fluoroquinolones were only included in a small percentage

of those resistant isolates – in the case of enrofloxacin, less than 4% for any of the 3 major BRD pathogens[98]. Other studies have demonstrated very similar findings[97,107], however another recent study from 2017 showed higher levels of resistance to enrofloxacin, so it is possible that these patterns are changing[101]. Recently, Japanese researchers have observed resistance rates in fluoroquinolone antimicrobials to have increased up to 4-fold over the period of 2006 to 2009, from 4.8% to 18.8%[108]. Fluoroquinolones have been in use for BRD treatment a decade longer in Japan than in North America, which may contribute to this increase[109].

1.12.2 Genetic mechanisms of multi-drug resistance

Recently, Michael et al. found 12 antimicrobial resistance genes within an integrative conjugative element (ICE) in an isolate of *P. multocida* from bovine respiratory tract infections[110]. An ICE can introduce new DNA into bacteria. This ICE, designated ICEPmu1, contains the resistance genes *aad*A25 (streptomycin/spectinomycin), *str*A and *str*B (strepto-mycin), *aad*B (gentamicin), *aph*A1 (kanamycin/neomycin), *tet*R-*tet(*H) (tetracycline), *flo*R (chloramphenicol/florfenicol), *sul*2 (sulfonamides), *erm(*42) (tilmicosin/clindamycin), and *msr* (E)-*mph*(E) (tilmicosin/tulathromycin)[110]. The presence of these 12 resistance genes in a single ICE demonstrates the potential for transfer of multiple antimicrobial resistance genes in one horizontal gene transfer event[110]. Klima et al. found *M. haemolytica*, *P. multocida*, and *H. somni* in lung samples from cattle in Texas and Nebraska possessing ICE that conferred resistance for up to seven different antimicrobial classes[95]. In their study, 45% of all bacterial isolates displayed resistance to three or more antimicrobials. Thirty-three percent of *M. haemolytica* isolates, 37.5% of *P. multocida* isolates, and 30% of *H. somni* were resistant to more than seven

antimicrobial classes, including aminoglycosides, penicillins, fluoroquinolones, lincosamides, macrolides, pleuromutilins, and tetracyclines[95]. The ability of the BRD pathogens to confer resistance to multiple antimicrobial drugs in a single gene transfer is very concerning and could severely decrease the effectiveness of the available antimicrobials.

1.13.1 Impact of Antimicrobial Resistance on Clinical Efficacy

As new antimicrobials have become available over the last thirty years for treatment of BRD in cattle, resistance from BRD pathogens has developed to those antimicrobials. Over that same time, antimicrobial susceptibility testing (AST) has made it easier to determine which antimicrobials are most likely to be effective. However, there are limitations to applying AST to clinical outcomes in treating BRD. One of the most significant limitations to AST is that it takes several days to get results. This means that clinically the selection of an antimicrobial to treat a particular case of BRD or for use in metaphylaxis on a group is based on past experience and testing by the clinician, not the actual sensitivity profile of the pathogen being treated. Another limitation discussed earlier is the disease state of the animal prior to treatment. Clinical scores are often used in studies on antimicrobial effectiveness, and these range from slightly ill to moribund[74]. When lungs are examined at slaughter, 68% of cattle that have signs of pneumonia at slaughter were never treated for BRD[74]. Antimicrobials are only likely to be effective if given early in the progression of BRD, and sick animals must be detected by feedlot personnel, regardless of the sensitivity profile of the pathogen being treated. Finally, clinical efficacy is determined by the susceptibility of the organism to the selected antimicrobial. As mentioned earlier, veterinary specific interpretive criteria to help correlate the *in vitro* test

result with clinical outcome that we have today are very helpful. Apley et al. showed that the clinical success rate when treating isolates of *M. haemolytica* categorized as susceptible was 84.9%. In contrast, the success rate in treating animals with isolates categorized as either intermediate or resistance was only 38.9%[111]. Clinical efficacy often seems to be directly linked to *in vitro* susceptibility testing, although at times this association is not as clear[112].

1.14.1 Conclusion

Finding ways to treat and prevent disease in beef cattle using methods such as improved biosecurity and effective treatment methods for BRD is important for the future health of the industry. There is a need for more research on biosecurity practices in cattle and their effect on animal health. Due to the structure of the Canadian cattle industry, exclusion biosecurity cannot be reasonably achieved in beef herds. However, based on the available research from other countries, there may be biosecurity actions that can be undertaken to help limit the introduction of disease. Purchasing of new animals into a herd has the greatest negative impact on animal health from a biosecurity perspective. Based on that information, limiting new introductions into cow-calf herds to a minimum should help reduce disease. Testing the newly introduced animals for diseases such as BVD will likely also reduce the transmission of certain diseases. Exposure to cattle from other farms also increases the risk so limiting the use of community pastures and avoiding fence line contact whenever possible may have health benefits. Hygiene practices seem to play a lesser role in disease transmission; however, for certain diseases there can be a positive impact from improved hygiene.

There is a need to better understand the biosecurity practices that exist on Canadian beef farms. This study set out to quantify animal introductions into herds, where and how cattle mix, and other aspects of biosecurity in beef production. As well, this study looked at how biosecurity practices impact animal health in those herds. By doing so, recommendations can be developed to help producers make changes to biosecurity that would have the most benefit in improving animal health in their herds.

Over the last thirty years several new antimicrobials have become available to treat BRD in cattle, and at the same time resistance to those antimicrobials has increased. Also, it seems that the longer an antimicrobial is in use for, the greater the number of resistant isolates that are documented. Together, this would lead to the conclusion that over time the control of BRD will rely on either the development of newer, more effective antimicrobials, or a change in production and management methods so that antimicrobials are not required as frequently. Improving biosecurity methods used by cow-calf producers should reduce the need for antimicrobials. Changing the source of calves from the auction market to a single source reduces mixing and may decrease the need for antimicrobial use as well. Programs such as the preconditioning of calves have shown to dramatically decrease morbidity and mortality[66]. Finally, faster testing to allow for susceptibility testing chute-side and appropriate antimicrobial selection at the time of treatment through whole genome sequencing is being explored. Multiple new strategies will be required to reduce the need for and use of antimicrobials.

By studying the impact of source and commingling on both the prevalence of BRD pathogens and antimicrobial resistance of those pathogens, we hoped to be able to find ways to help reduce the use of antimicrobials to control BRD. Does purchasing calves from a single source of calves reduce the BRD risk because they are exposed to less pathogens? Or is it the type of BRD pathogens that are different? Finally, what impact does antimicrobial resistance have on the morbidity and mortality of feedlot cattle? These are some questions we hoped to answer.

1.15.1 Objective of Research

The overall objective of this thesis is to better understand ways to prevent disease in cattle, other than using antimicrobials or vaccines. Several studies have been published recently with information coming from the WCCSN. These studies have looked at vaccine usage in western Canadian cow-calf herds[113] and antimicrobial usage in those herds[114]. The focus of this thesis is to look at other factors that are associated with cattle health in cow-calf herds and in the feedlot. Factors such as preventing disease from entering a herd through biosecurity, and how mixing of cattle in the auction market can impact the BRD pathogens isolated and their resistance patterns.

The first objective of this thesis was to describe current biosecurity practices in cow-calf herds in western Canada and examine the potential association of those practices with animal health. Specifically, the study examined the association between biosecurity and Johne's disease, bovine respiratory disease, and calf diarrhea in those herds.

The second objective of this thesis was to look at the effect that source of cattle has on the prevalence and antimicrobial resistance of BRD pathogens: *M. haemolytica, P. multocida,* and *H. somni.* Mixing of cattle through the auction market is suspected of being a major risk factor in the development of BRD. The study examined the BRD pathogens isolated and their resistance patterns in single source calves (RANCH) vs auction market derived (AUCT) calves that are mixed. As well, the research looked at treatment for BRD and death and the association to prevalence and antimicrobial resistance of BRD pathogens. The aim was to better understand how source can affect the types of BRD pathogens that are observed, and the impact that has on morbidity and mortality in the feedlot. Similar to the first objective, the goal

was to find ways to reduce BRD, without necessarily relying on the use of antimicrobials or vaccination.

Chapter 2. Biosecurity practices in western Canadian cow-calf herds and their association with animal health

Biosecurity practices of beef cow-calf herds in Western Canada have not been studied extensively, nor has their association with herd health. A survey was sent to 103 cow-calf producers with biosecurity and animal health questions. The results showed that certain decisions around biosecurity such as purchasing adult animals and community pasture grazing are associated with BRD and calf diarrhea in those herds.

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Chapter 2

Biosecurity practices in western Canadian cow-calf herds and their association with animal health

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2.1 Abstract

Biosecurity practices of beef cow-calf herds in Western Canada have not been studied extensively. Neither is there a good understanding of their association with herd health. A survey was sent to 103 cow-calf producers who are part of the Western Canadian Cow-Calf Surveillance network. Eighty-one questionnaires were returned. Questions were asked about current inventory, other animals on the farm (dairy cattle and other species), purchased animals, source of purchased cattle, intake management of purchased cattle (i.e. disease testing and vaccinations), commingling with other herds, potential risks from people and equipment, and general herd biosecurity, as well as disease history. All the herds purchased bulls during the 2014-2017 study period, 54% of herds purchased heifers and 42% purchased cows. The use of standard biosecurity practices was generally low with 30% of producers keeping purchased animals separate and 30% vaccinating new additions. None of the evaluated biosecurity practices were associated with reporting Johne's disease. The purchase of over 10 bulls and the purchase of any number of cows were associated with an outbreak of Bovine Respiratory Disease (BRD). Not vaccinating animals purchased into the herd and use of community pasture were also associated with a BRD outbreak. Outbreaks of calf diarrhea were associated with the purchase of 10 or more bulls, the use of community pasture, as well as leasing and sharing bulls. Biosecurity is not emphasized on cow-calf farms in western Canada and the purchase of breeding animals and using community pasture are risk factors for BRD and calf diarrhea.

2.2 Introduction

Globally there is a recognized need to reduce antimicrobial drug usage, making prevention of disease a top priority particularly as the worldwide demand for beef continues to increase. The objective of biosecurity is to prevent new pathogens from entering a livestock operation and also to reduce the spread of any existing pathogens within that premises[16].

The beef industry in Canada presents some unique challenges to implementing and maintaining adequate biosecurity protocols. There are a relatively large number of cow-calf operations, just under 73,000[5], concentrated mainly in western Canada. Their production is funneled into a small number of feedlots; in Alberta and Saskatchewan there are only 163 feedlots with average annual capacity of 1000 head or higher, and together they feed 1.5 million head of cattle[115]. This results in a large amount of mixing of cattle from various farms, often as they pass through auction markets on the way to a feedlot. This challenge of the industry structure is coupled with uncertainty regarding the level of knowledge about basic biosecurity practices among beef producers, consistent with that reported in other countries[11,12,15,20,116]. In Canada the Canadian Food Inspection Agency has published the Canadian Beef Cattle On-Farm Biosecurity Standard, which has recommendations for best practices in biosecurity for beef producers[117]. It is uncertain to what extent these practices are followed. There is limited information about biosecurity practices in beef cow-calf farms in Canada[45,46,118,119]. Previous research relevant to the current study found that cows bred on community pastures were more likely to be pregnant and less likely to have an abortion if they had been vaccinated for Bovine Viral Diarrhea Virus (BVDV) and Bovine Herpesvirus Type 1 (BHV-1)[45,46].

In the United States, the National Animal Health Monitoring System (NAHMS) found over two thirds of cow-calf ranches added new cattle to the herd within the previous 3 years[19]. As well, two thirds of producers did not quarantine new additions to the herd and less than 5% tested new cattle for diseases such as BVD and Johne's[19].

Several studies have shown that biosecurity can have an impact on animal health. Cardwell et al. found that biosecurity advice tailored to the producer by their herd veterinarian reduced seropositivity to BVDV and *Leptospirosis hardjo* on beef farms in the United Kingdom[14]. Presi et al. has shown that farms that bring in new livestock and use communal summer grazing are more likely to introduce BVDV infection into the herd[120]. Two other studies also showed that purchase of new animals into the herd increased the risk of BVDV[51,121]. Dias et al. found that buying cattle and renting pasture from other farmers were risk factors for bovine herpesvirus infection[54]. Bringing new cattle into the herd has been shown to be a significant risk factor associated with the presence of bovine tuberculosis[47–49]. In a western Canadian study, purchased animals had a 2.3 times higher odds of being *Mycobacterium avium paratuberculosis* (MAP) positive[57].

Similar results can be found in other areas of animal agriculture. In a study of Dutch dairy farms, farms that purchased cattle or shared pasture (termed as 'open' farms) differed in performance from farms that did not ('closed' farms). The results showed that the 'closed' farms incurred lower costs for veterinary services, had a lower average age at first calving, and a higher birth rate per 100 dairy cows[44]. Laanen et al. looked at biosecurity measures in Belgian pig farms and

found that increased biosecurity resulted in improvements in daily weight gain and feed conversion. They also found that as biosecurity improved there was a decreased use of antibiotics for prophylaxis[61].

The objectives of this study were to describe current biosecurity practices in cow-calf herds in western Canada and examine the potential association of those practices with animal health. Specifically, this study examined the association between biosecurity and Johne's disease, bovine respiratory disease, and calf diarrhea in those herds.

2.3 Materials and Methods

2.3.1 Ethics Statement

This study was approved by the University of Saskatchewan's Animal Research Ethics Board (#20140003) and the Human Behavioural Research Ethics Board (#14-07).

2.3.2 Herd recruitment

A biosecurity questionnaire was distributed to 103 cow-calf producers in western Canada participating in the Western Canadian Cow-Calf Surveillance Network (WCCCSN) in July 2017. One hundred and twenty-three producers had originally been recruited but at the time of this study the WCCSN consisted of a convenience sample of 103 cow-calf producers in the Canadian provinces of Alberta, Saskatchewan, and Manitoba. The 2011 Census of Agriculture[122] was used to determine recruitment targets for herd numbers in various geographic regions representative of reported herd density. The targeted distribution of moderately sized herds

(100-300 cow-calf pairs) and larger herds (>300 cow-calf pairs) were also determined from 2011 Census of Agriculture data. Local veterinary clinics were asked to assist in the recruitment of herds from their clientele. Criteria for recruitment included those clients that were interested in participating, herds which routinely pregnancy tested their herd, and producers that kept basic production records. Interested producers were paid a yearly honorarium to be part of the WCCCSN and were asked to complete approximately 3 surveys per year.

2.3.3 Survey content

The questionnaire contained the following sections related to biosecurity: current inventory, other animals on the farm (dairy cattle and other species), purchased animals, source of purchased cattle, where cattle were sold, intake procedures applied to purchased cattle (i.e. disease testing and vaccinations), commingling with other herds, potential risks from exposure to people and equipment, animal health practices, and general biosecurity within the herd. Questions were asked about animal movements onto and off the farm and other sources of commingling such as community pastures. Cleaning of tools and equipment was examined, as was other common biosecurity practices such as the separation of sick animals from healthy ones. The questionnaire also asked about diseases within the herd and antimicrobial use for potential associations with biosecurity practices. See Appendix 1 for a copy of the questionnaire.

Prior to full distribution, the questionnaire was sent to 5 cow-calf producers who were not study participants for pretesting and to gather feedback about the questions and suggestions

for improvements in wording and clarity. The questionnaires were distributed in June 2017 to the WCCCSN participants who could either fill out a paper copy and return it by mail or complete the identical questionnaire online.

2.3.4 Data management and statistical analysis

Data from the biosecurity survey were collected and entered into a commercial spreadsheet program (Excel 2017; Microsoft Corp., Redmond, Washington, USA). One producer was removed from the analysis because of incomplete survey data. Data were then imported into a statistical software package (Stata/IC version 15.1, Stata, College Station, Texas, USA) for analysis. The study population was described using descriptive statistics. Herd size was categorized as large (having 300 or more cows when completing the survey in 2017) or moderate (less than 300 cows).

Three health-related outcomes were examined to identify any associated biosecurity factors: the producer reported an animal diagnosed with Johne's disease; the producer answered yes to "Have you had an outbreak (treated more than 10%) of animals for shipping fever/pneumonia in the last 5 years?"; and the producer answered yes to "Have you had an outbreak (treated more than 10%) of animals for calf diarrhea and/or coccidiosis in the last 5 years?". Each outcome was examined separately using logistic regression, and results are reported as odds ratios (OR) with 95% confidence intervals (95% CI). All potential risk factors were screened using unconditional analysis; factors with $P<0.2$ were considered for inclusion in the final multivariable models. Manual stepwise backward selection was used to develop a main effects

model, retaining only variables in which P<0.05. The final model was checked for confounding with the variable herd size.

2.4 Results

2.4.1 Herd demographics

Eighty-one questionnaires were completed with the last one being returned in May 2018, resulting in a response rate of 79%. Herds ranged in size from 34 cows to over 2500, with a median of 312 cows (interquartile range (IQR): 161 to 331). Participants reported a median of 11 breeding bulls (IQR: 7 to 21), 49 replacement heifers (IQR: 29 to 83), and 193 calves (IQR: 131 to 312), and 22 feeder calves (IQR: 3 to 111). Thirty-one herds were large (≥300 cows) and 49 were moderate (<300 cows). A total of 95% of respondents reported having commercial cows, 22% had purebred cattle, 37% had calves that were being backgrounded (i.e. fed on a lower energy ration over the winter prior to entering the feedlot or summer grazing), and 9% also had a feedlot. Of the respondents 38 herds were in Alberta, 25 herds were in Saskatchewan, and 17 herds were in Manitoba.

2.4.2 Cattle purchases made by producers

All producers reported buying at least one bull between 2014 and 2017 (Table 2.1). The next most common cattle purchased were heifers (54% of herds), cows (42% of herds), foster calves (22% of herds), and feeder calves (17% of herds). Over that same time period, the median number of bulls purchased was 10, heifers were 32, cows were 15, foster calves was 1, and feeder calves were 200.

2.4.3 Cattle movements

Producers were asked where they purchased cattle from and where they sold cattle to in the previous 12 months (Table 2.2 and Table 2.3). Three options were given; auction market, another farm (cattle purchased or sold directly from or to a different farm), and private sale (a sale with a limited number of sellers but could be at any location such as an exhibition grounds or auction market (i.e. a bull sale)). Again, the most common cattle type purchased was bulls with 74% of herds purchasing bulls from private sales. Almost half (43%) of herds purchased bulls directly from other farms. Heifers were purchased from other farms in 25% of participating herds; 19% purchased heifers at a private sale and 14% bought heifers from an auction market. Fifteen percent of producers purchased a foster calf from another farm in the last 12 months. Ten percent of producers purchased feeder calves from auction markets and four percent purchased feeder calves through private sales. Finally, cows were bought from another farm in 8% of herds in the previous 12 months; 6% purchased cows through private sales and 5% purchased cow through auction markets.

Most cattle were sold through auction markets; 91% of producers sold cows at the auction market, 86% sold bulls, and 72% and 70% sold feeder steers and heifers, respectively. The next most common location for selling cattle was directly to another farm; 29% of producers sold bulls to another farm, while 27% sold heifers to another farm. Sixteen percent of producers sold foster calves to another farm. Finally, a smaller number of cattle were sold through private sales with 12% of producers selling bulls and heifers in a sale.

2.4.4 Biosecurity practices of cow calf herds in western Canada

Only 30% of producers kept purchased animals separate from the herd for a period of time, and only 30% vaccinated newly purchased animals (Table 2.4). Few producers asked about disease history when purchasing new cattle (16%), but most did ask about vaccination history (78%) prior to purchase decisions. Custom feeding (feeding cattle for a fee) and custom calving (feeding and calving cows for a fee), practices which would potentially bring new animals into the herd on a yearly basis, were not common with only 12% and 6% of producers participating in these activities, respectively. Community pastures, which mixes herds for summer grazing, were used commonly (30%), and 21% of producers took cattle to livestock shows. Only 6% of producers had a bull sale on their farm and 31% of producers leased bulls. As well, 19% of producers in the study restricted access of visitors to their farm, although 27% of farms had hosted visitors from another county in the last 3 years, a potential source of foreign animal diseases (Table 2.4). Most producers used the same equipment for handling manure and feeding cattle (79%), and only 22% reported that they cleaned equipment after handling manure.

2.4.5 Services provided to producers by a veterinarian.

Almost all producers (97%) indicated they had a working relationship with a veterinarian (Table 2.5). The three most common veterinary services used were bull breeding soundness evaluation (97%), pregnancy diagnosis (95%), and seeking treatment advice (94%). The least

common service requested was assistance with setting up written biosecurity protocols at only 3%.

2.4.6 Health-related outcomes

Interdigital phlegmon of cattle, more commonly known as footrot, was the most common disease in this study with 86% of producers reporting that they had treated at least one case in the last 5 years. Almost a third of producers (31%) reported that Johne's disease had been diagnosed in their herd in the past 5 years (Table 2.7). A total of 72% of producers had treated at least one case of pneumonia or BRD and 83% of producers had treated at least one case of calf diarrhea (Table 2.6). Outbreaks were defined as a situation where a producer treated 10% or more of their cattle for a particular disease in a single year; pneumonia (BRD) outbreaks were reported in 19% of herds, 22% of cow-calf producers reported having an outbreak of calf diarrhea in the past 5 years and coccidiosis outbreaks were reported in 16% of herds. Abortion outbreaks where more than 5% of the cow herd aborted in a single year over the last 5 years were only reported in 4% of herds.

2.4.7 Factors associated with having Johne's disease diagnosed in a herd.

Producers were asked if they had a case of Johne's disease diagnosed in the herd. There is a possibility that some herds may have had cows with Johne's disease but may not have been aware as it had not been diagnosed or tested for. There were a number of factors unconditionally associated ($P<0.20$) with reporting that a herd had a previous Johne's disease diagnosis (Table 2.8). They included herd size greater than or equal to 300 cows, the purchase

of 10 or more bulls from 2014 to 2017, new animals purchased are not kept separate for a period of time, new animals not vaccinated prior to adding them to the herd, producer does not ask if John's disease is present in the source herd, producer has taken cattle to a show in the last year, and the producer had a bull sale on the farm in the last year. The exposure variables of heifers purchased and cows purchased were not considered for the final model even though producers that purchased more than 10 cows or 10 heifers from 2014 to 2017 was significant at $P<0.20$. The reason for this is heifers purchased and cows purchased were not significant when considering those producers that purchased less than 10 cows or heifers. The only variable found to be significant ($p<0.05$) in the final model was the exposure variable of new animals are not vaccinated prior to adding them to the herd. However, when herd size was added to the model to check for confounding, it did have a greater than 20% effect on the exposure variable and was therefore retained in the model. This resulted in the exposure variable of new animals not vaccinated prior to adding them to the herd becoming not significant. Thus, no exposure variables were found to have a significant impact on whether a herd had a diagnosis of Johne's disease.

2.4.8 Factors associated with bovine respiratory disease outbreaks in a herd

Approximately one in five producers (19%) reported having an outbreak of bovine respiratory disease (BRD) in the previous 5 years. Unconditional associations ($P<0.20$) with various biosecurity management factors are reported individually with the herd outcome of having a BRD outbreak in the past 5 years in Table 2.9. A final model was developed that also included herd size as a potential confounder. Herd size did not change important effect estimates by >

20%, so it was not retained in the final model. In the final model, producers that purchased greater than 10 bulls from 2014-2017 (OR: 9.70, 95% CI: 1.68 to 56.0, *P* = 0.011), bought cows in a private sale in the last 12 months (OR: 20.7, 95% CI: 1.25 to 342, *P* = 0.034), bought cows from another farm in the last 12 months (OR: 12.2, 95% CI: 1.11 to 133, *P* = 0.041), did not vaccinate purchased animals (OR: 10.8, 95% CI: 1.22 to 95.0, *P* = 0.032), and used community pasture grazing in 2017 (OR: 6.2, 95% CI: 1.26 to 30.5, *P* = 0.025), had greater odds of reporting a BRD outbreak in the last 5 years than producers that did not report these factors.

2.4.9 Factors associated with an outbreak of calf diarrhea

A number of herds had either an outbreak of calf diarrhea (22%) or coccidiosis (16%) (Table 2.6). Upon examining factors unconditionally associated (P<0.20) with a producer reporting a calf diarrhea and/or coccidiosis outbreak (Table 2.10), a final model was developed that also included herd size as a potential confounder. Herd size did not change important effect estimates by > 20%, so it was not retained in the final model. In the final model, producers that purchased greater than 10 bulls from 2014-2017 (OR: 3.27, 95% CI: 1.16 to 9.21, *P* = 0.025), used community pasture for grazing in 2017 (OR: 2.86, 95% CI: 0.98 to 8.32, *P* = 0.054), and leased or shared bulls in the last 3 years (OR: 2.86, 95% CI: 0.98 to 8.32, *P* = 0.054) had greater odds of reporting an outbreak of calf diarrhea and/or coccidiosis in the last 5 years.

2.5 Discussion

Beef cow calf herds in western Canada are typically extensively managed (i.e. predominantly spend time grazing on pasture) and this type of management does not easily allow for exclusion

biosecurity practices that may be practiced in other livestock systems. There is very little information available in the literature regarding the typical biosecurity practices in cow calf herds in North America. Most of the available information for western Canada is from a series of studies by Waldner et al[45,46,123]. These studies mostly focused on cow attributes, herd management, environmental factors, and other history gathered from western Canadian cow calf herds. They did provide some insights into biosecurity practices such as the impact of community pasture and vaccination status on the incidence of abortions and non-pregnancy in these herds. The current study provided new insights into the general lack of basic biosecurity practices in western Canadian cow calf herds. It also demonstrated the potential negative health effects of some of those practices such as adding new adult cattle into the herd and communal grazing.

Introducing new animals into a herd presents one of the highest risks for introducing disease[43]. In this study all herds purchased bulls in the time period of 2014-2017 and over half of the herds purchased heifers as well, indicating that introduction of new animals into the herd was a common practice. Introduction of new cattle into a herd has been studied as a means of introduction of bovine tuberculosis[47–49], BVDV[50–52,120], BHV-1[53,54], and MAP[55–59]. Most bulls and heifers were purchased from either private sales or from other farms. This is potentially less risky from a biosecurity perspective than purchases made from an auction market where there is significant mixing of cattle from multiple farms. Chi et al. looked at how to control disease transmission in dairy cattle and found that because auctions handle cattle from many farms,

there is greater contact with cattle from multiple sources, and therefore more exposure to various infectious diseases[124].

Biosecurity precautions that would be considered standard practice in other areas of animal agriculture were not common in this study. Less than a third of producers kept new additions separate and vaccinated new animals. Additionally, many producers mixed their cows with other herds in the summer grazing period using community pasture. There was substantial mixing of cattle in other ways as well such as custom feeding of calves and taking cattle to shows. Finally, only 19% of herds had restricted access for visitors. Interestingly, these results are very similar from studies done in England[11], Australia[20], Finland[12], and Belgium[15]. This suggests that exclusion biosecurity for cattle farms the world over is not seen as a priority, and probably not perceived as having substantial economic benefit. Partly this can be attributed to the fact that beef cattle are more commonly raised extensively (on pasture), not intensively (in a confined space). Beef cattle in the North American production system also move from breeding farm to backgrounding units to finishing feedlot, thereby encouraging the buying, selling, and mixing of cattle along the production chain. Ribble et al. in a large Canadian study found that increased mixing or commingling of calves from different ranches increased the risk of fatal pneumonia in those calves[125]. Other studies how shown similar increased risk of BRD from mixing calves[71,126].

Previous studies have shown that the two most significant calfhood diseases are BRD and calf diarrhea[118,119]. In the current study purchase of cows into the herd had a significant impact on

the odds of having a BRD outbreak. Purchasing bulls and leasing or sharing bulls also had a significant effect on the odds of an outbreak of calf diarrhea. This seems to demonstrate that bringing in adult cattle has an impact on diseases that are primarily a concern in calves, BRD and calf diarrhea. We expected to find that cow-calf herds primarily have problems with BRD when they purchase feeder cattle, which often have BRD when on feed, and problems with calf diarrhea when purchasing foster calves, which often have diarrhea due to failure transfer of passive immunity. There has been limited study in this area, with most research from cross-sectional surveys that are not able to establish causation. Increasing herd size and commingling of adults can increase the risk of preweaning BRD and calf diarrhea[68,118,127]. The cows and bulls themselves could be carrying pathogens as commensal organisms in their respiratory or gastrointestinal tracts. Alternatively, transmission could be from more mechanical vectors such as cattle trailers that haul the cattle, or the clothes and boots of producers, employees, or visitors. There are many potential ways that producers could mitigate this risk. Careful cow and bull selection for purchase based on known disease history and vaccination status of the source herd would be the primary means of reducing disease transmission. Use of artificial insemination reduces the need to purchase as many bulls, which could lower risk by reducing the number of herds that bulls are sourced from. However, estrus synchronization has been shown to increase BRD risk[68]. Finally, good hygiene practices such as cleaning trailers and clothing has been shown to reduce disease transmission in the case of other diseases[62–64]; however, its uncertain of the impact these practices would have on reducing BRD and calf diarrhea.

Using community pasture was the other factor that increased the risk of both BRD and calf diarrhea. This is the practice of mixing multiple cow-calf herds together in the same pasture during the summer grazing period in western Canada. This practice was common in the current study with 30% of producers using communal grazing in the year of study. This compares to 20 -22% in other Canadian studies[128,129]. Cows sent to community pasture are more likely to mix with herds of differing biosecurity status. Cows grazed on community pastures and not vaccinated for BVDV or BHV-1 were more likely to abort in one study[46]. A similar study by the same author also found that cows bred on community pasture and not vaccinated for BHV-1 and BVDV were less likely to be pregnant[45]. A Brazilian study found that communal grazing increased the risk of BHV-1 infection[54], and a Swiss study found that the risk of BVDV introduction was higher in herds that grazed communally[120]. Based on this research the increased risk of disease introduction from communal grazing seems to be prevalent in other countries as well.

It is interesting to note that BRD and calf diarrhea in pre-weaned calves are often found together[68,130]. They potentially share common risk factors such as housing density and poor hygiene[69,119,130]. In the current study 9 of the 15 herds that reported having a BRD outbreak, also reported having an outbreak of calf diarrhea. Other aspects of pasture grazing that have been shown to increase the risk of BRD in pre-weaned calves are increasing the number of cows, more intensive grazing practices and estrus synchronization programs[131]. This suggests that factors such as increased mixing and density of cows increases the risk of BRD on pasture. Based on that information and the increased risk of BRD and calf diarrhea outbreaks shown in

this study, finding alternatives to community pasture should be a consideration for producers. Purchase of individually owned pastures is probably the best solution. Where this isn't feasible due to cost or availability, options such as splitting community pastures into smaller sections to reduce the mixing of herds and developing similar biosecurity protocols to the other producers, should be considered.

The last factor associated with increased risk of BRD, although not an increased risk of calf diarrhea, was not vaccinating purchased animals upon arrival. The efficacy of vaccinating calves to prevent BRD is well established[70,71,127,132–134]. The questionnaire did not distinguish between the vaccination of adult new arrivals or calves. The findings of this study that purchase of adult animals increases BRD risk in calves would support vaccination of adult new arrivals. Recent work on vaccination practices from herds in the WCCSN showed that 91% of cows and 96% of replacement heifers are vaccinated at least once for BVDV and BHV-1[113], so this practice is commonplace already. This research would suggest that vaccinating purchased cattle for the common viral and bacterial BRD pathogens is a sound biosecurity practice.

There is potential in this study, like all survey-based research, for recall bias. It may have been difficult for a producer to recall all the purchases made and selling of animals in the last number of years. However, this is helped somewhat by the fact that most of these activities do not vary substantially on each farm from year to year. In the same way, it is likely that a producer does not change their biosecurity practices appreciably from year to year. So, for example, the

effect of practices such as community pasture grazing in the previous year can be extrapolated over time.

Another criticism is that the study does not represent a random sample. The WCCSN has herds recruited through local veterinary practices in western Canada. This could result in herds that are more likely to be involved with their local veterinarian. In turn, this could influence their knowledge and application of biosecurity practices.

2.6 Conclusion

It is interesting that the introduction of adult animals into a herd has such a significant association with diseases that are primarily a concern in calves prior to and just after weaning, namely BRD and calf diarrhea. The mechanism of how these pathogens spread from the newly introduced cattle into calves is an area that requires further study. Community pasture grazing was the other factor that was associated with both BRD and calf diarrhea outbreaks. Multiple studies from other areas of the world show similar results[44–46,54,120]. It would seem that purchase of new animals and community pasture grazing are two aspects of cow-calf production that can compromise biosecurity and affect animal health and warrant caution on the part of the producer. This study demonstrates there is minimal consideration of biosecurity on cow-calf operations in western Canada. Efforts should be made to reduce the introduction of new cattle into cow calf herds and to improve isolation and vaccination protocols for these cattle on cow-calf operations. As well communal grazing should be used as minimally as is feasible.

2.7 Tables

Table 2.1 Cattle purchases made by producers 2014-2017 reported by 80 cow-calf producers surveyed in western Canada (n=80).

	2017		2016		2015		2014		Overall	
	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle purchased, median (5^{th} – 95^{th} percentile)	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle purchased, median (5^{th} – 95^{th} percentile)	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle purchased, median (5^{th} – 95^{th} percentile)	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle purchased, median (5^{th} – 95^{th} percentile)	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle purchased, median (5^{th} – 95^{th} percentile)
Bulls	91%	3 (1-12)	89%	3 (1-10)	90%	2 (1-10)	91%	2 (1-10)	100%	10 (3-40)
Cows	8%	37 (1-136)	17%	11 (1-138)	22%	36 (3-200)	18%	18 (1-400)	42%	32 (1-543)
Heifers	28%	18 (1-200)	43%	10 (1-121)	33%	11 (1-118)	28%	11 (1-73)	54%	15 (2-387)
Foster Calves	10%	1 (1-4)	6 %	2 (1-5)	8%	2 (1-3)	6%	1 (1-3)	22%	1 (1-14)
Feeder Calves	9%	42 (3-10000)	11%	210 (1-10000)	15%	200 (2-10000)	9%	900 (2-10000)	17%	200 (8-40000)

Table 2.2 Locations cattle purchased from in the 12 months previous to the survey reported by 80 cow-calf producers surveyed in western Canada (n=80).

	Auction Market		Another Farm		Private Sale	
	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle type purchased, median (5^{th} – 95^{th} percentile)	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle type purchased, median (5^{th} – 95^{th} percentile)	Percentage of Producers who purchased cattle type % (n=80)	For those producers purchasing, number of cattle type purchased, median (5^{th} – 95^{th} percentile)
Bulls	0%	0	43%	2 (1-20)	74%	3 (1-11)
Cows	5%	20 (11-43)	8%	29 (1-94)	6%	2 (1-46)
Heifers	14%	20 (3-300)	25%	8 (1-73)	19%	3 (1-69)
Foster Calves	0%	0	15%	1 (1-4))	0%	0
Feeder Calves	10%	121 (1-1800)	4%	200 (1-3066)	0%	0

Table 2.3 Locations cattle sold to in the 12 months previous to the survey reported by 80 cow-calf producers surveyed in western Canada (n=80).

	Auction Market		Another Farm		Private Sale	
	Percentage of Producers who sold cattle type % (n=80)	For those producers selling, number of cattle type sold, median (5^{th} – 95^{th} percentile)	Percentage of Producers who sold cattle type % (n=80)	For those producers selling, number of cattle type sold, median (5^{th} – 95^{th} percentile)	Percentage of Producers who sold cattle type % (n=80)	For those producers selling, number of cattle type sold, median (5^{th} – 95^{th} percentile)
Bulls	86%	3 (1-10)	29%	6 (1-36)	12%	42 (1-82)
Cows	91%	24 (6-89)	14%	21 (1-1200)	4%	40 (33-50)
Heifers	35%	11 (2-67)	27%	25 (2-70)	12%	7 (1-57)
Foster Calves	2.5%	3 (1-4)	16%	3 (1-5)	0.0%	0
Feeder Heifer	70%	50 (5-175)	12%	64 (4-1500)	2.5%	53 (6-100)
Feeder Steer	72%	74 (8-300)	19%	105 (1-600)	2.5%	163 (135-190)

Table 2.4 Responses of producers in survey to general biosecurity questions (n=80).

Survey Questions	Yes	No	Under Certain Circumstances
New animals purchased kept separate for a period of time.	30%	46%	24%
New animals are vaccinated prior to adding them to the herd.	30%	68%	
Producer asks about disease history prior to purchasing new animals.	16%	64%	17%
Producer asks about vaccination history prior to purchasing new animals.	78%	20%	1%
Producer has custom fed calves on their farm in the last 3 years.	12%	85%	
Producer has custom calved cows on their farm in the last 3 years.	6%	93%	
Producer uses community pasture for summer grazing	30%	69%	
Producer has taken cattle to a show in the last year	21%	78%	
Producer had a bull sale on their farm in the last year	6%	93%	
Producer has leased bulls for use on their farm in the last 3 years	31%	67%	
Producer restricts access of people from other farms to their cattle.	19%	63%	16%
People from other countries had visited the producers farm in the last 3 years.	27%	70%	
Producer uses the same equipment for manure handling and feeding cattle.	79%	19%	
Producer cleans and disinfects loader after handling manure.	22%	57%	

Table 2.5 Services provided to producers by their veterinarian (n=79) (one producer did not complete this section of the survey)

Relationship that producers have with their veterinarian and services that are provided. (n=79)	Yes
Producer has a working relationship with a veterinarian.	97%
Producer uses their veterinarian for the following services:	
Pregnancy Diagnosis	95%
Bull Testing	97%
Body Condition Scoring	24%
Routine Post Mortems of Dead Cattle	49%
Trichomoniasis Testing of Bulls	21%
Treatment of sick animals	72%
Assisting with calving difficulty: ie. C-section	89%
Advice regarding vaccines	92%
Treatment advice	94%
Biosecurity advice	28%
Disease prevention advice	67%
Written vaccine protocols	32%
Written treatment protocols	27%
Written biosecurity protocols	3%
Assistance with quality assurance programs	9%
Marketing advice	5%
Staff employee or family member training	14%
Feed analysis or ration formulation	14%
Advice regarding nutrition	29%
Testing for other infectious diseases (e.g. Johne's, BVD, etc)	42%

Table 2.6 Health related outcomes when producers were asked questions about diseases that they observe in their herds (n=80).

Health Related Outcome (n=80)	Percentage of herds that have treated an animal for the disease	Percentage of herds that have had an outbreak[a] of the disease
Shipping Fever / Pneumonia	72%	19%
Calf Diarrhea / Scours	83%	22%
Coccidiosis	58%	16%
Infectious Bovine Rhinotracheitis	6%	0%
Bovine Viral Diarrhea	6%	0%
Pinkeye	69%	16%
Footrot	86%	12%
Trichomoniasis	1%	0%
Vibriosis	3%	1%

[a] Outbreak defined as treating equal to or more than 10% of animals in the herd for the specified disease.

Table 2.7 Health related outcomes when producers were asked questions about diseases that they observe in their herds (n=80).

Health Related Outcome (n=80)	Yes	No	Missing
Producer had more than 5% of their herd abort in a single calving season.	4%	94%	3%
Producer has had Johne's Disease diagnosed in their herd.	31%	68%	1%

Table 2.8 The unconditional associations of exposure variables to outcome (Answered Yes to "Have you had Johne's disease diagnosed in your herd?")

Exposure Variables	Odds Ratio	95% Confidence Intervals		P-value[a]
		Lower	Upper	
Cattle have contact with Dairy Cattle: no contact with Dairy cattle	2.26	0.30	17.1	0.43
Herd Size ≥300 Cows: <300 cows	3.02	1.13	8.07	**0.027**
1-10 Bulls Purchased from 2014-2017	1			
10 or more Bulls Purchased from 2014-2017	2.29	0.87	6.04	**0.095**
1-10 Cows Purchased from 2014-2017	1.70	0.35	8.22	0.51
10 + Cows Purchased from 2014-2017	2.02	0.71	5.75	**0.19[b]**
1-10 Heifers Purchased from 2014-2017	1.50	0.44	5.17	0.52
10 + Heifers Purchased from 2014-2017	2.14	0.71	6.49	**0.18[c]**
1 + Foster Calves Purchased from 2014-2017	0.42	0.11	1.63	0.21
1 + Feeder Calves Purchased from 2014-2017	2.08	0.62	6.99	0.24
Purchased Bulls from Another Farm in the previous 12 months	0.68	0.26	1.81	0.44
Purchased Bulls from a Private Sale in the previous 12 months	0.74	0.25	2.20	0.59
Purchased Cows from Another Farm in the previous 12 months	2.50	0.46	13.4	0.29
Purchased Cows from a Private Sale in the previous 12 months	0.53	0.06	5.04	0.58
Purchased Heifers from Auction Market in the previous 12 months	0.92	0.52	7.02	0.33
Purchased Heifers from Another Farm in the previous 12 months	0.97	0.32	2.95	0.96
Purchased Heifers from a Private Sale in the previous 12 months	2.52	0.32	2.95	0.96
Purchased Foster Calves from Another Farm in the previous 12 months	0.80	0.19	3.34	0.76
Purchased Feeder Calves from Auction Market in the previous 12 months	1.34	0.29	6.15	0.70
Purchased Feeder Calves from Another Farm in the previous 12 months	1.11	0.10	12.9	0.93
New animals purchased are not kept separate for a period of time.	0.52	0.20	1.39	**0.19**
New animals are not vaccinated prior to adding them to the herd.	0.29	0.10	0.80	**0.017**
Producer does not ask about disease history prior to purchasing new animals.	0.65	0.24	1.75	0.39
Producer has Feeder cattle that have direct contact with Cows.	0.50	0.03	7.45	0.61
Producer does not ask if Johne's disease is present in source herd.	0.31	0.06	1.50	**0.15**
Producer does not ask about vaccination history prior to purchasing new animals.	0.45	0.12	1.76	0.25
Producer has custom fed calves on their farm in the last 3 years.	1.49	0.38	5.85	0.57

Producer has custom calved cows on their farm in the last 3 years.	1.48	0.23	9.46	0.68
Producer uses community pasture for summer grazing.	1.90	0.70	5.21	0.21
Producer has taken cattle to a show in the last year.	2.35	0.78	7.10	**0.13**
Producer had a bull sale on the farm in the last year	3.55	0.55	22.7	**0.18**
Producer has leased bulls for use on their farm in the last 3 years.	1.30	0.48	3.56	0.61
Producer restricts access of people from other farms to their cattle.	1.33	0.50	3.55	0.57
People from other countries had visited the producers farm in the last 3 years.	0.75	0.25	2.22	0.60
Producer uses the same equipment for manure handling and feeding cattle.	0.91	0.27	3.01	0.88
Producer cleans and disinfects loader after handling manure.	1.41	0.52	3.85	0.50

[a] P-value , 0.20 retained for consideration in the final multivariable models.

[b]Not considered for final model as overall p-value for cows purchased was >0.20.

[c]Not considered for final model as overall p-value for heifers purchased was >0.20.

Table 2.9 The unconditional associations of exposure variables to outcome (answered YES to the question, "have you had an outbreak (treated more than 10%) of animals for shipping fever/pneumonia in the last 5 years?") (n = 80 herds)

Exposure Variables	Odds Ratio	95% Confidence Intervals		P-Value[a]
		Lower	Upper	
Herd Size ≥300 Cows: <300 cows	1.50	0.48	4.64	0.49
1-10 Bulls Purchased from 2014-2017	1.00			
10 or more Bulls Purchased from 2014-2017	4.02	1.15	14.01	**0.03**
1-10 Cows Purchased from 2014-2017	1.36	0.24	7.78	0.73
10 + Cows Purchased from 2014-2017	1.25	0.36	4.34	0.73
1-10 Heifers Purchased from 2014-2017	1.25	0.34	4.53	0.73
10 + Heifers Purchased from 2014-2017	0.32	0.06	1.65	**0.17**
1 + Foster Calves Purchased from 2014-2017	0.89	0.22	3.61	0.87
1 + Feeder Calves Purchased from 2014-2017	0.74	0.15	3.76	0.72
Purchased Bulls from Another Farm in the previous 12 months	2.34	0.74	7.38	**0.15**
Purchased Bulls from a Private Sale in the previous 12 months	0.96	0.27	3.43	0.95
Purchased Cows from Another Farm in the previous 12 months	4.92	0.88	27.36	**0.07**
Purchased Cows from a Private Sale in the previous 12 months	7.63	1.15	50.64	**0.04**
Purchased Heifers from Auction Market in the previous 12 months	0.42	0.05	3.54	0.42
Purchased Heifers from Another Farm in the previous 12 months	1.09	0.30	3.91	0.89
Purchased Heifers from a Private Sale in the previous 12 months	0.59	0.12	2.96	0.52
Purchased Foster Calves from Another Farm in the previous 12 months	0.82	0.16	4.18	0.81
Purchased Feeder Calves from Auction Market in the previous 12 months	1.58	0.28	8.82	0.60
New animals purchased are not kept separate for a period of time.	1.02	0.33	3.15	0.97
New animals are not vaccinated prior to adding them to the herd.	3.07	0.63	14.94	**0.17**
Producer does not ask about disease history prior to purchasing new animals.	1.05	0.32	3.45	0.94
Producer has Feeder cattle that have direct contact with Cows.	0.50	0.03	8.71	0.63
Producer does not ask if Johne's disease is present in source herd.	0.66	0.12	3.65	0.64
Producer does not ask about vaccination history prior to purchasing new animals.	1.58	0.43	5.81	0.50
Producer has custom fed calves on their farm in the last 3 years.	2.04	0.46	9.02	0.35
Producer has custom calved cows on their farm in the last 3 years.	1.09	0.11	10.51	0.94
Producer uses community pasture for summer grazing.	3.50	1.10	11.17	**0.03**
Producer has taken cattle to a show in the last year.	3.27	0.97	11.08	**0.06**

Producer has leased bulls for use on their farm in the last 3 years.	2.24	0.71	7.07	**0.17**
Producer restricts access of people from other farms to their cattle.	1.79	0.57	5.60	0.32
People from other countries had visited the producers farm in the last 3 years.	0.93	0.26	3.30	0.91
Producer uses the same equipment for manure handling and feeding cattle.	1.66	0.33	8.28	0.54
Producer cleans and disinfects loader after handling manure.	1.58	0.50	4.98	0.43

[a] P-value , 0.20 retained for consideration in the final multivariable models.

Table 2.10 The unconditional associations of exposure variables to outcome (answered YES to the question, "have you had an outbreak (treated more than 10%) of animals for Calf Diarrhea and/or Coccidiosis in the last 5 years?")

Exposure Variables	Odds Ratio	95% Confidence Intervals		P-value[a]
		Lower	Upper	
Cattle have contact with Dairy Cattle: no contact with Dairy cattle	2.04	0.27	15.34	0.49
Herd Size ≥300 Cows: <300 cows	2.28	0.88	5.90	**0.09**
1-10 Bulls Purchased from 2014-2017	1.00			
10 or more Bulls Purchased from 2014-2017	2.72	1.04	7.11	**0.04**
1-10 Cows Purchased from 2014-2017	1.27	0.28	5.85	0.76
10 + Cows Purchased from 2014-2017	2.15	0.77	6.00	**0.15**
1-10 Heifers Purchased from 2014-2017	0.92	0.29	2.89	0.88
10 + Heifers Purchased from 2014-2017	0.52	0.17	1.64	0.27
1 + Foster Calves Purchased from 2014-2017	1.07	0.35	3.28	0.91
1 + Feeder Calves Purchased from 2014-2017	3.96	1.15	13.65	**0.03**
Purchased Bulls from Another Farm in the previous 12 months	2.17	0.84	5.59	**0.11**
Purchased Bulls from a Private Sale in the previous 12 months	0.93	0.32	2.71	0.89
Purchased Cows from Auction Market in the previous 12 months	0.60	0.06	6.09	0.67
Purchased Cows from Another Farm in the previous 12 months	1.96	0.37	10.45	0.43
Purchased Cows from a Private Sale in the previous 12 months	1.28	0.20	8.17	0.79
Purchased Heifers from Auction Market in the previous 12 months	0.67	0.16	2.77	0.58
Purchased Heifers from Another Farm in the previous 12 months	1.05	0.36	3.05	0.93
Purchased Heifers from a Private Sale in the previous 12 months	1.88	0.60	5.91	0.28
Purchased Foster Calves from Another Farm in the previous 12 months	0.94	0.25	3.44	0.92
Purchased Feeder Calves from Auction Market in the previous 12 months	3.56	0.78	16.25	**0.10**
Purchased Feeder Calves from Another Farm in the previous 12 months	0.94	0.08	10.89	0.96
New animals purchased are not kept separate for a period of time.	1.41	0.55	3.56	0.47
New animals are not vaccinated prior to adding them to the herd.	1.06	0.38	2.91	0.92
Producer does not ask about disease history prior to purchasing new animals.	1.06	0.40	2.83	0.91
Producer has Feeder cattle that have direct contact with Cows.	3.00	0.20	45.24	0.43

Producer does not ask if Johne's disease is present in source herd.	0.47	0.11	2.05	0.31
Producer does not ask about vaccination history prior to purchasing new animals.	1.29	0.41	4.04	0.66
Producer has custom fed calves on their farm in the last 3 years.	3.43	0.07	1.14	**0.08**
Producer has custom calved cows on their farm in the last 3 years.	3.19	0.05	2.00	0.22
Producer uses community pasture for summer grazing.	2.73	0.14	0.99	**0.05**
Producer has taken cattle to a show in the last year.	2.06	0.16	1.45	**0.20**
Producer had a bull sale on the farm in the last year	0.47	0.23	19.98	0.51
Producer has leased bulls for use on their farm in the last 3 years.	2.40	0.16	1.12	**0.08**
Producer restricts access of people from other farms to their cattle.	0.67	0.55	4.02	0.44
People from other countries had visited the producers farm in the last 3 years.	1.14	0.31	2.45	0.80
Producer uses the same equipment for manure handling and feeding cattle.	1.05	0.29	3.14	0.94
Producer cleans and disinfects loader after handling manure.	0.68	0.53	4.04	0.46

[a] P-value , 0.20 retained for consideration in the final multivariable models.

Chapter 3. Antimicrobial Resistance in Bovine Respiratory Disease: Auction Market and Ranch Raised Calves

Calves from the auction market (n=299) and calves from a single ranch source (n=300) were tested for prevalence and antimicrobial sensitivity of three major BRD bacterial pathogens (*Mannheimia haemolytica* (MH), *Pasteurella multocida* (PM) and *Histophilus somni* (HS)) at arrival and again later in the feeding period. In the auction market calves the prevalence of MH decreased and the prevalence of HS increased over the feed period. In the single source ranch calves the prevalence of all three BRD pathogens decreased. In most cases antimicrobial resistance increased over the period except in the case of MH isolates in the single source ranch calves where antimicrobial resistance decreased.

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Chapter 3

Antimicrobial Resistance in Bovine Respiratory Disease: Auction Market and Ranch Raised Calves

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3.1 Abstract

Bovine respiratory disease (BRD) is the most significant disease in the feedlot industry. This study aims to compare the changes in prevalence and antimicrobial sensitivity of three major BRD bacterial pathogens at arrival and again later in the feeding period in feedlot calves derived from the auction market and from a single ranch source. The animals used were 299 auction market-derived (AUCT) and 300 ranch-sourced (RANCH) beef calves for a commercial feedlot. Calves were sampled with a deep nasal pharyngeal swab (DNS) at the time of entry to the feedlot and again at 64-168 days after arrival. The swabs were cultured within 24 hours of sampling followed by antimicrobial sensitivity testing of isolates of *Mannheimia haemolytica* (MH), *Pasteurella multocida* (PM) and *Histophilus somni* (HS). In the AUCT calves, the prevalence of calves with MH decreased from 37.8% to 20.3% (P <0.001) and the prevalence of calves with HS increased from 17.1% to 30.4% (P = 0.001) over the sampling period. There was a significant increase in calves with isolates that were not sensitive to tulathromycin from the first to second test of all bacterial pathogens. Also in AUCT calves there was a significant increase in calves with PM isolates not sensitive to florfenicol and oxytetracycline, and calves with HS isolates not sensitive to oxytetracycline and tilmicosin. In the RANCH calves, prevalence of calves with MH isolates dropped from 29.4% to 20.4% (P =0.01), from 60.0% to 43.4% for PM (P <0.001), and from 39.8% to 6.1% for HS (P <0.001). In these calves there was a significant increase in PM samples not sensitive to oxytetracycline, tilmicosin, tulathromycin and florfenicol. There was a significant decrease in MH isolates that were not sensitive to oxytetracycline, tilmicosin and tulathromycin. Almost all isolates were sensitive to ceftiofur or

enrofloxacin. Antimicrobial resistance of BRD pathogens and prevalence of bacterial pathogens can vary between auction market-derived and single source calves over the feeding period.

3.2 Introduction

Bovine Respiratory Disease (BRD) is the leading cause of sickness and death in feedlot beef cattle in North America[135]. A lack of effective antimicrobials has the potential to further increase that impact. Despite thousands of studies over the last 30 years[75], BRD still remains a major problem in cattle production.

There is a clear trend of increasing resistance to antimicrobials in the major BRD pathogens of *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni*[90,93,97,135,136]. Resistance to tetracyclines is the most common, particularly in *M. haemolytica* and *P. multocida,* with multiple studies since 1988 showing less than 50% of isolates susceptible to tetracycline[89,90,93,97]. The next most common is resistance to the macrolide class of antimicrobials, including drugs such as tilmicosin, gamithromycin, tulathromycin, and tildipirosin. Susceptibility to drugs in this class has been steadily decreasing since 1990 when tilmicosin, the first macrolide available in Canada, was introduced[89,90]. For the most part, susceptibility of the major BRD pathogens to florfenicol, the fluoroquinolones, and ceftiofur remains high, most often between 90 and 100%[89,90,97,98]. Two recent and somewhat alarming studies have shown nearly 100% resistance to multiple antimicrobials in *Mannheimia haemolytica* after cattle have only been in a feedlot for a short period of time[135,136].

As antimicrobials become less effective there will be a need to reduce morbidity and mortality in feedlot calves through means other than the use of antimicrobials. One way to potentially reduce the risk of BRD in feedlot calves is by acquiring calves for the feedlot directly from a known single source instead of multiple unknown sources. Step et al.[71] showed that single source calves were less likely to be treated for BRD than auction market-derived calves, and calves that were weaned 45 days prior to feedlot entry also were less likely to be treated. In a large Canadian study Ribble et al. found that mixing and commingling of calves from multiple ranches at the auction market increased the risk of fatal pneumonia in the feedlot[125]. There is also the process known as preconditioning, where calves are vaccinated, weaned, dehorned, dewormed, castrated, and trained to eat from a bunk prior to entry into the feedlot. In many cases with this practice there are single or fewer sources, and less mixing. Preconditioning has been shown to reduce morbidity and mortality in the feedlot[70,73]. Making strategic management decisions on the source of calves being purchased and how much commingling has occurred in those calves seems to have a significant impact on the development of BRD.

The objective of this study was to describe the prevalence and antimicrobial sensitivity of 3 major bovine respiratory pathogens (*Mannheimia haemolytica, Pasteurella multocida and Histophilus somni*) in calves derived from the auction market and those from a single source ranch. A secondary objective was to compare the results in these calves at arrival and again later in the feeding period.

3.3 Materials and Methods

3.3.1 Ethics Statement

The research protocol was reviewed and approved by the University of Saskatchewan Animal Care Committee, AUP #20140003.

3.3.2 Animals

Recently weaned steers and heifers of various mixed beef breeds were used for this study. The study was conducted at a commercial feedlot with an 8000 head one-time capacity. The feedlot typically buys auction market-derived, recently weaned calves each fall. They also feed calves from their own commercial cow-calf herd. A sample of 299 auction market-derived calves (AUCT) were randomly selected on arrival at the feedlot for study. As well, 300 calves from the above-mentioned commercial cow-calf herd (RANCH), were randomly selected on arrival at the feedlot. The calves all entered the feedlot in November and December 2017.

3.3.3 Study design

Each calf had a deep nasopharyngeal swab (DNS) performed at the time of processing on entry to the feedlot. The double guarded swab (Reproduction Provisions LLC**,** Walworth, WI**)** was advanced up the ventral meatus of the nose to the level of the medial canthus of the eye, a cotton tipped swab was advanced into the deep nasopharynx, and the swab was swirled on the mucosa approximately 6-10 times, as described elsewhere[137]. Depending on the size of the group being processed samples were collected from every 2nd or 3rd calf as they came through the chute – for example if the group being sampled was approximately 300 calves, then a sample was collected from every 3rd calf to collect around 100 samples for that day.

These samples were placed into Ames media (Copan Diagnostics Inc, Marrieta, CA) and transported in cooled containers to Prairie Diagnostics Laboratory in Saskatoon, Saskatchewan overnight. Isolates were initiated the following morning on 5% Columbia sheep blood and Chocolate agar plates and incubated at 35°C for 18 hours in an environment containing 5% CO_2, for isolation of *Histophilus somni*, *Mannheimia haemolytica*, and *Pasteurella multocida*. Bacterial colonies were examined for cultural characteristics such as production of yellow pigment (*H. somni*), β-hemolysis (*M. haemolytica*), and mucoid appearance (*P. multocida*), at 18 and 48 hours of incubation. The microorganisms of interest were identified using the Matrix Assisted Laser Desorption and Ionization Time of Flight (MALDI-TOF) Mass Spectrometry System. Briefly, individual bacterial colonies were transferred onto the stainless steel MALDI-TOF target in duplicate. Each target well was overlaid with 1 µl of α-cyano-4- hydroxycinnamic acid (HCCA) matrix, and the mass spectra were acquired using MALDI-TOF MF, Microflex LT system in a linear positive mode. Instrument calibration was performed using standard reference *Escherichia coli*. For bacterial identification, MALDI Biotyper 3.1.66 was used. The cut-off scores used for bacterial identification were ≥2.0. Only isolates that positively identified with scores equal or greater than 2.0 were included in this study. Positive isolates of *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni* were frozen at -80 ^{0}C for later sensitivity testing, as described elsewhere[137].

Sensitivity testing was by broth microdilution (Sensititre, Thermofisher Scientific, Nepean, ON, Canada) using a commercially available panel (BOPO6F custom bovine plates, Thermofisher

Scientific, Nepean, ON, Canada). These plates look for sensitivity to the following antimicrobials: ceftiofur, tiamulin, chlortetracycline, gentamicin, florfenicol, oxytetracycline, penicillin, ampicillin, danofloxacin, enrofloxacin, sulphadimethoxine, neomycin, trimethoprim/ sulfamethoxazole, spectinomycin, tylosin tartrate, tulathromycin, tilmicosin, and clindamycin. Briefly, the bacteria are inoculated into a series of wells on the plate containing the specific antimicrobial in increasing concentrations. The Sensititre plates used have a 96 well microtiter plate format containing doubling dilutions. Each plate also contains positive and negative controls[138,139]. The MICs are determined using an automated viewing device by observing the lowest concentration of antimicrobial agent that completely inhibits growth of the organism[138,139].

Isolates were categorized as resistant to an antimicrobial according to minimum inhibitory concentrations (MIC) defined by the Clinical and Laboratory Standards Institute for ceftiofur (≥ 8 μg/mL), enrofloxacin (≥ 2 μg/mL), florfenicol (≥ 8 μg/mL), penicillin (≥ 1 μg/mL), oxytetracycline (≥ 8 μg/mL), tilmicosin (≥ 32 μg/mL, for *M. haemolytica*), and tulathromycin (≥ 64 μg/mL)[140]. The CLSI breakpoints were not available for ampicillin, clindamycin, chlortetracycline, danofloxacin (for *H. somni*), gentamycin, spectinomycin, tiamulin, tilmicosin (for *P. multocida* and *H. somni*), trimethoprim/sulfamethoxazole, tylosin, and neomycin.

Each calf was treated on arrival with a subcutaneous injection of a long-acting macrolide to control BRD (tulathromycin, Draxxin, 2.5 mg/kg, Zoetis, Kirkland, QC, Canada), then weighed and vaccinated against infectious bovine herpes virus-1 (BHV-1), bovine viral diarrhea virus

(BVDV; types I and II), bovine parainfluenza-3 (Pi3), bovine respiratory syncytial virus (BRSV), *Mannheimia haemolytica, Histophilus somni* and clostridial pathogens (Bovishield Gold One Shot, Zoetis, Kirkland, QC, Canada) and Vision 8 Somnus, (Merck Animal Health, Kirkland, QC). The calves were also administered an anthelminthic (Bimectin, Bimeda-MTC, Cambridge, ON, Canada). In addition, auction market-derived heifers received 1mg cloprostenol in the muscle (Estrumate, Merck Animal Health, Kirkland, QC) to induce abortion.

Steers and heifers were housed separately by sex and fed in large outdoor dirt-floor pens in groups of 100 to 250 cattle. The study cattle remained in the larger groups with which they entered the feedlot; that is, AUCT cattle and RANCH cattle did not mix. All cattle received two doses of chlortetracycline (aureomycin, Zoetis, Kirkland, QC, Canada) within the first 28 days on feed (DOF) to prevent histophilosis as per standard feedlot procedure. A dose consisted of feeding 6 g of chlortetracycline per animal per day for 7 days in the total mixed ration and doses generally occurred during the second and fourth weeks on feed for each pen. Calves were identified by radio frequency ear tag.

A second DNS was collected from enrolled calves. These samples were also submitted for culture and sensitivity testing as described above. The AUCT calves received another vaccination against BHV-1 and Pi3 (Bovi-shield IBR-Pi3, Zoetis, Kirkland, QC, Canada) at the time of the second swab. This was an average of 76 days after the first swab. A total of 217 AUCT calves were resampled. The RANCH calves did not receive a vaccination at the time of the second swab and a change in feedlot protocol delayed resampling until an average of 153 days

after the first swab. A total of 279 RANCH calves were resampled. Calves that were not resampled were lost to follow-up due to death or being sold from the feedlot.

Cattle were observed daily by experienced pen checkers for detection of clinical illness. Cattle with one or more visual signs of BRD (e.g. depression, nasal or ocular discharge, cough, increased respiratory rate or dyspnea) were removed from the pens by pen checkers and, if not previously treated for BRD or another disease, were treated for BRD. Calves that required a first treatment for a case of clinical BRD were administered enrofloxacin (Baytril 100, Bayer Animal Heath, Mississauga, ON) at 10 mg/kg. Calves that required a second treatment for BRD were given florfenicol (Nuflor, Merck Animal Health, Kirkland, QC) at 40 mg/kg. No calves in this study were treated more than 2 times.

3.3.4 Statistical analysis

Data was collected for each calf on the prevalence of positive isolates for the BRD pathogens (*M. haemolytica, P. multocida and H. somni).* Based on the available CLSI cut-points for each antimicrobial, BRD pathogens were classified as sensitive, resistant and intermediate. This data was entered into a commercial spreadsheet program (Excel 2017; Microsoft Corp., Redmond, Washington, USA) then imported into a statistical software package (Stata/IC version 15.1, Stata, College Station, Texas, USA) for analysis. Isolates that were classified as intermediate or resistant were grouped together and termed not sensitive, as compared to sensitive isolates. The prevalence of BRD pathogens and sensitivity data was summarized in two ways; prevalence

of positive BRD isolates and isolates that were not sensitive to antimicrobials, as well as looking at calves as matched pairs from the first to the second test.

The prevalence of positive isolates and the prevalence of isolates not sensitive to each antimicrobial for the three BRD pathogens were compared from the first test to the second test using McNemar's test for paired data within calf source groups. The same prevalence data for the three BRD pathogens was compared between AUCT calves and RANCH calves for the first test, using Fisher's exact test.

Treatment risk for BRD and crude mortality risk over the feeding period were compared between AUCT calves and RANCH calves using Fisher's exact test. Logistic regression models were used to determine whether isolation of BRD pathogens or antimicrobial resistance of BRD pathogens might be associated with treatment for BRD or crude mortality. Potential risk factors were screened with unconditional analysis; factors with $P<0.20$ were considered for inclusion in the final multivariable models. Finally, the association was examined between antimicrobial treatment for BRD and antimicrobial resistance (AMR) in *M. haemolytica, P. multocida and H. somni* on the 2nd test. All the final multivariable models were constructed in the same way. The final models included source (AUCT and RANCH) and the interaction of treatment and source. If the interaction was significant then the pairwise comparisons for treated and untreated AUCT and RANCH calves were reported. If the interaction was not significant, it was removed from the model and the effect of source was reported.

3.4 Results

3.4.1 Prevalence of positive isolates for *M. haemolytica, P. multocida*, and *H. somni*

At the first test there was a significantly higher culture prevalence for *M. haemolytica* in AUCT calves at 39.5% compared to 29.7% for RANCH calves ($P = 0.013$; Table 3.1). However, the RANCH calves had higher culture prevalence for *P. multocida* and *H. somni* at 60.0% ($P < 0.001$) and 38.7% ($P < 0.001$), respectively compared to 28.1% and 14.8% for the AUCT calves. In the AUCT calves, prevalence of positive isolates of *M. haemolytica* dropped significantly from 37.8% at the first test to 20.3% at the second test ($P < 0.001$; Table 3.2). There was no significant change in *P. multocida* culture prevalence from the first to second tests in AUCT calves, but positive *H. somni* isolates increased significantly from 17.1% to 30.4% ($P = 0.001$). From the first to the second test positive culture prevalence dropped significantly for all three pathogens in the RANCH calves (Table 3.2). For *M. haemolytica* prevalence dropped from 29.4% to 20.4% ($P = 0.01$), from 60.0% to 43.4% for *P. multocida* ($P < 0.001$), and from 39.8% to 6.1% for *H. somni* ($P < 0.001$).

3.4.2 Antimicrobial sensitivity of *M. haemolytica, P. multocida, and H. somni* isolates to the most commonly used antimicrobials

In the AUCT calves at the first test, 26.7% of the *M. haemolytica* isolates were not sensitive to oxytetracycline and 27.6% were not sensitive to tilmicosin (Table 3.3). The RANCH calves had similar results on arrival with 20.3% of *M. haemolytica* isolates not sensitive to oxytetracycline and 19.0% not sensitive to each tilmicosin and tulathromycin. In AUCT calves that were tested twice, there was a significant increase in calves not sensitive to tulathromycin on the second test; from 1.4% to 7.4% ($P = 0.04$). In the RANCH calves tested twice, calves with non-sensitive

isolates of *M. haemolytica* decreased significantly in the second test from 5.7% to 0.4% for oxytetracycline ($P < 0.001$), and from 5.4% to 0% for both tilmicosin and tulathromycin ($P < 0.001$).

For the *P. multocida* isolates in AUCT calves prevalence of non-sensitive bacteria was relatively low in the first test (Table 3.4). All isolates were sensitive to chlortetracycline, florfenicol, and tulathromycin, with only a few isolates not sensitive to oxytetracycline and tilmicosin. The pattern was similar in the RANCH calves for *P. multocida*, with only a few non sensitive isolates for each antimicrobial (Table 3.4). In the AUCT calves tested twice, the prevalence of calves with *P. multocida* isolates not sensitive to florfenicol increased significantly from 0% to 2.8% ($P = 0.03$). Similarly, non-sensitive oxytetracycline and tulathromycin isolates in calves increased from 0.5% to 3.7% ($P =0.04$) and 0% to 3.2% ($P = 0.01$), respectively. RANCH calves also had significant increases in non-sensitive *P. multocida* from the first to the second test. From 0.4% to 9.0% in the case of florfenicol ($P < 0.001$), from 0.4% to 10.0% for oxytetracycline ($P < 0.001$), from 1.8% to 14.3% for tilmicosin ($P < 0.001$), and from 0.4% to 9.7% for tulathromycin ($P < 0.001$).

Finally, looking at antimicrobial sensitivity for *H. somni* isolates, all of the isolates were sensitive to chlortetracycline and florfenicol on the first and second tests for AUCT and RANCH calves (Table 3.5). In AUCT calves on the first test, all the *H. somni* isolates were sensitive to oxytetracycline, tilmicosin, and tulathromycin. However, by the second test, 11.5% of calves had *H. somni* isolates that were not sensitive to oxytetracycline ($P < 0.001$), 9.7% of calves were

not sensitive to tilmicosin ($P < 0.001$), and 9.2% were not sensitive to tulathromycin ($P < 0.001$). In the RANCH calves on the first test, all the *H. somni* isolates were sensitive to oxytetracycline, tilmicosin, or tulathromycin. By the second test, there was an increase in calves with non-sensitive *H. somni* isolates to 0.7% for oxytetracycline, tilmicosin and tulathromycin. This increase was not significant.

3.4.3 Comparison of antimicrobial sensitivity of *M. haemolytica, P. multocida, and H. somni* isolates on arrival at the feedlot (first test).

There was a significantly higher prevalence of AUCT calves compared to RANCH calves with *M. haemolytica* isolates on the first test that were not sensitive to oxytetracycline (P =0.02) and tilmicosin (P = 0.01). When looking at tulathromycin, there was a significantly higher prevalence of RANCH calves with non-sensitive *M. haemolytica* isolates than AUCT calves (P =0.04) (Table 3.6). For both *P. multocida* and *H. somni,* there were not any significant differences in isolates or calves that were not sensitive to antimicrobials in the first test between the AUCT and RANCH calves. (Table 3.7 and Table 3.8).

3.4.4 Health outcomes in AUCT calves versus RANCH calves

The AUCT calves had significantly higher treatment risk for BRD at 14.4% compared to 9.0% in the RANCH calves (P = 0.043; Table 3.9). There was no significant difference in mortality risk between the two groups.

3.4.5 Effect of treatment for BRD on antimicrobial sensitivity

Cattle that had been treated for BRD were more likely to have isolates of *P.* multocida resistant to spectinomycin(odds ratio (OR): 3.09, 95% CI:1.09 to 8.75, P=0.034) and tilmicosin (OR: 3.27, 95% CI: 1.17 to 9.13, P=0.024) on the second test. Cattle that had been treated for BRD were more likely to have isolates of *H. somni* resistant to oxytetracycline (OR: 3.95, 95% CI: 1.13 to 13.8, P=0.032), tilmicosin (OR: 5.33, 95% CI: 1.51 to 18.8, P=0.009) and tulathromycin (OR: 3.86, 95% CI: 1.12 to 13.2, P=0.032) on the second test (Table 3.10).

Where the interaction between treatment for BRD and source of cattle (AUCT or RANCH) was significant, treated AUCT calves were more likely to have *P. multocida* resistant to florfenicol on the second test (OR: 28.0, 95% CI: 3.56 to 220, P=0.002) compared to untreated AUCT calves. Similarly, treated AUCT calves were more likely to have *P. multocida* resistant to oxytetracycline on the second test (OR: 13.3, 95% CI: 2.17 to 81.9, P=0.005) and *P. multocida* resistant to tulathromycin on the second test (OR: 18.2, 95% CI: 2.72 to 122, P=0.003) compared to untreated AUCT calves (Table 3.11). Treatment for BRD did not have these same effects in RANCH calves.

3.4.6 Effect of positive isolates on treatment for BRD and death

Calves that had positive isolates for *H. somni* on the first test were less likely to be treated for BRD (odds ratio (OR): 0.41, 95% CI: 0.20 to 0.86, *P*=0.019) than calves with negative isolates for *H. somni.*

In the unconditional analysis, there was a trend towards higher mortality in AUCT calves that had positive isolates for *M. haemolytica* on the first test (OR: 3.74, 95% CI: 0.95 to 14.8, P=0.06). However, in the final multivariable analysis including source the association between positive *M. haemolytica* isolates on the first test and death was not significant (OR: 2.07, 95% CI: 0.74 to 5.83, P=0.17).

3.5 Discussion

To the author's knowledge, this is the first study to look specifically at prevalence of BRD pathogens and antimicrobial sensitivity in ranch-raised calves compared to auction market-derived calves. Most of the information in the literature looks at auction market derived cattle[71,141,142]. One of the objectives of this study was to determine the effects of mixing cattle on the prevalence of BRD pathogens isolated and the antimicrobial sensitivity of those pathogens.

At 39.5%, this study had a higher prevalence of *M. haemolytica* isolates in auction market calves on arrival than has been found in previous studies, where prevalence ranged from 13% to 30%[94,137,143,144]. At 29.7%, the prevalence of *M. haemolytica* isolates for RANCH calves closely agreed with what has been found in auction market calves in other studies. The culture prevalence for *M. haemolytica* after calves have been in the feedlot for a period of time varied from 19% to 28% in other studies[94,137,143,144], closely agreeing with the findings of this study for AUCT and RANCH calves. The significant decrease in *M. haemolytica* culture prevalence for

both AUCT and RANCH calves in the current study is not a consistent finding in other studies[94,137]. One reason for this could be the timing of the second sample collection. Particularly in the RANCH calves, the sampled were collected farther along in the feeding period at an average of 153 days. Other studies have shown that isolation rates of *M. haemolytica* are higher when the animal is affected with BRD, which is typically earlier in the feeding period[94,144]. The RANCH calves having second samples taken later in the feeding period than the AUCT calves is certainly a possibly source of bias in the trial and may have affected the results.

For *P. multocida* isolates, there was a prevalence of 28.1% on arrival for AUCT calves, agreeing with other studies reporting 28%[137] and 25%[144]. The culture prevalence of *P. multocida* in the RANCH calves on arrival in the current study is much higher at 60.0%. The reason for this is not clear. The RANCH calves in this study had no previous exposure to calves or cows outside of their herd prior to entry into the feedlot. *P. multocida* culture prevalence did not change significantly from the first to the second test in AUCT cattle. In the RANCH cattle, *P. multocida* culture prevalence dropped significantly to 43.4% on the second test. This is consistent with a previous study from Saskatchewan in auction market derived calves[137], but another study from Oklahoma showed a significant increase in *P. multocida* isolates in cattle during the feeding period[144].

A similar pattern was observed for *H. somni* isolates on the first test. For AUCT calves on arrival, *H. somni* culture prevalence at 14.8% was similar to another study reporting 9%[137]. Again, the

RANCH calves had significantly higher culture prevalence of *H. somni* than the AUCT calves on arrival at 38.7%. The AUCT calves had a significant increase in *H. somni* isolates to 30.4% at the time of the second test, similar to the previously mentioned study from Saskatchewan[137]. The prevalence of *H. somni* isolates decreased significantly in the RANCH calves to 6.1%. Again, the reason for this is not clear. A limitation of this study is that all the RANCH samples came from a single source. It is possible that the ranch calves selected for the study are not representative of calves on other ranches, and that if we had included samples from other ranch raised calves, the isolation rates of *P. multocida* and *H. somni* would have been different.

The source of the calves, whether auction market derived or direct from the ranch, seems to have an effect on the risk of isolating BRD bacteria from DNS. It was not expected that the RANCH calves would have higher prevalence on the first test of *P. multocida* and *H. somni* isolates than the AUCT calves. Stroebel et al. showed that spending 24 hours in an auction market did not increase the rates of these same respiratory pathogens being isolated from calves, and those authors suggested that BRD pathogens are not very transmissible between calves[142]. It is possible the herd where the RANCH calves came from has a high amount of BRD pathogens circulating within the herd. This herd had the same ownership as the feedlot. The cow herd does not stay in the feedlot for an extended amount of time but it does have some contact during the year – such as use of facilities for pregnancy testing and shared feeding and bedding equipment.

Antimicrobial resistance in *M. haemolytica* samples of auction market derived calves on arrival at the feedlot is still relatively uncommon. *M. haemolytica* most commonly has resistance to tetracyclines, with studies showing 3% to 5% of *M. haemolytica* isolates resistant in auction market calves on arrival[107,145]. The current study had 26.7% of *M. haemolytica* isolates in AUCT calves not sensitive to oxytetracycline on arrival. That is much higher than what is reported in other studies. It could be that the prevalence of resistant bacteria is increasing over time, or that the cattle sampled had been previously treated with tetracyclines. Interestingly, the RANCH calves had 20.3% of *M. haemolytica* isolates not sensitive to oxytetracycline, higher than you might expect in calves that had not received antimicrobials prior to arrival at the feedlot. Many studies have looked at macrolide resistance in beef cattle arriving at a feedlot, particularly because this class of antimicrobial is used extensively for metaphylaxis. *M. haemolytica* resistant to tilmicosin in calves on arrival is uncommon, reported at ≤1% in three studies[107,141,145]. Two more recent studies on cattle in the United States have reported higher levels of resistance to tilmicosin, in the 19-20% range[101,131], on arrival to the feedlot in small groups. The current study found 27.6% of *M. haemolytica* samples in AUCT calves and 19% in RANCH calves were not sensitive to tilmicosin, again an increase over previous work.

Many studies have shown an increase in antimicrobial resistance after cattle have been in the feedlot for a period of time, although results can vary significantly. A recent Canadian study showed a significant increase in resistance of 4 to 28% to macrolides after 90 days in the feedlot[137], and other studies have shown resistance to macrolides approaching 100% after only 7-14 days in the feedlot[101,135]. In the current study, the AUCT calves did show resistance

increase significantly in *M. haemolytica* isolates while the cattle were in the feedlot to tulathromycin, but not to the other antimicrobials. Interestingly, the resistance pattern in the RANCH calves was the opposite. The prevalence of calves with *M. haemolytica* isolates not sensitive on the second sample was significantly less for oxytetracycline, tilmicosin, and tulathromycin. One possible reason for this is the longer time period between samples for RANCH calves compared to AUCT calves. However, this pattern was only observed in *M. haemolytica* isolates, not in *P. multocida* or *H. somni* isolates. The authors could not find any previous work demonstrating this pattern so it may warrant further investigation. Most research suggests steadily increasing prevalence of resistance in *M. haemolytica* isolates[90,97], which is certainly cause for concern.

There has been limited research into resistant *P. multocida* on arrival in DNS, with most of the research looking at animals that have BRD already. One relevant study by Ericksen et al. found less than 2% of *P. multocida* samples were not sensitive to antimicrobials on arrival at the feedlot[141], which is similar to our findings. The one exception in the current study is tilmicosin, which had 6.1% and 4.0% non-sensitive *P. multocida* in AUCT and RANCH calves, respectively. With no prior exposure to this antimicrobial in the RANCH calves, it is not clear why this would be the case. Both AUCT and RANCH calves had significant increases in *P. multocida* resistant to florfenicol, oxytetracycline, spectinomycin, and tulathromycin on the second test. The previously mentioned study by Ericksen et al. did not find this marked increase in resistant *P. multocida* in cattle on feed[141]. However, in studies looking at *P. multocida* in animals sick or dead from BRD, there is a very high prevalence of resistance to oxytetracycline, tulathromycin,

tilmicosin, and florfenicol[97,98]. The finding in the current study that animals that had been treated for BRD were more likely to have resistant *P. multocida,* along with the previously mentioned studies, would suggest that treatment is associated with a significantly increased risk of resistant *P. multocida.*

Similar to *P. multocida,* most of the research into antimicrobial resistance in *H. somni* has been done on animals that are sick or dead due to BRD, not DNS on arrival. Again, the most relevant study was done by Ericksen et al. where they found 42% of *H. somni* samples were not sensitive to tilmicosin and 38% were not sensitive to tulathromycin on arrival[141]. After 90 days, similar prevalence of resistance persisted with 45% of samples not sensitive to tilmicosin and 43% not sensitive to tulathromycin. The current study did not find such substantial resistance on arrival, although the number of non-sensitive samples increased significantly at the time of second sampling for the AUCT calves, but not the RANCH calves. The current study also found high levels of resistance in cattle treated for BRD, suggesting that treatment leads to increased resistance of BRD pathogens[90,97,98] .

Treatment for BRD was significantly higher in AUCT cattle than RANCH cattle. Step et al. found similar results[71]. The finding that a positive *H. somni* isolate was associated with a significantly lower risk of being treated for BRD is interesting and not found elsewhere in the literature. There has been extensive research into the nasopharyngeal microbiota of calves in the first few weeks after arrival at the feedlot. Principally those studies have shown that the bacterial population undergoes substantive change in that time period, often moving to predominately

Mycoplasma sp.[142,146]. The current study did not find an association between positive isolates of *M. haemolytica* in DNS on arrival at the feedlot and later treatment for BRD. Other studies agree with this finding, with *M. haemolytica* only being isolated in increasing numbers just before treatment for BRD[145], or at the time of treatment[144].

Similar to the current study, both Noyes et al. and Lamm et al. did not find an association between treatment with antimicrobials and subsequent resistance to antimicrobials in *M. haemolytica*[94,147]. However, Noyes et al. did show that calves were more likely to have *M. haemolytica* resistant to multiple antimicrobials when cattle in the same pen had been treated with antimicrobials[94]. Dedonder et al. found there was not a significant difference between calves mass medicated with gamithromycin and calves given saline on arrival in regards to the likelihood of culturing a resistant isolate of *M. haemolytica* or *P. multocida*[148]. In contrast, other studies have shown resistance to antimicrobials, sometimes as high as 100% resistance, in cattle treated metaphylatically[97,101,135]. The feedlot's protocol was to use enrofloxacin for the first treatment for BRD in an individual calf and florfenicol for the second treatment. It is important to note that the statistical analysis did not differentiate if calves were treated once or twice. There was no association between treatment for BRD and resistance to enrofloxacin in any of the BRD pathogens, although resistance to enrofloxacin was very low. There was a significant association between treatment for BRD and *P. multocida* not sensitive to florfenicol on the second test in AUCT cattle. Treatment for BRD was also associated with *P. multocida* and *H. somni* resistant to macrolides and oxytetracycline. Klima et al. and Michael et al. have shown that resistance genes for macrolides and tetracyclines can be present alone or they can be

grouped together[95,110]. These studies also showed that resistance genes are part of the integrative and conjugative element that can travel across genus boundaries and into *P. multocida* and *M. haemolytica. M. haemolytica, P. multocida*, and *H. somni* possess integrative conjugative elements that can confer resistance for up to seven different antimicrobial classes[95]. This may explain the resistance observed to macrolides and tetracyclines in treated animals when the treatment was not with those antimicrobials.

3.6 Conclusion

This study showed a significant difference between the prevalence of BRD bacteria on DNS in auction market derived cattle versus cattle from a single source. Although it might be reasonably expected that the BRD pathogens examined in this study would be less prevalent in single source calves, this was not the case. However, morbidity in auction market calves was significantly higher. This would suggest that the prevalence of BRD pathogens on DNS on arrival is not necessarily associated with morbidity. Other factors such as the stress of mixing and reestablishing a social dominance hierarchy could be more significant and is an area of further research.

Overall, the levels of antimicrobial resistance in this study were high when compared to previous studies. These results agree with other recent studies that show a trend towards increasing antimicrobial resistance. The finding of decreasing resistance only in RANCH calves that had *M. haemolytica* isolated on the second test is interesting and should be investigated in the future. Another interesting finding that should be examined more closely is that calves

with positive isolates for *H. somni* on the first test were less likely to be treated for BRD than calves with negative isolates for *H. somni.* There has been more research recently into the nasopharyngeal microbiome that may help to explain how different bacterial populations are either harmful or protective in cases of BRD[146].

Animals that are treated for BRD showing increased antimicrobial resistance in *P. multocida* and *H. somni* isolates is not surprising, but a helpful piece of information. It is also interesting that this pattern is not observed with *M. haemolytica.* This study shows that antimicrobial resistance in BRD pathogens is still a concern for the beef cattle industry, and that further research into non-medicinal prevention approaches such as altering cattle procurement sources are a potential mitigation strategy.

3.7 Tables

Table 3.1 Comparison of positive isolates on DNS for each BRD pathogen at first test on arrival at the feedlot between auction market derived and ranch raised calves.

	Auction Market Calves n=299 (%)	**Ranch Raised Calves n=300 (%)**	**P-value**
M. haemolytica positive isolates	39.5%	29.7%	0.013
P. multocida positive isolates	28.1%	60.0%	<0.001
H. somni positive isolates	14.8%	38.7%	<0.001

Table 3.2 Positive isolates on DNS in auction market and ranch raised calves for each of the BRD pathogens; *M. haemolytica, P. multocida and H. somni,* both on arrival at the feedlot (first test) and later on in the feeding period (second test), looking at matched pairs only.

M. haemolytica results	**Positive M. haemolytica isolates on 1st Test (%)**	**Positive M. haemolytica isolates on 2nd Test (%)**	**P-value**
Auction Market Calves (n=217)	37.8%	20.3%	<0.001
Ranch Raised Calves (n=279)	29.4%	20.4%	0.01
P. multocida results	**Positive P. multocida isolates on 1st Test (%)**	**Positive P. multocida isolates on 2nd Test (%)**	
Auction Market Calves (n=217)	30.9%	23.5%	0.08
Ranch Raised Calves (n=279)	60.0%	43.4%	<0.001
H. somni results	**Positive H. somni isolates on 1st Test (%)**	**Positive H. somni isolates on 2nd Test (%)**	
Auction Market Calves (n=217)	17.1%	30.4%	0.001
Ranch Raised Calves (n=279)	39.8%	6.1%	<0.001

Table 3.3 Prevalence of *M. haemolytica* isolates and calves matched (first test to second test) not sensitive to antimicrobials on arrival at the feedlot (first test) and later on in the feeding period (second test) (samples classified as intermediate or resistant are classified as not sensitive).

Auction Market Calves:	**M. haemolytica isolates not sensitive on 1st Test (%) (n=116)**	**M. haemolytica isolates not sensitive on 2nd Test (%) (n=44)**	**Prevalence of matched calves with M. haemolytica isolates not sensitive on 1st Test (%) (n=217)**	**Prevalence of matched calves with M. haemolytica isolates not sensitive on 2nd Test (%) (n=217)**	**P-value for matched calves**
Ampicillin	0%	0%	0%	0%	-
Ceftiofur	0%	0%	0%	0%	-
Chlortetracycline	1.7%	11.4%	0.9%	2.3%	0.45
Danofloxacin	0%	0%	0%	0%	-
Enrofloxacin	0%	0%	0%	0%	-
Florfenicol	0%	0%	0%	0%	-
Gentamycin	0%	0%	0%	0%	-
Neomycin	26.7%	52.3%	12.0%	10.6%	0.76
Oxytetracycline	26.7%	52.3%	10.6%	10.6%	1.00
Penicillin	1.7%	2.3%	0%	0.5%	1.00
Spectinomycin	0%	0%	0%	0%	-
Tilmicosin	27.6%	50%	11.1%	10.1%	0.88
Trimethoprim/Sulfa	0%	0%	0%	0%	-
Tulathromycin	4.3%	36.4%	1.4%	7.4%	0.04
Ranch Raised Calves:	**M. haemolytica Isolates Not Sensitive on 1st Test (%) (n=79)**	**M. haemolytica Isolates Not Sensitive on 2nd Test (%) (n=57)**	**Prevalence of Calves with M. haemolytica Isolates Not Sensitive on 1st Test (%) (n=279)**	**Prevalence of Calves with M. haemolytica Isolates Not Sensitive on 2nd Test (%) (n=279)**	**P-value for matched calves**
Ampicillin	0%	0%	0%	0%	-
Ceftiofur	0%	0%	0%	0%	-
Chlortetracycline	5.1%	5.3%	1.4%	1.1%	1.00
Danofloxacin	0%	0%	0%	0%	-
Enrofloxacin	1.3%	0%	0.4%	0%	1.00
Florfenicol	0%	0%	0%	0%	-
Gentamycin	0%	0%	0%	0%	-
Neomycin	22.8%	10.5%	6.5%	2.2%	0.02
Oxytetracycline	20.3%	1.8%	5.7%	0.4%	<0.001
Penicillin	0%	8.8%	0%	1.8%	0.06
Spectinomycin	1.3%	0%	0.4%	0%	1.00
Tilmicosin	19.0%	0%	5.4%	0%	<0.001
Trimethoprim/Sulfa	0%	0%	0%	0%	-
Tulathromycin	19.0%	0%	5.4%	0%	<0.001

Table 3.4 Prevalence of *P. multocida* isolates and calves matched (first test to second test) not sensitive to antimicrobials on arrival at the feedlot (first test) and later on in the feeding period (second test) (samples classified as intermediate or resistant are classified as not sensitive).

Auction Market Calves:	**P. multocida isolates not sensitive on 1st Test (%) (n=82)**	**P. multocida isolates not sensitive on 2nd Test (%) (n=51)**	**Prevalence of matched calves with P. multocida isolates not sensitive on 1st Test (%) (n=217)**	**Prevalence of matched calves with P. multocida isolates not sensitive on 2nd Test (%) (n=217)**	**P-value for matched calves**
Ampicillin	1.2%	5.9%	0.5%	1.4%	0.63
Ceftiofur	0%	0%	0%	0%	-
Chlortetracycline	0%	0%	0%	0%	-
Danofloxacin	0%	0%	0%	0%	-
Enrofloxacin	0%	0%	0%	0%	-
Florfenicol	0%	11.8%	0%	2.8%	0.03
Gentamycin	17.1%	5.9%	4.2%	1.4%	0.15
Neomycin	84.2%	88.2%	24.9%	20.7%	0.33
Oxytetracycline	1.2%	15.7%	0.5%	3.7%	0.04
Penicillin	0%	0%	0%	0%	-
Spectinomycin	1.2%	17.7%	0.5%	4.2%	0.03
Tilmicosin	6.1%	17.7%	2.3%	4.2%	0.39
Trimethoprim/Sulfa	0%	0%	0%	0%	-
Tulathromycin	0%	13.7%	0%	3.2%	0.01
Ranch Raised Calves:	**P. multocida isolates Not Sensitive on 1st Test (%) (n=176)**	**P. multocida isolates Not Sensitive on 2nd Test (%) (n=121)**	**Prevalence of calves with P. multocida isolates Not Sensitive on 1st Test (%) (n=279)**	**Prevalence of calves with P. multocida isolates Not Sensitive on 2nd Test (%) (n=279)**	**P-value for matched calves**
Ampicillin	0.6%	0%	0.4%	0%	1.00
Ceftiofur	0%	0%	0%	0%	-
Chlortetracycline	1.1%	11.6%	0.4%	5.0%	0.001
Danofloxacin	0.6%	0.8%	0.4%	0.4%	1.00
Enrofloxacin	0%	0.8%	0%	0.4%	1.00
Florfenicol	1.7%	20.7%	0.4%	9.0%	<0.001
Gentamycin	15.9%	5.8%	9.7%	2.5%	<0.001
Neomycin	93.2%	89.3%	53.8%	38.7%	<0.001
Oxytetracycline	1.7%	23.1%	0.4%	10.0%	<0.001
Penicillin	0%	0%	0%	0%	-
Spectinomycin	1.7%	20.7%	0.4%	9.0%	<0.001
Tilmicosin	4.0%	33.1%	1.8%	14.3%	<0.001
Trimethoprim/Sulfa	0%	0%	0%	0%	-
Tulathromycin	1.7%	22.3%	0.4%	9.7%	<0.001

Table 3.5 Prevalence of *H. somni* isolates and calves not sensitive to antimicrobials on arrival at the feedlot (first test) and later on in the feeding period (second test) (samples classified as intermediate or resistant are classified as not sensitive).

Auction Market Calves:	**H. somni isolates Not Sensitive on 1st Test (%) (n=44)**	**H. somni isolates Not Sensitive on 2nd Test (%) (n=66)**	**Prevalence of calves with H. somni isolates Not Sensitive on 1st Test (%) (n=217)**	**Prevalence of calves with H. somni isolates Not Sensitive on 2nd Test (%) (n=217)**	**P-value**
Ampicillin	2.3%	1.5%	0.5%	0.5%	1.00
Ceftiofur	0%	0%	0%	0%	-
Chlortetracycline	0%	0%	0%	0%	-
Danofloxacin	0%	0%	0%	0%	-
Enrofloxacin	0%	0%	0%	0%	-
Florfenicol	0%	0%	0%	0%	-
Gentamycin	38.6%	54.6%	6.0%	16.6%	<0.001
Neomycin	86.4%	89.4%	14.3%	27.2%	<0.001
Oxytetracycline	0%	37.9%	0%	11.5%	<0.001
Penicillin	2.3%	1.5%	0.5%	0.5%	1.00
Spectinomycin	0%	6.1%	0%	1.8%	0.13
Tilmicosin	0%	31.8%	0%	9.7%	<0.001
Trimethoprim/Sulfa	4.6%	3.0%	0.9%	0.9%	1.00
Tulathromycin	0%	30.3%	0%	9.2%	<0.001
Ranch Raised Calves:	**H. somni isolates Not Sensitive on 1st Test (%) (n=102)**	**H. somni isolates Not Sensitive on 2nd Test (%) (n=17)**	**Prevalence of calves with H. somni isolates Not Sensitive on 1st Test (%) (n=279)**	**Prevalence of calves with H. somni isolates Not Sensitive on 2nd Test (%) (n=279)**	**P-value**
Ampicillin	0%	0%	0%	0%	-
Ceftiofur	0%	0%	0%	0%	-
Chlortetracycline	0%	0%	0%	0%	-
Danofloxacin	0%	0%	0%	0%	-
Enrofloxacin	0%	0%	0%	0%	-
Florfenicol	0%	0%	0%	0%	-
Gentamycin	30.4%	17.7%	10.8%	1.1%	<0.001
Neomycin	91.2%	100%	31.5%	6.1%	<0.001
Oxytetracycline	0%	11.8%	0%	0.7%	0.5
Penicillin	0%	0%	0%	0%	-
Spectinomycin	0%	0%	0%	0%	-
Tilmicosin	0%	11.8%	0%	0.7%	0.5
Trimethoprim/Sulfa	2.0%	0%	0.7%	0%	0.5
Tulathromycin	0%	11.8%	0%	0.7%	0.5

Table 3.6 Prevalence of *M. haemolytica* isolates and calves not sensitive to antimicrobials on arrival at the feedlot (first test) (samples classified as intermediate or resistant are classified as not sensitive).

	Auction market calves: prevalence of isolates not sensitive (%) (n=116)	**Ranch raised calves: prevalence of isolates not sensitive (%) (n=79)**	**P-value**	**Auction market calves: prevalence of calves not sensitive (%) (n=299)**	**Ranch raised calves: prevalence of calves not sensitive (%) (n=300)**	**P-value**
Ampicillin	0%	0%	-	0%	0%	-
Ceftiofur	0%	0%	-	0%	0%	-
Chlortetracycline	1.7%	5.1%	0.23	0.7%	1.3%	0.69
Danofloxacin	0%	0%	-	0%	0%	-
Enrofloxacin	0%	1.3%	0.41	0%	0.33%	1.00
Florfenicol	0%	0%	-	0%	0%	-
Gentamycin	0%	0%	-	0%	0%	-
Neomycin	26.7%	22.8%	0.62	10.4%	6.0%	0.05
Oxytetracycline	26.7%	20.25%	0.31	10.4%	5.3%	0.02
Penicillin	1.7%	0%	0.52	0.7%	0%	0.25
Spectinomycin	0%	1.3%	0.42	0%	0.3%	1.00
Tilmicosin	27.6%	19.0%	0.18	10.7%	5.0%	0.01
Trimethoprim/Sulfa	0%	0%	-	0%	0%	-
Tulathromycin	4.3%	19.0%	0.001	1.7%	5.0%	0.04

Table 3.7 Prevalence of *P. multocida* isolates and calves not sensitive to antimicrobials on arrival at the feedlot (first test) (samples classified as intermediate or resistant are classified as not sensitive).

	Auction market calves: prevalence of isolates not sensitive (%) (n=82)	**Ranch raised calves: prevalence of isolates not sensitive (%) (n=176)**	**P-value**	**Auction market calves: prevalence of calves not sensitive (%) (n=299)**	**Ranch raised calves: prevalence of calves not sensitive (%) (n=300)**	**P-value**
Ampicillin	1.2%	0.6%	0.535	0.3%	0.3%	1.00
Ceftiofur	0%	0%	-	0%	0%	-
Chlortetracycline	0%	1.1%	1.00	0%	0.7%	0.50
Danofloxacin	0%	0.6%	1.00	0%	0.3%	1.00
Enrofloxacin	0%	0%	-	0%	0%	-
Florfenicol	0%	1.7%	0.554	0%	1.0%	0.25
Gentamycin	17.1%	15.9%	0.857	4.7%	9.3%	0.04
Neomycin	84.2%	93.2%	0.039	23.1%	54.7%	<0.001
Oxytetracycline	1.2%	1.7%	1.00	0.3%	1.0%	0.62

Penicillin	0%	0%	-	0%	0%	-
Spectinomycin	1.2%	1.7%	1.00	0.3%	1.0%	0.62
Tilmicosin	6.1%	4.0%	0.528	1.7%	2.3%	0.77
Trimethoprim/Sulfa	0%	0%	-	0%	0%	-
Tulathromycin	0%	1.7%	0.554	0%	1.0%	0.25

Table 3.8 Prevalence of *H. somni* isolates and calves not sensitive to antimicrobials on arrival at the feedlot (first test) (samples classified as intermediate or resistant are classified as not sensitive).

	Auction market calves: prevalence of isolates not sensitive (%) (n=43)	**Ranch raised calves: prevalence of isolates not sensitive (%) (n=102)**	**P-value**	**Auction market calves: prevalence of calves not sensitive (%) (n=299)**	**Ranch raised calves: prevalence of calves not sensitive (%) (n=300)**	**P-value**
Ampicillin	2.3%	0%	0.297	0.3%	0%	0.50
Ceftiofur	0%	0%	-	0%	0%	-
Chlortetracycline	0%	0%	-	0%	0%	-
Danofloxacin	0%	0%	-	0%	0%	-
Enrofloxacin	0%	0%	-	0%	0%	-
Florfenicol	0%	0%	-	0%	0%	-
Gentamycin	39.5%	30.4%	0.335	5.7%	10.3%	0.05
Neomycin	86.1%	91.2%	0.378	12.4%	31.0%	<0.001
Oxytetracycline	0%	0%	-	0%	0%	-
Penicillin	2.3%	0%	0.297	0.3%	0%	0.50
Spectinomycin	0%	0%	-	0%	0%	-
Tilmicosin	0%	0%	-	0%	0%	-
Trimethoprim/Sulfa	4.7%	2.0%	0.582	0.7%	0.7%	1.00
Tulathromycin	0%	0%	-	0%	0%	-

Table 3.9 Comparison of health outcomes (treatment for BRD and crude mortality) in auction market derived and ranch raised calves.

Health Variable	**Experimental Group**		**RR (95% CI)**	**P-Value**
	Auction Derived	**Ranch Raised**		
No. of Animals – First Test	299	300		
Treatment for BRD, %	14.4	9.0	1.6 (1.0-2.5)	0.043
Crude Mortality, %	3.3	1.7	2.0 (0.7-5.8)	0.204

Table 3.10 Cattle that had been treated for Bovine Respiratory Disease had the following significant outcomes, where the interaction between source of cattle (auction market vs ranch) and treatment for BRD was not significant.

Outcome	Odds Ratio	95% Confidence Intervals		P-value
		Lower	Upper	
P. multocida resistant to spectinomycin on 2nd test	3.09	1.09	8.75	0.034
P. multocida resistant to tilmicosin on 2nd test	3.27	1.17	9.13	0.024
H. somni resistant to oxytetracycline on 2nd test	3.95	1.13	13.8	0.032
H. somni resistant to tilmicosin on 2nd test	5.33	1.51	18.8	0.009
H. somni resistant to tulathromycin on 2nd test	3.86	1.12	13.2	0.032

Table 3.11 Cattle that had been treated for Bovine Respiratory Disease had the following significant outcomes, where the interaction between source of cattle (auction market vs ranch) and treatment for BRD was significant.

Outcome	Odds Ratio	95% Confidence Intervals		P-value
		Lower	Upper	
P. multocida resistant to florfenicol on 2nd test				
Treated auction calves vs untreated auction calves	28.0	3.56	220	0.002
Treated ranch calves vs untreated ranch calves	1.50	0.37	6.12	0.572
P. multocida resistant to oxytetracycline on 2nd test				
Treated auction calves vs untreated auction calves	13.3	2.17	81.9	0.005
Treated ranch calves vs untreated ranch calves	1.28	0.31	5.17	0.734
P. multocida resistant to tulathromycin on 2nd test				
Treated auction calves vs untreated auction calves	18.2	2.72	122	0.003
Treated ranch calves vs untreated ranch calves	1.34	0.33	5.46	0.680

Chapter 4

Objective, discussion, general conclusions and future research

4.1 Objectives

The overarching aim of this thesis was to better understand ways to prevent disease in cattle by looking at how biosecurity and cattle mixing impact health outcomes. In order to achieve this aim, two separate studies were conducted. The first, chapter 2, was a survey of biosecurity practices of beef cow-calf producers in western Canada. The survey looked at common biosecurity practices of cow-calf producers and the associations between those practices and common diseases that are a concern for producers, and the upstream owners of the calves such as feedlot operators. The purpose of this was to help inform the cow-calf industry about the biosecurity measures that are currently being used that are having a negative effect on animal health. At the same time there is acknowledgment that total exclusion of pathogens is impossible in the beef sector. The second study, chapter 3, looked at how the source of cattle impacts both the prevalence and antimicrobial resistance of the common BRD pathogens *M. haemolytica, P. multocida,* and *H. somni.* As well, this study looked at treatment for BRD and mortality and their association with the prevalence and antimicrobial resistance of these BRD pathogens. The purpose of this second study was to better understand how the source of purchased cattle can affect the types of BRD pathogens that are seen in the feedlot and the impact this has on morbidity and mortality in the feedlot. Again, the aim of this study was to identify ways to reduce BRD, such as by changing source and reducing commingling of cattle.

4.2 Discussion

There have been many studies done around the world looking at the topic of biosecurity, in both the beef cattle industry and in other areas of animal agriculture. However, there has not been any done in Canada looking specifically at beef cattle. Chapter 2 found that many of the standard biosecurity practices that would be common in the swine and poultry sectors are not commonly practiced in the Canadian beef industry. Only 30% of producers kept new additions separate from the main herd and 30% vaccinated new additions. Mixing of cattle was common with 30% of producers using community pastures for grazing. These results are similar to results found in many other countries[11,12,15,20]. This would lead us to believe that biosecurity in beef cattle is impacted by how they are raised, the fact they graze pastures extensively, and that they are marketed and moved from farm-to-farm throughout their life. These characteristics of the beef industry appear to be part of the beef production system the world over.

Chapter 2 also showed the significance of purchasing adult cattle in the spread of BRD and calf diarrhea. We expected to find that cow-calf herds primarily have problems with BRD when they purchase feeder cattle, which often have BRD, and problems with calf diarrhea when purchasing foster calves, which often have diarrhea due to failure transfer of passive immunity. Instead, the purchase of cows and bulls was shown to be significantly associated with these diseases. The other association identified was with community pasture. There have been other studies that have also shown that community pasture is associated with the spread of cattle disease[54,120]. Finally, not vaccinating new arrivals was associated with BRD outbreaks.

Vaccination of cattle has been shown many times to reduce BRD[70,71,133,149], so we would expect that not vaccinating would increase the occurrence of BRD outbreaks.

A limitation of the study in Chapter 2 is that as it is a cross-sectional survey so we can only establish associations, not causation. Further research, such as using a case-control study or clinical trial, would be required to try and establish causation of practices such as the purchase of cows and use of community pasture. Another limitation is that in looking at only 81 producers across western Canada, there is the potential that those producers are not representative of the industry as a whole. However, this study does provide a good basis for biosecurity practices in cow-calf herds in western Canada, as well as providing some areas where improvements can be made to reduce disease.

Most studies on antimicrobial resistance have looked at cattle that are sick or have died due to BRD[90,93,97]. More recently, there have been studies looking at antimicrobial resistance on arrival and later on in the feeding period in groups of cattle regardless of disease state[135,136,141]. However, those studies have been on auction market cattle, not single source or ranch raised cattle. Chapter 3 looked at the prevalence of BRD pathogens and antimicrobial resistance comparing cattle that have been mixed (auction market cattle) to cattle from a single source. Overall, the prevalence of BRD pathogens isolated in this study was high when compared to other studies. Interestingly, the RANCH cattle had higher prevalence of both *P. multocida* and *H. somni* on arrival than the AUCT cattle, but lower prevalence of *M. haemolytica.* All of the RANCH cattle came from a single source, so it is not clear if the high prevalence of *P. multocida*

and *H. somni* is unique to the cattle of this ranch or if this is something that is common when cattle are not mixed. Stroebel et al. showed that 24 hours in an auction mart does not increase the rates of these respiratory pathogens being cultured in calves and that the BRD pathogens are not very transmissible between calves[142]. Because the calves from this herd had not been exposed to other cattle prior to sampling, we would assume transmission of the BRD pathogens was from the adult cows and bulls in the herd. This provides an interesting connection with Chapter 2, where the study demonstrated that introducing adult cows and bulls increased the odds of having a BRD outbreak in a herd. An area of further study would be to better understand how these pathogens transmit from the cows to the calves, as well as possible ways to decrease that transmission to reduce BRD pathogens in those calves.

Chapter 3 also agreed with a trend seen in other studies showing increasing antimicrobial resistance in recent years[90,97,135,136,141]. The study added to that knowledge by showing some differences between auction market calves and single source calves. One interesting finding was that the RANCH calves had substantial levels of resistance to oxytetracycline, tilmicosin, and tulathromycin in *M. haemolytica* on arrival. Because we know the herd the RANCH calves came from, we can be reasonably certain that these calves had not been treated with antimicrobials prior to this testing. This demonstrates that resistant *M. haemolytica* can transmit to calves and does not require exposure to antimicrobials for that resistance to develop. This is an area where further research could study how that transmission occurs and investigate methods to prevent that transmission. In both the AUCT calves and RANCH calves, antimicrobial resistance increased from the first to the second test. The only exception was

with *M. haemolytica* in the RANCH calves, where the amount of antimicrobial resistance decreased significantly over the feeding period. The AUCT calves showed an increase in antimicrobial resistance. This is an area for further research to see if this repeatable, and if so, to investigate the mechanism. These results also highlight another potential limitation of the study, which is the difference in time between the first and second samples in the AUCT calves and the RANCH calves. With the RANCH calves being sampled at an average of 153 days on feed versus 76 days for the AUCT calves this may explain some of the difference in antimicrobial resistance patterns.

Another finding in Chapter 3 was that isolation of *M. haemolytica* on arrival did not appear to be associated with treatment for BRD; however, isolation of *H. somni* on arrival was associated with a decreased odds of requiring treatment for BRD. This research does seem to show that the type of BRD pathogens isolated impacts subsequent odds of treatment. This is an area of further research. Understanding what types of bacteria increase or decrease the odds of treatment could lead to an intervention or even methods to alter the microbiome to reduce BRD.

Finally, Chapter 3 showed that treatment for BRD was associated with antimicrobial resistance in *P. multocida* and *H. somni,* but not in *M. haemolytica.* An area of further research would be to investigate why there is a difference between the BRD pathogens. The odds of resistance to florfenicol, oxytetracycline, and tulathromycin were much higher in treated AUCT calves than

RANCH calves. This may be due to previous exposure to these antimicrobials, although further investigation into why this would be the case is needed.

4.3 General Conclusions

The two studies helped answer some important questions for the beef industry. Chapter 2 underlined the importance of caution when introducing new adult animals into a herd, such as breeding cows and bulls, and the risks posed by these introductions to the health of young calves. It also showed that communal grazing practices increases the risk of disease in young calves. Chapter 3 demonstrated that in AUCT calves the prevalence of *M. haemolytica* decreased over the feeding period and *H. somni* increased. In RANCH calves, the prevalence of *M. haemolytica, P. multocida,* and *H. somni* all decreased over the feeding period. Generally, there was an increase in resistant isolates over the feeding period, but surprisingly, there was a decrease in *M. haemolytica* isolates that were resistant to oxytetracycline, tilmicosin and tulathromycin. The source of calves affected the prevalence of BRD pathogens cultured on arrival – the prevalence of *M. haemolytica* was higher in AUCT calves and the prevalence of *P. multocida* and *H. somni* was higher in RANCH calves. The odds of a calf having *P. multocida* and *H. somni* resistant to multiple antibiotics was higher if they had been treated. This study demonstrated the importance of reducing commingling in cattle when we are looking for ways to reduce disease transmission.

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Appendix

Western Canadian Cow-Calf Surveillance Network
Survey 12 Biosecurity Practices in Cow-Calf Herds

THIS QUESTIONNAIRE IS PART OF THE RESEARCH FOR THE BCRC- FUNDED DISEASE SURVEILLANCE NETWORK.

Your participation is voluntary. All of your responses will be kept confidential. Return of our questionnaire by mail, will indicate your consent to participate in the survey and have your responses summarized in the final report.

- **Please answer each question in the questionnaire.**
- **Please add any comments you may wish to make at the end of the questionnaire.**
- **Please return the questionnaire in the provided stamped envelope.**
- **Pages have questions both sides**
- **Please send back each page of the questionnaire**
- **Answer each question as best as you can. If something else should have been asked or included, please write us a note to explain.**

Please enter your name: _____

If you have any questions regarding the questionnaire, feel free to call:

Dr. Trent Wennekamp; (780) 808-0099

Or e-mail twennekamp@lah.ca

Western Canadian Cow-Calf Surveillance Network
Survey 12 Biosecurity Practices in Cow-Calf Herds

For all of the following questions:

*Please do **not** leave blank spaces. **Enter** zero if no animals in that category (or not applicable if the question does not apply to you or not answered if you choose not to answer.)*

Please answer questions looking back over the previous 3 years.

Biosecurity is: Those practices that prevent disease from entering, spreading or being released from livestock operations.

This survey is concerned with how disease may enter into or come out of your cow calf operation, and the effect those diseases may have on your herd.

1. Current inventory: How many of each type of animal do you have in your herd currently?

Number of BULLS _____

Number of MATURE COWS (Over 2 Years Old) _____

Number of REPLACEMENT HEIFERS (Under 2 Years Old) _____

Number of CALVES (Under 6 months of age) _____

Number of FEEDER CALVES _____

(Heifers or Steers over 6 months on feed or grass)

Table A.1 Other Animals on the Farm: Please circle yes or no if you have other animals on the farm. Also, please give us the number of other animals, and if they have contact with your Beef Cattle. (Contact would be fence line contact, or mingling with the cattle).

	Animals on farm?	If Yes, How many?	Contact with Cattle?
Dairy Cattle	YES or NO		YES or NO
Horses	YES or NO		YES or NO
Goats	YES or NO		YES or NO
Sheep	YES or NO		YES or NO
Elk	YES or NO		YES or NO
Bison	YES or NO		YES or NO
Other? (please list)			
_____	YES or NO	_____	YES or NO
_____	YES or NO	_____	YES or NO

2. ***Purchased Animals: Please look back over the last 3 years (since 2014) as well as 2017 and tell us how many head of each animal type you purchased or added into your cow calf herd.***

Under each year please fill in approximately the number of animals of each type you have added into the herd:

For example, the table below shows that in each year over the last 3 years as well as this year Producer A purchased 5 bulls and 30 mature cows:

	2017	**2016**	**2015**	**2014**
Bulls	5	5	5	5
Mature Cows	30	30	30	30

Table A.2

	2017	**2016**	**2015**	**2014**
Bulls				
Mature Cows (Over 2 Years Old)				
Heifers (4 months to 2 Years Old)				
Foster Calves (Under 30 days Old)				
Feeder Calves / Backgrounding /Grass Calves (Heifers and Steers)				
Other (please describe) _____				

3. ***Please list in the table below the number of animals from each source which you PURCHASED cattle in the last 12 months.***

For example, in the table below Producer A purchased 5 bulls: 3 from a local purebred breeder and 2 from a bull sale. As well, he bought 30 mature cows: 20 from a sale at the auction market and 10 from a neighbor's farm.

	Auction Market	Another Farm	Sale (ie. Bull Sale)
Bulls	0	3	2
Mature Cows	20	10	0

Table A.3:

	Auction Market	Another Farm	Sale (ie. Bull Sale)
Bulls			
Mature Cows (Over 2 Years Old)			
Heifers (4 months to 2 Years Old)			
Foster Calves (Under 30 days Old)			
Feeder Calves / Backgrounding /Grass Calves (Heifers and Steers)			
Other (Please Describe) _____			

4. ***Please list in the table below the number of animals to each source you SOLD cattle in the last 12 months.***

For example, last fall Producer A sold 20 replacement heifers to a neighbor. He also sold 50 feeder heifers at the auction market.

	Auction Market	Another Farm	Sale (ie. Bull Sale)
Replacement Heifers (Under 2 Years Old)	0	20	0
Foster Calves (Under 30 Days Old)	0	0	0
Feeder Heifers	50	0	0

Table A.4:

	Auction Market	Another Farm	Sale (ie. Bull Sale)
Bulls			
Mature Cows (Over 2 Years Old)			
Replacement Heifers (Under 2 Years Old)			
Foster Calves (Under 30 Days Old)			
Feeder Heifers			
Feeder Steers			

5. ***When you purchase or add new animals to the herd, do you keep them separate from the rest of herd for a period of time?***

☐**Yes. For how long? _____**

☐ **No**

☐ **Under certain circumstances. Please elaborate:**

_____

_____

6. ***When you purchase or add new animals to the herd, do you vaccinate them for any diseases prior to adding them to the herd?***

☐ **Yes. What vaccine(s) do you give them? _____**

☐ **No**

7. ***If you indicated above that you have purchased calves to feed in the last 3 years, describe the contact that these calves have with the cow herd (Select the highest level of contact even if it is for a brief part of the time period) (please select ONE)***

☐ **Commingle**

☐ **Fence line contact**

☐ **Same farm but no contact**

☐ **Fed on different farm**

☐ **Other (please describe) _____**

8. ***Do you ask about disease history when you are buying cattle? For example, do you ask if a farm has had a history of Johne's disease prior to buying replacement heifers? (please select ONE)***

☐**Yes. What diseases do you inquire about?** _____

☐ **No**

☐ **Under certain circumstances. Please elaborate:**

_____

_____

9. ***Do you ask about vaccination history when you are buying cattle? (please select ONE)***

☐**Yes**

☐ **No**

☐ **Under certain circumstances. Please elaborate:**

_____

_____

10. ***Have you done any custom feeding on your farm in the last 3 years? (please select ONE)***

☐**Yes** ☐ **No**

11. ***Have you done any custom calving on your farm in the last 3 years? (please select ONE)***

☐**Yes** ☐ **No**

Commingling: Please answer the following questions on how your cattle mix with other cattle:

12. ***Are you using a community pasture for summer grazing in the 2017 grazing season? (please select ONE)***

☐**Yes** ☐ **No**

If YES please answer the next two questions

13. How many of each animal type do you send to community pasture?

Number of BULLS _____

Number of COWS _____

Number of REPLACEMENT HEIFERS _____

Number of CALVES _____

14. What will be the total number of other herds that your herd was exposed to during communal grazing in 2017?

_____ ___ Enter number of herds (If you're not sure, just give an approximate number.)

15. ***Have you, or will you, take some of your cattle to shows during the 2017 year? (please select ONE)***

☐**Yes** ☐ **No**

If YES please answer the next two questions

16. How many shows do you go to in an average year?

_____ ___ Enter number of shows

17. ***Have you ever had to treat an animal (i.e. for pneumonia) that was taken to a show? (please select ONE)***

☐**Yes** ☐ **No**

18. ***Did you have a bull sale on your farm in 2017? (please select ONE)***

☐**Yes** ☐ **No**

19. ***If yes, do other producers sell bulls in your sale? (Please select ONE)***

☐ **Yes. How many other producers sell bulls in your sale? _____**

☐ **No**

☐ **Not Applicable**

20. ***Have you leased bulls or shared bulls during a single breeding season from another producer in the last 3 years? (please select ONE)***

☐**Yes** ☐ **No**

Managing People, Equipment and Vehicles.

21. ***Do you restrict the access of people from other farms to your cattle? (please select ONE)***

☐**Yes**

☐ **No**

☐ **Under certain circumstances. Please elaborate:**

_____

_____

22. ***Have you had anyone from a country other than Canada visit your farm in the last year? (Please select ONE)***

☐ **Yes. What countries?** _____

☐ **No**

23. ***Do you use the same equipment (i.e. tractor, front end loader) for manure handling and feeding cattle? (please select ONE)***

☐**Yes** ☐ **No**

24. ***If yes, do you clean and disinfect your front end loader after handling manure? (please select ONE)***

☐**Yes** ☐ **No** ☐ **Not Applicable**

25. ***How often are the following items cleaned and/or disinfected on your farm? (Please check ONE column for each item)***

Table A.5

	With Every Use	Every 2-3 Uses	Every 4-6 Uses	Once per Year	Never	Item Not Used
Cattle Trailer						
Calving Tools (ie. Chains, jack)						
Boots						
Clothing						
Tube Feeder for Calves						
All Terrain Vehicle						
Veterinary Supplies (ie. Multi-use Syringes)						
Calving Barn						
Front End Loader / Tractor						

Managing Animal Health Practices.

26. ***Do you have a working relationship with a veterinarian or veterinary practice? (Please select ONE)***

☐ **Yes. How many times per year does your veterinarian visit your farm? _____**

☐**No**

27. ***What services does your veterinarian typically provide to you in a year? (Please select ALL THAT APPLY)***

- ☐ **Pregnancy diagnosis**
- ☐ **Bull testing**
- ☐ **Body condition scoring**
- ☐ **Routine post mortems of dead animals**
- ☐ **Trichomoniasis testing of bulls**
- ☐ **Treatment of sick animals when necessary**
- ☐ **Assisting with calving difficulty: C-section/Hard Pulls**
- ☐ **Advice regarding vaccines**
- ☐ **Treatment advice**
- ☐ **Biosecurity advice**
- ☐ **Disease prevention advice**
- ☐ **Written vaccine protocols or standard operating procedures**
- ☐ **Written treatment protocols or standard operating procedures**
- ☐ **Written biosecurity protocols or standard operating procedures**
- ☐ **Assistance with Quality Assurance Programs**
- ☐ **Marketing advice**
- ☐ **Staff, employee or family member training**
- ☐ **Feed analysis or ration formulation**
- ☐ **Advice regarding nutrition**
- ☐ **Testing for other infectious diseases (e.g. Johnes, BVD, etc.)**

Biosecurity Within Your Herd

Please answer the following questions based on the following scenarios:

28. "One day in early June after the cows have gone to summer pasture, you find a cow that had her third calf that year is looking much thinner than the other cows. She looks like she may have had some diarrhea as well. You have had Johne's disease in your herd in the past and you suspect this cow may have Johne's." What do you do? (Please check those that apply)

☐ **Separate the cow from the rest of the herd and observe**

☐ **Remove calf to put on another cow and cull the sick cow.**

☐ **Leave as is until fall and cull cow at that time.**

☐ **Ensure calf is recorded and is NOT kept in herd as a replacement.**

☐ **Do nothing and see how cow progresses.**

☐ **Make a plan to remove Johne's in your herd with your veterinarian.**

29. "You find a 2 week old calf in the calving area with severe diarrhea (scours). The calf is able to stand and suck, but is definitely weakened." What do you do? (Please check those that apply)

☐ **Bring the cow and calf into the barn to treat the calf.**

☐ **Treat calf out in calving area and leave the calf there.**

☐ **Separate cow and calf from herd for at least a few days.**

☐ **Clean and disinfect anything the calf touched (tube feeder, etc)**

Disease Within Your Herd

30. Have you had to treat an animal in your herd for the following diseases in the last 5 years?
How many OUTBREAKS of the following infectious disease have you had your herd in the last 5 years?
For this survey we will define an OUTBREAK as a situation where you had to treat at least 10% of the group, or at least 10% were affected. For example, last spring you treated 5 out of 50 calves for calf scours = an outbreak.

Table A.6

Disease	Treated Animal for this disease in last 5 years? (Please circle ONE)	Had an Outbreak in last 5 years? (Please circle ONE)	How many Outbreaks?
Shipping Fever/Pneumonia	YES or NO	YES or NO	
Scours / Calf diarrhea	YES or NO	YES or NO	
Coccidiosis	YES or NO	YES or NO	
Infectious Bovine Rhinotracheitis (IBR)	YES or NO	YES or NO	
Bovine Viral Diarrhea (BVD)	YES or NO	YES or NO	
Pinkeye	YES or NO	YES or NO	
Footrot	YES or NO	YES or NO	
Trichomoniasis	YES or NO	YES or NO	
Vibriosis	YES or NO	YES or NO	

31. ***Have you had 5% or more of your herd abort their calves in a single calving season in the last 5 years? (Please select ONE)***

☐ **Yes** ☐**No**

If YES please answer the next two questions

32. How many times has this occurred in the past 5 years?

_____ ___ Enter number of times

33. What was the cause of the abortion, if it was diagnosed?

_____

_____

34. ***Have you had Johne's Disease diagnosed in your herd? (Please select ONE)***

☐ **Yes** ☐**No**

Please RANK the following options in the order that best represents your management practices.

Leave those you don't consider blank. (1 is the highest rank, i.e. the most important)

35. Rank all of the following factors that you would typically consider when deciding what ANTIMICROBIALS to use on your operation.

____ **Microbial cost**

____ **Historical effectiveness**

____ **Convenience (1 dose vs multiple doses)**

____ **Route of administration (SC, IM, in feed, oral bolus, other)**

____ **Withdrawal time**

____ **Written treatment protocol from veterinarian**

____ **Advertising or information from other information sources**

____ **Advice from another producer**

____ **Other (Please specify): _____**

____ **Not applicable – I don't use antimicrobials**

Do you have any other questions or comments that you would like to share with us?

Thank you so much for taking the time to complete this survey.
Your responses will provide valuable information to the
Canadian beef industry!