NUTRITIONAL AND MANAGEMENT STRATEGIES FOR HIGH-RISK BEEF CALVES DURING THE RECEIVING PERIOD

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NUTRITIONAL AND MANAGEMENT STRATEGIES

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Abstract: Crossbred beef steers (n = 605; initial BW = 255 ± 8.3 kg) were randomly assigned to 1 of 2 treatments upon arrival to the feedlot. Steers were either administered metaphylactic antimicrobial treatment at arrival (MET) or received no antimicrobial treatment (CON). No differences in BW existed between CON and MET steers throughout the experiment ($P \geq 0.44$). Average daily gain was greater ($P < 0.01$) for MET steers than for CON steers from d 0 to 14. Performance and hematological differences were evaluated within CON steers that were either treated (TRT) or not treated (NTRT) for BRD. Body weight was consistently greater ($P < 0.02$) for NTRT steers compared to TRT steers; however, no differences ($P \geq 0.12$) in ADG were detected. Neutrophil counts tended ($P = 0.08$) to be greater for NTRT steers than for TRT steers, but no further differences ($P \geq 0.16$) in leukocyte concentrations existed. Treated CON steers had lower ($P \leq 0.05$) hematocrits, hemoglobin, and mean corpuscular hemoglobin than NTRT steers. In Exp. 2, newly received heifers (n = 557; initial BW = 230 ± 33 kg) were randomly allocated to diets containing 15% roughage (R15), 30% roughage (R30), or 45% roughage (R45). Heifer BW decreased linearly ($P \leq 0.01$) with decreasing roughage inclusion after d 28 of the experiment. There was a linear decrease ($P \leq 0.01$) in ADG as roughage concentration increased. Dry matter intake increased linearly ($P \leq 0.01$) and G:F linearly decreased ($P \leq 0.04$) as dietary roughage concentration increased. No responses (L, $P \geq 0.44$; Q, $P \geq 0.11$) were detected for overall BRD treatment or other clinical measures. Roughage concentration had no impact ($P \geq 0.11$) on serum metabolites. In Exp. 3, newly received heifers were randomly assigned to receive a nutrient-rich bolus at processing (BOL) or received an empty gelatin bolus (CON). No differences ($P \geq 0.11$) in BW, ADG, DMI, G:F, or health outcome were detected between treatments. Glucose concentrations were greater ($P < 0.01$) for CON cattle on d 14; however, no further differences ($P \geq 0.20$) in metabolite concentrations were observed.

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LIST OF ABBREVIATIONS

ACTH	Adrenal cortex thyroid hormone
ADG	Average daily gain
APP	Acute phase proteins
BCv	Bovine coronavirus
BHv-1	Bovine herpes virus
BRD	Bovine Respiratory Disease
BRSv	Bovine respiratory syncytial virus
BUN	Blood urea nitrogen
BVDv	Bovine viral diarrhea virus
BW	Body weight
CBC	Complete blood count
CS	Covariance structure
DFM	Direct-fed microbial
DMI	Dry matter intake
DOF	Days on feed
EBW	Empty body weight
G:F	Gain to feed ratio
HCW	Hot carcass weight
HPA	Hypothalamic-pituitary-adrenal-axis
HS	*Histophilus somni*
IBR	Infectious bovine rhinotracheitis virus
IFN- ɣ	Interferon- ɣ
IG	Immunoglobulin
IL	Interleukin

LPS	Lipopolysaccharide
MB	*Mycoplasma bovis*
MH	*Mannheimia haemolytica*
MHC	Major histocompatibility complex
MLV	Modified-live vaccine
NAHMS	National Animal Health Monitoring System
NEFA	Non-esterified fatty acid
NK	Natural killer
PAMP	Pathogen associated molecular patterns
peNDF	Physically effective neutral detergent fiber
PI	Persistently infected
PI-3	Parainfluenza-3 virus
PM	*Pasteurella multocida*
PTF	Probability of treatment failure
PUN	Plasma urea nitrogen
TH1	T-helper-1 cells
TH2	T-helper-2 cells
TM	Trace mineral
TNF- α	Tumor necrosis factor- α
VAST	Veterinary Antimicrobial Susceptibility Testing
VFD	Veterinary feed directive
WSBRC	Willard Sparks Beef Research Center
SS	Severity score
RBC	Red blood cell
WBC	White blood cell

CHAPTER I

INTRODUCTION

A continued area of interest among animal scientists has been to evaluate management strategies that reduce the incidence of bovine respiratory disease (BRD). Bovine respiratory disease continues to be the most frequent and costly disease among all beef cattle diseases. Carlos-Valdez et al. (2016) reported that approximately 75% of morbidity and over 50% of feedlot mortality is caused by BRD, and it has been reported that the majority of BRD occurs within the first 45 d following arrival (Sanderson et al., 2008). The National Animal Health Monitoring System (NAHMS) estimated that 16.2 % of all cattle placed in feedlots exhibit clinical signs of BRD during the feeding phase (NAHMS, 2013). Of the 16.2 % of cattle with BRD symptoms, NAHMS (2013) reported that 87.5 % of those animals were treated, which incurred direct treatment costs of $23.60 per BRD case. Moreover, the economic damages associated with BRD are estimated to exceed $3 billion globally (Watts and Sweeney, 2010). These economic losses can primarily be attributed to increased death loss, treatment costs, reductions in performance, and reduced carcass value (Ives and Richeson, 2015).

Bovine respiratory disease is a multi-factorial disease that generally involves

environmental and psychological stressors coupled with pathogenic viruses and bacteria that predispose cattle to infection (Taylor et al., 2010a; Carlos-Valdez et al., 2016). Furthermore, chronic infection can lead to further debilitation, decreased performance, and even mortality, which ultimately accentuates the importance of a strong, functioning, and responsive innate and adaptive immune response to immunological challenges (Ackermann et al., 2010). In brief, innate immunity is a non-self-recognition and non-specific immune response to foreign pathogens; whereas, adaptive immunity is the product of somatic diversification and selective clonal expression and can be further divided into the humoral immune response and the cellular immune response (Yuan et al., 2014). Together, the innate and adaptive immune responses work to decrease adherence, migration, and proliferation of pathogens in the host, while also mounting antibody responses against pathogenic organisms (Ives and Richeson, 2015).

The host's immune system is often compromised through stress-induced immunosuppression, which allows for viral pathogens and bacteria to proliferate in the respiratory tract to cause BRD. Lighter-weight calves purchased from sale barns appear to be at greatest risk for BRD (Taylor et al., 2010a). The NAHMS (2013) survey reported a mortality rate of 4 % for cattle weighing less than 317 kg that were treated for BRD. Death loss was reduced to 3.6 % in cattle treated once for BRD that were over 317 kg when placed into the feedlot. Cattle at high risk of developing BRD generally experience intense stressors from the time at which abrupt weaning process begins (Duff and Galyean, 2007) through the relocation and arrival process to the feedlot (Earley et al., 2007), which will be further described throughout the review of literature.

It has been suggested that one obstacle preventing the successful management of BRD is the segmented infrastructure of the beef industry (Ives and Richeson, 2015). Ives and Richeson (2015) further elaborate that the production phase commonly consists of calves changing ownership on multiple occasions, and the resulting commingling of calves from different sources and exposures

allow ample opportunities for pathogens associated with BRD to colonize the lower respiratory tract. Commingling, in combination with other stressors result in immunosuppression and subsequent BRD.

The use of preconditioning programs and metaphylaxis have been found throughout the literature to be effective in improving the health and overall economic value of calves while reducing feedlot morbidity and mortality (Ives and Richeson, 2015; Abell et al., 2017). Preconditioning programs are designed to increase the ability of the immune response to react to pathogens involved with BRD by the preparation for stressful events prior to being enrolled into the marketing process (Thrift and Thrift, 2011). A few common stressful events calves may experience include weaning, unfamiliarity with bunk feeding and feed ingredients, transport stress, commingling, arrival processing and castration, and environmental changes. The use of metaphylaxis upon arrival to the feedlot has consistently shown to reduce animal morbidity and mortality in stressed calves (Ives and Richeson, 2015). Metaphylaxis is implemented in many feedlots when calves arrive that have been subjected to many of the stressors previously listed. These stressed calves have a high risk of succumbing to BRD. The decision to administer a certain antimicrobial to groups of arriving cattle is dependent primarily on the efficacy and cost effectiveness of each antimicrobial (Abell et al., 2017).

Antimicrobial use in livestock production continues to face public scrutiny. This intense public scrutiny emanates from concern over the use of antimicrobials shared within humans and animals in feeding operations, antimicrobial resistance, and potential antimicrobial residuals in meat (Dennis et al., 2018). There has been an increase in effort over the past decade by both livestock producers and research scientists to promote the judicious use of antimicrobials, with specific emphasis in developing advanced biomarker detection systems to facilitate targeted identification of animals needing treatment, and non-antibiotic alternatives for those where treatment is indicated (Kayser et al, 2019; von Konigslow et al., 2019). Among the many biomarkers, bovine hematology may serve as a useful measure to aid in improving disease diagnosis and may serve as an indicator of future mortality or morbidity (von Konigslow et al., 2019). Rapid chute-side leukocyte differential

tests are currently a popular area of BRD research, as rapid tests allow antimicrobials to be selectively administered to animals based on objective hematology rather than a subjective decision to administer group metaphylaxis at arrival.

Nutritional implications on BRD in feedlot cattle have been heavily researched. Particularly, diet energy density and diet roughage concentration have been considered important factors in reducing BRD incidence. An increase in energy intake is necessary for newly received calves to support inflammatory processes, regain purchase weight, and offset the characteristically low DMI levels observed (Richeson et al., 2019). In a summary of 18 experiments, Krehbiel et al. (2011) reported only 83.4 of morbid and 94.6 % of newly-received calves consumed feed by d 7 following feedlot arrival. Richeson et al. (2019) further explains the traditional thoughts regarding receiving diet formulation which suggest that receiving calves should be offered greater concentrations of roughage in the diet in addition to long-stem hay in order to acclimate microbes and minimize digestive upsets resulting from a low rumen pH. Unfortunately, much of the research concerning roughage level and energy density was conducted before the widespread use of fibrous by-products. At the same time, increased levels of roughage in diets are difficult for feedlot mills to manage. Therefore, it has become evident that energy density and roughage inclusion in receiving diets should be revisited to determine implications on health and performance.

Additional attention has been placed in recent years on natural alternatives to antimicrobials that improve performance and health outcomes in newly received feedlot cattle. Investigation into nonantimicrobial feed additives such as direct-fed microbials (DFM) and trace mineral (TM) supplementation strategies has been heavily investigated to address the health and nutrition challenges of newly received feedlot cattle (Smock et al., 2020). Moreover, livestock producers are searching for alternative feed additives to antimicrobials to improve growth and well-being of livestock (Broadway et al., 2015). One strategy to prevent colonization of pathogenic organisms during immunosuppressive events is the supplementation of DFM, as it has been suggested that DFM

possess the ability to bind to and remove pathogenic microorganisms (Walsh et al., 2007). Direct-fed microbials are natural occurring bacterial supplements that were originally designed for post-ruminal effects; however, beneficial effects to ruminal function have been noted (Beauchemin et al., 2003).

The following review of literature was prepared to discuss the etiology and pathogenesis of BRD. Moreover, this review will discuss some relationships associated with immunology, nutrition, and management of newly-arrived beef calves to the feedlot. This review will also discuss technological advances in leukocyte detection devices, provide historical and present ideology of nutritional management of newly received beef calves upon feedlot arrival, and will investigate previous literature concerning the use of multiple feed additives as immune modulators for receiving beef calves. Ultimately, this review will provide a preface to the experiments presented in this dissertation, which: 1) Investigated the effect of metaphylaxis administered to newly received calves and determined prediction biomarkers in hematology results for BRD; 2) Investigated energy density and roughage inclusion in receiving calf diets; 3) Investigated the use of a nutritional bolus containing immune modulators administered at arrival to highly stressed beef calves.

CHAPTER II

REVIEW OF LITERATURE

BOVINE RESPIRATORY DISEASE IN FEEDLOT CATTLE

Bovine respiratory disease (**BRD**) is the most threatening and costly disease to cattle production in North America (Taylor et al., 2010). Newly arrived, highly stressed calves are at greatest risk to develop BRD, and animal morbidity and mortality attributed to BRD generally occurs soon after feedlot arrival (Loneragan et al., 2001). Bovine respiratory disease causes detrimental effects to productivity from receiving throughout the finishing phase, and to final carcass quality. Despite years of research dating back to the late 1800's and advancements in vaccines and in antimicrobials, reports suggest that the prevalence of BRD remains unchanged (Holland et al., 2010; Ives and Richeson, 2015; Peel, 2020). It has even been reported that death loss due to BRD among feedlot cattle has increased 23.1% from 1999 to 2011 (Theurer et al., 2021)

To date, economic losses from BRD are greater than any other beef cattle disease. The financial impact of BRD to the beef industry is astronomical, with estimates ranging from $800 million to $1 billion annually (Griffin, 1997; Chirase and Greene, 2001). Galyean et al. (1999) reported that 1.5 to 2.7 per 100 animals marketed die in the feedlot, and that 70% of those deaths.

are directly attributed to BRD. Financial losses can be attributed primarily to mortality, the cost of antibiotics, reduced growth performance, and discounts in carcass quality (Gagea et al., 2006).

The economic effect of BRD on feedlot cattle during backgrounding and finishing phases was evaluated by Brooks et al. (2011). The authors reported that net returns during the combined backgrounding and finishing phases decreased as the number of BRD treatments increases. Additionally, Brooks et al. (2011) reported that on average, cattle had $111.12, $92.51, $59.98, and $20.62 greater returns than chronically ill cattle when treated 0, 1, 2, or 3 times for BRD. Similarly, Schneider et al. (2009) evaluated the effect of BRD on feedlot performance and carcass traits using data collected from Midwestern feedlots encompassing 5,976 total animals. Incidence rate of BRD was 8.17% and lung lesions were present in 61.9% of these cattle at slaughter. Schneider et al. (2009) reported that average daily gain (**ADG**), hot carcass weight (**HCW**), and marbling score were all negatively affected by BRD. Furthermore, the decrease in performance and carcass merit translated to a decline of $23.23, $30.15, and $54.01 in carcass value when comparing non-treated cattle with cattle treated 1, 2, or 3 times. In agreement with Schneider et al. (2009), Wilson et al. (2017a) observed that increasing the number of times cattle were treated for BRD linearly increased days on feed (**DOF**) and decreased HCW, rib eye area, and quality grades. It was interesting to note that Wilson et al. (2017a) reported that calves treated multiple times for BRD are able to reach similar compositional endpoints as their untreated pen mates with increased DOF; however, it seemed unlikely that quality grade and carcass yield would recover.

Introduction to stress concepts and categorical levels of risk

The pathogenesis of BRD in newly received feedlot cattle is defined by stress and unfavorable environmental factors that predispose the animal to infection with viral agents that cause damage to host immune mechanisms such that commensal bacteria can become pathogenic and cause bronchopneumonia (Mosier, 2014). Moreover, the pathogenesis of BRD is dependent

upon complex interactions of environmental, infectious, and host factors. Though the respiratory system contains a dynamic set of defense mechanisms, these mechanisms are susceptible to failure as a result of stress, glucocorticoids, and viral infections (Caswell, 2014).

Stress is a widely used term that has over time attracted the use of many definitions. For the purpose of this literature review, the definition of stress reported by Aich et al. (2009) will be used, which defines stress as "psychologically perturbing condition that occurs in response to adverse external influences capable of affecting physical health". Psychological and physiological stress in both human and animal models has been linked to an increased incidence and severity of respiratory disease (Aich et al., 2009). Moreover, it is well known that both psychological and physical stress can alter certain physiological levels of endocrine hormones, chemokines, and cytokines. These stress responses can encompass either the entire body or specific cellular compartments and usually include physical perturbations. Altogether, these alterations may be immunosuppressive, which can lead to further disease susceptibility (Aich et al., 2009).

The detrimental effects stress elicits on the immune system and its coordinated responses have been well documented throughout literature. Stressors serve as both interoceptive and exteroceptive stimuli that elicit physiologic responses at in attempt to regain homeostasis. Attempt to regain homeostatic control within the body is accomplished by the activation of the hypothalamic-pituitary-adrenal axis (**HPA**) and the sympathetic nervous system (Carroll and Forsberg, 2007). As previously mentioned, stress has been associated with immunosuppressive effects; however, Carroll and Forsberg (2007) contend that not all stress is immunosuppressive. Moreover, Carroll and Forsberg (2007) report that there may be a differentiation in immunostimulatory effects caused by acute and chronic stress; whereas acute stress may be immunoenhancing and chronic stress may be immunosuppressive. Richeson et al. (2016) described acute stress as stress that lasts less than 24 h, while chronic stress lasts greater than 24 h.

Bovine respiratory disease is often recognized in the stocker or feedlot segments of cattle production; however, most BRD cases are initiated prior to transportation because risk factors can occur beginning at the ranch of origin (Wilson et al., 2017b). In commercial production, risk factors are used to assign a categorical risk classification to a group of receiving cattle such as low, medium, or high-risk classifications. These risk designations generally influence how cattle are managed upon arrival. General animal attributes considered when assigning risk classifications are distance traveled, weight, age, sex, extreme weather changes, dust, dehydration, fasting length, degree of anticipated hypoxia, acute metabolic disturbances, and the degree of commingling (Cusack et al., 2003; Taylor et al., 2010a; Avra et al., 2017). Ultimately, the most stressful events that calves encounter are during weaning, transportation, and feedlot entry, which lead to multiple physiological, nutritional, and immunological changes (Arthington et al., 2008). Calves at highest risk of developing fatal BRD are generally 400-600 lb beef calves that have no prior processing (including castration or vaccination for respiratory pathogens), have undergone abrupt weaning, have been transported and commingled with cattle from multiple sources, and have been taken to the feedlot (Griebel et al., 2014).

To date, there are many predisposing factors to BRD which would cause cattle to be classified in an increased risk category. Calves in the weaning process often experience extreme stress during maternal separation, especially when the weaning process occurs abruptly. Hickey et al. (2003) evaluated the effect of abrupt weaning of suckler calves and reported increases in the neutrophil:lymphocyte ratio, plasma cortisol concentrations, and nor-adrenaline concentrations for calves abruptly weaned. Calves that are abruptly weaned, or that are sold as “unweaned” at the sale barn generally sell below market value for comparable calves that are weaned as there is an increased risk assumed by the buyer assumes with regard to the animal’s health and performance in the stocker or feedlot production segments. Arthington et al. (2008) evaluated the performance and stress response of beef steers at the feedlot in response to pre-shipping

management strategies. Calves were either weaned on the day of shipping, creep-fed before weaning and shipping, weaned and provided supplement on pasture before shipping, or early weaned at 70 to 90 d of age and kept on pasture until shipping. The authors reported that ADG, dry matter intake (**DMI**) and gain to feed ratio (**G:F**) were all significantly greater for the early-weaned cattle compared to the control group. Moreover, the results of this experiment suggested that preshipping management appears to affect the acute phase protein response in receiving stressed steers.

Additional important risk factors that calves are subjected to during the marking processes to stocker or feedlot operations associated with the development of BRD are transportation and the commingling with other calves. Transportation is a necessary component of cattle production and is also a significant stressor that causes a quantifiable biological response that can be associated with an increased incidence and severity of BRD (Earley et al., 2017). Cattle in transit commonly encounter psychological stress such as restraint in addition to physical stress such as hunger, injury, disease, and environmental pressure (Arthington et al., 2003). Both endocrine and hematological measures indicative of transportation stress have been documented by many researchers (Arthington et al., 2003; Chirase et al., 2014; Earley et al., 2017). In a review of the relationship between transportation and BRD, Earley et al. (2017) stated that decreases in glucocorticoid receptor and β-adrenergic receptor expression in lymphocytes have been observed, while increases in epinephrine, norepinephrine, and circulating cortisol have been reported in nearly all transportation studies. Blood glucocorticoid levels have been linked to immune system suppression and increased susceptibility to disease (Wilson et al., 2017b). Transportation stress has also been shown to upregulate the immune response, including total white blood cell (**WBC**), neutrophil, basophil, hematocrit, and hemoglobin counts, while concomitantly decreasing lymphocyte responsiveness to mitogen stimulation and eosinophil and monocyte counts (Arthington et al., 2003; Earley et al., 2017). Buhler et al. (2019) reported that

stress can also exacerbate the shedding of viral respiratory pathogens, which will be discussed in greater detail. Chirase et al. (2004) also proposed that marketing stressors such as transportation stress precipitate oxidative stress, which would ultimately reduce antioxidant defense and increase total body lipid peroxidation.

Calves in transportation from the ranch of origin to stocker or feedlot facilities are often commingled with cattle from other sources at sale barns, order-buyer facilities, or at their destination through sorting. The transportation process in addition to the commingling of cattle between differing sources of origin often causes additional social stress while simultaneously resulting in exposure to additional isolates of viral and bacterial pathogens (Wilson et al., 2017b). Step et al. (2008) evaluated the effect weaning management and commingling had on receiving performance and BRD incidence following arrival to the feedlot. The authors reported that cattle retained on a ranch for 45 d after weaning exhibited less morbidity and less subsequent health costs than cattle that were commingled or sent directly to the feedlot after weaning.

Many of these risk factors reviewed have been recognized by research scientists and commercial producers previously; however, Avra et al. (2017) went on to quantify the probability of treatment failure in relation to independent risk factors. The authors classified independent variables in their model as arrival month, weight, sex, risk classification (high vs. low), DOF at first treatment, and rectal temperature at time of first BRD treatment. Subsequent interactions between independent variables were also evaluated. Cattle were classified as treatment failures if they were retreated or died. Probability of initial treatment failure (**PTF**) was greatest from April to June and increased as BW decreased. Initial treatment failure also increased with high-risk calves compared to low-risk calves and was greatest for calves on feed from 11 to 20 d.

The implication stress has on feedlot health and performance outcomes is not fully understood but has continued to be investigated by researchers and producers. Managing these

stressful events that cattle endure while in marketing channels to reduce the intensity of the immunosuppression and subsequent financial losses attributed to BRD has become a primary focus for livestock producers that have long-term financial interest in cattle health and performance. Understanding the implications of pre-arrival management on economical returns at the feedlot is paramount. Unfortunately, there is little incentive for producers who cease animal ownership prior to feedlot placement to provide additional labor and cost for the sake of providing a greater health outcome at the feedlot with regard to BRD. Together, the lack in incentivized management combined with the geographical segmentation between calf origin and feedlot placement has provided little to no change in the manner of which cattle are marketed in the U.S.

Infectious agents of bovine respiratory disease

Bovine respiratory disease is a disease complex that develops in response to interactions between stressful events and respiratory pathogens. These respiratory pathogens can cause pneumonia outbreaks in neonatal, weaned, growing calves, and adult cattle that may lead to debilitation, decreased performance, and death. It may take one or a combination of stressors to initiate BRD, and the infectious agents associated with this complex disease are ubiquitous among cattle populations (Cusack et al., 2003). It is generally accepted that the pathogenesis of BRD typically involves viral or parasitic infections that are of enough virulence to damage innate respiratory disease mechanisms, suppress the host immune system, or both. This immune suppression further allows pathogenic bacteria that enter the lungs via droplet particles to colonize in the upper respiratory tract and ultimately initiate BRD (Griffin et al., 2010). Moreover, there is an increased risk for bacterial respiratory infections to become fatal following a primary viral infection. This phenomenon called “viral-bacterial synergy” was first established in humans following influenza epidemics, but this synergism has also been reported throughout literature with regard to the bovine species (Aich et al., 2009). The synergistic relationship

between viruses and bacteria can ultimately cause a more severe BRD case (Urban-Chmiel and Grooms, 2012; Carlos-Valdez et al., 2016).

Viruses are equipped with a wide range of abilities which allow a successful establish an environment suitable for colonization of pathogenic bacteria. Some viruses can enhance adhesion of bacteria to virus-infected cells via alterations in mucosal surfaces. Most viruses that predispose the host to pneumonia replicate in the nasal cavity before reaching the lung (Caswell, 2014). These viral agents can cause severe damage to respiratory clearance mechanisms and lung parenchyma, which could facilitate the translocation of bacteria from the upper respiratory tract to establish infection in a compromised lung (Taylor et al., 2010a). Furthermore, bacterial colonization is induced more rapidly in areas where virus-induced mucosal erosion is present rather than intact mucosa. Collectively, virus-induced infections can result in an increase in the release of cytokines that increase the migration of inflammatory processes and products such as neutrophils, which results in greater adherence of bacteria to bronchial epithelial cells (Urban-Chmiel and Grooms, 2012). Booker et al. (2008) were able to quantitatively demonstrate the synergism between several etiologic agents by using immunohistochemical staining. The authors used histopathological findings in 90 calves diagnosed at necropsy with BRD to investigate relationships between pathogenic agents and found that 96% of bovine viral diarrhea virus (**BVDv**) positive animals were also positive for *Mannheimia haemolytica* (**MH**). In addition, Booker et al. (2008) reported that 80% of animals positive for *Histophilus somni* (**HS**) were also positive for *Mycoplasma bovis* (**MB**).

The most recognized causative viruses involved in the progression of the multi-faceted BRD complex are infectious bovine rhinotracheitis virus (**IBR**), bovine herpes virus (**BHv-1**), BVDv, parainfluenza 3 (**PI-3**), bovine coronavirus (**BCv**), and bovine respiratory syncytial virus (**BRSv**; Urban-Chmiel and Grooms, 2012; Caswell, 2014; Moiser, 2014; Baptiste and Kyvsgaard, 2017). A survey conducted in 1991 that included 233,450 cattle at 6 different feedlot operations

found that 68, 13, 57, and 27% of cattle were positive for BVDv, BHv-1, PI-3, and BRSv, respectively (Cusack et al., 2003). There are 3 BHv-1 subtypes based on antigenic and genomic differences (BHv-1.1, BHv-1.2a, and BHv-1.2b). Bovine herpes virus is capable of replicating in mucosal cells, submucosa tissue, and in connective tissue near the tracheal rings. Bovine herpes virus infection will lead to establishment of latency, with recrudescence often occurring under stress (Cusack et al., 2003). The destruction of epithelium of the upper respiratory tract by BHv-1 ceases ciliary activity and ultimately causes secondary bronchopneumonia. Other common associations with BHv-1 are fetal infections, abortion, and reproductive tract disease (Fulton, 2009). Bovine viral diarrhea virus has arguably received more attention than any other virus in connection with BRD. Bovine viral diarrhea virus is grouped into 2 sub-genotypes of BVDv-1 and BVDv-2. This virus impairs humoral antibody production, depresses monocyte chemotaxis, impairs myeloperoxidase antibacterial system in polymorphonuclear leukocytes, and seems to be mediated by initial hyperplasia of all lymphoid organs within 10 d of infection. Collectively, these attributes of BVDv enhance pathogenic colonization of the lungs and exacerbate the pulmonary pathology (Cusack et al., 2003). The unique aspect of BVDv compared to other viral agents in that cattle can become persistently infected (**PI**) through intrauterine exposure. These PI-BVDv calves continually shed the virus increasing the risk of infection for cohorts or animals in adjacent pens (Taylor et al., 2010a). Several experiments have reported that PI-BVDV exposure increases the risk for BRD treatment, which is significant as 30% or more pens may contain PI-BVDv calves (Taylor et al., 2010a). Therefore, it has been reported that the identification and removal of PI-BVDv animals is crucial to control programs; however, some experiments have observed no effect of PI-BVDv exposure on morbidity, mortality, or performance (Taylor et al., 2010a). Bovine respiratory syncytial virus and PI-3 act similarly to BHv by causing destruction to the ciliated respiratory epithelium (Cusack et al., 2003). Infection of alveolar macrophages is caused by BRSv, which causes depression in local cellular immunity. Infection with BRSv can also cause loss of cilia 1 to 2 d post-infection and cellular necrosis at 4

to 7 d post-infection (Caswell, 2014). Although PI-3 does replicate in both upper and lower respiratory tract epithelial cells, most damage occurs primarily in the lower respiratory tract (Cusack et al., 2003). The lower tract infection of PI-3 causes bronchitis, bronchiolitis, and alveolitis. Infection of PI-3 is similar to BRSv infection in that PI-3 affects innate pulmonary defense mechanisms by infecting alveolar macrophages, which allows the escalation of secondary bacterial pneumonia.

Most infectious bacteria are incapable of inducing significant disease without the presence of concurrent infections and other physiologic stressors (Griffin et al., 2010). It is well recognized that the synergistic relationship between viral infections and MH leads to the colonization of bacterial pathogens in the lower respiratory tract (Urban-Chmiel and Grooms, 2012). Common bacterial pathogens associated with BRD in cattle include MH, *Bibersteinia trehalose*, HS, *Pasteurella multocida* (**PM**), MB, and *Trueperella pyogenes*. These commensal bacteria exist within polymicrobial biofilms within healthy cattle and may coexist in bacterial combinations such as HS and PM (Mosier, 2014). The biofilm creates an environment that protects the bacterial population from toxins, antimicrobials, and other adverse agents, while simultaneously allowing the bacteria to co-exist with the host. It is generally through biofilm dispersal that bacteria associated with BRD become pathogenic and begin to systemically colonize deeper within the lung. This biofilm dispersal is trigged by alterations in the biofilm microenvironment caused by stressors, nutrient concentration changes, hypoxia, or adverse temperatures (Mosier, 2014). Once the active pathogenic bacteria have become established within the lung, the bacteria cause damage to the host through virulence factors. A few widely recognized virulence factors are leukotoxin and lipopolysaccharide endotoxin. These toxins initiate coagulation cascades that result in an increased vascular permeability which leads to an accumulation of inflammatory cells, edema, and both intravascular and extravascular fibrin deposition in the lung. Endotoxins also activate granulocytes and macrophages that are

responsible for protection against pathogenic bacteria; however, this accumulation of granulocytes and macrophages causes increased tissue damage (Cusack et al., 2003). The severity of disease is generally enhanced with combinations of pathogenic organisms such as MH with MB and/or BHV-1, HS with BRSv, and MB with BHv-1 (Mosier, 2014).

The most predominant bacterial pathogen associated with BRD is MH, which was formally known as Pasteurella haemolytica (Griffin et al., 2010). *Mannheimia haemolytica* exists in the upper respiratory tract as normal flora in healthy calves, and of the 12 serotypes, the most predominate serotype isolated from clinically normal cattle is A2 (Griffin et al., 2010). Once the commensal relationship between MH bacteria and the host is disrupted by the previously mentioned stressors, serotype A1 becomes the prominent organism and is primarily responsible for the onset of bronchopneumonia. The prevalence of the A1 serotype of MH seems to increase with colder temperatures; however, the combination of colder temperatures and viral infection quickly trigger MH and exacerbate colony size (Griffin et al., 2010; Caswell, 2014). *Mannheimia haemolytica* impairs phagocytosis by producing a leukotoxin that is active against phagocytes and that also neutralizes macrophages. Neutrophils are also destroyed by extracellular fractions of MH. Ultimately, phagocytes are attracted to infected regions equipped with reactive oxygen metabolites which are normally used to destroy bacteria. These reactive oxygen compounds may be released in an uncontrolled manner as the phagocytes are impaired or killed, thereby, exacerbating pneumonia by pulmonary inflammation (Cusack et al., 2003; Griffin et al., 2010). *Mannheimia haemolytica* leukotoxin produced at high concentrations can directly cause lung lesions by impairing leukocytes such that cell death will occur due to necrosis (Griffin et al., 2010). *Pasteurella multocida* has 5 serogroups and 16 serotypes, but the most common PM isolated in BRD cases is A:3. *Pasteurella multocida* is identified regularly in younger cattle affected with BRD and normally occurs during times of intense stress. This bacterium is easily isolated from nasal secretions and can be found in 20 to 60% of clinically normal cattle, which

suggests PM is also a commensal organism (Griffin et al., 2010). *Histophilus somni* is an additional commensal organism found in 15 to 50% of newly received cattle, but these bacteria prefer to colonize the lower respiratory tract. Virulence factors produced by HS outer membrane proteins and lipooligosaccharide are similar to the virulence factors produced by MH; however, HS also produces additional histamines and exopolysaccharides which aid in the progression of BRD. *Histophilus somni* is able to spread quickly through via an immunoglobulin-binding protein which directs cytotoxic activities towards endothelial cells. Pneumonia caused by HS is extremely difficult to differentiate from pneumonia caused by other respiratory pathogens, as fibrin deposition is commonly associated with pneumonia caused by PM and MH. Diseases commonly associated with HS are fibrinopurulent bronchopneumonia, laryngitis, thromboembolic meningoencephalitis, polyarthritis-polyserositis, and fibrinous pericarditis (Griffin et al., 2010). It is often debated whether or not MB causes primary infection or if MB is limited to the role of a secondary pathogen that colonizes in an infected lung after previous infection. *Mycoplasma bovis* is commonly found concurrently with BVDv and in cases of chronic pneumonia (Fulton, 2009). *Mycoplasma bovis* can translocate between respiratory cells to enter the blood stream and MB is often associated with the respiratory form of mycoplasmosis. Nodules of caseous necrosis surrounded by consolidated lungs and the subsequent lung lesions are often associated with MB (Griffin et al., 2010).

Murray et al. (2017) conducted an examination of pathogens associated with 136 weaned cattle that were submitted for postmortem examination in Ireland. The authors' examination concluded that dual infections between pathogenic organisms were detected in 58% of the lungs examined. *Mannheimia haemolytica* and HS were the most frequent combination of respiratory pathogens detected. *Mannheimia haemolytica* alone was the most frequent pathogen found (43%), followed by HS. The most frequently observed viral agents observed by Murray et al. (2017) were PI-3 and BRSv. Booker et al. (2008) conducted a similar evaluation of

histopathological findings in 90 feedlot calves diagnosed at necropsy with BRD. The authors found MH and MB to be the most commonly identified infectious agents involved with the BRD cases. Immunohistochemical staining revealed that 96% of animals positive for BVDv were also positive for MH, and that 80% of animals positive for HS were also positive for MB (Booker et al., 2008). Gagea et al. (2006) evaluated the prevalence of pathogens in BRD cases in 99 calves within 72 Ontario beef feedlots. Fibrinosuppurative bronchopneumonia accounted for 49% of major diseases detected. Pathologic investigation reported by Gagea et al. (2006) revealed that MB and HS were identified in 36 and 8% of all fatal fibrinosuppurative bronchopneumonia cases, respectively. Additionally, viral respiratory disease accounted for 19% of all bronchopneumonia cases, with BVDv, BRSv, BHv, and PI-3 identified in 35, 9, 6, and 3%, respectively. *Mannheimia haemolytica* was isolated in 27% of the lungs, followed by PM and HS at 19 and 14%, respectively. Gagea et al. (2006) concluded by reporting that pneumonia, specifically within the first 2 months following arrival, was the leading cause of mortality representing 69% of total deaths.

Immune response mechanisms

Immunity is recognized as an organism's ability to resist infectious disease caused by harmful microorganisms (Yuan et al., 2014). Viral challenges have the ability to influence immunity by modifying the innate and adaptive immune system response through alterations in alveolar macrophage function, lymphocyte proliferation suppression, induced apoptosis, and through changes to cytokine and other inflammatory mediator releases (Urban-Chmiel and Grooms, 2012). Immunity is generally classified as innate or adaptive, which refers to a natural or specific immune response, respectively.

The innate immune system is considered as the first line of defense against pathogens and represents a diverse set of defense mechanisms that are non-antigen specific. Innate immune

factors include physical barriers designed to exclude invading pathogens, as well as defense mechanisms that can act non-specifically against an array of invading organisms. Cells in this response rely upon recognition of variously stimulatory molecules that are highly conserved among bacterial, viral, and parasitic organisms. The ability to recognize such molecules are germline encoded in the host and do not depend upon previous exposure to sensitize the immune system or prepare it to respond (Yuan et al., 2014). Innate immune responses generally begin to occur within 0 to 4 h post antigen exposure. Characteristics of innate immunity are physical barriers, chemical barriers, the complement system, phagocytes, macrophage derived cytokines, and beneficial microorganisms in the respiratory tract that compete against foreign pathogenic organisms (Galyean et al., 1999; Carroll and Forsberg, 2007). The robustness and effectiveness of the innate immune response is generally thought to be impaired by direct physical damage or insult, dehydration, nutritional status, genetics, and certainly stress (Carroll and Forsberg, 2007). A strong and functional innate immune system is typically capable of preventing disease caused by pathogenic organisms by blocking the infectious agents via barriers or through rapid detection and elimination. Physical barriers of innate immunity include skin, mucosal secretions, tears, stomach acid, and urine. Collectively, the primary responsibility of these barriers and antigen-nonspecific cellular components is to provide the necessary time required by the adaptive portion of the immune system to mount an antibody response to a specific pathogen, which can take up to several weeks (Carroll and Forsberg, 2007).

There are 5 types of white blood cells that are commonly identified and quantified in routine blood analyses, which are all classified as leukocytes (Nicholson, 2016). Neutrophils, monocytes, basophils, and eosinophils are primarily produced in bone marrow and are collectively parts of the innate immune response. Alternatively, lymphocytes, sub-divided into T-cells and B-cells, are apart of adaptive immunity. Natural killer (**NK**) cells are also classified as

lymphocytes but are considered to be part of the innate immune response as these cells have no memory functions (Nicholson, 2016).

Neutrophils are considered the first line of defense and are the dominant WBC analyzed in a complete blood cell (**CBC**) count. Neutrophils migrate to the site of damaged tissue or to the site of infection within 2 h and quickly begin processing and killing pathogenic organisms via phagocytosis. There are multiple stages of neutrophil development, with the most common stage in circulation being segmented neutrophils. Segmented neutrophils have eosinophilic cytoplasm because of the presence of cytoplasmic granules (Jones and Allison, 2007). An additional commonly recognized neutrophil stage are immature band neutrophils, which are released into circulation with acute inflammation and are characterized by morphologic horseshoe shape. Accelerated changes to neutrophil abundance and morphology are indicative of severe inflammation, which is generally caused by gram-negative bacteria and septic shock (Jones and Allison, 2007). General increases in circulating neutrophil concentration are termed neutrophilia. Neutrophilia is caused by the presence of mild inflammation or can occur in response to infectious processes, tissue injury, neoplastic diseases, and some noninflammatory conditions (Jones and Allison, 2007). Conversely, neutropenia is caused by severe acute inflammatory diseases that commonly include sepsis, mastitis, pneumonia, *Salmonella* infection, or can be observed with bone marrow injury.

Eosinophils are a classification of WBC that are produced primarily in response to parasites and allergens. Eosinophils are equipped with cytotoxic granule proteins that are virulent to protozoa, fungi, and bacteria (Jones and Allison, 2007). Eosinophilia results from parasitic migration, interstitial pneumonia, and autoantibody formation. Eosinopenia may occur in response to acute inflammatory processes or a stress response, and tends to be greater in concentration in adult cattle than for younger calves. Basophils are typically lower in concentration for cattle, but generally are produced in response to allergic reactions and various

inflammatory processes. Basophils release inflammatory mediators such as heparin and histamine to control allergic reactions. Monocytes are involved with immune response processes and are called macrophages after they exit blood circulation and enter tissues. Once in the tissue, macrophages are capable of phagocytosis of infectious organisms and numbers may increase in response to chronic inflammation, tissue necrosis, hemolysis, or a stress response (Jones and Allison, 2007). Low concentrations of monocytes may be indicative of endotoxemia and viremia.

The cellular component of the immune system consists of phagocytes, NK cells, and additional cells that release inflammatory mediators (Carroll and Forsberg, 2007). Neutrophils, monocytes, macrophages, and dendritic cells are the primary phagocytic cells of innate immunity. These phagocytic cells of immunity recognize pathogen associated molecular patterns (**PAMP**) by using pattern recognition receptors. These pathogen receptors can be classified as either circulating humoral proteins, endocytic receptors, or toll-like receptors that are expressed on the surface of the cell. Pathogen associated molecular pattern molecules generally associated with infectious pathogens including lipopolysaccharide (**LPS**) from gram-negative bacterial cell walls, peptidoglycans, lipoteichoic acids from gram-positive bacterial walls, sugars such as glycolipids and glycoproteins, bacterial (non-methylated) DNA, double-stranded RNA (which is unique to some viruses), teichoic acid, cytokine-phosphate-guanine, lipopeptides, mycobacteria, and fungal cell wall glucans (Carroll and Forsberg, 2007; Ackermann et al., 2010). All major viral and bacterial pathogens in cattle produce some type of PAMP that are recognized by epithelia and alveolar and intravascular macrophages. The result of PAMP recognition is that the phagocytic cells are activated to the site of infection where they are able to engulf and kill pathogens before the pathogenic organisms have opportunity to further proliferate (Carroll and Forsberg, 2007). Recognition of PAMPs also results in a wide-array of other responses which collectively produce the characteristics of inflammation, including local blood flow; increased vascular permeability; and even potentially systemic signs and symptoms, including fever.

Natural killer cells are a type of lymphocyte but are not included as part of adaptive immunity. Natural killer cells are equipped with dissimilar mechanisms to the PAMP recognition of phagocytic cells at an attempt to protect against pathogenic agents. These NK cells require no activation and target abnormal cells by binding to cell and releasing a chemical burst. This burst of chemical disrupts the cellular membrane, which further allows extracellular fluid to penetrate and rupture the target cell. Furthermore, NK cells aid in the activation of immunological responses by stimulating the secretion of proinflammatory cytokines such as interleukin (**IL**) -1, IL-6, IL-12, tumor necrosis factor-α (**TNF-α**), and interferon-ɣ (**IFN- ɣ**) by macrophages and monocytes (Carroll and Forsberg, 2007). The cascade of proinflammatory cytokines released act to activate the acute phase response, as well as serve regulatory purposes for the febrile response. The most notable reaction of the acute phase response is the synthesis and release of acute phase proteins (**APP**) from the liver, but also includes fever, increases in WBC's, lethargy, anorexia, depression, and alterations in plasma Fe, Zn, and Cu (Carroll and Forsberg, 2007). These proinflammatory cytokines help to regulate the febrile response by inducing the production of prostaglandin E2. Furthermore, cytokines induce negative feedback inhibition of cytokine gene expression by acting on the pituitary to increase adrenal cortex thyroid hormone (**ACTH**) concentrations. This stimulation of ACTH increases the release of cortisol, which is the primary glucocorticoid released by the adrenal cortex. The resulting febrile response stimulated by proinflammatory cytokines ultimately aids in killing pathogens via the stimulation of immune cells, as well as accelerating the enzymatic processes of which kill the pathogens (Carroll and Forsberg, 2007).

Acute phase proteins synthesized in the liver by hepatocytes function as proteinase inhibitors, enzymes, coagulation proteins, metal-binding proteins, and transport proteins (Carroll and Forsberg, 2007). These APP can be positively or negatively influenced by proinflammatory cytokines such as IL-1, IL-6, and TNF-α. Acute phase proteins produced by hepatocytes can have

both direct and indirect roles in eliciting the immune response. Positive APP increase dramatically in the plasma concentrations in response to infection and cytokine stimulation. Common APP heavily evaluated in research and used as indicators of acute and chronic inflammation in cattle are haptoglobin, serum amyloid A, ceruloplasmin, α1-acid glycoprotein, and fibrinogen (Carroll and Forsberg, 2007).

Adaptive immunity is conceptually different than innate immunity as adaptive immunity results in defense abilities uniquely targeted to a particular target (be that of a bacterial cell, viral proteins, toxin, etc.). Adaptive immune responses are a product of selective clonal expression and somatic diversification which is stimulated only after it is found that a particular cell has relatively high affinity for a specific antigen of an invading pathogen. Adaptive, or "acquired" immunity, represents part of the immune system that mounts a specific immune response for each antigen it encounters. Importantly, once activated by a specific antigen, the acquired immune response will be long-lived, and prepared to respond immediately should that antigen or associated pathogen be encountered again. The capability to retain memory of previous infections is crucial to the ability of the immune system to mount an effective immune response to harmful pathogens. These memory-like features protect both the host from reinfection and limit the spread of infection in a community. Immune memory is distributed throughout the body by circulating antibodies that reach everywhere circulation does and can also develop outside the bloodstream within tissues (Nicholson, 2016). Adaptive immunity can be further divided into humoral and cell-mediated immunity (Galyean et al., 1999; Yuan et al., 2014)

The acquired immune response is most easily recognized by the production of antibodies that target specific antigens and also possess immunologic memory (Carroll and Forsberg, 2007). This segment is termed humoral immunity. However, there is also a cell-mediated immunity arm of acquired immunity that results in proliferation and long-term retention of cell lines with strong affinity for particular antigens. Humoral immunity is mediated by B-lymphocytes that respond to

antigens to become antibody producing cells and memory cells. Antibodies are free-floating molecules that circulate in the blood and may be secreted to mucosal surfaces. Antibodies can bind and inactivate their target, and mark it for destruction. This response of B-lymphocytes is critical for defense against extracellular microbial infection, but can also be useful for preventing cellular entry by viruses.

Cell-mediated immunity (CMI) is the second arm of the acquired immune response. The CMI response is associated with T-lymphocytes and cytokines, and provides defense against intracellular pathogens and tumor cells (Galyean et al., 1999). The B-lymphocytes ingest and process antigens for presentation to T-lymphocytes (Carroll and Forsberg, 2007). Antibodies presented by B-cells are called immunoglobulins (IG), which are present on the surface of B-cells and are used as antibody receptors. Immunoglobulins are antigen-specific receptors that are formed by the combination of 2 identical heavy and 2 identical light chains that is comprised of 3 globular domains connected by 2 binding linker domains (Nicholson, 2016). Antibodies bind firms to the target antigen at one end, and on the other end, antibodies signal to other immune cells. Antibodies are subdivided into antibody isotopes, which are classified as IG-M, IG-A, IG-D, IG-G, and IG-E. Immunoglobulin-M is secreted as pentamer that functions as a naïve B-cell receptor and produces natural antibodies that complement T-cell activation. Immunoglobulin-A is secreted into mucus as a dimer for mucosal immunity. Immunoglobulin-D is a naïve B-cell receptor, and IG-G is secreted as a monomer for opsonization and complement activation. Lastly, IG-E is secreted bound mostly to cells that aid in defense against parasites and allergens (Nicholson, 2016).

T-lymphocytes, commonly called T-cells, develop in the thymus and are crucial for both forms of acquired immunity. T-lymphocytes are subdivided into T-helper-1 cells (TH1) and T-helper-2 cells (TH2). The T-helper cells are able to produce cytokines that allow other T and B cells to grow and divide, which help to increase production of cells to fight future infection.

Ultimately, it is the cytokine profile that directs the initial adaptive immune response into primarily TH1 (favoring CMI) or TH2 (favoring humoral immunity) by dictating T-helper cell proliferation and differentiation (Carrol and Forsberg, 2007). Antigen receptors from lymphocytes recognize cell-surface molecules on APC that are known as the major histocompatibility complex (MHC). The major histocompatibility complex are molecules that are a combination of material derived from the environment and are bound in flexible holds of the MHC molecule that hold it in place (Nicholson, 2016). The MHC directs MHC-antigen complexes to a cell's surface where the complexes can be detected by additional lymphocytes. Lymphocytosis, characterized by an increase in lymphocyte concentrations, is commonly associated with chronic viral infections, pyogenic conditions, or autoimmune diseases, and lymphopenia is generally associated with increased stress, increased corticosteroid concentrations, acute viral and bacterial infections, endotoxemia, BVDv infection, and other immunodeficiencies. It is common to associate lymphocyte and neutrophil concentrations during CBC differentials. The ratio of neutrophils to lymphocytes in clinically normal cattle is generally 1:2 in adult animals but varies greatly in newly received calves (Jones and Allison, 2007). Immune systems addressed in this review are complex and integrated, and these integrated systems are all tasked with solving these immunological challenges.

Management of newly received feedlot cattle

The management of feedlot calves prior to transportation, while in transit, and during the first few weeks following arrival to the feedlot is critical in order to minimize detrimental decreases in feedlot morbidity and mortality, as well as other performance measures such as ADG and carcass characteristics during the growing and finishing period. Ideally, newly-received calves should have adequate time to distribute the stress load induced by weaning over time, and that these receiving calves should also have been placed into preconditioning programs where they would undergo a vaccination program, increase energy input via supplemental feed, and gain

exposure to bunk feeding and general watering systems. Additionally, backgrounding allows additional time for recovery from castration and other management procedures that ultimately cause suppression of the immune system via stress and infection. Unfortunately, the beef cattle industry is highly segmented and it is unrealistic to assume that all calves entering the feedlot have been allowed these opportunities for preparation to arrive at the feedlot. Often, little to no previous health history is known for calves bought from auction markets and placed into feedlots, which ultimately causes processing and nutrition protocols to be based on but not limited to the sale location, distance traveled, weather, weight, and sex of the animals. Ultimately, the goal of any receiving protocol should be to minimize stress, injury, and disease transmission calves are subjected to prior to and during arrival, while also maximizing energy intake once in feed pens. Receiving protocols for both processing and nutritional management of calves entering the feedlot have been of great interest in recent years. Implications of the management and consequential stress induced prior to arrival to the feedlot have been previously reviewed; therefore, the management of newly received calves described in this section will focus on the common feedlot management practices of receiving cattle once arrived to the feedlot.

Processing is collectively known as a series of both medicinal and nutritional management activities cattle are subjected to following arrival to best enhance health and performance outcomes in the feedlot. The majority of respondents in a survey conducted by Samuelson et al. (2016) reported that 66.7% of feedlot clients allowed 12 to 24 h for cattle to rest following feedlot arrival. Urban-Chmiel and Grooms (2012) suggested that it may be beneficial to allow 1 h of rest for every 1 h of transit. Processing regimen include the administration of vaccines, growth-enhancing implants, anthelmintics, parenteral vitamins, ancillary therapeutic treatments, and prophylactic medication (Taylor et al., 2010; Wilson et al., 2015). In addition, the castration of bulls, abortion of pregnant heifers, and dehorning or tipping of horns are other common stressful procedures completed at time of initial processing following arrival.

Vaccination is a tool used commonly to prevent disease and is a cornerstone of animal health management (Richeson et al., 2016). Vaccination is an attempt to build immunological protection against important pathogens involved in BRD by stimulating antibody titer production similar to that of natural exposure to an antigen (Urban-Chmiel and Grooms, 2012; Wilson et al., 2017b). Research has demonstrated that vaccination can reduce the risk of BRD when given appropriately by providing the vaccine to an immunocompetent animal (Urban-Chmiel and Grooms, 2012). The U.S Feedlot Survey indicated that 95.1 % of feedlots vaccinated for BVDv, while 93.2, 55.1, and 61.4% of cattle were vaccinated for IBR, PI-3, and BRSv, respectively (NAHMS, 2013). Conversely, vaccine-induced titers are not always correlated with protection against disease, and failure of vaccines to provide sufficient disease protection may be caused by incorrect timing of administration, failure of stressed calves to respond appropriately to pathogenic challenges, and the increased susceptibility of stressed calves to viral and bacterial pathogens. Just as important, time is required for the immune system to respond to vaccination. If a calf has already been exposed to various pathogens and is incubating disease, vaccination is unlikely to result in an immune response quickly enough to prevent clinical disease. While more effective vaccines and therapeutic agents are available today as compared to 1983, evidence of efficacy regarding administration of respiratory vaccines is equivocal at best (Fulton, 2009; Taylor et al., 2010b). The overall consensus among most scientists is that vaccination is best accomplished as part of a preconditioning program.

Richeson et al. (2016) investigated immunosuppression by mimicking stress via dexamethasone administration and evaluating subsequent immunological responses to a multivalent respiratory vaccine containing replicating and nonreplicating agents. Thirty-two animals were identified as seronegative to infectious IBRv, BVDv, BRSv, and PI-3 and were randomly assigned to 3 treatments. Treatment groups consisted of acute immunosuppression (0.5 mg/kg BW dexamethasone at d 0), chronic immunosuppression (0.5 mg/kg BW dexamethasone

on d -3 to 0), and a control group (no dexamethasone). Richeson et al. (2016) reported that acute and chronic immunosuppression with dexamethasone blunted the APP response following multivalent respiratory vaccination on d 0, and also reported that immunosuppression was greatest for the chronic treatment group and least for the control group that received no dexamethasone. The acute and chronic treatment groups were observed to have greater IBRv and BVDv-specific antibody titers for the live-attenuated vaccine. Conversely, the MH-antibody response for the inactivated toxoid agent was reduced for the acute and chronic treatment groups. The authors speculated that these data may indicate consequential effects of modified-live vaccination (**MLV**) or inactivated vaccination administered to stressed, newly received beef cattle. Furthermore, the authors state that the antigenicity and replication of MLV agents may be detrimental to health or growth, but inactivated formulations may reduce the immune response in stressed calves (Richeson et al., 2016).

It is a common procedure to castrate all bulls that enter feedlot production. Castration is a stressful event, thus making the practice a risk factor for BRD. Roughly 15 million bulls are castrated each year in the U.S. (Ball et al., 2018). Castration is deemed a necessary in order to improve human and animal safety, as bulls tend to become more aggressive thus making them more difficult to handle. Castration of bulls also limits undesired breeding and improves carcass characteristics by reducing the number of dark cutters and increasing the amount of marbling and muscle tenderness (Wilson et al., 2017b; Roberts et al., 2018).

Physiological and behavioral responses differ based on castration method. Roberts et al. (2018) reported that 52.3% of bulls are surgically castrated upon arrival to the feedlot, while 41.1% on band castrated and 6.6% are not castrated at all. An additional method of castration recently reviewed is the use of an injectable product consisting of zinc acetate neutralized by L-histidine; however, data tends to show minimal efficacy of this method. Ball et al. (2018) evaluated zinc injection as a means of castration in comparison to band castration and a control of

no castration. These authors reported that zinc injection resulted in sterilization, but animals on this experimental treatment had testosterone concentrations more similar to the intact bulls than for the banded animals. Roberts et al. (2018) evaluated the effect of castration method and use of meloxicam on inflammation, performance, and carcass characteristics in feedlot cattle. These authors castrated via surgically or via band, and cattle were or were not given meloxicam. Roberts et al. (2018) reported that both castration methods reduced feedlot performance, but the reduction in performance occurred at different times. Surgically castrated calves had less performance during the first week post-castration, while banded calves had less performance during the second week post-castration. Meloxicam improved overall ADG for both surgical and banded castration methods. The beneficial effects of meloxicam administration following castration have also been reported by Coetezee et al. (2012). Taylor et al. (2010a) reported that given the immunosuppressive nature of increased cortisol levels, castrating older bulls may put them at greater risk for BRD than bulls castrated at an earlier age. Data overall suggests that castration is least immunosuppressive while completed at an early age, and that castration at the feedlot consistently reduces ADG and is immunosuppressive in nature (Taylor et al., 2010a).

Dehorning, anthelmintic treatment, and administration of a growth promoting implants are other routine procedures commonly performed at processing. Cattle entering the feedlot with horns are generally tipped due to increased bunk space requirements and subsequent concern regarding feed intake. Additionally, cattle with horns pose a greater safety concern to humans and other animals within the pen (Wilson et al., 2017b). The dehorning processes has been associated with hormonal measures indicative of stress such as cortisol, thus constituting this process as a risk factor for BRD. Dehorned cattle at initial processing has been reported to decrease ADG throughout the receiving period, and it has also been reported that dehorned cattle have numerically greater morbidity (Wilson et al., 2017b). Increases in BRD have been reported in groups where greater than 30% of calves were dehorned (Taylor et al., 2010a). Research

regarding the effects of an anthelmintic administered at processing on BRD incidence has been somewhat inconclusive. Taylor et al. (2010b) reviewed literature regarding anthelmintic administration and reported only one experiment that found a negative impact of anthelmintic on health and subsequent BRD, while others studies either showed a positive influence or no influence at all of an anthelmintic administered on arrival. Steroidal implants have been used in all segments of the beef cattle industry to improve growth and performance for over 50 years (Carvalho et al., 2020). It has been reported that steroidal implants are of the few processing products administered that immediately began to physiologically direct an animal into a positive energy balance. One could hypothesize based on that speculation that the use of implants may reduce the incidence of BRD. Investigation into implant use was conducted by Poe et al. (2013) and Richeson et al. (2015). Overall investigation by these authors concluded that administering implants do not influence health or vaccine responses in stressed cattle.

Consideration towards delaying partial processing events until cattle have time to acclimate to their environment has been heavily examined in recent years (Taylor et al., 2010a; Taylor et al., 2010b; Urban-Chmiel and Grooms, 2012; Wilson et al., 2017b). It has been speculated that vaccination at time of arrival processing may be detrimental, or at least ineffectual, as stressed calves may have previously been exposed to pathogens and are presumably experiencing some level of immunosuppression (Wilson et al, 2017b; Richeson and Falkner, 2020). Richeson and Falkner (2020) reported that for vaccination to be effective, a vaccine against BRD antigens should be administered several weeks before homologous our heterologous challenge. Furthermore, the interaction between stress and vaccination for pathogens involved with BRD is influenced by the type of vaccine antigen (MLV vs killed), acute infection, and natural and genetic variation of stress (Richeson and Falkner, 2020). Poe et al. (2013) evaluated the effect of on-arrival pentavalent respiratory vaccination timing with or without a hormonal growth implant in newly received stocker calves. Cattle in this experiment

were vaccinated on arrival or were 14 d post arrival. These authors reported that time of vaccination did not influence overall ADG or morbidity rate, but vaccination at arrival did increase BVDv type 1a antibody titers (Poe et al., 2013). In a similar experiment, Richeson et al. (2009) investigated the effect of clostridial or MLV vaccination administered on arrival or 14 d post arrival on health, performance, stress, and immune measures in newly received beef calves. The results reported by Richeson et al. (2009) concluded that performance and morbidity were not influenced by treatment, and that BVDv titer concentrations were greater for the early vaccination group than for the delayed treatment group. Other experiments have reported greater morbidity in calves when processing was delayed and also reported that delaying processing has resulted in greater initial BRD cases occurring over time (Taylor et al., 2010b). In summary, the most ideal time to vaccinate cattle against BRD is when cattle are in a state of immunologic homeostasis and free of acute infection; specifically, vaccination should be applied when cattle are at least several weeks before stressful events or BRD challenges are expected (Richeson and Falkner, 2020).

Delaying castration is one processing procedure reported to have negative implications on growing and finishing calf performance (Zweiacher et al., 1979; Taylor et al., 2010a). An experiment was conducted by Zweiacher et al. (1979), in which the authors evaluated differences in performance and health outcomes between bulls that were castrated upon feedlot arrival, 1-wk post arrival, or 2-wk post arrival and the authors compared these responses to that of steers purchased at a similar time. The authors reported that steer performance was greater than for any castration method. Additionally, bulls castrated on arrival had greater gains than for either delayed castration treatment group. Health was most improved for steers than for any of the castration treatment groups. Conversely, a review of castration management by Taylor et al. (2010a) reported that some experiments have found no association between delayed castration and BRD. Although difficult to assess, Taylor et al. (2010a) speculated that the indicative nature

of poor management related to non-castrated calves may have more association with disease than castration itself.

The experiment by Poe et al. (2013) also evaluated delaying implant administration along with vaccine administration on the health and performance of newly received beef calves. Results reported by Poe et a. (2013) concluded that delaying implant administration did not influence ADG or morbidity outcomes. More recently, Richeson et al. (2015) investigated the use of delaying implant administration for 14 or 28 d in stocker cattle on performance and immunity. These authors concluded that there are no clear benefits to delaying growth implants, and that implants did not affect health or vaccine responses in newly received calves.

The experiences calves endure in the segmented beef cattle industry to arrive in feedlot production are generally immunosuppressive in nature. Immune suppression and the subsequent increases in morbidity and decreases in performance may be exacerbated by the manner of which animals are managed upon arrival. Ultimately, management protocols should not be homogenous for any given set of cattle, as management prior to feedlot arrival can vary substantially. This review of literature regarding the management processes of newly received beef cattle suggests a lack in evidence to discontinue current practices. An overwhelming theme in this review is that given modern advances in pharmaceutical products available, BRD and subsequent feedlot performance measures are best secured by properly managing calves prior to marketing, which primarily includes disbursement of stresses over a greater length of time, such as weeks before being introduced into a differing production system.

METAPHYLACTIC USE OF ANTIMICROBIALS

Cattle producers often compromise when purchasing cattle that will perform well in feedlot production. Higher purchase prices are generally indicative of healthier animals that are less likely to become morbid and more likely to exceed average performance. Alternatively, cattle

purchased at lower or discounted prices are often associated with greater risk of morbidity and mortality and are less likely to perform well under normal conditions (Dennis et al., 2018). Cattle buyers often categorize prospective cattle into risk categories based on expected morality risk, cattle performance, feeding location, and time of year. Variables of animal assessment are often weight, age, comingling status, distance traveled to the feedlot, season, and prior health treatments previously administered (Dennis et al., 2018). It is well understood that cattle classified as high-risk often require additional management. Groups of high-risk cattle are generally light weight, recently weaned, highly commingled, are of auction market origin, and have experienced extended transport time (Ives and Richeson, 2015). These high-risk groups of cattle are often more susceptible to BRD; therefore, the need for antimicrobial treatment for BRD is typically greater than that of low risk cattle.

The percentage of mortality associated with BRD has remained relatively unchanged despite years of improved understanding of BRD and advancements in antimicrobial technologies (Ives and Richeson, 2015). One hypothesis for lack in BRD progression is that infrastructure of the beef industry has not changed throughout the years (Nickell and White, 2010; Peel, 2020). Nonetheless, one management practice that has consistently shown to reduce morbidity and mortality is the use of antimicrobial metaphylaxis upon feedlot arrival (Ives and Richeson, 2015).

Previous justification in support of metaphylaxis

Metaphylaxis is the procedure of timely administering an FDA-approved antimicrobial to a group of animals with the goal of eliminating or minimizing an expected outbreak of disease (Edwards, 2010). Treatment of a population is often preferred to traditional selective individual treatment in groups at high risk of developing BRD, as identifying BRD in calves objectively is difficult and labor intensive (Nickell and White, 2010). The decision to utilize metaphylaxis on a group of newly received cattle is generally made prior to or immediately upon arrival to the

feedlot. Oftentimes, feedlot managers may make the decision to administer a metaphylactic antimicrobial to cattle not originally on a metaphylaxis protocol if the overall morbidity of a group surpasses a certain predetermined threshold. In a survey conducted by NAHMS (2013), the authors reported that 59.3% of feedlots utilized metaphylaxis for BRD control. In feedlots with 8,000 or more cattle weighing 700 lb or less, 92.6% of feedlots used metaphylaxis. Only 59.0% of feedlots utilized metaphylaxis on cattle that were 317 kg or greater. A feedlot survey conducted by Samuelson et al. (2016) concluded that 83.3, 39.4, and 6.09% of feedlots administered metaphylactic treatment to high, medium, and low risk cattle. There are several antibiotics authorized to be used for metaphylactic treatment, and the 3 most common antibiotics reported in the NAHMS (2013) survey were tilmicosin, tulathromycin, and ceftiofur. Guidelines that determine the implementation of metaphylactic treatment on or post-arrival are that cattle must appear clinically ill on arrival, current morbidity patterns must be identified, observed reduction in feed intake, elevations in body temperature, and proven efficacy of products labeled for the control of BRD (Nickell and White, 2010).

Efficacy of metaphylaxis

Judicious use of metaphylaxis has been reported throughout literature to be an efficient and cost-effective method to control the spread of bacterial pathogens associated with BRD in high risk calves (Edwards, 2010). Metaphylactic treatment of cattle can be accomplished by parenteral administration or through feed and water. While published data are generally in agreement that metaphylaxis aids in health and performance outcomes in newly received calves, some reports have suggested that differences in health outcomes exists between different classes of antimicrobials. A metanalysis completed by Abell et al. (2017) revealed that metaphylactic antimicrobials have proven to offer different effects on BRD morbidity and mortality in stocker and feedlot operations (Abell et al., 2017). Nonetheless, current literature has deemed metaphylaxis as an important method to reduce morbidity and mortality in calves.

An experiment conducted by Word et al. (2020) evaluated the effect of metaphylactic antimicrobial administration on the health, antimicrobial usage, and productivity of newly-received male calves. Calves in the experiment were administered either ceftiofur crystalline free acid, tilmicosin phosphate, or were assigned to a negative control receiving no treatment. Word et al. (2020) reported that metaphylactic administration of either antimicrobial improved animal well-being by reducing both morbidity rates and the total number of days animals presented clinical illness, but no differences existed between antimicrobial treatments. In their experiment, calves receiving metaphylaxis had 25.2% lower morbidity rates and had improved ADG and G:F during the first 14 d following administration. Word et al. (2020) observed no differences in total antimicrobial usage between the metaphylaxis and control calves in their experiment. Duff et al. (2000) conducted 2 experiments to evaluate pre-shipping and arrival medication, and also feeding chlortetracycline at arrival on the health and performance newly received beef calves. Duff et al. (2000) compared metaphylactic treatment prior to or at arrival to a control group receiving no treatment in their first experiment, and the authors added the use of feeding chlortetracycline in their second experiment. Duff et al. (2000) reported no differences in ADG, DMI, or G:F among metaphylactic treatments in either experiment. The percentage of steers treated for BRD decreased compared to the control group in the authors' first experiment, while similar results were reported for their second experiment. The authors reported that for their second experiment, the number of steers treated for BRD decreased for the arrival treatment compared to the steers administered an antimicrobial prior to shipping. Numerous other experiments have documented improvements in animal health and performance when newly received calves were administered metaphylactic antimicrobial treatments at arrival (Duff and Galyean, 2007; Taylor et al., 2010b; Wilson et al., 2017b; Munoz et al., 2020).

Antimicrobial resistance and residues

In recent years, public concern over the use of antimicrobials used in both human and animal operations, antimicrobial resistant bacteria, and antimicrobial residues in meat has escalated. Disease monitoring organizations have claimed that injudicious use of shared-class antimicrobials is occurring in livestock production (Dennis et al., 2018). Of the greatest concern are the antibiotic growth promoters that have both human and veterinary medical applications or antibiotics that share a common antibiotic family class with antibiotics essential for treatment of bacterial diseases in humans. Furthermore, there is evidence to support that antibiotic-resistant bacteria can be transferred from livestock to humans. Antibiotics utilized in livestock production for nontherapeutic application are generally administered in the diet during times of high disease risk and often improve performance and feed efficiency (Alexander et al., 2008). Using antimicrobials as prophylaxis, metaphylaxis, or growth-enhancing drugs can result in resistance of MH to a large number of antibiotics (Griffin et al., 2010); thus, governmental regulatory agencies have established the veterinary feed directive (**VFD**), which mandates that antimicrobial drugs are administered under the regulation of licensed veterinarians.

Numerous studies have documented cases of antimicrobial resistance in BRD pathogens (Alexander et al., 2008; Cameron and McAllister, 2016; Crosby et al., 2018; Holman et al., 2019; Coetzee et al., 2020). Antimicrobial resistance can be evaluated by veterinary-specific breakpoints that are determined by the Veterinary Antimicrobial Susceptibility Testing Subcommittee (**VAST**). The VASTS selects breakpoints as defined by susceptible, intermediate susceptibility, or resistant (Griffin et al., 2010). These breakpoints are then applied to combinations of diseases, pathogens, animal species, and antimicrobial regimens. The serial dilution method and disk-diffusion method are the 2 primary approaches to susceptibility testing. Serial dilution testing utilizes microwell plates that contain predetermined concentrations of selected antimicrobials that are inoculated with broth containing a standardized number of bacteria, and the presence of growth in the well determines the breakpoint value (Griffin et al.,

2010). The disk-diffusion utilizes a standard bacterial inoculum that are streaked onto an agar plate for 16 to 18 h. Zones of inhibition are measured and compared with interpretive zone-size criteria and the following breakpoint can be determined (Griffin et al., 2010).

The development of widespread resistance of BRD pathogens to therapeutic antimicrobial agents would be economically devastating to the cattle industry (Watts and Sweeney, 2010). Decreasing resistance of BRD pathogens to antimicrobial agents, as well as the occurrence on resistance of microbials to shared-class antimicrobials may be accomplished through prudent use of antimicrobials. Unfortunately, metaphylactic use of antimicrobials may expose more bacteria to antimicrobial selection, thus, increasing resistance (Cameron and McAllister, 2016). Judicious use can be defined as the cost-effective use of antimicrobials which maximizes clinical therapeutic effect while minimizing both drug-related toxicity and the development of antimicrobial resistance (Baptiste and Kyvsgaard, 2017). The livestock industry will continue to face additional stringent regulations such as the VFD and state mandated antibiotic-use policies. Most importantly, consumers of animal protein are concerned with traceability and are continuing to direct their buying decisions towards products that have been marketed with labels of judicious and sustainable use of antibiotics or products that have never been administered antibiotics.

Selective treatment of BRD using leukocyte differential cell counts

With ever-increasing demand by consumers to raise livestock devoid of antibiotics and increasing regulations regarding judicious use of antimicrobials, pressure and increased scrutiny has been placed on livestock producers to focus on reducing the use of metaphylactic antimicrobial administration. Furthermore, criteria for sustainable beef production has included the enhancement of economic viability, efficient resource use, maintenance of animal health and well-being, and judicious use of pharmaceutical products (Word et al., 2020). It has been

suggested that the combination of clinical observations and rectal temperature commonly used to determine an animal's treatment eligibility has both a sensitivity and specificity near 60%. This suggests that nearly 40% animals are inaccurately treated, while 40% of animals truly succumbed to BRD are not treated (Baruch et al., 2019). Historically, metaphylaxis administered to calves at high risk of developing BRD has been the most cost-effective and least labor-intensive practice to reduce morbidity and mortality. In recent years, increased scrutiny over antimicrobial usage has caused innovators in livestock production to develop alternative methods which identify BRD on an individual animal basis. Resulting selective antimicrobial treatment strategies have been developed recently that aim to reduce antimicrobial usage at time of arrival.

Advances in the understanding of biomarkers in high risk calves have demonstrated promise in the ability to detect and predict BRD in recent years (von Konigslow et al., 2019). Specifically, understanding leukocyte differential counts may provide a means to refine treatment protocols when interpreted in conjunction with clinical exam findings in high risk receiving calves and may ultimately be a viable alternative to antimicrobial metaphylaxis in livestock production. Leukocyte counts, leukograms, and sequential leukograms may be used for health assessments, disease diagnostics, and to establish prognosis (von Konigslow et al., 2020). Recent work has focused on identifying clinically measurable risk factors that affect mortality in calves, and rapid chute-side cell counters using leukocyte data to make clinical decisions upon have emerged into the industry.

Von Konigslow et al. (2019) conducted an experiment to validate an automated leukocyte counter, the QScout BLD test (Advanced Animal Diagnostics, Morrisville, NC). The authors collected blood samples from 235 calves upon arrival and compared leukocyte differential counts between the QScout and manual microscopy. Comparison of leukocyte counts was completed by using Lin's concordance correlation coefficient. The authors further evaluated the test results to determine if leukocyte cell counts differed in classification as being below, within, or above

reported 95% reference intervals. Von Konigslow et al. (2019) reported excellent agreement between neutrophil counts, fair agreement for lymphocyte counts, fair agreement for the neutrophil to lymphocyte ratio, and slight agreements for monocyte counts and eosinophil counts. The authors reported only a 4.2% and 5.8% disagreement in classification for neutrophils and lymphocytes, respectively, while monocyte and eosinophil counts differed in agreement of classification by 23.3% and 70.3%, respectively (von Konigslow et al., 2019). In an additional experiment completed by von Konigslow et al. (2020), the authors evaluated leukocyte differential counts collected by the QScout machine at both arrival and 72 h post arrival. The authors attempted to use these data to determine morbidity risk, mortality risk, and growth during the receiving period. The authors concluded that lymphocyte counts between 4.8 and 5.8×10^9 cell/L decreased the probability of mortality and that neutrophil counts greater than 6.0×10^9 cells/L decreased the probability of mortality (von Konigslow et al., 2020). Both von Konigslow et al. (2019) an (2020) suggested that machine leukocyte differential cell counts have the potential to identify high risk calves that might require treatment for BRD.

Data regarding the utility of chute-side leukocyte analyzers as BRD detection and prevention tools are limited. Nonetheless, utilization of these machines may allow livestock operations an opportunity to make informed decisions that reduce antimicrobial cost without sacrificing health and production or increasing morbidity and mortality. Additionally, these machines may be a viable alternative and sustainable solution to metaphylaxis if proven accurate and may further aid in decreasing the rate of microbial resistance. Management limitations for these detection systems do exist to become fully operational in livestock production; more specifically, if these detection systems are to become operational in confinement feedlot systems. These rapid leukocyte analyzers must have the ability to return a quick result, samples must be reasonably quick to obtain, and it must be minimally invasive to the animal (von Konigslow et

al., 2020). Economic evaluation with regard to the risk classification must also be taken into consideration.

DIETARY MANAGEMENT OF RECEIVING CATTLE

Scientists have investigated various nutritional strategies to understand and enhance the immune system of receiving feedlot cattle for more than 3 decades (Carroll and Forsberg, 2007). Yet, discrepancies still exist with regard to nutritional recommendations for receiving cattle, which is presumably attributed to the inconsistency in pre-arrival management and inherent variability in the level of stress cattle are subjected to pre and post-feedlot arrival. Years of research in the realm of calf nutrition has concluded that nutrient availability, or lack thereof, influences all physiologic processes within the body including the immune system (Carrol and Forsberg, 2007). Lightweight, newly received calves face stress associated with weaning, transportation, marketing, commingling, and management procedures. A major consequence and somewhat resulting paradox of the chronic stress imposed on these calves is the deficiency in nutrient intake required to support immunological and growth processes.

Receiving management of newly received calves can have long-term consequences, or benefits, with regard to cattle health and performance throughout the growing and finishing period. Appropriate management procedures for receiving feedlot calves are highly dependent on many external variables, but ultimately the arrival protocols set forth should find realistic balances between labor and mill capabilities and the physiological demand of the newly received group, while maintaining maximum biosecurity measures. When surveyed by Samuelson et al. (2016), the majority of surveyed nutritionists reported their clients allowed cattle to rest for 12 to 24 h following feedlot arrival. Categorical risk classification, season of purchase, calf genetics, length of time in the marketing process, and previous management if known should all be taken into consideration when designing a receiving, processing, and feed protocol. Feed protocols set

forth for receiving cattle have important implications with regard to overall animal health and performance. Feed protocols for newly received calves should be designed to achieve nutrient intake such that deficiencies are corrected and performance is established, while simultaneously taking into consideration ruminal integrity and rate of digestive disorders. Much of this review covering dietary management of newly received calves will focus on literature surrounding intake management and ration formulation as it relates to balancing energy density with animal health and performance.

Intake management for receiving cattle

Appropriate management of the diet formulation and feed delivery programs for newly received calves is essential to recovery from shipping stress, and key components of successful programs include establishing adequate intake through highly-palatable and digestible diets when getting calves off to a healthy start (Krehbiel et al., 2011). When considering the role of nutrition in BRD, it has been suggested that achieving adequate dietary intake of nutrients may be more important than what ingredients are included in the ration (Taylor et al., 2010b). Feedstuffs provided at the feedlot are oftentimes unfamiliar to newly received calves. Unfamiliarity with common feedstuffs, combined with increasing levels of immunosuppression, generally prevent highly stressed, newly received beef calves from establishing intakes necessary to support immune modulation and performance.

Feed intake of high risk newly received calves generally averages only 1.5% of BW during the first 2 wk following arrival (Galyean et al., 1999; Krehbiel et al., 2011). It has also been well-documented that stressed calves display different eating habits than non-stressed calves (Galyean et al., 1999). A review conducted by Krehbiel et al. (2011) reported that only 83.4% of morbid calves had consumed feed by d 7 following feedlot arrival, while 94.6% of healthy calves

consumed feed in the same time. Additionally, DMI of morbid calves was 58, 68, and 88% of healthy calves across d 1 to 7, 1 to 14, and 1 to 56, respectively

It is obvious that the lack of intake or fluctuations in intake exhibited by newly received calves create unique challenges with regard to quickly reestablishing homeostasis via intake of nutrients. As such, nutritionists must consider low DMI of stressed receiving calves when formulating rations to meet nutrient requirements. Stressed calves do not have increased nutrient requirements compared non-stressed counterparts; however, nutrients oftentimes need to be formulated in greater concentrations than established requirements to offset lower DMI observed by newly received calves (Krehbiel et al., 2011). Ration composition and bunk management for newly received calves has been an area of research interest for decades. Bunk management is dynamic and can vary to the type of diet, class of cattle, climatic conditions, bunk space allocated, and the overall marketing objective of the cattle (Pritchard and Bruns, 2003). The overall objective of bunk management is to reduce variability in intake, and the role bunk management as it relates to BRD is unclear. The relationship between feed management, diet type, feed intake, animal performance, BRD, and incidence of metabolic disorders is also somewhat unclear, but has gathered attention in recent years (Schwartzkopf-Genswein et al., 2003; Tomczak et al., 2019). Much of the literature dating back to the 1970's has focused on the nutrient composition, energy density, and roughage inclusion required in receiving diets to maximize performance while maintaining health and ruminal integrity. Complexity regarding these topics still exists as cattle have continued to change over the years, management practices and understanding of biological processes has improved, current BRD detection systems have become less subjective, and current feedstuffs used in rations have changed primarily due to the addition of byproduct feeds of the ethanol industry. Nonetheless, opportunity still exists to improve our understanding of nutritional strategies that mitigate instance of BRD while improving growing and finishing

performance, especially as pressure for livestock production to discontinue antibiotic use continues to rise.

Impact of diet energy and roughage on receiving characteristics

High risk, newly received calves are often more prone to arrive to the feedlot in a catabolic state. The catabolic state is generally a result of sustained feed and water deprivation calves endure during marking and in transit. This negative energy balance, combined with low DMI of the newly received calves early in the receiving period, increases susceptibility of the immune system to become compromised and subsequently leads to a greater risk for morbidity and decreased performance (Richeson et al., 2019). Evaluation of diet energy density and subsequent roughage inclusion level have been investigated frequently by scientists. Current dogma with regard to ration formulation for receiving calves is that morbidity and mortality are decreased as roughage level increases (Richeson et al., 2019). Alternatively, this dogma would suggest that performance is increased as diet energy density increases and as diet roughage level decreases. However, it is speculated that increases in performance would offset losses due to morbidity (Rivera et al., 2005). Samuelson et al. (2016) reported that nutritionists on average formulate receiving diets to contain 40.7% roughage. Additionally, their survey suggested that nutritionists incorporate grain into the diet at 30 to 40% on a DM basis (Samuelson et al., 2016). Unfortunately, many experiments conducted to evaluate energy density or roughage inclusion are inherently confounded, as energy concentrations are commonly altered by changing dietary roughage concentration. Nonetheless, numerous research experiments have been executed to assess biological responses to altering energy and roughage concentrations in diets offered to receiving cattle.

Lofgreen et al. (1975) evaluated energy level in receiving diets for highly stressed calves recently exposed to shipping stress. Lofgreen et al. (1975) utilized 395 calves in a series of 4

experiments. In their first experiment, 117 calves were assigned to 1 of 3 treatment diets containing either 20, 55, or 72% concentrate. Percent of calves requiring treatment was lower for the 72% concentrate ration than for the 55% ration, and the morbidity was greatest for the intermediate diet; however, medication cost increased as concentrate increased because of the greater number of treatments per calf. Energy intake and subsequent ADG increased as percent concentrate of the ration increased. In the authors' second experiment, 107 calves were assigned to diets consisting of 55, 72, or 90% concentrates with NEg levels of 46, 50, and 54 mcals/kg. The authors followed these calves through slaughter, for a total of 253 d. Calves on the 72% diet consumed more feed than cattle consuming the 55 and 90% diets. In their third experiment, Lofgreen et al. (1975) removed the 55% concentrate diet and added a self-selection group. Contrary to the first 2 experiments, no increases in morbidity were observed for cattle on the high concentrate diet. Cattle on the self-selection group preferred the higher energy feed. Lastly, in their fourth experiment, 59 steers were used to evaluate the effect of free choice long-stem alfalfa hay on health and performance. Providing long-stem hay did not influence health or performance.

More recent experiments have been conducted to evaluate diet energy density and roughage level. Fluharty and Loerch (1996) completed 3 experiments to evaluate the effects of energy source and level on performance of newly received calves using corn silage-based diets. The authors reported no differences in morbidity for the 70, 75, 80, or 85% concentrate rations. Fluharty and Loerch (1996) also reported no differences in performance or efficiency between the 4 diets in their second experiment. Calves fed more energy dense diets in their third experiment had greater ADG, DMI, and G:F. Fluharty and Loerch (1996) concluded that receiving diets containing at least 16% CP and 70% concentrates are beneficial to calves during the first week of arrival. Berry et al. (2004a) utilized 572 calves to evaluate dietary energy and starch concentrations on growth and performance characteristics of newly received calves. The authors' experimental design was able to eliminate confounding effects of roughage and energy

concentration. Cattle were randomly assigned to 1 of 2 dietary energy levels (0.85 or 1.07 mcal NEg/kg) and 1 of 2 dietary starch levels (34 or 48% ME from starch). No energy × starch interactions for performance or health were observed, and ADG and G:F were not affected by treatment. The authors reported no difference in morbidity for calves fed high-energy compared to calves fed low energy diets; however, high-starch fed calves had numerically greater morbidity. Berry et al. (2004a) concluded that performance was not influenced by dietary energy or starch concentration. A follow-up experiment completed by Berry et al. (2004b) concluded that diet had minimal effects on APP.

Overall, the rationale for starting cattle on diets with greater roughage inclusion levels is based on a perceived advantage of reducing morbidity and mortality and increasing DMI as well as rumen health, while the rationale for starting cattle on diets with less roughage and subsequently greater energy-density is based on the improvements in performance and profitability (Rivera et al., 2005). Rivera et al. (2005) used a mixed model regression on existing data to evaluate relationships between dietary energy and roughage concentrations and reported that morbidity due to BRD slightly decreased as dietary roughage concentration increased. Additionally, the model created by Rivera et al. (2005) reported that a decrease in morbidity by feeding a 100% roughage diet would not offset the loss in ADG and resulting profit generated by feeding a 40% roughage diet. The authors speculated that optimum dietary strategy would be to feed a 50 to 70% concentrate, milled diet, which would allow cattle to perform well without negatively influencing economical returns. Rivera et al. (2005) reported that cattle receiving higher energy-dense rations may be able to mount a more intensive immune response at arrival, but these results are in disagreement with cytokine concentrations reported by various other authors (Richeson et al., 2019).

This review of literature tends to agree with Richeson et al. (2019), who reported that existing literature suggests cattle perform better at greater levels of energy density and lower

levels of roughage; however, greater performance may come at the expense of increased morbidity rates. Richeson et al. (2019) also suggested it is possible that acidotic cattle are incorrectly diagnosed with BRD, as clinical signs of acidosis are analogous with BRD. This theory seems probable, as the transition from forage-based to grain-based diets is challenging in newly received calves. Rapid adaptation to energy dense diets creates a greater proportion of propionate, which can further augment performance, but also elevates risk of ruminal acidosis (DeClerck et al., 2020). Lastly, foundational research concerning the debate regarding energy density and roughage inclusion level lacks the evaluation of fibrous by-products that contribute a large percentage of the diet in today's feedlot industry (Samuelson et al., 2016; Richeson et al., 2019). These by-products have minimal amounts of starch and have shown to favorably influence ruminal characteristics such as pH. Collectively, research is needed to address effects of dietary energy density and roughage inclusion level on the health and performance of newly received stressed calves with rations that include fibrous by-products such as corn gluten feed and distillers grains (Richeson et al., 2019).

Additional nutrient considerations for receiving diets

Protein deposition is largely dependent upon energy intake, as energy intake is the first limiting factor involved with weight gain. Furthermore, newly received calves are likely to have low capacity for protein deposition due to lower net levels of energy intake (Galyean et al., 1999; Krehbiel et al., 2011). The general dogma regarding CP concentration in receiving diets is that ADG increases as CP concentration increases, but these increases in performance occur at the expense of greater morbidity. The experiment conducted by Fluhart and Loerch (1996) reported that calves fed diets containing 16% CP had greater DMI, ADG, and feed efficiency than calves fed diets containing 12.5% CP, but no association in BRD was noted. Conversely, numerous experiments have reported that CP concentration appears similar to energy density such that increases in CP concentration result in increased morbidity (Taylor et al., 2010b). Other studies

have reported linear increases in ADG and G:F with increasing MP concentrations at the expense of increasing the amount of treated calves (Galyean et al., 1999). Duff and Galyean (2007) concluded that morbidity from BRD increases with increasing concentrations of CP in diets offered to receiving calves, but with observed increases in ADG and DMI. These authors attributed the paradoxical response to either inaccurate diagnosis of BRD, morbid calves fed greater CP concentrated diets had greater performance than morbid calves on lower CP diets, or that performance by healthy calves consuming greater CP concentrated diets was greater than healthy calves fed lower CP concentrated diets (Duff and Galyean, 2007).

Complex relationships exist between levels of micronutrients, immune function, disease resistance, and growth in cattle (Spears, 2000). The effect of mineral and vitamin concentration and source in diets fed to receiving calves has been somewhat inconclusive on receiving characteristics. Vitamin deficiencies have been linked to immune system disorders for centuries, and development and function of the immune system can be linked to adequate levels of all vitamins (Carroll and Forsberg, 2007). Vitamins increase leukocyte concentrations and play important roles in minimizing tissue damage from reactive oxidative species (Carroll and Forsberg, 2007). Samuelson et al. (2016) reported that 68.2% of nutritionists considered the full value of the major mineral concentrations, while 45.5% of nutritionists considered only the partial value of TM concentrations in the basal diet. Nonetheless, formulated concentrations of vitamins and minerals in receiving diets likely need to be increased to meet established requirements and offset the lower DMI of receiving cattle.

NON-MEDICATED FEED ADDITIVES IN RUMINANT PRODUCTION

Scientists have increased research efforts towards finding viable antibiotic alternatives in recent years. Increased pressure for livestock producers to lessen or discontinue antibiotic therapy due to antimicrobial resistance and food safety concerns has shifted focus of livestock producers

from parental antimicrobials to feed additives. As a result of increasing antibiotic scrutiny, the European Union has placed a ban on the use of antibiotics for production purposes in animal diets, and the U.S implemented the VFD (Walsh et al., 2007). Thus, more livestock producers are seeking non-antimicrobial alternatives to prevent colonization of pathogenic microorganisms, increase performance, decrease digestive disorders, and increase overall animal well-being.

Ruminant nutritionists and microbiologists have been interested in manipulating the rumen microbial ecosystem to improve production efficiency (Elghandour et al., 2015). The most common microbial alternatives researched have been the inclusion of bacterial and fungal microorganisms as DFM. Common microorganisms used as DFM for ruminants are lactic acid producing bacteria, lactic acid utilizing bacteria, or other species such as *Lactobacillus*, *Streptococcus*, and *Megasphaera elsdenii*. Several fungal species such as *Saccharomyces* and *Aspergillus* have been identified as useful lactic-related DFM as well (Elghandour et al., 2015). Direct-fed microbials were originally designed to benefit intestinal processes such as establishing desirable gut microflora and preventing the proliferation of pathogenic organisms. In recent years, there has been indication that certain DFM may have positive effects in the rumen, such as decreasing the potential for ruminal acidosis (Krehbiel et al., 2003).

Numerous additional feed additives have been of interest in recent years. Chromium supplementation has been studied for decades and has demonstrated to be important in ruminant nutrition. Chromium propionate is the only source of chromium permitted for supplementation to cattle in the United States. Chromium propionate supplementation has been demonstrated to alter glucose and lipid metabolism and has appeared to favorably enhance the immune system (Bernhard et al., 2012). Numerous additional supplements have been demonstrated to enhance metabolism and immune function. Supplementation of yeast cell wall components such as beta glucans has also reported to have beneficial immunomodulatory effects (Salinas-Chavira et al., 2018). Collectively, investigation into DFM and other performance and immune-enhancing

additives has yielded mixed results, especially in regard to newly received stressed calves. Research evaluating the reliability and utility of such additives warrants further investigation.

Chemistry and mode of action of direct-fed microbials

Direct-fed microbials have been utilized by the livestock industry for over 30 years with the focus of utilization centered around the ability to accelerate the establishment of the intestinal microflora involved with feed digestion and promotion of gut health and integrity. More recently, additional sophisticated mixtures of DFM have been developed that target to improve fiber digestion, prevent acidosis, increase growth and feed efficiency, and enhance the immune system (McAllister et al., 2011). The U.S. FDA has defined DFM as a source of live, naturally occurring microorganisms, and DFM for ruminants include fungi and bacterial organisms. In a review by Krehbiel et al. (2003) the authors summarized that feeding bacterial DFM to feedlot cattle results in a 2.5 to 5% increase in ADG, a 2% improvement in feed efficiency, and a 6 to 7 kg improvement in carcass weight, with inconsistent effects on DMI.

Microbial cultures have been developed to potentially replace or reduce antibiotic use in ruminants and other species (Krehbiel et al., 2003). Unlike antibiotics that have direct bactericidal or bacteriostatic effects on bacteria, DFM function through indirect mechanisms such as alteration to intestinal microbiome, intestinal efficiency enhancement, and modulation of the host innate immune system (Buntyn et al., 2016). The increased attention generated by DFM has caused animal scientists to attempt to improve our understanding of the biological mechanisms of action. To date, some research has reported benefits for the use of DFM, whereas numerous results indicate little to no effect on health and feedlot characteristics.

Adeyemi et al. (2019) recently explored the effects of dietary supplementation of a *Saccharomyces cerevisiae*-based DFM on growth, immune gene expression, serum biochemistry, and plasma metabolome of newly weaned beef calves during a 42 d period. These authors

allocated 40 single-sourced Angus steers to either a basal diet with no additive or a basal diet top-dressed with 19 g of DFM. Adeyemi et al. (2019) reported that supplementation of the DFM increased final BW, tended to improve G:F, and had no effect on DMI. Additionally, DFM supplementation increased serum calcium, total protein, albumin, and the expression of some immune-related genes involved in detecting PAMP. Metabolome analysis indicated that DFM supplementation increased metabolite concentrations and tended to lower fecal pH. Adeyemi et al. (2019) concluded that *Saccharomyces cerevisiae* supplementation as a DFM was effective in improving performance, nutritional status, and health in newly weaned beef steers.

Broadway et al. (2020) evaluated feeding 13 g/hd per d of *Bacillus subtilis* PB6 (CLOSTAT) to weaned Holstein steers confirmed not shedding *Salmonella*. *Bacillus subtilis* PB6 is a bacterial DFM stimulated by low pH and bile salts that initiates small intestinal activity by passing through the rumen as a spore (Smock et al., 2020). Treatments were arranged in a 2 × 2 factorial design with CLOSTAT serving as one factor and the inoculation of *Salmonella* serving as the second factor. Calves were harvested either at 48 h or 96 h post-challenge. Broadway et al. (2020) reported that CLOSTAT reduced *Salmonella* concentrations for calves harvested at 48 h but no differences were reported in *Salmonella* concentrations for cattle harvested at 96 h. CLOSTAT supplemented calves displayed increased WBC and lymphocyte counts and also had increased concentrations of IL-6 and IFN-y. Broadway et al. (2020) concluded that CLOSTAT supplemented calves reduced *Salmonella* presence in the gastrointestinal tract while simultaneously reducing the challenge severity.

Impact of beta-glucans as immune modulators

Yeast products are fed to livestock often as live yeast (considered a DFM), as a yeast cell wall, or as a combination. A major component of the yeast and yeast cell wall is a polysaccharide such as a β-D-glucan (Broadway et al., 2015). β-glucans are extracted from the cell walls of

yeast, fungi, and some cereal grains and reportedly have immune modulatory effects (Tao et al., 2015). These polysaccharides are able to directly interact with immune cells and are able to bind bacteria to prevent attachment and pathogenic colonization in the gastrointestinal tract. Additionally, β-D-glucans may possibly possess antioxidant and antitumor properties and have reportedly been involved with the releasement of cytokines from macrophages and modulation of other immune cells. Salina-Chavira et al. (2018) stated that yeast cell wall supplementation has been associated with enhanced immune status and increases in ADG and feed efficiency.

Experiments evaluating β-D-glucan supplementation in ruminants are limited. (Tao et al., 2015) investigated the effects of β-D-glucan supplementation on nutrient digestibility and serum profiles in pre-ruminant Holstein calves. Holstein calves were allocated to 6 treatment groups, which included a control receiving no supplement or supplemented groups with either 25, 50, 75, 100, or 200 mg of yeast β-D-glucan. Tao et al. (2015) reported that yeast supplementation quadratically increased IgG and IgM concentrations, while supplementation decreased serum triglyceride and cholesterol concentrations. β-D-glucan supplementation in their experiment did not affect total protein, albumin, serum urea nitrogen, or glucose. The authors concluded that yeast β-D-glucan supplementation at 75 mg/kg can improve nutrient digestibility and enhance immunity by increasing immunoglobulin concentration. Other experiments have reported increases in DMI, protein digestibility, increases in ADG and carcass weight, and possible increases in immune stimulation by the supplementation of β-D-glucans (Grove et al., 2006; Cherdthong et al., 2018; Salinas-Chavira et al., 2018).

Chromium propionate and butyric acid supplementation

Chromium is required for insulin metabolism and subsequent nutrient uptake by peripheral cells. Chromium is also a component of glucose tolerance factor that potentiates the action of insulin (Kegley and Spears, 1995; Yari et al., 2010). In 2009, the USDA Center for

Veterinary Medicine permitted the use of chromium propionate up to 0.50 mg/kg as a source of supplemental chromium. In recent years, chromium propionate has been found to enhance insulin sensitivity, growth performance, and health in the feedlot (Smock et al., 2020). It has also been suggested that chromium modifies glucose metabolism through an oligopeptide known as chromodulin, which consist of glycine, cysteine, aspartate, and glutamate (Bernhard et al., 2012).

Bernhard et al. (2012) investigated supplementing chromium propionate (KemTRACE Chromium propionate 0.04%, Kemin Industries, Des Moines, IA) on glucose and lipid metabolism of newly received steers. The authors supplemented chromium propionate to add 0 or 0.2 mg/kg to the basal diet. No effect of chromium propionate supplementation was observed for glucose concentration, glucose clearance rates, or pre-infusion insulin concentrations. However, chromium supplemented calves tended to have greater insulin concentrations post-infusion, which caused an increase in the insulin to glucose ratio. Additionally, non-esterified fatty acid (NEFA) concentrations for the chromium supplemented steers were lower for both pre and post-infusion. Bernhard et al. (2012) concluded that chromium propionate supplementation can alter lipid metabolism, which suggested that steers had less dependence on lipid metabolism for energy. Kneeskern et al. (2016) conducted a similar study to evaluate the effect of chromium propionate supplementation on growth, insulin, glucose, and carcass characteristics in beef cattle. The authors reported that chromium propionate supplementation did not affect glucose or insulin metabolism, but supplementation did increase dressing percentage and tended to decrease intramuscular fat, with no observed effects on performance (Kneeskern et al., 2016).

Butyric acid supplementation has been evaluated for growth responses in monogastric animals but has recently been identified as a potential beneficial supplement in ruminants. Butyric acid is a short-chain fatty acid that is produced by microbial fermentation primarily in the large intestine. Butyric acid is also known to be involved in the mucosal immune response and to have anti-inflammatory effects (Kaczmarek et al., 2016). Short-chain fatty acids have shown potential

as effective supplements in antibiotic-free conditions, and when used as a feed additive for broiler chickens, butyric acid has shown beneficial effects on the development of intestinal epithelium and control of pathogenic bacteria. Furthermore, butyrate can serve as an energy source for gut enterocytes, which may increase the growth and overall absorptive surface area of the villi (Pascual et al., 2020).

Limited data exist that evaluates encapsulated butyric acid in beef cattle. Kaczmarek et al. (2016) conducted 2 experiments to evaluate the effect protected calcium butyrate has on growth and nutrient digestibility in broiler chickens. The authors reported that apparent total tract digestibility, apparent metabolizable energy, and feed conversion were improved by calcium butyrate supplementation. Kaczmarek et al. (2016) reported that calcium butyrate supplementation also improved feed conversion and increased cysteine, glycine, and alanine digestibility relative to the negative control. The authors concluded that butyrate supplementation improved digestion and absorptive processes in broilers. In contrast, an experiment conducted by Pascual et al. (2020) concluded that feeding sodium butyrate to broiler chickens had no effect on performance and gut response in chickens.

CONCLUSIONS FROM THE LITERATURE

It is apparent from this review that the U.S beef industry has yet to overcome the monumental management challenges and economic losses encountered as a result of BRD in feedlot production, despite improvements in parental pharmaceuticals, management procedures, and increased comprehension of the multifaceted BRD complex. Rapid leukocyte analysis is becoming increasingly more available as means for the early detection of BRD. Debate surrounding dietary energy and roughage concentrations throughout the literature has seemed to support increasing energy density in receiving diets at the expense of slight morbidity increases. Feed additives such as DFM, beta-glucans, and direct VFA supplementation seem promising for

both beef and dairy cattle with regard to increasing performance and health characteristics. As long as BRD remains a critical threat to U.S. beef production, progress must be made towards reducing BRD incidence in an era of increasing antimicrobial scrutiny. This will require continual research and development of early detection systems and new nutritional management strategies.

CHAPTER III

INVESTIGATION INTO THE EFFICACY OF METAPHYLAXIS AND HEMATOLOGY PARAMETERS ASSOICATED WITH INSTANCE OF BOVINE RESPIRATORY DISEASE

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ABSTRACT

The objective was to determine the effect of metaphylaxis on performance and health characteristics in newly received beef cattle, as well as to evaluate potential relationships among hematology parameters as the indicators relate to bovine respiratory disease BRD prediction. Three blocks of steers (n = 605; initial BW = 255 ± 8.3 kg) were procured from livestock buying stations in Louisiana in September 2018. Steers were weighed on d -1 and assigned randomly to 1 of 2 treatments. Treatments were: 1) cattle receiving no antimicrobial treatment at arrival (CON) or 2) cattle administered metaphylaxis at arrival (MET; tildipirosin). Treatments were balanced within pen (n = 24 pens). Animal served as the experimental unit and animals from both treatments were assigned randomly to pens. Performance and hematological data

were analyzed using the MIXED and GLIMMIX procedures of SAS 9.4, respectively. No differences ($P \geq 0.44$) in BW were observed between CON and MET steers throughout the entire experiment. Cattle receiving metaphylaxis had greater ($P < 0.01$) ADG from d 0 to 14 compared to CON steers, but no additional differences ($P \geq 0.16$) in ADG during the 56 d receiving experiment were detected. Performance and hematological effects were evaluated between treated (TRT) and non-treated (NTRT) steers within the CON cattle. Body weight was greater ($P \leq 0.02$) at all time points for non-treated CON cattle compared to CON cattle treated for BRD; however, no differences ($P \geq 0.12$) in ADG were detected between the treated and non-treated groups of steers. Neutrophil counts tended ($P = 0.08$) to be greater for non-treated CON steers, but no other differences ($P \geq 0.16$) in leukocyte counts were observed. Treated CON steers had lower ($P \leq 0.05$) hematocrits, hemoglobin, and mean corpuscular hemoglobin than non-treated CON steers. Overall, metaphylaxis administered to steers in the current experiment had minimal impact on performance during the receiving period after d 14. Steers enrolled in this experiment were likely not sufficiently immunocompromised that the value of metaphylaxis was economically realized. Cellular components related to erythrocyte indices such as hematocrit percent and hemoglobin concentration were lower for cattle selectively treated for BRD compared to non-treated cattle, which suggests that evaluation of these parameters with regard to their ability to indicate BRD may be beneficial.

Key Words: bovine respiratory disease, hematology, metaphylaxis, disease prediction

INTRODUCTION

Bovine respiratory disease (BRD) is multi-faceted and involves a number of environmental factors, host factors, and management practices that all ultimately challenge animal's ability to remain immunocompetent and perform well in the feedlot (Abell et al., 2017). The percentage of morbidity and mortality associated with BRD has remained relatively

unchanged despite years of improved understanding of BRD and advancements in antimicrobial technologies (Ives and Richeson, 2015). One hypothesis for the lack in progression towards BRD prevention is that the infrastructure of the beef industry has not changed for several decades (Nickell and White, 2010; Peel, 2020). Nonetheless, one management practice that has consistently shown scientific evidence of efficacy in cost-effectively reducing instance of BRD and subsequent costs associated with the disease complex is use of metaphylaxis following arrival to the feedlot (Edwards, 2010; Taylor et al., 2010; Ives and Richeson, 2015).

Metaphylaxis is an animal management practice where an FDA-approved antimicrobial is administered to a group of cattle at high-risk of developing BRD in order to eliminate or reduce the onset of the disease (Dennis et al., 2018). Metaphylaxis is also indicated for use in high-risk animals when the number of clinical cases within a group reaches a set threshold such that the remainder of in-contact animals are simultaneously treated to restrict the spread and impact of the disease (Baptiste and Kyvsgaard, 2017). The decision to use metaphylaxis on a newly received group of cattle is generally made prior to or immediately upon arrival to the feedlot. A survey conducted by NAHMS (2013) reported that 59.3% of feedlots utilized metaphylaxis for BRD control, and a subsequent survey completed by Samuelson et al. (2016) concluded that feedlot administered metaphylactic treatment to 83.3, 39.4, and 6.09% of high, medium, and low risk cattle, respectively. Published data generally supports that metaphylaxis is effective in reducing clinical illness in newly received cattle, but effects on performance have been variable. Additionally, public scrutiny regarding antimicrobial usage in animals harvested for human consumption has increased in recent years due to concern over the use of antimicrobials used in both human and animals, antimicrobial resistance, and potential antimicrobial residuals in meat (Dennis et al., 2018). This increase in scrutiny has led researchers to search for additional management practices that improve the industry's judicious use of antimicrobials. Quantifying hematology parameters for use as BRD prediction measures have garnered interest in recent years

and may provide a method to selectively treat animals at greater risk of developing BRD rather than treating a group of cattle simultaneously based on risk classification. Therefore, the objective of this study is to investigate potential predictive indices of hematology parameters as the indicators relate to subsequent BRD treatment. An additional objective of this experiment was to evaluate the effect of metaphylaxis on performance characteristics in newly received beef cattle.

MATERIALS AND METHODS

All live animal procedures for the current experiment were approved by the Oklahoma State University Institutional Animal Care and Use Committee (Animal Care and Use Protocol number: AG-19-8). This experiment was conducted at the Willard Sparks Beef Research Center (WSBRC) located in Stillwater, OK.

Cattle background and arrival procedures

A total of 605 crossbred beef steers (BW = 255 ± 8.3 kg) were procured from a livestock buying station in Louisiana and then transported approximately 966 km to the WSBRC at Oklahoma State University. Steers arrived to the WSBRC in 3 groups (blocks) in September of 2018. Immediately upon arrival to the research feedlot (d -1), cattle were weighed (Avery Weigh-Tronix; Fairmont, MN) and administered individual identification tags. Ear notch samples were also collected upon arrival to test for infection with bovine viral diarrhea virus (**BVDv**). Steers were then allowed 12 to 24 h of rest in holding pens containing *ad libitum* access to prairie hay and water before initial processing on d 0.

At initial processing (d 0), cattle were weighed, vaccinated against clostridial pathogens *Clostridium chauvoei*, *Clostridium novyi*, *Clostridium perfringens* C and D, *Clostridium septicum*, *Clostridium sordellii*, and *Moraxella bovis* (Vision 7 20/20 with SPUR; Merck Animal Health, Madison, NJ) and against viral pathogens bovine herpesvirus-1, BVDv type 1 and 2, parainfluenza-3 virus, and bovine respiratory syncytial virus (Titanium 5 PH + M; Elanco Animal

Health, Greenfield, IN). Steers were also drenched with an oral anthelmintic (Safeguard; Merck Animal Health), given a topical insecticide (Standguard; Elanco Animal Health), and were administered a growth implant containing 80 mg of trenbolone acetate, 16 mg estradiol, and 29 mg tylosin tartrate (Component TE-IS; Elanco Animal Health) at processing. No cattle tested positive for BVDv. Cattle were sorted upon exiting the chute and were immediately allotted to their receiving pens following processing on d 0.

Experimental treatments and receiving management

Cattle were stratified by BW within block and were randomly assigned to 1 of 2 experimental treatments. Experimental treatments consisted of 1) cattle receiving no antimicrobial treatment at arrival (CON) or 2) cattle administered metaphylaxis at arrival (MET; tildipirosin, Merck Animal Health). Experimental treatments were randomly assigned to animal, and both experimental treatments were equally balanced within receiving pens. A total of 24 receiving pens were used during the receiving trial. Animal was considered the experimental unit for all analyses.

All animals were housed in 12.5 × 30.5 m soil-surfaced open-air receiving pens that contained continuous flow concrete watering tanks (Model J 360-F; Johnson Concrete, Hastings, NE) and a 12.2 m concrete bunk. Cattle were managed to target *ad libitum* access to water and feed throughout the entire duration of the experiment. The receiving diet (Table 3-1) fed to all steers during the experiment was formulated to meet or exceed NASEM (2016) nutrient requirements. Long-stem hay was provided at 0.91 kg per head daily for the first 4 d of the experiment. Feed bunks were read at 0530 and 1730 h and feed was mixed and delivered once daily by 0900 h using a trailer-mounted feed mixer (274-12B; Roto-Mix, Dodge City, KS). Feed calls were adjusted daily to target crumbs left in the bunk, and feed refusals were collected daily at 0600 h. Daily residual feed and feed refusals before BW collections were dried for DM

determination and the resulting feed DM was factored into DMI calculations. Ration samples were collected twice per week and dried in a forced air oven for 48 h at 60°C for DM determination. Weekly ration samples were composited by month and analyzed at a commercial laboratory (Servi-Tech Inc., Dodge City, KS) for determination of nutrient composition. Total digestible nutrients (TDN) were calculated by using the following equation: TDN = 93.59 – (ADF × 0.936). Net energy for maintenance (NE_m) and net energy for gain NE_g were calculated by the following equations: $NE_m = ((0.029 \times TDN) – 0.29)$; $NE_g = ((0.029 \times TDN) – 1.01)$.

Evaluation of BRD for antimicrobial treatment

Calves were evaluated daily by 2 trained personnel for the detection of clinical signs consistent with (or suggestive of) of BRD. Cattle were assigned severity scores (**SS**) based upon the DART system with modifications described by Wilson et al. (2016) and Step et al. (2008). Numerical SS range from 0 to 4. A SS of 0 indicated an animal was clinically normal, 1 indicated mild clinical signs, 2 indicated an animal exhibiting moderate clinical signs, 3 indicated severe clinical signs, and a SS of 4 would indicate a moribund animal requiring immediate attention. Animals that received a SS of 1 or greater were eligible to be taken to the processing chute for rectal temperature measurement (GL M-500; GLA Agricultural Electronics, San Luis Obispo, CA). Animals that received a subjective SS of 1 or 2 and had a rectal temperature greater than or equal to 40°C were eligible for antimicrobial treatment. Cattle that were assigned a SS of 3 or 4 received antimicrobial treatment regardless of rectal temperature. All cattle regardless of treatment status were immediately returned to their home pen.

All antimicrobials were administered subcutaneously according to the manufacturing label and Beef Quality Assurance Guidelines (NCBA, 2001). Cattle eligible for treatment were allowed to receive antimicrobial treatment up to 3 times on alternating sides of the animal. If an animal did not respond to antimicrobial treatment after the third treatment and continued to

receive a DART score of 1 or greater, the animal was labeled as chronic and removed from the experiment. Antimicrobial therapy with tildipirosin (Zuprevo; 4mg/kg, Merck Animal Health) was administered to the MET steers at arrival and was the first antimicrobial administered for BRD treatment for CON steers if treatment criteria was met. Following a moratorium of 168 h after Zuprevo administration, florfenicol (Nuflor; 40 mg/kg, Merck Animal Health) was administered if antimicrobial treatment criteria was met a second time. If treatment criteria were met for the third time following a Nuflor moratorium of 72 h, ceftiofur crystalline free acid (Excede; 6.6 mg/kg, Zoetis) was administered.

Data collection

Individual BW were recorded on d 0, 14, 28, 42, and 56. Body weight was recorded before feeding at approximately 0530 h with no feed or water withdrawal. All BW were adjusted using a calculated 2% pencil shrink (BW × 0.98). Average daily gain was calculated for each animal by dividing the individual weight gained during the period by the number of days on feed during the period. Performance and feed data for animals that died or were removed from the experiment were excluded from statistical analyses.

Hematology analysis was performed by collecting whole blood via jugular venipuncture from each animal on d 0 (n = 605) using 4 mL vacutainer tubes containing EDTA (BD Vacutainer; Thermo Fisher Scientific, Waltham, MA). Hematology analysis was performed for neutrophil, lymphocyte, monocyte, basophil, eosinophil, hemoglobin, hematocrit, platelet, red blood cell (**RBC**), mean corpuscular volume, mean corpuscular hemoglobin concentration, and mean corpuscular hemoglobin determination using an automated hemocytometer (ProCyte Dx Hematology Analyzer; IDEXX Laboratories, Inc., Westbrook, ME).

Statistical analysis

Data were analyzed using the MIXED and GLIMMIX procedures of SAS 9.4 (SAS Institute Inc., Cary, NC). Experimental treatments were arranged in a randomized complete block design (n = 3 blocks). Animal served as the experimental unit for all response variables, with treatment included as the fixed effect and block serving as a random effect. The MIXED procedure was used to evaluate performance differences between treatments, while the GLIMMIX procedure was used to compare differences in hematology parameters in CON calves that were subsequently treated for BRD.

RESULTS AND DISCUSSION

Animal performance

Performance data for CON and MET steers are presented in Table 3-2. There were no differences ($P \geq 0.44$) in BW between CON and MET steers throughout the entire length of the experiment. Average daily gain for the MET steers was greater ($P < 0.01$) during the first 14 d than for CON steers. No differences ($P \geq 0.16$) in ADG between treatments existed for the remainder of the experiment. Numerous experiments have documented benefits in performance in response to metaphylaxis on arrival. Word et al. (2020) evaluated metaphylaxis with ceftiofur crystalline free acid or tilmicosin phosphate versus a control group of lightweight males calves. The authors reported that metaphylaxis positively impacted ADG and G:F. Similar to the results of the current experiment, Word et al. (2020) reported that ADG and G:F were improved only for the initial 14 d on feed, but no differences were observed after 42 d. Improvements in gain observed for MET cattle the first 14 d are most likely a result of improvements in health due to the antibiotic treatment, and the lack in differences beyond the initial few weeks suggest that cattle not administered MET were able to naturally overcome stress or disease challenges by d 14. Duff et al. (2000) reported that tilmicosin phosphate given at arrival reduced morbidity by 25% compared to a negative control, but the authors found no differences in ADG, DMI, or G:F during

the 35 d receiving trial. Galyean et al. (1995) conducted 3 experiments to evaluate metaphylaxis with tilmicosin phosphate on health and performance of receiving calves. These authors reported that MET in all 3 experiments reduced the percentage of calves treated for BRD and also reported that in 2 of 3 experiments, ADG and DMI were unaffected. Guthrie et al. (2004) observed that MET improved ADG the first 102 d and increased final BW by 7.26 kg. In agreement, Munoz et al. (2020) reported that metaphylaxis with tulathromycin improved ADG from d 0 to 28 and improved overall BW while also reducing morbidity. Discrepancy between results published by Guthrie et al. (2004) and Munoz et al. (2020) compared to the current experiment may be explained by the difference in the severity of morbidity between experiments. In the current experiment, 11.4% of CON cattle were treated for BRD, while 56.5% and 53% of control cattle in their experiments became morbid, respectively. Furthermore, the overall lack in differences in performance data after d 14 suggests that cattle in the current experiment were less clinically ill overall than expected. Generally, high-risk cattle (light weight, recently weaned and highly commingled) are most benefitted by metaphylaxis (Ives and Richeson, 2015). Based on the performance results and clinical outcome, the cattle in the current experiment would be classified as medium-risk and thus would likely not benefit greatly from antimicrobial metaphylaxis (Wilson et al., 2017). A meta-analysis completed by Baptiste and Kyvsgaard (2017) suggested that metaphylaxis demonstrated moderate, yet highly variable risk reductions in BRD morbidity, and stated that BRD morbidity reductions were dependent on antimicrobial classes, metaphylaxis definition criteria, BRD morbidity rates, and the randomized controlled clinical trials evaluated.

Data evaluating differences in performance between CON steers that remained clinically healthy (NTRT) and CON steers that were treated for BRD (TRT) are presented in Table 3-3. Steer BW on d 0 was less ($P = 0.01$) for cattle that were eventually treated for BRD than for cattle not treated for BRD during the experiment. Body weight for TRT steers was less ($P \leq 0.02$) than BW for NTRT steers throughout the receiving period; however, no differences ($P \geq 0.12$) were

observed between ADG throughout the experiment. These data suggest that lighter weight cattle at arrival in the current experiment were at greater risk of BRD. Guthrie et al. (2004) reported that non-medicated control cattle outperformed similar calves eventually treated for BRD by 0.04 kg per d over 102 d on feed. The lack in differences in ADG between the 2 groups in the current experiment indicate that TRT steers were able to recover from disease challenge with antimicrobial treatment, and these data ultimately highlight that treated cattle have the potential to perform similarly to non-treated cattle. It can also be speculated that cattle treated for BRD are unable to fully recover BW through compensatory gain, which can have drastic indirect impacts on financial gain.

Hematology

Hematology data are presented in Table 3-4. We observed a tendency (P =0.08) for CON NTRT steers to contain greater neutrophil counts than CON TRT steers. No differences between treatments were observed ($P \geq 0.16$) for counts of lymphocytes, monocytes, eosinophils, or basophils. Both hematocrit percentage and hemoglobin were greater ($P \leq 0.05$) for NTRT steers than for the TRT steers. No differences were detected ($P \geq 0.11$) in red blood cell (RBC) counts, platelets, mean corpuscular volume, or mean corpuscular hemoglobin concentration; however, mean corpuscular hemoglobin was greater (P = 0.16) for the NTRT steers than for the TRT steers.

Most of the hematological data presented in this experiment fall within the respective reference range provided by Roland et al. (2014) and Jones and Allison (2017). Because these data are within established reference ranges, it is difficult to determine the biological significance between TRT and NTRT cattle. Also since cattle were only sampled at arrival, it is difficult to determine which direction blood differentials between TRT and NTRT are shifting. In the current experiment, TRT tended (P =0.08) to exhibit neutropenia relative to NTRT cattle. Neutropenia

occurs in ruminants during the first 1 to 2 d of severe, acute inflammation that is oftentimes caused by sepsis or pneumonia (Roland et al., 2014). Cattle in TRT group from the current experiment also displayed ($P \leq 0.05$) lower hematocrit percentage and hemoglobin concentration compared to NTRT cattle. Hemoglobin represents the oxygen-carrying capacity of the RBC, which may suggest that TRT were slightly anemic on arrival than NTRT. Mean corpuscular hemoglobin is an additional cellular measurement used to describe hemoglobin. In the present experiment, mean corpuscular hemoglobin was reduced in the TRT steers compared to the NTRT steers. Mean corpuscular hemoglobin can be used to further describe the differences in hemoglobin concentrations. No other differences in cellular blood parameters between NTRT and TRT cattle were observed in the current study. The lack in differences again may highlight that the cattle used in this experiment may not have been immunologically suppressed enough to justify the use of metaphylaxis.

CONCLUSIONS

Metaphylaxis in the current experiment improved performance early in the feeding period, but early improvements in gain were negated over the course of the experiment. No differences in arrival leukocyte data were present, which give no indication for key leukocytes that may be indicative of early-onset BRD. Cellular components related to erythrocyte indices such as hematocrit percent and hemoglobin concentration were lower for cattle selectively treated for BRD compared to cattle not treated, so further evaluation of these parameters with regard to the parameter's ability to indicate BRD is warranted. Ultimately, the low prevalence of BRD detected in this experiment suggests that metaphylaxis was not warranted, and further highlights the applicability for accurate rapid blood analyses for selective antimicrobial treatment for BRD as antimicrobial use could have been reduced.

Table 3-1. Composition of the common receiving diet[1]

Item	Value
Ingredient, % of DM	
Rolled corn	15.00
Prairie hay	28.44
Sweet Bran[2]	51.36
Dry supplement	5.20
Nutrient composition[3], DM basis	
Dry matter, %	69.67
CP, %	17.20
ADF, %	22.23
TDN, %	70.63
NE_m, Mcal/kg	1.65
NE_g, Mcal/kg	1.01
Ca, %	0.63
P, %	0.68
K, %	1.27
Mg, %	0.36

[1] Diet analyses for nutrient were performed by Servi-Tech Laboratories; Dodge City, KS.
[2] Sweet Bran (Cargill Inc., Dalhart, TX).
[3] All values are presented on a DM basis. Dry supplement was formulated to contain (% DM basis) 40.0% ground corn, 29.6% limestone, 20.0% wheat middlings, 7.0% urea, 1.0 % salt, 0.53% magnesium oxide, 0.51% zinc sulfate, 0.17% manganese oxide, 0.13% copper sulfate, 0.08% selenium premix (0.6%), 0.0037% cobalt carbonate, 0.32% vitamin A (30,000 IU/g), 0.10% vitamin E (500 IU/g), 0.009% vitamin D (30,000 IU/g), 0.20 % tylosin (Tylan-40, Elanco Animal Health, Greenfield IN) and 0.33% monensin (Rumensin- 90; Elanco Animal Health).

Table 3-2. Effect of metaphylactic antimicrobial treatment at arrival on performance characteristics in receiving steers

	Treatment[1]			
Item	CON	MET	SEM	*P*-Value
BW[2], kg				
d 0	256	255	8.3	0.94
d 14	265	267	8.8	0.44
d 28	299	301	10.3	0.50
d 42	322	324	10.3	0.52
d 56	347	349	9.1	0.58
ADG[3], kg				
d 0 to 14	0.69	0.87	0.120	<0.01
d 14 to 28	2.44	2.42	0.123	0.69
d 28 to 42	1.62	1.62	0.052	0.96
d 42 to 56	1.82	1.81	0.097	0.79
d 0 to 56	1.65	1.69	0.038	0.16

[1] Treatments included: CON = cattle receiving no antimicrobial treatment at arrival; MET = cattle administered metaphylaxis at arrival (tildipirosin; Merck Animal Health)

[2] Body weight was adjusted using a 2% calculated shrink

[3] Average daily gain was calculated from the individual shrunk BW gain, kg divided by the days on feed for each period

Table 3-3. Effect of respiratory treatment administered to non-metaphylaxis cattle on subsequent performance during the receiving period

	Treatment[1]			
Item	NTRT	TRT	SEM	*P*-Value
BW[2], kg				
d 0	258	241	6.5	0.01
d 14	267	249	6.7	<0.01
d 28	301	284	6.7	0.01
d 42	324	305	7.2	<0.01
d 56	349	332	7.2	0.02
ADG[3], kg				
d 0 to 14	0.72	0.60	0.141	0.41
d 14 to 28	2.44	2.51	0.104	0.54
d 28 to 42	1.64	1.49	0.115	0.20
d 42 to 56	1.78	1.96	0.111	0.12
d 0 to 56	1.65	1.65	0.052	0.93

[1] Treatments included: NTRT = steers that were not administered metaphylactic antimicrobial treatment upon arrival and that were not treated for BRD; TRT = steers that were not administered metaphylactic antimicrobial treatment upon arrival and that were subsequently treated for BRD

[2] Body weight was adjusted using a 2% calculated shrink

[3] Average daily gain was calculated from the individual shrunk BW gain, kg divided by the days on feed for each period

Table 3-4. Difference in cellular blood parameters between steers treated for bovine respiratory disease

Item	Treatment[1]		SEM	*P*-value
	NTRT	TRT		
Neutrophils, $n \times 10^3/\mu L$	4.8	3.8	0.56	0.08
Lymphocytes, $n \times 10^3/\mu L$	6.7	6.3	0.54	0.55
Eosinophils, $n \times 10^3/\mu L$	0.4	0.3	0.12	0.26
Basophils, $n \times 10^3/\mu L$	0.008	0.006	0.0023	0.53
Hematocrit, %	37.3	35.0	1.14	0.05
Hemoglobin, g/dL	12.2	11.4	0.33	0.02
Red blood Cells, $n \times 10^6/\mu L$	10.0	9.8	0.30	0.44
Platelets, $n \times 10^3/\mu L$	472.7	473.5	40.27	0.99
Mean corpuscular volume, fL	37.3	36.0	0.84	0.11
Mean corpuscular h., pg[2]	12.2	11.7	0.24	0.03
Mean corpuscular h. conc., g/dL[3]	32.8	32.6	0.36	0.59

[1] Treatments included: NTRT = steers that were not administered metaphylactic antimicrobial treatment upon arrival and that were not treated for BRD; TRT = steers that were not administered metaphylactic antimicrobial treatment upon arrival and that were subsequently treated for BRD

[2] Mean corpuscular hemoglobin, pg

[3] Mean corpuscular hemoglobin concentration, g/dL

CHAPTER IV

THE EFFECT OF ROUGHAGE INCLUSION LEVEL IN RECEVING DIETS ON PERFORMANCE, HEALTH, AND METABOLITE CHARACTERISTICS OF NEWLY RECEIVED BEEF CALVES

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ABSTRACT

Increasing roughage inclusion in receiving diets is thought to improve calf health at the expense of reduced performance in newly received beef calves. The first experiment evaluated the effects of increasing dietary roughage concentration on performance and clinical health in newly received high-risk heifers. Heifers (*n* = 557; initial BW = 230 ± 33 kg) were sourced from livestock auctions throughout central Oklahoma from April through October of 2019 in 7 groups. Heifers were weighed on d -1 and assigned randomly to pens which were randomly assigned to 1 of 3 dietary treatments including: 1) a diet containing 15% roughage (**R15**); 2) a diet containing 30% roughage (**R30**); and 3) a diet containing 45% roughage (**R45**). The randomized complete block design resulted in 9 pen replications per treatment. In Exp. 2, Angus steers (*n* = 12) and heifers

(n = 6; BW = 272 ± 28 kg) were acquired from a single ranch in central Oklahoma and used to evaluate the same dietary roughage treatments on serum glucose, lactate, blood urea nitrogen (**BUN**), and non-esterified fatty acid (**NEFA**) concentrations. Animals were randomly assigned to experimental treatments, with animal serving as the experimental unit in Exp. 2. Data were analyzed using PROC MIXED in SAS 9.4. Orthogonal contrasts were used in Exp. 1 to test for linear and quadratic responses. Metabolite models in Exp. 2 were analyzed using repeated measures with the effects of treatment, time, and treatment × time. There was a linear decrease in ADG ($P \leq 0.01$) with increasing roughage inclusion throughout the experiment leading to linear decreases ($P \leq 0.01$) in heifer BW with increasing dietary roughage after d 28. A linear increase ($P \leq 0.01$) was observed for overall DMI and G:F decreased linearly ($P \leq 0.04$) as dietary roughage concentration increased. No response ($P \geq 0.13$) was detected for animals treated once for bovine respiratory disease (BRD) or for overall antimicrobial treatments; however, a quadratic response was observed ($P = 0.02$) for the percent of cattle treated 3 times with decreasing roughage. No other responses ($P \geq 0.11$) were detected in animal health variables. In Exp. 2, no treatment × time interactions ($P \geq 0.45$) were present; however, tendencies were detected for BUN ($P = 0.07$) and NEFA ($P = 0.06$) concentrations. Treatment had no effect ($P \geq 0.11$) on serum glucose, lactate, BUN, or NEFA concentrations, but time impacted ($P \leq 0.02$) all metabolites. In summary, growth performance was improved in heifers as dietary roughage concentration decreased without impacting the number of animals requiring treatment for BRD. Dry matter intake increased as roughage level increased, which caused a linear reduction in G:F. Dietary roughage concentration had a minimal impact on serum metabolites in the current experiment. Our results suggest that by product-based diets containing 15% roughage improve receiving calf performance without negatively affecting health and metabolite characteristics.

Key Words: Bovine respiratory disease, dietary roughage, energy density, feedlot, receiving

INTRODUCTION

Newly received calves often arrive at the feedlot in a catabolic state induced by the sustained feed and water deprivation that animals endure during the marketing and transport processes (Richeson et al., 2019). The resulting negative energy balance, combined with traditionally low DMI post-arrival frequently observed in receiving calves, decreases immune function, which may lead to decreased performance and greater occurrence of health related issues due to bovine respiratory disease (BRD; Richeson et al., 2019). Thus, proper nutritional management of newly received calves is paramount to allow for recovery from stresses associated with shipping (Krehbiel, 2011; Wilson et al., 2017a).

Roughage level and energy density in receiving diets have been investigated by researchers and debated among nutritionists for decades (Lofgreen et al., 1975). Current dogma with regard to receiving calf nutrition is that performance and efficiency increase as roughage level in receiving diets decreases, but also that this performance increase comes at the expense of increased morbidity (Richeson et al., 2019). Samuelson et al. (2016) reported that nutritionists formulate receiving diets with roughage concentrations greater than 40% on average, while nutritionists frequently incorporate grain at 30 to 40% of receiving diets. Lofgreen et al. (1975) reported that increasing diet energy density improved performance and also concluded that morbidity may increase with increasing levels of dietary energy. A meta-analysis completed by Rivera et al. (2005) concluded that morbidity caused by BRD slightly increased as roughage inclusion level decreased. The authors suggested that providing diets containing 50 to 75% concentrate was optimum for starting light-weight, stressed, receiving cattle. Alternatively, Berry et al. (2004) reported no differences in morbidity among calves offered diets differing in diet energy and starch concentrations. Lastly, historical research to support recommendations regarding roughage and energy density in receiving diets lacks the inclusion of fibrous by-products that contribute a large percentage of the diet offered to receiving cattle U.S. feedlots today. Fibrous feed by-products provide an opportunity to increase diet energy density without

increasing dietary starch concentration (Richeson et al., 2019). Therefore, the objective of the current experiment was to determine the effect of roughage inclusion level and the subsequent differences in diet energy density on receiving calf performance, clinical health, and metabolite characteristics of newly received beef cattle.

MATERIALS AND METHODS

All live animal procedures for the current experiment were approved by the Oklahoma State University Institutional Animal Care and Use Committee (Animal Care and Use Protocol number: AG-19-8). This experiment was conducted at the Willard Sparks Beef Research Center (WSBRC) located in Stillwater, OK.

Cattle background and arrival processing

In Exp. 1, a total of 557 crossbred beef heifers (BW = 230 ± 33 kg) were purchased at livestock auctions throughout Oklahoma and sent to an order buyer facility in central Oklahoma. All heifers remained at the order buyer facility for at least 4 d before being transported approximately 1.5 h to the research location on April 4, 2019 (Block 1), May 13, 2019 (Block 2), June 10, 2019 (Block 3), July 22, 2019 (Block 4), August 19, 2019 (Block 5), October 9, 2019 (Block 6), and October 23, 2019 (Block 7). Immediately upon arrival to the research feedlot (d -1), cattle were weighed on validated individual scales (Avery Weigh-Tronix; Fairmont, MN) and administered individual identification tags. Calves were then allowed 12 to 24 h of rest in holding pens containing *ad libitum* access to prairie hay and water before initial processing on d 0. In Exp. 2, a total of 18 Angus-bred steers (n = 12) and heifers (n = 6; BW = 272 ± 28 kg) were acquired from a single-source ranch and were transported approximately 48 km to Stillwater, OK on December 17, 2019. Similar to the heifers in Exp. 1, cattle in Exp. 2 were weighed and administered individual identification tags on d -1 and were allowed 12 to 24 h of rest time in a common pen with *ad libitum* access to prairie hay and water before initial processing on d 0.

At initial processing (d 0), cattle enrolled in Exp. 1 and Exp. 2 were weighed, vaccinated against clostridial pathogens *Clostridium chauvoei*, *Clostridium novyi*, *Clostridium perfringens* C and D, *Clostridium septicum*, *Clostridium sordellii*, and *Moraxella bovis* (Vision 7 20/20 with SPUR; Merck Animal Health, Madison, NJ) and against viral bovine herpesvirus-1, bovine viral diarrhea virus type 1 and 2, parainfluenza-3 virus, and bovine respiratory syncytial virus (Titanium 5; Elanco Animal Health, Greenfield, IN). Cattle were also administered a *Mannheimia haemolytica* bacterin (Nuplura; Elanco Animal Health), drenched with an oral anthelmintic (Safeguard; Merck Animal Health), and an insecticide (Standguard; Elanco Animal Health) was applied topically. Heifers from Exp. 1 and Exp. 2 were administered a growth implant containing 80 mg of trenbolone acetate, 8 mg of estradiol, and 29 mg of tylosin tartrate (Component TE-IH; Elanco Animal Health), while steers in Exp. 2 were administered a growth implant containing 80 mg of trenbolone acetate, 16 mg estradiol, and 29 mg tylosin tartrate (Component TE-IS; Elanco Animal Health). Cattle were sorted upon exiting the chute and were immediately allotted to assigned receiving pens following processing on d 0.

Experimental treatments and receiving management

Experimental dietary treatments (DM basis) consisted of 1) a low roughage (**R15**) diet (Table 4-1; 15.0% prairie hay, 46.5% Sweet Bran (Cargill Inc.; Dalhart, TX), 32.5% rolled corn, and 6% dry supplement), 2) an intermediary roughage (**R30**) diet (30.0% prairie hay, 39.0% Sweet Bran (Cargill Inc.), 25% rolled corn, and 6% dry supplement), 3) or a high roughage (**R45**) diet (45.0% prairie hay, 31.5% Sweet Bran (Cargill Inc.), 25.0% rolled corn, and 6.0% dry supplement). Pen was considered the experimental unit in Exp 1. and animal was considered the experimental unit in Exp. 2. Experimental treatment diets were formulated to meet or exceed NASEM (2016) nutrient requirements. Cattle were stratified by BW within block and were randomly assigned to 1 of 3 experimental pens in both experiments. Experimental treatments were previously randomly assigned to receiving pen. A total of 27 receiving pens were used for

Exp. 1, with 9 replications per treatment. A total of 3 receiving pens were used for Exp. 2, with 4 steers and 2 heifers per pen.

All animals were housed in 12.5 × 30.5-m soil-surfaced, open-air receiving pens that contained continuous flow concrete watering tanks (Model J 360-F; Johnson Concrete, Hastings, NE) and 12.2 m concrete bunks, which provided approximately 46 cm of linear bunk space per animal for heifers in Exp. 1 and 152 cm of bunk space per animal in Exp. 2. Cattle received ad libitum access to water and experimental diets throughout the duration of the experiment. Long-stem hay was provided at 0.91 kg per head daily in the bunk for the first 4 d of the experiment. Feed bunks were read at 0530 and 1730 h and feed was mixed and delivered once daily at 0800 h by a trailer-mounted feed mixer (274-12B; Roto-Mix, Dodge City, KS). Feed calls were adjusted daily to target crumbs left in the bunk, and feed refusals were collected daily at 0600 h. Daily residual feed and feed refusals weighed before BW collections were dried for DM determination and the resulting feed DM was removed from DMI calculations. Ration samples were collected twice per week. Ration samples and feed refusals were dried in a forced air oven for 48 h at 60°C for DM determination. Weekly ration samples were composited by month and analyzed at a commercial laboratory (Servi-Tech Inc., Dodge City, KS) for determination of nutrient composition. Total digestible nutrients (TDN) were calculated as described by Weiss et al. (1992). Net energy used for maintenance (NE_m) and gain (NE_g) were calculated using equations provided by NASEM (2016). Particle size of prairie hay and Sweet Bran (Cargill Inc.; Dalhart, TX) were determined with a 3.8 L sample using a 3-sieve forage particle separator (Nasco; Fort Atkinson, WI). The sieves were shaken in one direction 5 times, rotated one quarter turn and repeated for a total of 8 sets or 40 shakes. The physically effective neutral detergent fiber (**peNDF**) for prairie hay and Sweet Bran was estimated by calculating the percent of the sample remaining in the top 3 sieves and multiplying by the NDF content of the feedstuff. To determine the peNDF from the roughage and Sweet Bran of each diet, the peNDF of each contributing

ingredient was multiplied by the percent inclusion in the diet. The respective peNDF values were then added to create total peNDF for the diet.

Evaluation of BRD for antimicrobial treatment

Calves were evaluated daily by 2 independent trained personnel for the detection of clinical signs indicative of (or consistent with) BRD. Cattle were assigned severity scores (**SS**) based upon the DART system with modifications described by Wilson et al. (2016) and Step et al. (2008). Numerical SS ranged from 0 to 4. A SS of 0 indicated an animal was clinically normal, 1 indicated mild clinical signs, 2 indicated an animal exhibiting moderate clinical signs, 3 indicated severe clinical signs, and a SS of 4 would indicate a moribund animal requiring immediate attention. Animals that received a SS of 1 or greater were eligible to be taken to the processing chute for rectal temperature measurement (GL M-500, GLA Agricultural Electronics, San Luis Obispo, CA). Animals that received a subjective SS of 1 or 2 and had a rectal temperature greater than or equal to 40°C were eligible for antimicrobial treatment. Cattle that were assigned a SS of 3 or 4 received antimicrobial treatment regardless of rectal temperature. All cattle regardless of whether or not antimicrobial treatment was administered were immediately returned to a home pen from the processing chute.

All antimicrobials were administered subcutaneously according to the manufacturer's label and Beef Quality Assurance Guidelines (NCBA, 2001). Cattle eligible for antimicrobial treatment were allowed to receive an antimicrobial up to 3 times on alternating sides of the animal. If an animal did not respond to antimicrobial treatment after the third antimicrobial administration and continued to receive a DART score of 1 or greater or continued to lose weight, the animal was labeled as chronic and removed from the experiment. Antimicrobial therapy with tilmicosin phosphate (Micotil; 10 mg/kg, Elanco Animal Health) was administered the first time treatment criteria was met. Following a moratorium of 120 h after tilmicosin administration,

florfenicol (Nuflor; 40 mg/kg, Merck Animal Health) was administered if antimicrobial treatment criteria was met a second time. If treatment criteria were met for the third time following a florfenicol moratorium of 72 h, ceftiofur crystalline free acid (Excede; 6.6 mg/kg, Zoetis) was administered.

Data collection

Individual BW was recorded for all heifers in Exp. 1 on d 0, 14, 28, 42, and 56. Body weight was recorded before feeding at approximately 0530 h with no feed or water withdrawal. All BW were adjusted using a calculated 2% pencil shrink (BW × 0.98). Individual BW were averaged within pen to calculate an average BW for the pen. Average daily gain was calculated for each animal by dividing the individual weight gained during the period by the number of days on feed during the period. Pen ADG was calculated by averaging individual ADG for each animal in a pen for that period. Dry matter intake was calculated within period by taking the total weight of DM fed divided by the number of cattle and the days on feed for that period. Gain to feed ratio was calculated within period by dividing pen ADG by the pen average daily DMI for each respective period.

Performance and feed data for animals that died or were removed from the experiment were excluded from statistical analyses. Intake data were corrected for mortalities and removals by removing an animal's average daily DMI from the pen until the animal ceased gaining BW. If an animal was not gaining BW, DMI for that animal was removed from the time the animal began to lose weight until the removal date using the NASEM (2016) net energy maintenance equation $NE_m = 0.077 \times (SBW)^{0.75}$.

All animals in Exp. 2 were bled via jugular venipuncture using 10 mL serum vacutainer tubes (BD Vacutainer; Thermo Fisher Scientific, Waltham, MA) to evaluate the metabolite responses of glucose, L-lactate, non-esterified fatty acids (**NEFA**), and blood urea nitrogen

(**BUN**) to dietary roughage treatments. Blood collections occurred on h 0 and d 1 (h 4), 2, 3, 4, 5, 6, 13, and 20 relative to h 0 when the animals were first fed dietary treatments following initial processing. Following blood collection, serum was harvested by centrifuging the whole blood at 1,294 × g for 10 min at 4°C (Sorvall RC6; Thermo Scientific, Waltham, MA). Serum was then stored at -80°C until further metabolite analyses could be conducted. Serum samples were thawed immediately before glucose, lactate, NEFA, and BUN analysis. Glucose and lactate were analyzed using an immobilized enzyme system (YSI Model 2950 D; YSI Inc., Yellow Springs, OH). Blood urea nitrogen was analyzed utilizing the methods described by Marsh et al. (1965) adapted for a 96-well plate. Serum was analyzed for NEFA concentration by use of a standard NEFA quantitation kit (NEFA-C Kit; WAKO Chemicals USA, Richmond, VA).

Statistical analysis

Data were analyzed using the MIXED procedure of SAS 9.4 (SAS Institute Inc., Cary, NC). In Exp. 1, experimental treatments were arranged in a generalized randomized complete block design (n = 7 blocks) with 9 pen replications per treatment. Pen served as the experimental unit for all dependent variables. Treatment was included in the model as the fixed effect and block served as a random effect. Linear and quadratic contrasts were performed for the main effects for the 3 experimental diets (R15, R30, and R45).

In Exp. 2, animal served as the experimental unit for all serum metabolite data. Metabolite data were assessed for normality using the Shapiro-Wilk test statistic in the UNIVARIATE procedure of SAS 9.4. Lactate and NEFA concentrations were determined to be non-normal and were logarithm (base 10) transformed to achieve normality. The covariance structure with the lowest Akaike information criterion was used for each variable. The fixed effect of treatment, day, and the resulting treatment × day interaction was used in the model to analyze the metabolite data, with pen serving as a random effect. Results were considered

significant where $P \leq 0.05$, and tendencies were identified where $0.05 > P \leq 0.10$. All performance and intake data from cattle removed in the experiment were excluded from the statistical analysis with the exception of the health variables.

RESULTS AND DISCUSSION

Animal performance

Performance data are presented in Table 4-2. As expected, there was no effect in BW ($P \geq 0.38$) on d 0. There were also no differences ($P \geq 0.13$) observed in BW between treatments on d 14. However, there was a linear increase ($P \leq 0.01$) in BW on d 28, 42, and 56 with decreasing diet roughage concentration. The lack of difference in BW on d 14 may have been the result of lower feed and thus energy intake due to the stressful transition to the feedlot and greater morbidity within first 2 wk following arrival. Dry matter intake was 2.2, 2.1, and 2.2% of BW during the first 14 d for the R15, R30, and R45 treatment groups, respectively. It has been reported that cattle only consume 0.5% to 1.5% of their BW during the first 2 wk after arrival to the feedlot (Krehbiel et al., 2011; Richeson et al., 2019). Average daily gain increased linearly ($P \leq 0.05$) with increasing dietary concentrate concentrations during the first 3 periods and also increased linearly ($P \leq 0.01$) throughout the entire experiment. However, no response in ADG from d 42 to 56 was observed ($P \geq 0.18$).

A tendency for a quadratic response ($P = 0.08$) in DMI was detected from d 0 to 14, where R45 tended to consume more feed than R30 but did not differ from R15. There was no response ($P \geq 0.24$) in DMI observed from d 14 to 28; however, DMI increased linearly ($P \leq 0.04$) for the last 2 periods with increasing roughage in the diet. Overall DMI ($P \leq 0.01$) throughout the experiment also increased linearly as roughage concentration increased. There was a linear decrease ($P \leq 0.04$) in G:F with increasing dietary roughage across all time periods during the experiment.

The linear trend for BW and ADG to increase as concentrate increased is expected, as intake of dietary energy was greater for the lower roughage diets. The trend for DMI to increase linearly as roughage level increased can be explained by caloric intake and limitations to ruminal capacity. Satiety in cattle consuming diets greater in roughage may only be met when maximum ruminal capacity or ruminal fill is reached. Alternatively, lower levels of intake have been reported in diets with greater caloric density due to negative chemical feedback mechanisms (Krehbiel et al., 2006). Diets in the current experiment contained 0.88, 0.69, and 0.59 Mcals NE_g/kg of DM for the R15, R30, and R45 diets, respectively; thus, the resulting average NE_g intake for each experimental group from d 0 to 56 would be 6.5, 5.3, and 4.8 Mcals NE_g per d, respectively. The performance trend in the current experiment aligns similarly to that reported by Lofgreen et al. (1975), in which multiple experiments evaluated energy level in receiving diets offered to high risk calves on performance and health characteristics. In their first experiment, Lofgreen et al. (1975) reported that performance was greater for the calves receiving the 1.10 Mcal diet than for the other 2 dietary treatments. Lofgreen et al. (1975) also reported that DMI was directly proportional to energy density in their first experiment, which is in disagreement with the results of the current experiment. Conversely, DMI of receiving calves decreased as Lofgreen et al. (1975) replaced the 0.84 Mcal diet with a 1.19 Mcal diet, which would align similarly with results from the current experiment. Berry et al. (2004) reported that performance, intake, and G:F were unaffected when diet starch concentration was increased from 18.8% to 26.9%. These authors also reported that energy density (0.85 vs. 1.07 Mcal/kg NE_g) had no effect on animal performance during a 42 d trial; however, a greater diet energy density in their experiment reduced overall experimental DMI (Berry et al., 2004). In a review of dietary roughage concentration conducted by Rivera et al. (2005), the authors reported that ADG and DMI were negatively affected by increasing dietary roughage concentration, which partially agrees with results from the current experiment, as results from the current experiment suggest that DMI increases proportionally to roughage level while ADG decreases. Research published

by Fluharty and Loerch (1996) suggests that DMI and ADG increase as percent concentrate in the ration increases. Diet composition in the current experiment may contrast greatly with others previously mentioned, as the diets in the current experiment contained more moisture and Sweet Bran, a wet corn gluten feed based by-product, which may provide some explanation for the discrepancy in DMI response. In the current experiment, the average diet DM was 72.9% (range = 71.59% to 74.23%), which can be primarily attributed to the increased inclusion rate of the Sweet Bran. Only Berry et al. (2004) indicated the diet DM of their experimental treatments, which averaged 89.4% DM; however, based on the dietary ingredients and respective level in the diet, it can be speculated that diet DM of Fluharty and Loerch (1996) and Lofgreen et al. (1975) would be greater than 85%. Overall, performance data from the current experiment agree with literature previously reported such that performance is increased as dietary energy density increases; however, few previously published experiments agree with the intake results of the current experiment.

Clinical Health

Clinical health data are presented in Table 4-3. Throughout the experiment, there was no linear response ($P \geq 0.38$) of treatment on clinical health outcome variables. There was one quadratic response ($P = 0.02$) detected for the percent of animals treated 3 times; however, caution should be taken interpreting these results due to the low number of animals ($n = 8$) treated 3 times. Current dogma in the beef industry with regard to ration formulation for receiving calves is that morbidity and mortality increase as roughage inclusion level decreases. Although no response existed for the total amount of animals treated for BRD in the current experiment, numerical differences and even a near-quadratic tendency for decreased morbidity as roughage level increases becomes apparent. Overall morbidity (13.8%) was less than expected in the current experiment (14.2, 15.7, and 11.4% for the R15, R30, and R45 diets, respectively; Table 4-

3). The low rates of morbidity observed may partially explain the lack in health differences between experimental treatments.

Similar trends in the response of morbidity to dietary treatment were observed between Exp. 1 conducted by Lofgreen et al. (1975) and the current experiment, where both experiments reported that a greater percentage of animals consuming the intermediate diet required treatment for BRD compared to the low and high concentrate diets. Lofgreen et al. (1975) reported that cattle were treated when rectal temperature exceeded 39.4°C. In contrast, Exp. 2 of Lofgreen et al. (1975), morbidity tended to increase with increasing concentrations of dietary energy. Richeson et al. (2019) suggested that cattle enrolled on the high concentrate diet in Exp 2. of Lofgreen et al. (1975) experiment may have exhibited greater morbidity due to a reduced energy intake and subsequent inability to mount an adequate immune response, or that the calves may have encountered ruminal acidosis. Energy intake for heifers was greatest on the R15 diet in the current experiment, which may describe why similar results in morbidity in this study were not observed. Richeson et al. (2019) further described that there are possible limitations in interpreting the results concluded by Lofgreen et al. (1975), as the authors used a small number of calves (range = 35 to 39 calves) within each treatment and only 2 pen replicates per treatment were used. The current experiment enrolled an average of 185 calves per experimental treatment and had 9 pen replications per treatment.

Fluharty and Loerch (1996) reported that no differences in calf morbidity existed between calves consuming diets containing 1.15, 1.21, 1.25, or 1.30 Mcal NE_g/kg, and the authors concluded that calves may benefit from high energy receiving diets containing 70 to 85% concentrate. Diets in the current experiment contained 85, 70, and 55% concentrate for the R15, R30, and R45 diets, respectively. Performance and clinical results from the current experiment agree with results published by Fluharty and Loerch (1996) in that heifers on the greater concentrate diets outperformed heifers consuming lower concentrate diets. Caution with data

interpretation is warranted, however, due to the numerical reduction (5.1%) in total morbidity from calves consuming the R15 diet compared to the R45 diet in the current experiment. Berry et al. (2004) observed no differences in the percent of calves requiring BRD treatment when calves were assigned to 1 of 2 dietary energy levels (0.85 or 1.07 Mcal NE_g/kg) and 1 of 2 dietary starch levels (34 or 48% of ME from starch). Numerical differences were observed in their experiment in which calves fed greater levels of starch had increased morbidity, and calves consuming lower levels of starch tended to have less third treatments for BRD.

In the meta-analysis conducted by Rivera et al. (2005), the authors reported that morbidity attributed to BRD increased slightly as dietary roughage concentration increased (% morbidity = 49.59 – 0.0675 × roughage %), but concluded that providing a 50 to 70% concentrate diet would be the optimum dietary strategy to enhance performance while negating negative effects on health in receiving cattle. For the present experiment, linear increases in BW, ADG, and G:F were observed for cattle receiving the 85% concentrate, 0.88 Mcal NE_g/kg ration (R15), with no significant, negative relationship in health detected. Much of the foundational research concerning dietary energy density and roughage inclusion level lacks the inclusion of fibrous by-products that contribute to a large percentage of the diet in today's feedlots (Samuelson et al., 2016; Richeson et al., 2019). Potentially, diets containing high energy, low starch fibrous by-products may reduce instance of BRD without compromising performance. Lower starch, high energy diets may also reduce the prevalence of digestive upsets such as clinical acidosis.

Metabolite Characteristics

Metabolite data from cattle in Exp. 2 are presented in Figures 1 and 2. There were no treatment × time interactions ($P \geq 0.45$) observed for glucose or lactate concentrations. However, tendencies for treatment × time interactions were detected for BUN ($P = 0.07$) and NEFA ($P = 0.06$) concentrations. Concentrations of BUN tended to be greater for animals consuming the R30

and R45 diets on d 13 than for animals consuming the R15 diet. Non-esterified fatty acid concentrations tended to be greater on d 1 for animals consuming the R30 and R45 diets than for animals consuming the R15 diet. Additionally, NEFA concentrations were greater for the R30 experimental group than for the R15 and R45 treatment groups on d 3. The main effect of treatment did not impact ($P \geq 0.11$) glucose and lactate concentrations; however, a time effect ($P \leq 0.02$) was observed for all metabolites. Glucose concentrations decreased the first 2 d following exposure to dietary treatments. Concentrations of glucose consistently remained at around 0.6 to 0.7 g/L from d 2 to 4, then increased to d 5, decreased to d 6, and increased to d 13. Lactate concentrations decreased from d 0 to 4 followed by a slight increase to d 20. Blood urea nitrogen concentration remained fairly steady from d 0 to h 4, increased substantially to d 1, then decreased over time to d 20. Blood NEFA concentrations decreased with no apparent trend from h 0 to d 4, which was then followed by a steady increase to d 20.

The cattle enrolled in Exp. 2 were different in makeup from the heifers enrolled in Exp. 1 with regard to previous management and at-arrival physiological condition. Cattle in Exp. 2 were less stressed overall, as the cattle were weaned, traveled less miles, were not commingled with cattle from other sources, had previous vaccination records, and were clinically healthy at arrival. Therefore, the metabolite data presented should be only used to assess dietary effects on metabolite characteristics in healthy (low-risk) receiving calves and should not be extrapolated to determine the same metabolite responses between dietary treatments in stressed high-risk calves subjected to shipping, commingling, and other stressful events during transition to the feedlot.

Elevations in glucose concentrations have been caused by stresses and the resulting glucocorticoid production (Apple et al., 1995; Donley et al., 2009). Disruptions in glucose homeostasis due to immunoactivation and resulting increase in glucose consumption of immune cells have also been reported (Kvidera et al., 2016). Although no glucocorticoids such as cortisol were measured in Exp. 2, it is plausible to speculate that the peak glucose concentrations

measured on d 0 resulted from stresses incurred during shipping, feedlot entry, and from handling and processing at the chute. Glucose concentrations declined quickly after processing and began to increase again around d 4, which presumably is a function of increased feed intake during the first 4 days on feed.

In general, the trend in lactate concentration tended to follow that of glucose. Lactate is formed from glucose during anaerobic glycolysis under conditions of (local or systemic) hypoxia, including dehydration, maximum muscle exertion, compartment syndrome or other muscle injury, or severely compromised respiratory system. As such, it is not unexpected that lactate trends in the current experiment tended to follow that of glucose concentration. The increased levels of lactate on d 0 are indicative of an increased stress response and subsequent switch of muscle metabolism to anaerobic from aerobic metabolism, which causes lactate to be transferred from the muscle and into the blood (Williams et al., 2019). No interaction or effect of treatment was detected for serum lactate. The reason for the numerical increase in lactate for the R45 treatment on d 13 is unknown to the authors.

Blood urea nitrogen concentrations peaked 24 h following processing followed by a gradual decline throughout the remaining 20 d. Blood urea nitrogen may reflect short-term dietary effects on rumen ammonia production and hepatic N turnover, which is plausible as the spike in BUN was 24 h following access to dietary treatments (Yari et al., 2010). These BUN data are indicative of an increased protein catabolism early in the receiving phase, and the resulting decrease following d 1 illustrates more reliance on dietary protein and less on muscle catabolism.

Serum NEFA concentrations are used to describe the extent of fat mobilization and are highly indictive of overall energy balance (Richeson et al., 2015; Buhler et al., 2019). Peak NEFA concentrations on d 0 likely reflect an overall negative energy balance as a result of the inherent stresses of transportation, receiving, and processing in combination with limited access to feed

prior to processing. The decline in serum NEFA concentrations indicates that animals regained reliance on dietary energy as nutrients required to regain homeostasis were exceeded. The tendency for reduced NEFA concentrations on d 1 may be a result of a greater level of energy intake for cattle consuming the R15 diet; however, an explanation for differences that tended to occur on d 3 is unknown. Collectively, minimal impacts of dietary treatments were observed on blood metabolites. It appears metabolite responses recorded in Exp. 2 were more reflective of an effect of typical transportation and processing procedures and time relative to feedlot arrival than dietary treatment. Further research should evaluate these responses to dietary treatments in high-risk calves subjected to additional stresses.

CONCLUSIONS

Previous literature has indicated that performance, intake, and feed efficiency increase as dietary roughage decreases, but that improvements in performance come at the expense of slight increases in animal morbidity. Much of the previous research pertaining to roughage inclusion and diet energy density for receiving cattle was conducted before the widespread use of fibrous by-products included in commercial feedlot diets today (Richeson et al., 2019). Feeding a receiving diet containing 15% roughage and 0.88 Mcal NE_g/kg in the current experiment provided superior performance without increasing the percentage of cattle treated for BRD. It should be noted that overall morbidity in this experiment did not exceed 16% for any experimental treatment, so caution is warranted interpreting clinical outcomes, as morbidity results may differ between dietary treatments when a greater percent of calves become morbid. Body weight, ADG, and G:F in the current experiment increased linearly while DMI decreased linearly as roughage inclusion level decreased. Negligible differences were detected between serum glucose, lactate, BUN, or NEFA concentrations between dietary treatments; however, further research evaluating similar metabolites in stressed high-risk calves is warranted. Collectively, providing energy dense, fibrous byproduct-based diets formulated that contain low

levels of roughage may be a suitable alternative to traditional receiving diets without compromising calf health.

Table 4-1. Ingredient and nutrient composition of experimental diets[1]

	Dietary Treatment[2]		
Ingredient, % of DM	R15	R30	R45
Rolled corn	32.50	25.00	17.50
Prairie hay	15.00	30.00	45.00
Sweet Bran[3]	46.50	39.00	31.50
Dry supplement[4]	6.00	6.00	6.00
Nutrient composition, DM basis			
Dry matter, %	71.59	73.02	74.23
Crude protein, %	16.94	15.96	14.98
Acid detergent fiber, %	18.10	22.6	28.93
peNDF[5], %	23.38	29.74	36.11
TDN[6], %	70.70	63.88	60.35
NE_m[7], Mcal/kg	1.47	1.26	1.15
NE_g[7], Mcal/kg	0.88	0.69	0.59
Ca, %	0.71	0.85	0.74
P, %	0.65	0.58	0.50
K, %	1.01	0.96	0.93
Mg, %	0.30	0.31	0.30

[1] Diet analyses were performed by Servi-Tech Laboratories; Dodge City, KS.

[2] Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement

[3] Sweet Bran (Cargill Inc., Dalhart, TX)

[4] Dry supplement was formulated to contain (% DM basis) 40.0% ground corn, 29.6% limestone, 20.0% wheat middlings, 7.0% urea, 1.0 % salt, 0.53% magnesium oxide, 0.51% zinc sulfate, 0.17% manganese oxide, 0.13% copper sulfate, 0.08% selenium premix (0.6%), 0.0037% cobalt carbonate, 0.32% vitamin A (30,000 IU/g), 0.10% vitamin E (500 IU/g), 0.009% vitamin D (30,000 IU/g), 0.20 % tylosin (Tylan-40, Elanco Animal Health, Greenfield IN) and 0.33% monensin (Rumensin- 90; Elanco Animal Health)

[5] Physically effective fiber proved by the prairie hay and Sweet Bran in the diet

[6] Calculated according to Weiss et al. (1992)

[7] Calculated according to NASEM (2016)

Table 4-2. Effect of roughage inclusion level in receiving diets on growth, performance, and feed efficiency in receiving heifers

	Dietary Treatment[1]				Contrasts	
Item	R15	R30	R45	SEM[2]	Linear	Quadratic
BW[3], kg						
d 0	225	225	226	7.9	0.26	0.38
d 14	244	243	241	8.8	0.13	0.95
d 28	267	263	259	9.5	<0.01	0.89
d 42	288	280	272	8.3	<0.0001	0.99
d 56	309	301	291	9.8	<0.0001	0.69
ADG[4], kg						
d 0 to 14	1.38	1.28	1.11	0.134	0.04	0.73
d 14 to 28	1.59	1.45	1.29	0.114	0.05	0.94
d 28 to 42	1.50	1.17	0.89	0.160	<0.0001	0.84
d 42 to 56	1.56	1.54	1.40	0.140	0.18	0.51
d 0 to 56	1.51	1.36	1.17	0.058	<0.0001	0.53
DMI[5], kg						
d 0 to 14	4.94	4.77	5.02	0.212	0.54	0.08
d 14 to 28	7.60	7.65	7.82	0.348	0.24	0.70
d 28 to 42	8.54	8.81	9.15	0.455	0.04	0.89
d 42 to 56	8.82	9.45	10.36	0.477	<0.001	0.60
d 0 to 56	7.45	7.62	8.07	0.346	<0.01	0.41
G:F[6]						
d 0 to 14	0.279	0.275	0.223	0.0298	0.04	0.28
d 14 to 28	0.212	0.190	0.166	0.0144	0.03	0.96
d 28 to 42	0.176	0.134	0.099	0.0187	<0.0001	0.74
d 42 to 56	0.176	0.163	0.133	0.0118	<0.001	0.31
d 0 to 56	0.204	0.180	0.146	0.0075	<0.0001	0.24

[1] Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement

[2] n = 9 pens per treatment

[3] Body weight was adjusted using a 2% calculated shrink

[4] Pen ADG was calculated from individual shrunk BW gain, kg divided by days on feed for each period

[5] Pen DMI was calculated from total DMI for the pen for each period divided by the total steers and days on feed in each period

[6] Pen G:F was calculated by dividing the ADG for the pen by the average daily DMI for the pend for each respective period

Table 4-3. Effect of roughage inclusion level in receiving diets on clinical health outcomes of newly received beef heifers

	Dietary Treatment[1]				Contrasts[3]	
Variable	R15	R30	R45	SEM[2]	L	Q
BRD treatment, %						
Treated once[4]	14.17	15.74	11.40	4.372	0.53	0.44
Treated twice[5]	3.36	6.10	2.08	1.656	0.59	0.11
Treated thrice[6]	0.95	2.96	0.00	0.969	0.38	0.02
Total antimicrobial treatments[7], %	18.07	24.40	13.00	6.245	0.44	0.13
Days to first treatment	8.00	8.15	6.19	2.006	0.53	0.65
Rectal temperature, °C	40.32	40.12	40.24	0.211	0.74	0.38
Severity score[8]	1.28	1.57	1.24	0.167	0.86	0.11

[1] Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement

[2] n = 9 pens per treatment

[3] L = linear, Q = quadratic; *P*-value shown

[4] Percentage of cattle treated once for BRD

[5] Percentage of cattle treated twice for BRD

[6] Percentage of cattle treated thrice for BRD

[7] Total antimicrobial treatments were calculated by dividing the total number of animals treated within a pen by the sum of animals within the pen

[8] Severity scores were calculated by dividing the sum of the severity scores within a pen by the sum of animals treated within a pen

Figures

Figure 4-1a. Effect of dietary treatment on serum glucose concentrations in newly received beef heifers. Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement. There was no treatment × time interaction ($P = 0.92$) or treatment effect ($P = 0.96$) on serum glucose concentrations. However, time did effect ($P < 0.01$) serum glucose concentrations. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 4-1b. Effect of dietary treatment on serum lactate (logarithm base 10) concentrations in newly received beef heifers. Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement. There was no treatment × time interaction ($P = 0.45$) or treatment effect ($P = 0.11$) for serum lactate concentrations. There was a time effect ($P = 0.02$) on serum lactate. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 4-2a. Effect of dietary treatment on blood urea nitrogen (BUN) concentrations in newly received beef heifers. Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement. There was a tendency for a treatment × time interaction ($P = 0.07$) for BUN concentrations. No treatment effect ($P = 0.73$) was observed for serum BUN concentrations; however, a time effect ($P < 0.01$) for serum BUN concentration was detected. Values plotted

represent least squares means ± SE of the mean, calculated for 6 animals per experimental group. Within time points, the slice output option of SAS (SAS Inst. Inc., Cary, NC) was used to perform mean separations. [x,y]Means with different superscripts tend to differ ($P \leq 0.10$).

Figure 4-2b. Effect of dietary treatment on non-esterified fatty acid (NEFA) concentrations (logarithm base 10) in newly received beef heifers. Treatments included (DM basis): R15 = 15% prairie hay, 46.50% Sweet Bran, 32.50% rolled corn, 6% dry supplement; R30 = 30% prairie hay, 39% Sweet Bran, 25% rolled corn, 6% dry supplement; R45 = 45% prairie hay, 31.50% Sweet Bran, 17.50% rolled corn, 6% dry supplement. There was a tendency for a treatment × time interaction ($P = 0.06$) for NEFA concentrations. No treatment effect ($P = 0.47$) was observed for serum NEFA concentrations; however, a time effect ($P < 0.01$) for serum NEFA was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group. Within time points, the slice output option of SAS (SAS Inst. Inc., Cary, NC) was used to perform mean separations. [x,y]Means with different superscripts tend to differ ($P \leq 0.10$).

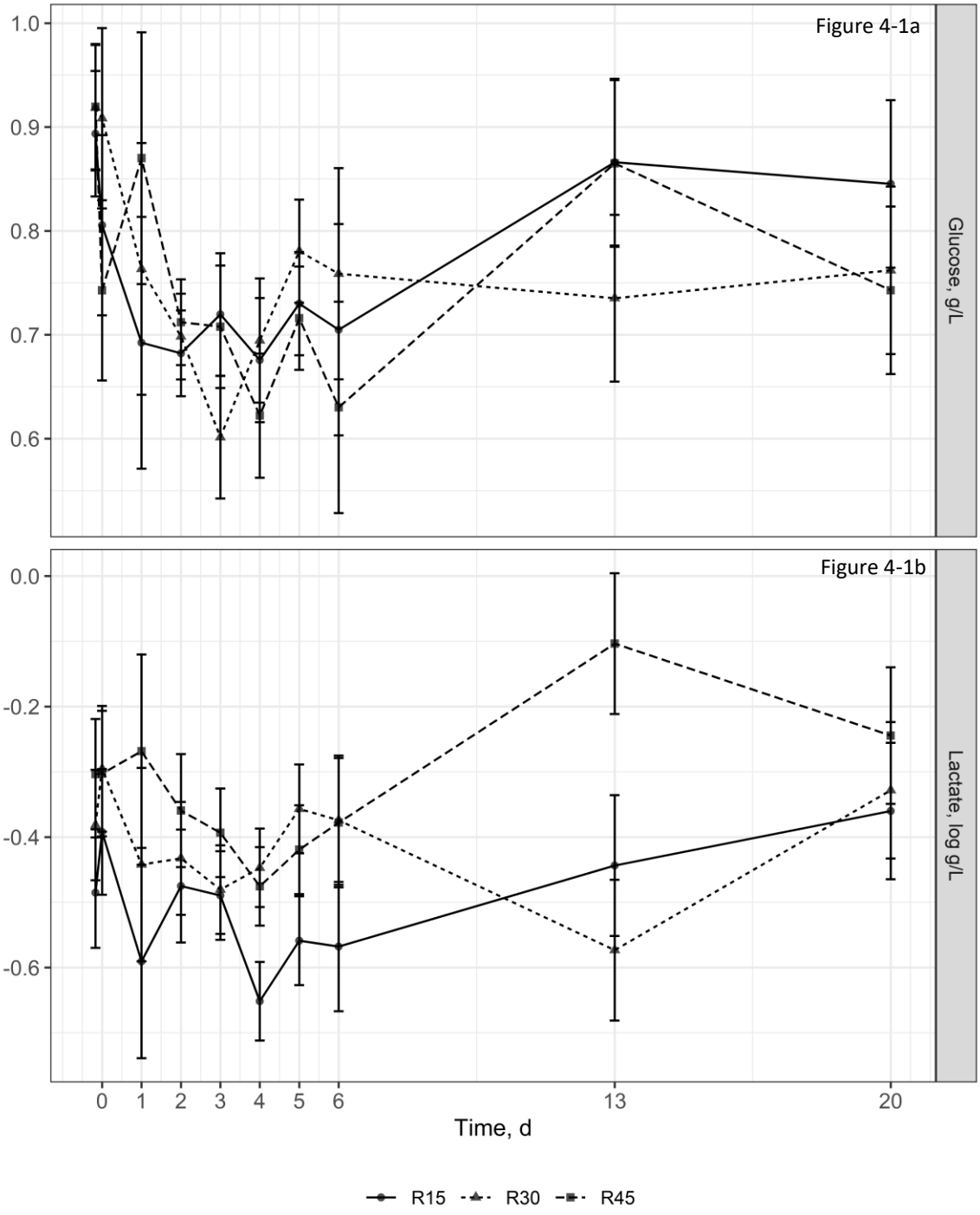
Figure 4-1a
1.0
0.9
0.8
0.7
0.6
Glucose, g/L
Figure 4-1b
0.0
-0.2
-0.4
-0.6
Lactate, log g/L
0
1
2
3
4
5
6
13
20
Time, d
R15
R30
R45

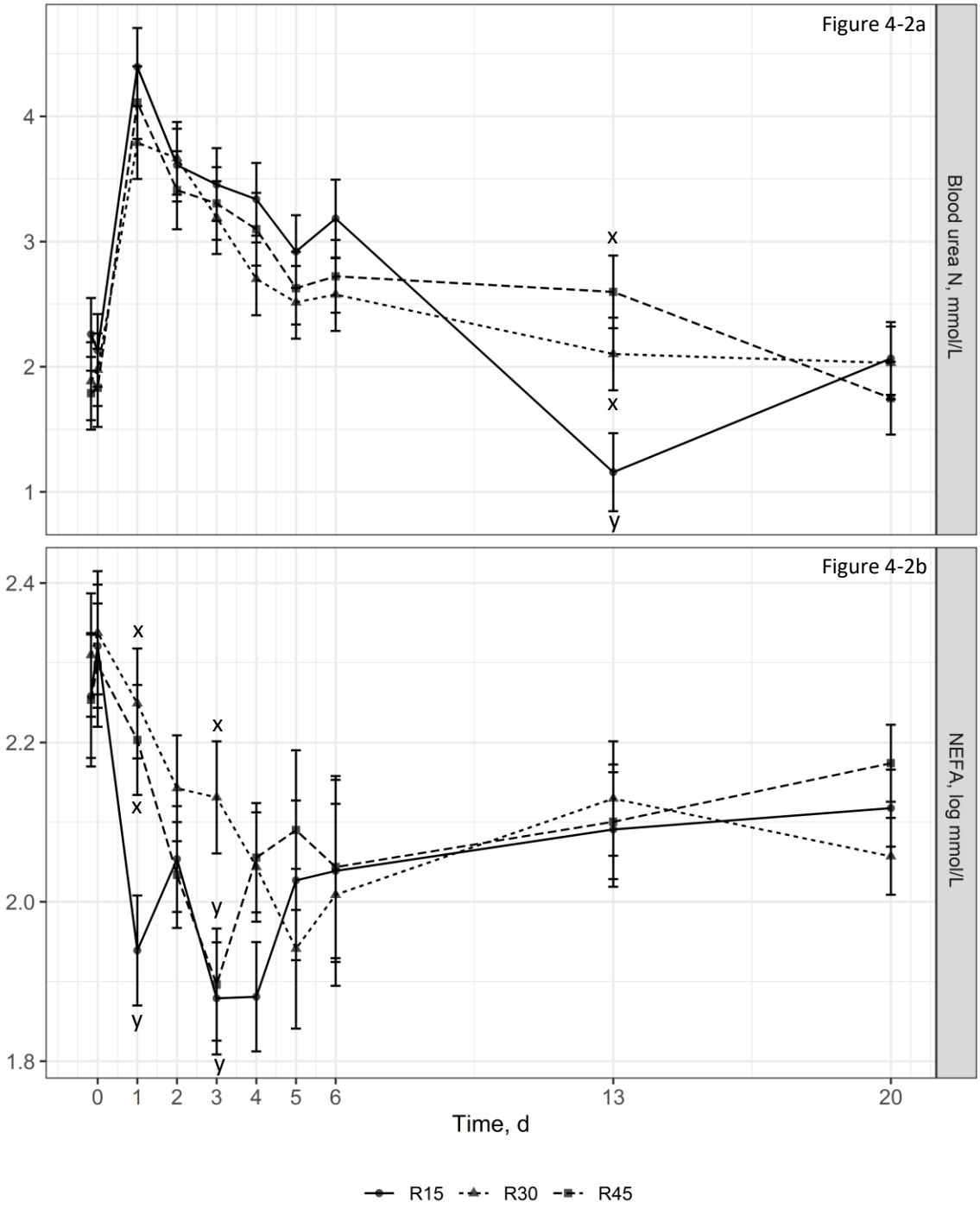
Figure 4-2a
Blood urea N, mmol/L
4
3
2
1
x
x
y
Figure 4-2b
NEFA, log mmol/L
2.4
2.2
2.0
1.8
x
x
y
x
y
y
0
1
2
3
4
5
6
13
20
Time, d
R15
R30
R45

CHAPTER V

EFFECT OF A NUTRITIONAL BOLUS ADMINISTERED AT ARRIVAL ON THE PERFORMANCE, HEALTH, AND METABOLITE CHARACTERISTICS OF NEWLY RECEIVED BEEF HEIFERS

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ABSTRACT

The study objective was to determine the effects of a nutrient-rich bolus containing a *Bacillus subtilis* direct-fed microbial (DFM), chromium propionate, beta-1,3-glucan, and a combination of butyric acid and zinc on the performance, health, and metabolite characteristics of newly received heifers during a 56 d receiving period. Four blocks of heifers (*n* = 576; initial BW = 187 ± 12.4 kg) were procured from livestock auctions throughout Alabama, Mississippi, and Oklahoma in February of 2020. Heifers were weighed on d -1 and assigned randomly to 1 of 2 experimental treatments. Treatments were: 1) a negative control (CON; placebo empty gelatin bolus) and 2) a

nutrient-rich bolus (BOL; containing 13 g *B. subtilis*, 3.9 g chromium propionate, 1 g beta-1,3-glucan, and 4 g of encapsulated butyric acid and zinc). Treatments were administered at initial processing along with the standard processing regimen. Blood samples were collected on d 0, 7, and 14 relative to treatment administration to evaluate hematological responses, as well as to determine glucose, lactate, plasma urea nitrogen (PUN), and non-esterified fatty acid (NEFA) concentrations. The experiment used a randomized complete block design with 12 pens per treatment. Pen served as the experimental unit for all response variables. Data were analyzed using PROC MIXED procedure of SAS 9.4. Throughout the experiment, no differences were detected for animal BW, ADG, G:F, or for DMI ($P \geq 0.11$). There were also no effects ($P \geq 0.19$) of treatment on clinical health outcomes. No treatment × time interactions ($P \geq 0.32$) or treatment effects ($P \geq 0.34$) were observed for hematological variables. A treatment × time interaction ($P < 0.01$) was observed for glucose concentrations on d 14, but no other treatment × time interactions ($P \geq 0.20$) were present for plasma lactate, PUN, or NEFA concentrations. All plasma metabolites were impacted ($P \leq 0.0001$) by time. The nutrient-rich experimental bolus administered at processing had no impact on animal performance, health, or plasma metabolites in the current experiment.

Key Words: beta glucan, chromium propionate, direct-fed microbial, high-risk calves, receiving cattle

INTRODUCTION

Scientist are continually working towards finding viable antibiotic alternatives for livestock production. Increased pressure has been placed on livestock producers to lessen or discontinue antibiotic use due to concerns of antimicrobial resistance and antibiotic residues in meat harvested for human consumption. This increase in antibiotic scrutiny has caused the European Union to place bans on the use of antibiotics for production purposes in animal diets

and has caused the U.S. to implement the veterinary feed directive (**VFD**; Walsh et al., 2007). Thus, finding alternatives that prevent pathogen colonization, increase performance, and improve overall animal well-being continues to be an important area of research.

Ruminant nutritionists and microbiologists are interested in manipulating the rumen environment to improve production efficiency and clinical health (Elghandour et al., 2015). To date, most antimicrobial alternatives have included supplying bacterial or fungal microorganisms as direct-fed microbials (**DFM**). Chromium propionate supplementation has also been repeatedly shown to favorably enhance the immune system, as well as alter glucose and lipid metabolism. Chromium propionate is the only source of chromium currently permitted for use in cattle diets in the United States (Bernhard et al., 2012). More recently, there has been interest in the supplementation of beta-glucans for immunological and performance benefits. However, little is known about the effects beta-glucan supplementation on calf health and performance during periods of stress. Additionally, feed additives that supply readily available energy substrates to cattle withdrawn from feed or water for extended periods of time may prove beneficial to stressed, newly received feedlot calves as these calves have characteristically low intake of energy and nutrients during the first wk to 2 wk following arrival. Antibiotic alternatives that are targeted to provide stimulation to the immune system, protection against harmful pathogens, and nutrition to newly-received calves may reduce incidence of bovine respiratory disease (**BRD**) and enhance animal performance during the receiving period. Thus, the objective of this experiment was to evaluate the effects of a bolus containing a *B. subtilis* DFM, beta-glucan, chromium propionate, and butyric acid zinc supplement on the performance, health, and metabolite characteristics in newly received, highly-stressed heifers.

MATERIALS AND METHODS

All live animal procedures for the current experiment were approved by the Oklahoma State University Institutional Animal Care and Use Committee (Animal Care and Use Protocol number: AG-19-8). This experiment was conducted at the Willard Sparks Beef Research Center (WSBRC) located in Stillwater, OK.

Cattle background and arrival procedures

A total of 576 crossbred beef heifers (BW = 187 ± 12.4 kg) were procured from livestock auctions throughout Alabama, Mississippi, and Oklahoma and transported approximately 966, 837, and 97 km, respectively to the WSBRC at Oklahoma State University. Heifers arrived at the WSBRC on February 10, 2020 (Block 1), February 11, 2020 (Block 2), February 12, 2020 (Block 3), and February 13, 2020 (Block 4). Immediately upon arrival to the research feedlot (d -1), cattle were weighed (Avery Weigh-Tronix; Fairmont, MN) and administered individual identification tags. Calves were then allowed 12 to 24 h of rest in holding pens with *ad libitum* access to prairie hay and water before initial processing on d 0. Ear notch samples were also collected upon arrival to test for infection with bovine viral diarrhea virus (**BVDv**). Two animals from block 1 were identified as BVDv infected calves; thus, those animals were commingled with all other calves in block 1 to ensure equal exposure among all calves in the group. The BVDv calves were then removed from the study on d 0 at processing.

At initial processing (d 0), cattle were weighed, vaccinated against clostridial pathogens *Clostridium chauvoei*, *Clostridium novyi*, *Clostridium perfringens* C and D, *Clostridium septicum*, *Clostridium sordellii,* and *Moraxella bovis* (Vision 7 20/20 with SPUR; Merck Animal Health, Madison, NJ) and against viral pathogens bovine herpesvirus-1, BVDv type 1 and 2, parainfluenza-3 virus, and bovine respiratory syncytial virus (Titanium 5; Elanco Animal Health, Greenfield, IN). Cattle were also administered a *Mannheimia haemolytica* bacterin (Nuplura; Elanco Animal Health), drenched with an oral anthelmintic (Safeguard; Merck Animal Health),

given a topical insecticide (Standguard; Elanco Animal Health) and administered a growth promoting implant containing 80 mg of trenbolone acetate, 8 mg of estradiol, and 29 mg of tylosin tartrate (Component TE-IH; Elanco Animal Health) at processing. Cattle were sorted upon exiting the chute and were immediately assigned to receiving pens following processing on d 0.

Experimental treatments and receiving management

Cattle were stratified by BW within block and randomly assigned to 1 of 2 experimental treatments. Experimental treatments consisted of 1) a negative control (CON; placebo empty gelatin bolus) and 2) a nutrient-rich bolus [BOL; containing 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries]. The amount of each ingredient placed within the bolus was based on manufacturer recommendations. Experimental treatments were randomly assigned previously to receiving pens. A total of 24 receiving pens were used, with 12 replications per treatment. Hematology and metabolite data were pooled by animal and averaged within pen. Thus, pen was considered the experimental unit for all performance, clinical health, hematology, and metabolite analyses.

All animals were housed in 12.5 × 30.5 m soil-surfaced open-air receiving pens that contained continuous flow concrete watering tanks (Model J 360-F; Johnson Concrete, Hastings, NE) and a 12.2 m concrete bunks. Cattle were managed to target *ad libitum* access to water and feed throughout the entire duration of the experiment. The receiving diet (Table 5-1) fed to all heifers during the experiment was formulated to meet or exceed NASEM (2016) nutrient requirements. Long-stem hay was provided at 0.91 kg per head daily in the bunk for the first 4 d of the experiment. Feed bunks were read at 0530 and 1730 h and feed was mixed and delivered once daily by 0900 h using a trailer-mounted feed mixer (274-12B; Roto-Mix, Dodge City, KS).

Feed calls were adjusted daily to target crumbs left in the bunk, and feed refusals were collected daily at 0600 h. Daily residual feed and feed refusals before BW collection days were dried for DM determination and the resulting feed DM was factored into DMI calculations. Ration samples were collected twice per week. Ration samples and feed refusals were dried in a forced air oven for 48 h at 60°C for DM determination. Weekly ration samples were composited by month and analyzed at a commercial laboratory (Servi-Tech Inc.; Dodge City, KS) for determination of nutrient composition. Total digestible nutrients (TDN) were calculated by using the following equation: TDN = 93.59 – (ADF × 0.936). Net energy for maintenance (NE_m) and gain (NE_g) were calculated using the following equations: NE_m = ((0.029 × TDN) – 0.29); NE_g = ((0.029 × TDN) – 1.01).

Evaluation of BRD for antimicrobial treatment

Calves were evaluated daily by 2 trained personnel for the detection of clinical signs compatible with (or suggestive of) BRD. Cattle were assigned severity scores (**SS**) based upon the DART system with modifications described by Wilson et al. (2016) and Step et al. (2008). Numerical SS ranged from 0 to 4. A SS of 0 indicated an animal was clinically normal, 1 indicated mild clinical signs, 2 indicated an animal exhibiting moderate clinical signs, 3 indicated severe clinical signs, and a SS of 4 would indicate a moribund animal requiring immediate attention. Animals that received a SS of 1 or greater were eligible to be taken to the processing chute for rectal temperature measurement (GL M-500, GLA Agricultural Electronics, San Luis Obispo, CA). Animals that received a subjective SS of 1 or 2 and had a rectal temperature greater than or equal to 40°C were eligible for antimicrobial treatment. Cattle that were assigned a SS of 3 or 4 received antimicrobial treatment regardless of rectal temperature. All cattle regardless of whether or not antimicrobial treatment was administered were immediately returned to the respective home pen from the processing chute.

All antimicrobials were administered subcutaneously according to the manufacturer's label and Beef Quality Assurance Guidelines (NCBA, 2001). Cattle eligible for antimicrobial treatment were allowed to receive an antimicrobial up to 3 times on alternating sides of the animal. If an animal did not respond to antimicrobial treatment after the third antimicrobial administration and continued to receive a DART score of 1 or greater and continued to lose weight, the animal was labeled as chronic and removed from the experiment. Antimicrobial therapy with tilmicosin phosphate (Micotil; 10 mg/kg, Elanco Animal Health) was administered for the first treatment. Following a moratorium of 120 h after tilmicosin phosphate administration, florfenicol (Nuflor; 40 mg/kg, Merck Animal Health) was administered if antimicrobial treatment criteria was met for the second time. If treatment criteria were met for the third time following a florfenicol moratorium of 72 h, ceftiofur crystalline free acid (Excede; 6.6 mg/kg, Zoetis) was administered for the third, and final treatment.

Data collection

Individual BW was recorded on d 0, 7, 14, 28, 42, and 56. Body weight was recorded before feeding at approximately 0530 h with no feed or water withdrawal. All BW were adjusted using a calculated 2% pencil shrink (BW × 0.98). Individual BW were averaged within pen to calculate an average BW for the pen. Average daily gain was calculated for each animal by dividing the individual weight gained during the period by the number of days on feed during the period. Pen ADG was calculated by averaging individual ADG for each heifer in a pen for that period. Dry matter intake was calculated within period by taking the total weight of DM fed provided to the feed bunk minus any orts that were collected from the bunks divided by the number of heifers × days in the feeding period. Gain to feed ratio was calculated within period by dividing pen ADG by the pen average daily DMI for each respective period.

Performance and feed data for animals that died or were removed from the experiment were excluded from statistical analyses. Intake data was corrected for mortalities and removals by removing each animal's average daily DMI from the pen until the heifer ceased gaining BW. If an animal was not gaining BW, DMI for that animal was removed from the time the animal began to lose weight until the removal date using the NASEM (2016) net energy maintenance equation $NE_m = 0.077 \times (SBW)^{0.75}$ and the calculated NE_m of the diet.

Hematology and metabolite analyses were performed by collecting whole blood via jugular venipuncture on a subset of heifers (n = 72; 3 heifers per pen) using 10 ml vacutainer tubes containing EDTA (BD Vacutainer; Thermo Fisher Scientific, Waltham, MA). Blood collections for all analyses occurred on d 0 (h 0), 7, and 14. All collection time points are in relation to when the animals received the placebo or experimental bolus. Hematology analysis was performed for white blood cell (**WBC**), lymphocyte, monocyte, neutrophil, basophil, eosinophil, hemoglobin, hematocrit, platelet, red blood cell (**RBC**), mean corpuscular hemoglobin concentration, and mean corpuscular hemoglobin determination using an automated hematology analyzer (Abaxis Vetscan; Zoetis). Additionally, plasma harvested from whole blood was analyzed for determination of glucose, lactate, non-esterified fatty acids (**NEFA**), and plasma urea nitrogen (**PUN**) concentrations. Following blood collection, plasma used for metabolite analyses was harvested by centrifuging the whole blood at 1,294 × g for 10 min at 4°C (Sorvall RC6; Thermo Scientific). Plasma was then stored at -80°C until further metabolite analyses. Plasma samples were thawed at room temperature immediately before glucose, lactate, NEFA, and PUN analysis. Glucose and lactate were analyzed using an immobilized enzyme system (YSI Model 2950 D; YSI Inc., Yellow Springs, OH). Plasma urea nitrogen was analyzed utilizing the methods described by Marsh et al. (1965) adapted for a 96-well plate. Plasma was analyzed for NEFA concentration by use of a standard NEFA quantitation kit (NEFA-C Kit; WAKO Chemicals USA, Richmond, VA).

Statistical analysis

Data were analyzed using the MIXED procedure of SAS 9.4 (SAS Institute Inc; Cary, NC). Experimental treatments were arranged in a generalized randomized complete block design (n = 4 blocks) with 12 pen replications per treatment. Pen served as the experimental unit for all response variables, with treatment included as the fixed effect and block serving as a random effect. Metabolite data were assessed for normality using the Shapiro-Wilk test statistic in the UNIVARIATE procedure of SAS 9.4. Lactate and NEFA concentrations were determined to be non-normal and were logarithm (base 10) transformed to achieve normality. The covariance structures (**CS**) within the model were compared for both hematology and metabolite data, and the best fit CS (CS with the lowest Akaike information criterion) was used. Repeated measures for the fixed effects of treatment, day, and the resulting treatment × day interaction was used in the model to analyze the hematology and metabolite data, with pen serving as a random effect. Glucose and lactate concentrations on d 0 were used in the model as covariates. Results were considered different where $P \leq 0.05$, and tendencies were defined where $0.05 > P \leq 0.10$. All performance and intake data from heifers removed in the experiment were excluded from the statistical analysis with the exception of the health analysis.

RESULTS AND DISCUSSION

Animal performance

Performance data are presented in Table 5-2. There were no differences ($P \geq 0.79$) in BW between treatments throughout the experiment. Heifer BW for both treatments decreased from d 0 to 7, then increased throughout the remainder of the experiment. The slight reduction in BW observed on d 7 is likely due to continued body catabolism of fat and tissue reserves during the first wk, as the DMI intake for both treatments groups from d 0 to 7 (2.3 kg) was insufficient for positive energetic accretion. Dry matter intake in newly received, high risk calves is

characteristically low and averages only 1.5% of BW during the initial 2 wk after arrival to the feedlot (Krehbiel et al., 2011). The decline in BW from d 0 to 7 in the current experiment likely represents a period of slow initial transition to the feeding management and concomitantly low DMI. The reduction in BW from d 0 to 7 is supported by the negative ADG observed for both treatments from d 0 to 7. While ADG did not differ, cattle administered the nutritional bolus lost less weight numerically (-0.43 vs -0.24 kg; $P = 0.16$) the first week following arrival to the feedlot.

There were no differences ($P \geq 0.11$) in heifer ADG throughout the entire experiment. There were also no differences ($P \geq 0.35$) in DMI between treatments during the experiment, except from d 42 to 56, where the CON heifers tended ($P = 0.06$) to consume more feed than the BOL heifers. There were also no differences ($P \geq 0.19$) in G:F measurements between experimental treatments.

The experimental bolus in the current experiment contained a *B. subtilis* DFM, chromium propionate, beta-1,3-glucan, and a butyric acid and zinc molecule. The aforementioned additives have been suggested in previous literature to positively influence performance and intake, as well as have direct implication on immune regeneration during intense periods of stress. Chromium has been recommended to enhance insulin metabolism and optimum uptake of nutrients by peripheral cells (Yari et al., 2010). Several studies have demonstrated chromium propionate to be effective in improving performance in beef cattle, while others have observed no differences. Moonsie-Shageer and Mowat (1993) reported a 23% increase in ADG when cattle were fed 0.2 and 1 ppm of supplemental chromium compared to a control. Sousa et al. (2020) also stated that calves supplemented with chromium had greater ADG than non-supplemented calves. In contrast, Kegley and Spears (1995) reported no differences in performance between heifers supplemented with various chromium or chromium-yeast additives. Kneeskern et al. (2016) evaluated chromium propionate supplementation on growth characteristics and concluded that chromium

propionate supplementation had no impact on ADG, DMI, or G:F. Similarly, Van Bibber-Krueger et al. (2016) reported that finishing heifers receiving a chromium yeast supplement showed no improvements in BW, ADG, or DMI. Smock et al. (2020) reported that chromium supplementation in their experiment actually led to a 9 kg reduction in final BW.

Bacillus subtilis is a bacterial DFM that is stimulated by an acidic environment and bile salts and initiates small intestinal activity when activated (Smock et al., 2020). Payling et al. (2017) reported that *B. subtilis* supplementation increased BW, ADG, and G:F in grower pigs. Smock et al. (2020) evaluated *B. subtilis* supplementation on growth characteristics in newly received calves and concluded that both DMI and performance were improved by *B. subtilis* supplementation. Conversely, results reported by Wilson et al. (2019) suggests that *B. subtilis* supplementation in feedlot heifers offered no performance benefit, but the authors did observe increases in feed efficiency.

Experiments evaluating beta-glucan or butyric acid supplementation in ruminants are limited. Beta-glucan supplementation has been previously associated with immune enhancement and increased ADG and feed efficiency. Butyric acid and zinc have both demonstrated to be key regulators in intestinal barrier function, and both have been suggested to have consistent beneficial effects toward gut health (Mani et al., 2019). Cherdthong et al. (2018) investigated beta-glucan supplementation on feed intake in beef cattle, and the authors reported that beta-glucan supplementation at 4.7 g improved feed intake, as well as intake and digestibility of crude protein (**CP**). Salinas-Chavira et al. (2018) reported that beta-glucan supplementation to calf-fed Holstein heifers at 195 mg/kg improved ADG and DMI.

While previous experiments have documented improvements with feeding similar ingredients that were included in the current experimental bolus, no benefits were observed in the present experiment. One possible explanation for the lack in differences between treatments is

that the experimental bolus may have contained insufficient amounts of these additives to substantiate increases in overall performance and health. Additionally, any potential benefits offered by the ingredients may have been short-lived when administered at the current amounts. Any observed improvements in performance characteristics from bolus administration would be due to impacts of a singular bolus given at arrival processing at the feedlot. Therefore, it is reasonable to expect that no differences in performance would be seen at subsequent weight collections (d 28, 42, and 56) if differences in performance during the first few wk following feedlot arrival were not observed.

Clinical Health

Clinical health data are presented in Table 5-3. No differences in clinical health outcomes were detected ($P \geq 0.45$) between experimental treatment groups. The total percent of antimicrobial treatments administered for each experimental treatment remained around 30%, with negligible differences in the number of calves requiring 1, 2, or 3 antimicrobial treatments for BRD. Natural alternatives to antibiotics such as yeast-based products, DFM, or chromium have been reported to have positive effects both directly and indirectly on the immune system and subsequent biomarkers, thus mitigating effects related to stress and disease (Spears, 2000; Broadway et al., 2015). Smock et al. (2010) found that both *B. subtilis* and chromium propionate supplementation independently reduced overall treatment rates for BRD, and the authors also reported that *B. subtilis* supplementation reduced antimicrobial cost by $3.50 per animal. Moonsie-Shageer and Mowat (1993) similarly reported that chromium supplementation reduced morbidity as well as rectal temperatures in feedlot steers. Broadway et al. (2015) reported that yeast and yeast cell wall products such as beta-glucans interact indirectly with immune cells by binding bacteria to prevent pathogenic colonization. Results reported by Finck et al. (2015) suggest that yeast based supplements including yeast cell wall products may offer improvements in cattle health during the receiving period. Overall data evaluating the effects of the various

additives included in the bolus in the current experiment on clinical health outcomes are limited. In the current experiment, no health benefits due to bolus administration were observed, presumably due to the low amount of total additives consumed. Cattle likely need daily supplementation following arrival for these additives to have effect on clinical health outcome.

Hematology

Hematology analyses are presented in Figures 5-1 through 5-6. No treatment × time interactions ($P \geq 0.29$) were observed for any hematological response variables. Similarly, no treatment differences ($P \geq 0.20$) for hematological responses were observed. However, time impacted many of the hematological response variables measured. A time effect ($P \leq 0.03$) was observed for lymphocytes, eosinophils, hemoglobin, hematocrit, platelets, RBC, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentrations. Time also tended to impact ($P = 0.10$) WBC counts. No effect of time ($P \geq 0.15$) was observed for basophils, monocytes, or neutrophil counts.

Platelet counts, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentrations responded similarly throughout the receiving experiment. Concentrations of these response variables increased from d 0 to d 7, then declined from d 7 to 14. In contrast, hematocrit percent, hemoglobin, and RBC counts declined rapidly from d 0 to d 7, followed by a slower and more steady decline in concentrations from d 7 to d 14. All values presented in the current experiments for hematological variables fall within the normal reference intervals for bovine hematology reported by Roland et al. (2014). Although no effect of treatment was reported for hematological variables in the current experiment, numerous other studies have demonstrated these additives can alter blood cell differentials and humoral responses in cattle. Broadway et al. (2020) evaluated feeding 13g/hd per d of *B. subtilis* to weaned Holstein steers and reported that *B. subtilis* supplemented calves displayed increased WBC and lymphocyte counts. Moonsie-Shageer

and Mowat (1993) reported a positive linear response in blood hematocrit percentage and a negative linear response in cortisol concentrations with increasing levels of chromium supplementation. Lastly, Kegley and Spears (1995) found that peripheral lymphocytes from chromium supplemented steers had a greater blastogenic response than non-supplemented steers. Additional research evaluating supplementation of these additives on hematological variables is warranted.

Metabolite Characteristics

Plasma metabolite data are presented in Figures 5-7 and 5-8. A treatment × time interaction ($P < 0.01$) was detected for glucose concentrations. On d 14, glucose concentrations in CON heifers were greater than concentrations exhibited by BOL heifers. No further interactions ($P \geq 0.20$) or treatment effects ($P \geq 0.33$) for metabolites were observed. Time did have an impact ($P \leq 0.0001$) on all plasma metabolites in this experiment. Glucose and PUN concentrations quickly increased from d 0 to 7, then slightly increased from d 7 to 14. Lactate and NEFA concentrations both decreased rapidly from d 0 to 7 and then continued to decrease at a slower rate from d 7 to 14.

Supplementation of the additives used such as chromium have reportedly had more profound impacts on blood metabolites than performance characteristics. Bernhard et al. (2012) investigated chromium propionate supplementation on glucose and lipid metabolism in feedlot cattle during the receiving period. The authors indicated that chromium propionate supplementation increased the insulin to glucose ratio, as well as increased NEFA concentrations during a glucose tolerance test. Likewise, Spears et al. (2012) reported that chromium propionate impacted insulin sensitivity and the ratio of insulin to glucose. The opposite was observed by Hayirli et al. (2001), whom reported that the molar ratio of insulin to glucose was greater for animals not supplemented with chromium. The authors also reported that chromium

supplementation did not affect liver triglyceride or NEFA concentrations. Similarly, Ghorbani et al. (2002) and Kneeskern et al. (2016) reported that blood glucose concentrations were not altered by DFM and chromium propionate supplementation, respectively. Tao et al. (2015) reported that beta-glucan supplementation decreased serum triglyceride concentrations and increased total cholesterol. Van Bibber-Krueger et al (2016) concluded that a combination of yeast and chromium propionate did not affect plasma glucose or lactate concentrations. Chromium priopionate supplementation alone also had no impact on serum NEFA concentrations in an experimented conducted by Yari et al. (2010).

CONCLUSIONS

In the present experiment, the nutritional feed additives were administered once orally in a gelatin capsule upon arrival with the goal of decreasing time to regain metabolic homeostasis, thus hopefully improving receiving health and performance early in the receiving period. The results of this experiment indicate that providing a nutrient-rich bolus at the levels administered does not benefit performance, health, or metabolite characteristics in receiving cattle. It is difficult to compare results from the current experiment to others previously reported as supplementation strategies, durations, and overall additive supplement intakes differ greatly. This experiment provides evidence that cattle likely need additional days of supplementation following arrival for feed additives to have measurable effects on performance or clinical health outcomes.

Table 5-1. Composition of the common receiving diet[1]

Item	Value
Ingredient, % of DM	
Rolled corn	15.00
Prairie hay	28.44
Sweet Bran[2]	51.36
Dry supplement	5.20
Nutrient composition[3], DM basis	
Dry matter, %	70.67
CP, %	16.80
ADF, %	25.80
TDN, %	66.93
NE_m, Mcal/kg	1.54
NE_g, Mcal/kg	0.94
Ca, %	0.75
P, %	0.66
K, %	1.36
Mg, %	0.32

[1] Diet analyses for nutrient were performed by Servi-Tech Laboratories; Dodge City, KS.
[2] Sweet Bran (Cargill Inc., Dalhart, TX).
[3] All values are presented on a DM basis. Dry supplement was formulated to contain (% DM basis) 40.0% ground corn, 29.6% limestone, 20.0% wheat middlings, 7.0% urea, 1.0 % salt, 0.53% magnesium oxide, 0.51% zinc sulfate, 0.17% manganese oxide, 0.13% copper sulfate, 0.08% selenium premix (0.6%), 0.0037% cobalt carbonate, 0.32% vitamin A (30,000 IU/g), 0.10% vitamin E (500 IU/g), 0.009% vitamin D (30,000 IU/g), 0.20 % tylosin (Tylan-40, Elanco Animal Health, Greenfield IN) and 0.33% monensin (Rumensin- 90; Elanco Animal Health).

Table 5-2. Effect of a nutrient-rich bolus administered at arrival on growth, performance, and feed efficiency in receiving heifers

	Treatment[1]			
Item	CON	BOL	SEM[2]	*P*-value
BW[3], kg				
d 0	188	187	4.2	0.85
d 7	185	185	4.9	0.95
d 14	203	203	4.1	1.00
d 28	221	221	4.7	1.00
d 42	247	248	3.9	0.89
d 56	268	266	4.2	0.79
ADG[4], kg				
d 0 to 7	-0.43	-0.24	0.129	0.16
d 7 to 14	2.51	2.46	0.182	0.71
d 14 to 28	1.25	1.25	0.188	0.98
d 28 to 42	1.94	1.99	0.140	0.51
d 42 to 56	1.47	1.30	0.091	0.11
d 0 to 56	1.43	1.42	0.043	0.75
DMI[5], kg				
d 0 to 7	2.31	2.35	0.200	0.67
d 7 to 14	4.79	4.92	0.238	0.39
d 14 to 28	6.45	6.30	0.247	0.35
d 28 to 42	8.07	8.07	0.262	0.95
d 42 to 56	9.03	8.70	0.297	0.06
d 0 to 56	6.75	6.66	0.247	0.51
G:F[6]				
d 0 to 7	-0.195	-0.127	0.0649	0.25
d 7 to 14	0.528	0.507	0.0498	0.39
d 14 to 28	0.190	0.198	0.0230	0.48
d 28 to 42	0.243	0.249	0.0222	0.58
d 42 to 56	0.162	0.149	0.0073	0.19
d 0 to 56	0.212	0.214	0.0052	0.71

[1] Treatments included: CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries)

[2] n = 12 pens per treatment

[3] Body weight was adjusted using a 2% calculated shrink

[4] Pen ADG was calculated from individual shrunk BW gain, kg divided by days on feed for each period

[5] Pen DMI was calculated from total DMI for the pen for each period divided by the total steers and days on feed in each period

[6] Pen G:F was calculated by dividing the ADG for the pen by the average daily DMI for the pend for each respective period

Table 5-3. Effect of a nutrient-rich bolus administered at arrival on clinical health outcomes of newly received beef heifers

	Treatment[1]			
Variable	CON	BOL	SEM[2]	*P*-value
BRD treatment, %				
Treated once[3]	25.3	26.4	4.67	0.73
Treated twice[4]	2.7	1.7	0.96	0.43
Treated thrice[5]	2.0	0.9	0.79	0.24
Total antimicrobial treatment[6], %	30.4	29.6	5.75	0.85
Days to first treatment	7.5	7.9	1.04	0.71
Rectal temperature, °C	40.2	40.4	0.09	0.19
Severity score[7]	1.24	1.13	0.059	0.19

[1] Treatments included: CON = negative control empty gelatin bolus; BOL = a nutrient-rich bolus containing 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries)

[2] n = 12 pens per treatment

[3] Percentage of cattle treated once for BRD

[4] Percentage of cattle treated twice for BRD

[5] Percentage of cattle treated thrice for BRD

[6] Total antimicrobial treatments were calculated by dividing the total number of animals treated within a pen by the sum of animals within the pen

[7] Severity scores were calculated by dividing the sum of the severity scores within a pen by the sum of animals treated within a pen

Figures

Figure 5-1a. Effect of experimental bolus percent lymphocyte counts in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.53$) or treatment effect ($P = 0.90$) on lymphocyte counts; however, a time effect ($P = 0.03$) for lymphocyte counts was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-1b. Effect of experimental bolus white blood cell (WBC) concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.50$), treatment effect ($P = 0.35$), or time effect ($P = 0.11$) detected for WBC concentration. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-2a. Effect of experimental bolus on monocyte counts in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.66$), treatment effect ($P = 0.69$), or time effect ($P = 0.64$)

detected for monocyte counts. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-2b. Effect of experimental bolus on neutrophil counts in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.86$), treatment effect ($P = 0.88$), or time effect ($P = 0.87$) detected for neutrophil counts. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-3a. Effect of experimental bolus on basophil counts in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.64$), treatment effect ($P = 0.34$), or time effect ($P = 0.13$) detected for monocyte counts. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-3b. Effect of experimental bolus on eosinophil counts in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.79$) or treatment effect ($P = 0.86$) on eosinophil counts;

however, a time effect ($P < 0.01$) for eosinophil counts was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-4a. Effect of experimental bolus on hematocrit percentage in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.73$) or treatment effect ($P = 0.73$) on hematocrit percentage; however, a time effect ($P < 0.0001$) for hematocrit percentage was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-4b. Effect of experimental bolus on hemoglobin concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.63$) or treatment effect ($P = 0.49$) on hemoglobin concentrations; however, a time effect ($P < 0.0001$) for hemoglobin concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-5a. Effect of experimental bolus on platelet concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no

treatment × time interaction ($P = 0.32$) or treatment effect ($P = 0.96$) on platelet concentrations; however, a time effect ($P < 0.01$) for platelet concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-5b. Effect of experimental bolus red blood cell (RBC) concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.74$) or treatment effect ($P = 0.76$) on RBC concentrations; however, a time effect ($P < 0.0001$) for RBC concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-6a. Effect of experimental bolus on mean corpuscular hemoglobin concentrations (MCHC) in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.37$) or treatment effect ($P = 0.52$) on MCHC concentrations; however, a time effect ($P < 0.01$) for MCHC concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-6b. Effect of experimental bolus on mean corpuscular hemoglobin (MCH) in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium

propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.45$) or treatment effect ($P = 0.54$) on MCH concentrations; however, a time effect ($P < 0.01$) for MCH concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-7a. Effect of experimental bolus on plasma glucose concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was a treatment × time interaction ($P = 0.01$) for plasma glucose concentrations. There was also a treatment effect ($P = 0.02$) and time effect ($P < 0.0001$) observed for plasma glucose concentrations. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-7b. Effect of experimental bolus on plasma lactate concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.20$) or treatment effect ($P = 0.90$) observed for plasma lactate concentrations. However, a time effect ($P < 0.0001$) was overserved to impact plasma lactate concentrations. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-8a. Effect of experimental bolus on plasma urea nitrogen (PUN) concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.97$) or treatment effect ($P = 0.34$) on PUN concentrations; however, a time effect ($P < 0.0001$) for PUN concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

Figure 5-8b. Effect of experimental bolus on non-esterified fatty acid (NEFA) concentrations in newly received beef heifers. CON = negative control; empty gelatin bolus; BOL = a nutrient-rich bolus containing: 13 g *B. subtilis* (CLOSTAT; Kemin Industries, Des Moines, IA), 3.9 g chromium propionate (KemTRACE Chromium; Kemin Industries), 1 g beta-1,3-glucan (Aleta; Kemin Industries), and 4 g of encapsulated butyric acid and zinc (ButiPEARL-Z; Kemin Industries). There was no treatment × time interaction ($P = 0.76$) or treatment effect ($P = 0.33$) on NEFA concentrations; however, a time effect ($P < 0.0001$) for NEFA concentration was detected. Values plotted represent least squares means ± SE of the mean, calculated for 6 animals per experimental group.

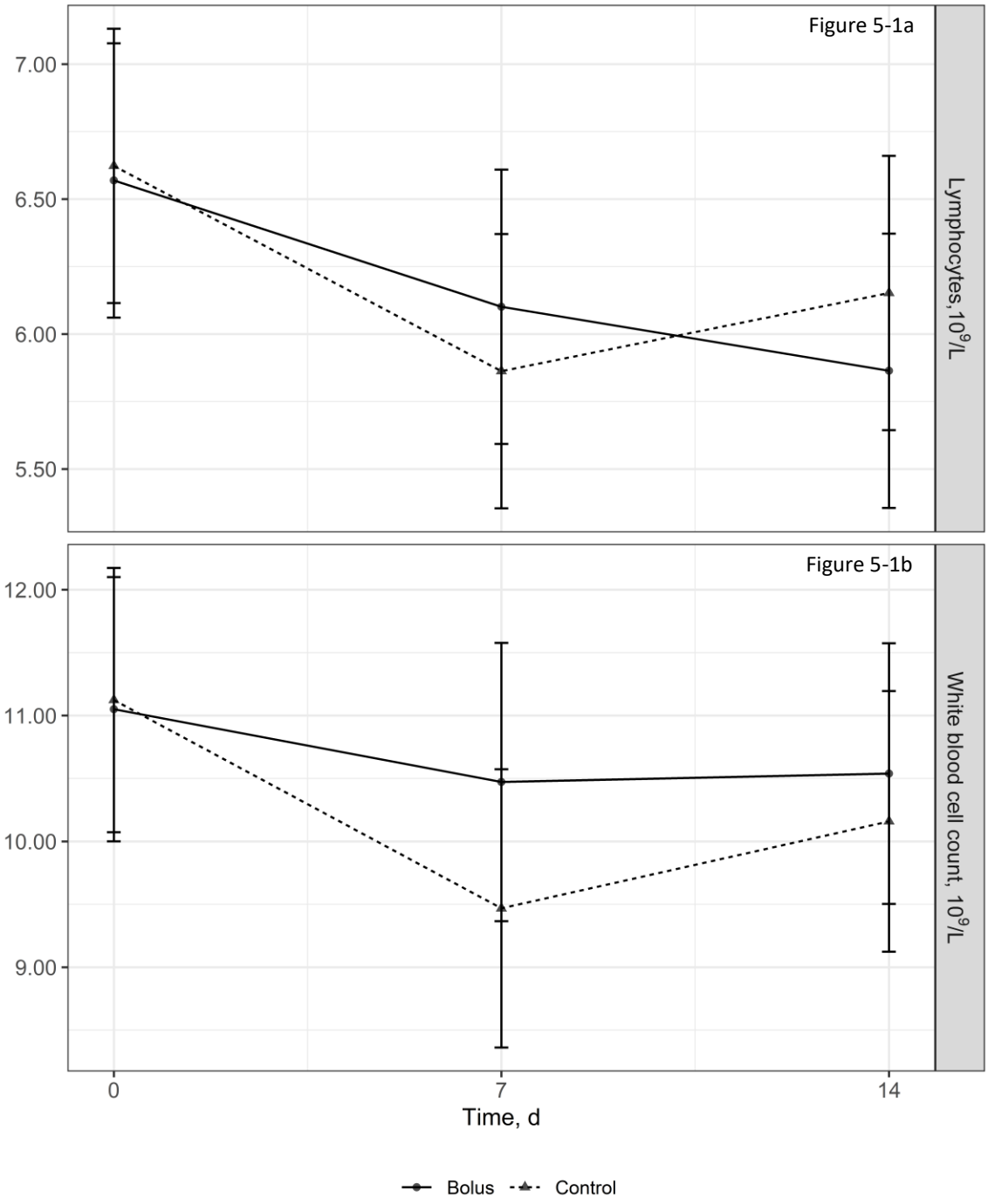
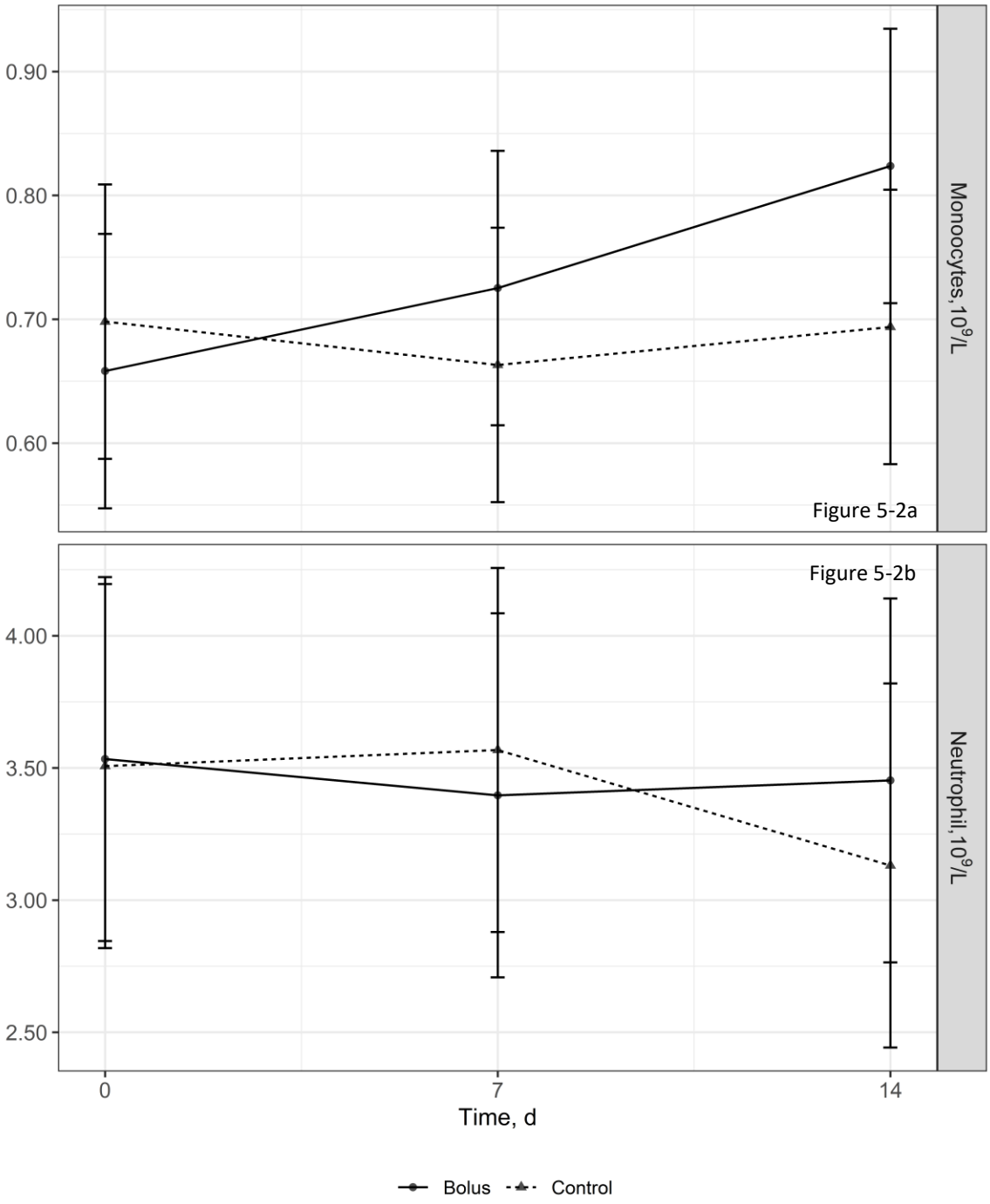
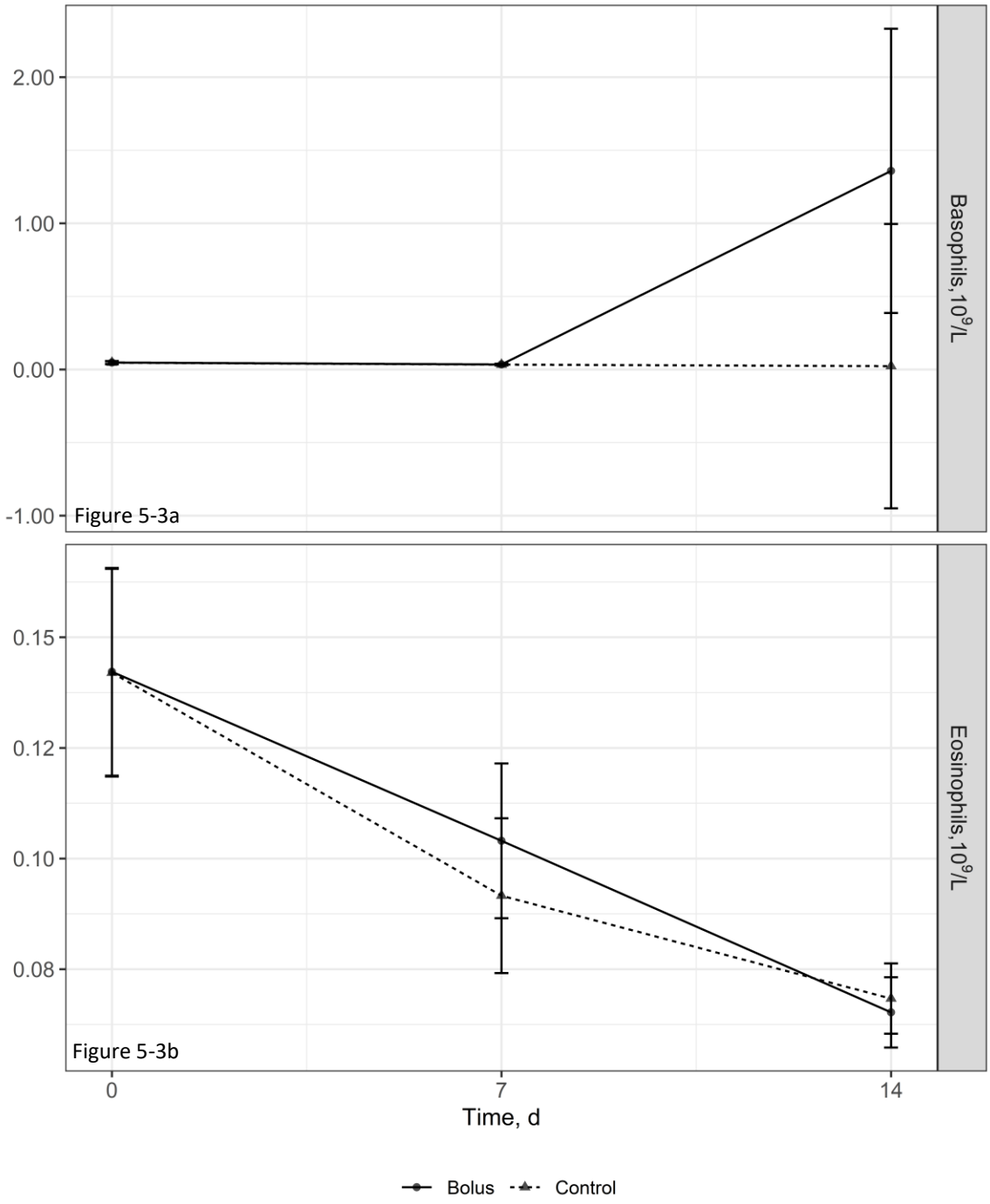


Figure 5-1a
7.00
6.50
6.00
5.50
Lymphocytes, 10^9/L
Figure 5-1b
12.00
11.00
10.00
9.00
White blood cell count, 10^9/L
0
7
14
Time, d
Bolus
Control


0.90
0.80
0.70
0.60
Monoocytes, 10^9/L
Figure 5-2a
Figure 5-2b
4.00
3.50
3.00
2.50
Neutrophil, 10^9/L
0
7
14
Time, d
Bolus
Control


2.00
1.00
0.00
-1.00
Basophils, 10^9/L
Figure 5-3a
0.15
0.12
0.10
0.08
Eosinophils, 10^9/L
Figure 5-3b
0
7
14
Time, d
Bolus
Control

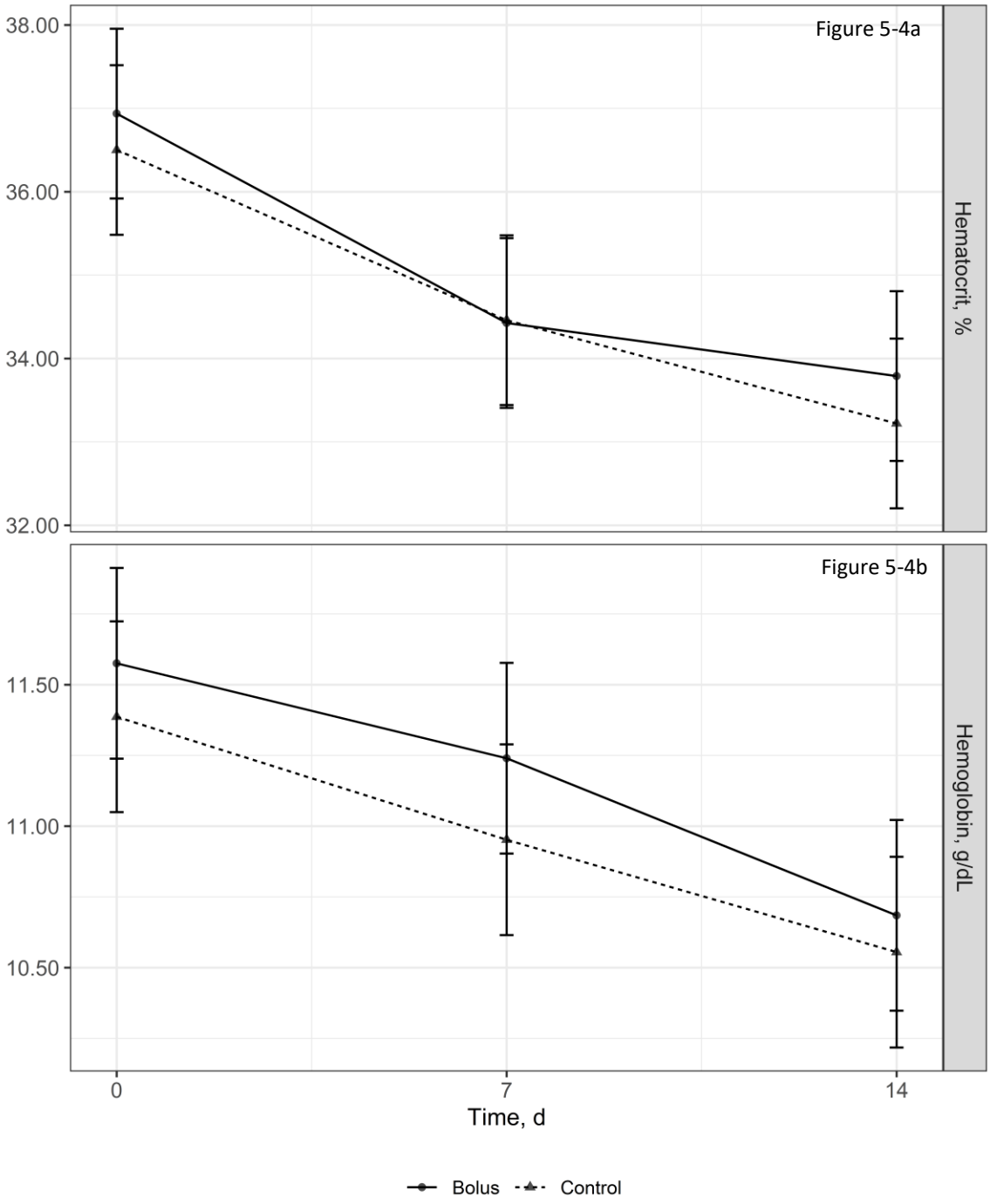


Figure 5-4a
38.00
36.00
34.00
32.00
Hematocrit, %
Figure 5-4b
11.50
11.00
10.50
Hemoglobin, g/dL
0
7
14
Time, d
Bolus
Control

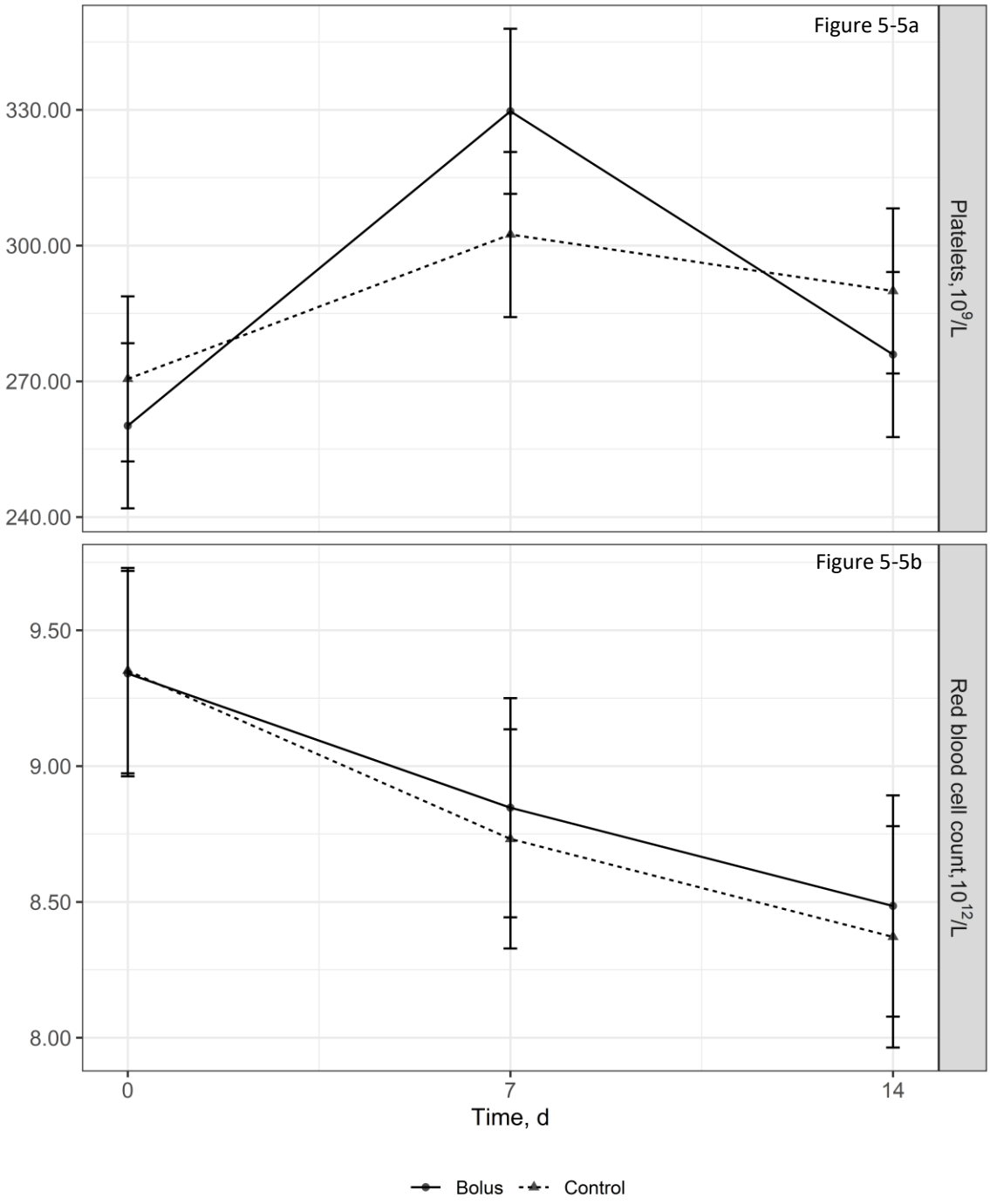


Figure 5-5a
330.00
300.00
270.00
240.00
Platelets, 10^9/L
Figure 5-5b
9.50
9.00
8.50
8.00
Red blood cell count, 10^{12}/L
0
7
14
Time, d
Bolus
Control

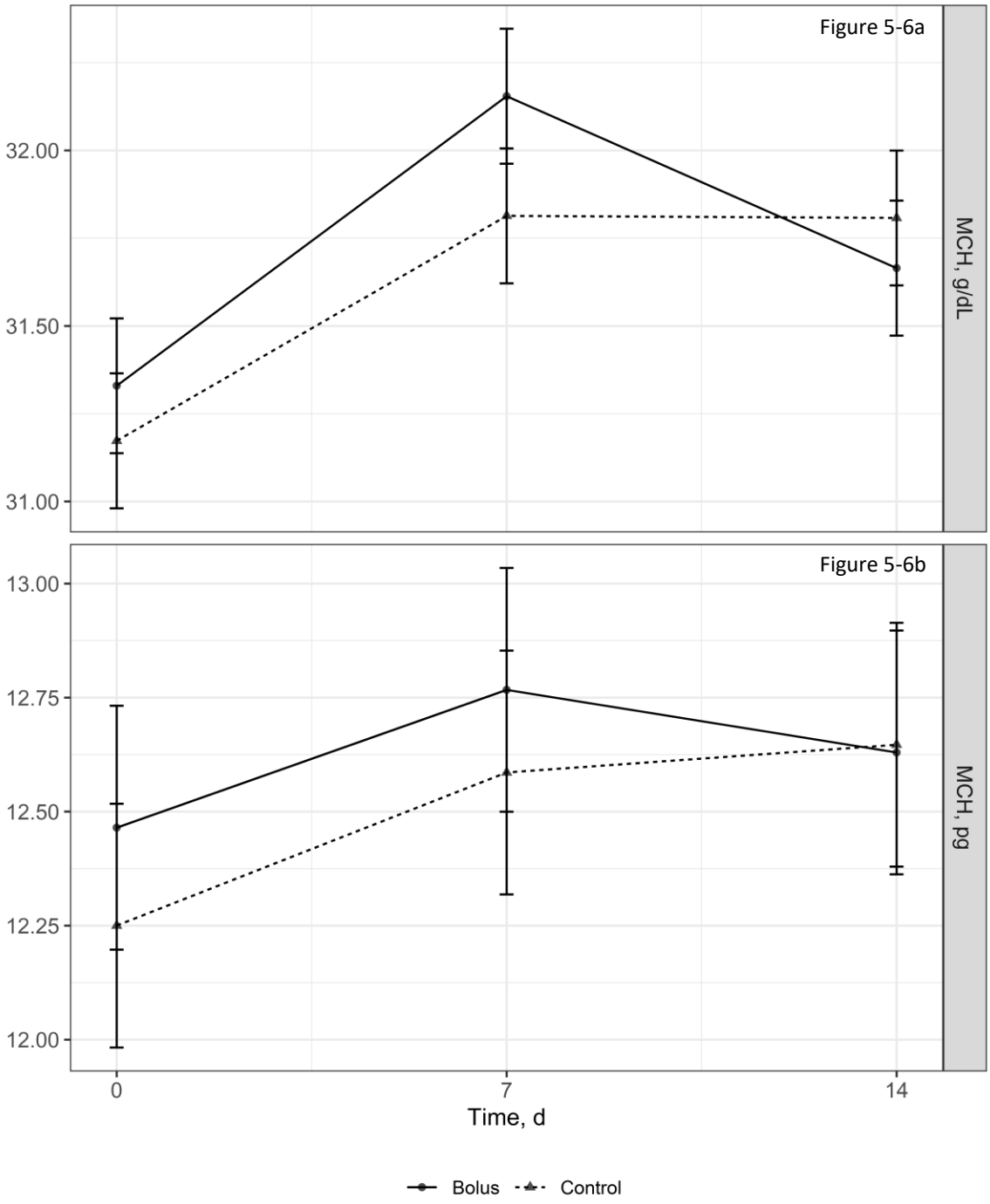


Figure 5-6a
32.00
31.50
31.00
MCH, g/dL
Figure 5-6b
13.00
12.75
12.50
12.25
12.00
MCH, pg
0
7
14
Time, d
Bolus
Control

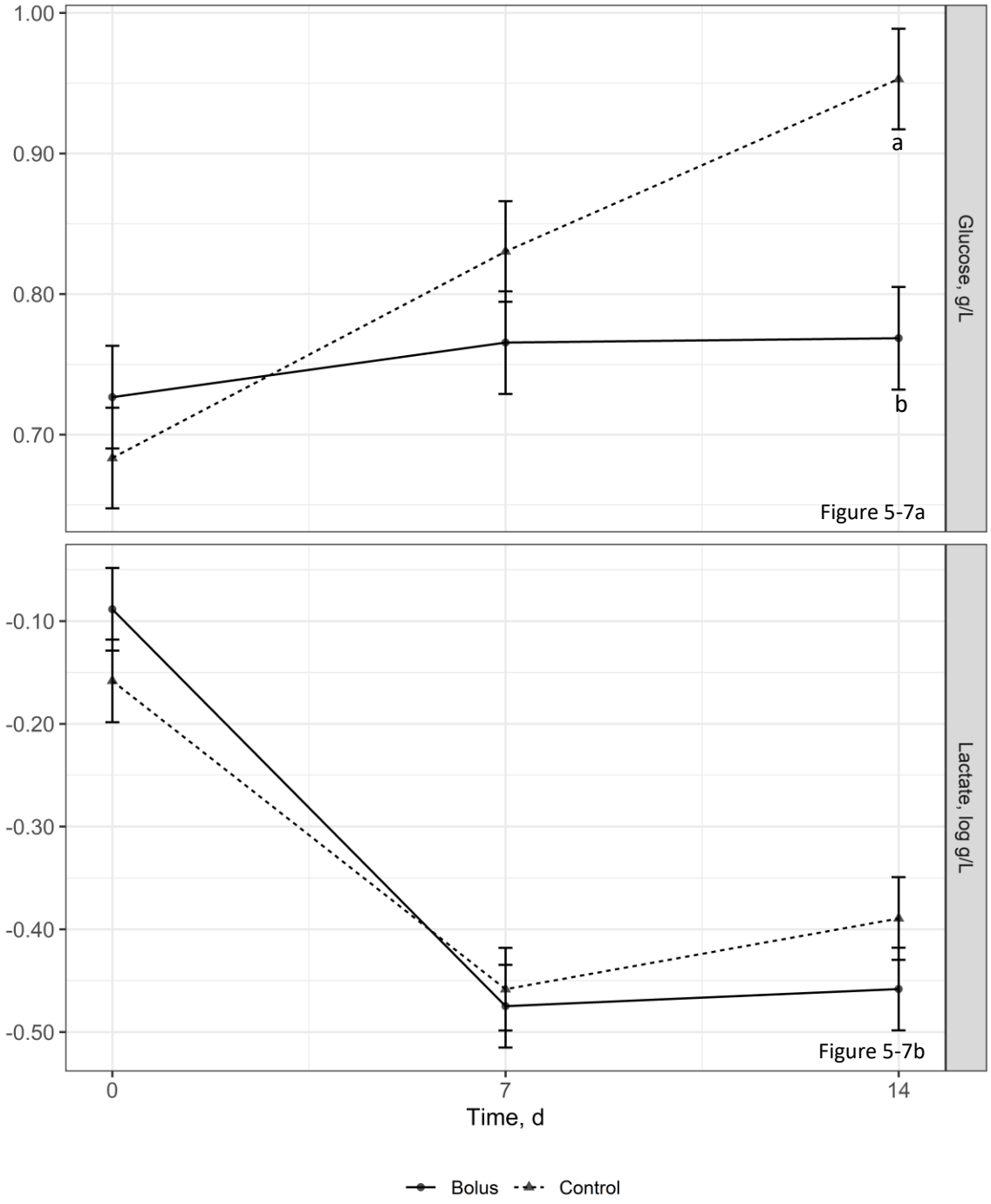
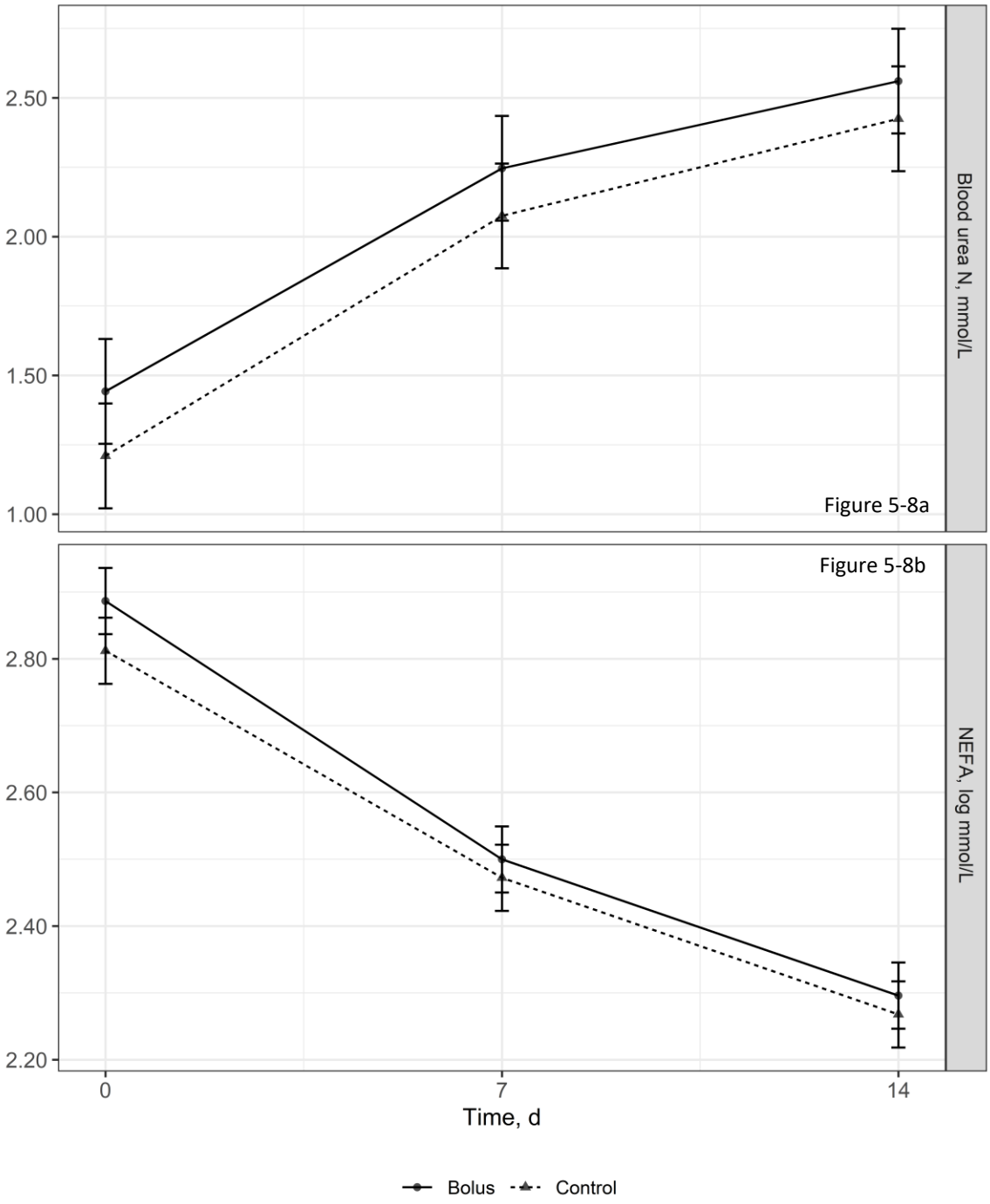


Figure 5-7a

Figure 5-7b


2.50
2.00
1.50
1.00
Blood urea N, mmol/L
Figure 5-8a
Figure 5-8b
2.80
2.60
2.40
2.20
NEFA, log mmol/L
0
7
14
Time, d
Bolus
Control

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