2017

Productivity measures in beef cows and calves following a single subcutaneous injection of extended-release eprinomectin

Claire Andresen
Iowa State University

Productivity measures in beef cows and calves following a single subcutaneous injection of extended-release eprinomectin

by

Claire Elizabeth Andresen

A thesis submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Animal Science

Program of Study Committee:
Patrick Gunn, Co-Major Professor
Dan Loy, Co-Major Professor
Troy Brick
Lee Schulz

The student author, whose presentation of the scholarship herein was approved by the program of study committee, is solely responsible for the content of this thesis. The Graduate College will ensure this thesis is globally accessible and will not permit alterations after a degree is conferred.

Iowa State University

Ames, Iowa

2017

TABLE OF CONTENTS

Page ii

Page iii

Page iv

NOMENCLATURE

ADG	average daily gain
AI	artificial insemination
BCS	body condition score
BW	body weight
CAB	Certified Angus Beef
CONV	conventional
DMI	dry matter intake
DOR	doramectin
EPR	extended-release eprinomectin
F:G	feed to gain
FAMACHA	Faffa Malan Chart
FEC	fecal egg counts
FECRT	fecal egg count reduction test
GABA	gamma-amino butyric acid
GIN	gastrointestinal nematodes
HCW	hot carcass weight
IgE	immunogolublin E
IgG1	immunoglobulin G1
IL4	interleukin 4
KPH	kidney, pelvic, heart fat
L_1	first stage larvae
L_2	second stage larvae

L_3	third stage larvae
L_4	fourth stage larvae
REA	ribeye area
TCSCF	Tri-County Steer Carcass Futurity
Th2	T helper cell 2
W.A.A.V.P	World Association for the Advancement of Veterinary Parasitology
YG	yield grade

ACKNOWLEDGMENTS

I would like to thank my major professors. Thank you, to Dr. Patrick Gunn for your support and guidance throughout my time here at Iowa State. To Dr. Dan Loy, thank you for stepping in as my on-campus advisor and offering learning and extension opportunities. I would also like to thank my committee members for mentoring me through my program. To Dr. Troy Brick, thank you for providing advice and resources throughout my project. To Dr. Lee Schulz, thank you for your expertise and guidance.

I would like to thank my fellow graduate students Caitlin Wiley and Colby Redifer for their help with research. Thank you to my office mates past and present for providing encouragement, office entertainment, and frequent caffeine runs.

A big thank you to the McNay Farm staff and the Beef Teaching Farm staff here at Iowa State for assistance with data collection.

I would like to express a special thank you to the Iowa Beef Center for many opportunities to be involved in beef extension and research during my time here at Iowa State.

To my family and friends, a heartfelt thank you for your love, support, and encouragement in everything that I do. A very special thank you to my parents, Lyle and Stacey, for your unfailing belief that I can accomplish anything I put my mind to.

Finally, thanks to God, who makes all things possible, for directing my path and sustaining me with His unfailing love. (Proverbs 19:21)

ABSTRACT

The effect of a single subcutaneous injection of extended-release eprinomectin for parasite control on cow/calf performance was evaluated in a pair of studies. In the first study, a fall-calving Angus herd was utilized. Mature cows were treated with either extended-release eprinomectin (EPR) or a conventional injectable anthelmintic (CONV). Cows treated with EPR had better maintenance of BCS through calving and into breeding. Subsequent pregnancy rates were greater for EPR than CONV cows. Furthermore, calves from EPR dams were younger at weaning, but had greater weaning weights than calves from CONV dams. From the same fall-calving Angus herd, replacement heifers were either treated with EPR or CONV. Weights taken post-treatment demonstrated heavier BW, greater weight gain, and greater ADG, for EPR heifers. Both conception to AI and overall pregnancy rates were greater for EPR heifers. Also, a greater proportion of EPR heifers calved in the first 21 days of the subsequent calving season.

A second study was conducted to elucidate the effects of a single injection of extended-release eprinomectin on economically relevant production variables in beef cows and calves as well as subsequent feedlot health, performance and carcass traits of calves. Animals from 13 cooperator herds across 7 states were stratified within herd by cow age, calf birth date, calf birth BW, and calf sex and assigned to 1 of 2 treatments; injectable doramectin (DOR) or injectable extended-release eprinomectin (EPR). There was no difference in cow BW at the start or end of the grazing season, resulting in no differences in BCS, change in BW or ADG over the course of the grazing season. Fecal samples collected at treatment indicated no difference in fecal egg count (FEC) at the start of the grazing season. However, subsequent samples collected at the end of the grazing season showed lower FEC for EPR cows and a greater overall reduction in FEC over the course of the grazing season. EPR cows had a lower incidence of pinkeye, however,

there was no differences in calf pinkeye. Fly counts conducted indicate no difference in fly burden between treatment groups. There was no difference in reproductive success including conception to AI, overall breeding season pregnancy rates, calving interval, and calving distribution. There was no difference in calf treatment BW, weaning BW, or pre-weaning ADG.

Following weaning, a subset of calves from each herd at the discretion of the cooperator were shipped to Tri-County Steer Carcass Futurity (TCSCF) for the finishing phase. At initiation of the feeding phase, calf BW did not differ. While EPR calves tended to be heavier at re-implantation, final BW and overall ADG were not different between treatments. Despite a lack of differences in feedlot performance, morbidity was lower for EPR calves indicating these calves were healthier throughout the feeding phase. However, evaluation of carcass performance showed no difference in HCW, dressing percent, backfat, KPH, REA, YG or marbling score. Analysis of quality grade indicated higher average quality grade for EPR calves as well higher percentage of calves that graded average choice or higher. There were no differences in the percentage of steers that graded low choice or lower. Economic analysis indicates an opportunity for producers operating on a retained ownership platform who treated with EPR to realize a profit above the initial cost of treatment through improved health status during the feeding phase. An overall lack of performance differences observed in the current study may likely be a function of low FEC in participating herds.

In summary, results from these studies indicate that certain environmental conditions can result in improved performance following treatment with extended-release eprinomectin. Benefits from anthelmintic administration to suckling calves pre-weaning may extend to the feedlot phase. Opportunities to capitalize on initial treatment investment are evident, but are dependent on the size of the production response and the economic conditions at time animals are marketed.

CHAPTER 1.

INTRODUCTION

All grazing animals are exposed to parasites and acquire some level of parasitic infection throughout the grazing season. If not managed properly, these parasites result in costly consequences to both animal health and a producer's bottom line (Hawkins, 1993). Gastrointestinal parasites are estimated to cost the U.S. cattle industry approximately $3 billion annually (Bagley et al., 1998). However, the costs of parasitism are difficult to quantify as infections are typically subclinical in nature. Gastrointestinal parasites can create nutritional inefficiencies in livestock and greatly reduce performance resulting in economic losses (Bagley et al, 1998). The resulting losses from subclinical infections are subtle yet costly to the beef industry.

While parasites pose a potentially severe health risk, pharmaceutical intervention in the form of anthelmintic treatment has been proven to reduce worm burdens in cattle and improve performance across all segments of the beef industry. Deworming during the grazing season has been shown to improve cow/calf production parameters including calf performance, cow performance, reproductive success, and milk production (Stuedemann et al., 1989; Wohlgemuth et al., 1990; Stromberg et al., 1997; Hersom et al., 2011). Furthermore, deworming has been implicated for improved lifetime performance and health for both replacement heifers and feedlot animals (Mejia et al., 1999; Clark et al., 2013, 2015). Although highly advantageous for producers, a large portion of the cowherd is never dewormed including unweaned calves (38%), replacement heifers (25%), weaned calves (41%), and mature cows (13%) (NAHMS, 2008).

Anthelmintic technologies have long been used in animal agriculture and have been a stable in ruminant production systems (Sutherland and Scott, 2010). The development began in the 1960's and continued through the late 1990's with the arrival of newer, more effective products (McKellar and Jackson, 2004). Most products currently available have a range of effectiveness from 28 to 35 days. While these products have broad-spectrum action, and come in convenient dosing forms, they are short-duration treatment options.

Few developments for alternative or new anthelmintic technologies have been made in the last decade. However, in 2012, Merial, Inc. released the extended-release version of their injectable anthelmintic drug, eprinomectin. This product label claims 100-150 days of parasite protection with one injection. Research analyzing plasma concentration of eprinomectin over the extended-release period shows effective plasma concentrations up to 150 days post-administration (Solls et al., 2013). While this product has proven to reduce worm burdens and improve weight gains, investigations have been primarily made into the stocker segment of the beef industry (Rehbein et al., 2013a; Rehben et al., 2013b, Clark et al., 2014). Little research has been focused on other production setting including cow/calf and feedlot. Therefore, the development of a newer, novel anthelmintic warrants investigation into its effects in alternative production systems as well as its impact on reproductive success, as this has been largely understudied in response to anthelmintic treatment.

CHAPTER 2. LITERATURE REVIEW

2.1 Introduction

The goal of this literature review is to describe the parasites found in ruminants, their impact in grazing animals, as well anthelmintic products available and to help control parasites. Finally, the impact of animal performance following anthelmintic treatment and the economic implications associated with anthelmintic treatment will be described.

2.2 Common parasites in cattle

Parasitism is equal to the summation of effects from all gastrointestinal nematodes (GIN) species and stages present in the host at any given time (Sutherland and Scott, 2010). There is a diverse variety of GIN that infect cattle and their effects on cattle health and productivity are equally diverse and pose the greatest health threat to grazing cattle. Gastrointestinal nematodes are species-specific to the host they inhabit and their ability to develop to an infectious stage is highly dependent on a multitude of environmental factors including temperature, humidity, pasture type, pasture management, and grazing behavior (Stromberg and Gassbarre, 2006; Fox et al., 2013). While most parasite species have a life cycle of approximately 6-8 weeks, longer grazing seasons can facilitate recycled infections, which increase worm burdens (Williams and Loyacano, 2001).

2.2.1 Parasite life cycle

While variations exist between species of parasites, the general life cycles for GIN in cattle are largely similar (Zajac, 2006; Sutherland and Scott, 2010; Ballweber, 2014). GIN can live both on pastures and within their host, however, an entire lifecycle cannot be carried out in a single location (Zajac, 2006; Sutherland and Scott, 2010).

A nematode lifecycle begins when an egg, produced by an adult within the host, is expelled into the environment via fecal excrement (Sutherland and Scott, 2010). Typically, within 24 hours of being excreted, eggs will hatch into their first larval stage (L_1; Ballweber, 2014). Following hatching from the egg, L_1 larvae will undergo two molts as it develops to the second larval stage (L_2) followed by the third larval stage (L_3; Zajac, 2006).

While a large amount of eggs may be deposited onto the pasture, a very small percentage actually develop to an infective stage, estimated in a range from 3% to 30% depending on species and environmental impacts (Ciordia and Bizzell, 1963; Williams and Bilkovich, 1971). This survival rate is strongly impacted by a number of highly variable factors. Two of these factors of considerably great importance are temperature and humidity (Armour, 1980; Stromberg, 1997; Stromberg and Gasbarre, 2006; Yazwinski and Tucker, 2006, and Taylor et al., 2007). Both of these factors have been strongly implicated in development, survival, migration, and infectivity of GIN (Ciordia, and Bizzell, 1963; Armour, 1980; Stromberg, 1997; Stromberg and Gasbarre, 2006; Yazwinski and Tucker, 2006, and Taylor et al., 2007). A range between 6° C and 32° C has been established with an optimum temperature of 25° C for development of the free-living stages nematodes (Ciordia and Bizzell, 1963). While humidity in the air is important, other sources of moisture including moisture in the manure pat itself, the soil, the vegetation, and drainage all play an important role in the GIN life cycle (Armour, 1980). The survival of free-living GIN and overall lifespan of GIN is also greatly impacted by nutritional status of the parasite (Klass, 1977; Yazwinski and Tucker, 2006; Sutphin and Kaeberlein, 2008). Most interestingly, studies have noted a negative correlation between nutritional status and lifespan such that nutritional restriction increases lifespan (Klass 1977; Sutphin and Kaeberlein, 2008). The mechanisms for this correlation are not well understood but are believed to be founded in decelerated aging process (Sutphin and Kaeberlein, 2008). These optimum conditions for longevity are an interesting contrast to the environment found within the host they inhabit.

Migration of the L_3 larvae is extremely important for transmission to the host as well as subsequent survival and development into the adult stages (Stromberg and Gasbarre, 2006). There are a number of environmental factors that play a role in the migration of L_3 larvae including pasture-type, topography, drainage, pasture management, grazing behavior and moisture which all impact GIN ability to migrate away from manure pats and onto surrounding herbage for uptake into the host (Stromberg and Gasbarre, 2006; Fox et al., 2013). A continuous film of moisture on the herbage is imperative to larval migration away from the fecal pat and to a location where it can be ingested by the host (O'Connor et al., 2006). While potentially not a factor for more hardy species that can withstand dry conditions (Silva et al., 2008) time of day could potentially impact larval migration (Krecek et al., 1995). Increased moisture in the morning and evening have been shown to increase larval migration during these times and possibly increase infection risk in grazing animals (Krecek et al., 1995; Chaudary et al., 2008). Also, height of pasture being grazed can play a role in risk of GIN infection for grazing animals. When grass is adequate, cattle can selectively graze areas away from fecal pats that have concentrated parasite populations (Stromberg and Gasbarre et al., 2006; Fox et al., 2013). However, when pasture resources are limited, cattle cannot be as selective which may increase infection risk (Fox et al., 2013).

Grazing management can be implemented to control uptake of parasites on pasture and help mitigate risk of infection to grazing livestock. Limiting the length of the grazing season or amount of grazing time per day can reduce parasite intakes in grazing animals (Charlier et al., 2005; Yazwinski and Tucker, 2006). Different types of forage have also been implicated in reducing the ability of parasites to migrate and therefore be ingested by the host (Morely and Donald, 1980; Yazwinski and Tucker, 2006; Fox et al., 2013) where pasture species with higher moisture retention may contribute to greater larval migration (Niezen et al., 1998; Amaradasa et al., 2010). Herbage species that contain natural anthelmitic compounds may reduce larval migration (Niezen et al., 1998). Maintaining adequate pasture resources can also reduce exposure of livestock to concentrated GIN populations on livestock by dilution of contamination (Brundson, 1980; Stromberg et al., 2006; Fox et al., 2013). Resting pastures can allow natural removal of parasites by environmental factors without reinfection by grazing animals (Morely and Donald, 1980; Brundson, 1980). In the wake of anthelmintic resistance, which will be discussed, grazing management is an important source of biological control of GIN populations on pasture and subsequent infection in grazing livestock.

The parasitic phase of the GIN life cycle cannot begin until the L3 larvae interacts with the host which usually occurs by ingestion of GIN by the host from herbage while grazing. Soon after ingestion, L_3 larvae reside in their respective intestinal area where they will exert their parasitic effect (Stromberg and Gasbarre, 2006). In the same manuscript, authors identified that shortly after reaching the area they will primarily affect, they develop into an immature adult (L_4) stage. It is at the stage (L_4) that some species of worms are able to arrest their development in a process called hypobiosis (Sutherland and Scott, 2010). While the mechanisms of hypobiosis are not well understood, some factors believed to trigger this arrest stage are immune status of the host, season or climate, and possibly response to alterations in hormones (Sutherland and Scott, 2010). It has been suggested that hypobiosis is a mechanism by which GIN can synchronize their life cycle with current conditions, either in the host or external environment (Michel, 1976). While hypobiosis occurs during adverse conditions, ingestion of arrested, less pathogenic larvae has been implicated as a mechanism for lessening the impact of parasitic infection by storing dormant larvae instead of pathogenic adults (Schad, 1977). After a period of hypobiosis, resumption of development of inhibited larvae can account for the occurrence of clinical parasitic infection in animals who have not been recently exposed to contaminated pasture (Armour and Duncan, 1987).

If there is no arrest stage, GIN will develop into reproductively mature adults within 2 to 4 weeks of ingestion of the L_3 stage and will begin producing eggs to be excreted in the feces (Ballweber, 2014). This time between ingestion of the L_3 larvae and subsequent detection of eggs in the feces is termed the pre-patent period and is dependent on species and host environment (Sutherland and Scott, 2010; Ballweber, 2014).

Other limitations to lifespan are host immunity. Initially, established worms may not be effected, but subsequent ingested GIN lifespans may be impacted once an immune response by the host has been mounted (Sutherland and Scott, 2010). Primary parasitic infections have been shown to block host immune response (Behnke et al., 1983). Studies down with *Ostertagia ostertagia* infections in cattle have demonstrated suppression of lymphocyte reactivity as well as suppressed cellular and antibody responses during initial stages of parasite infection (Klesius, 1988). However, subsequent infections allow for a mounted immune response by the host and can influence secondary GIN infections (Keymer and Hiorns, 1986).

2.2.2 Gastrointestinal nematodes in cattle

While a large number of GIN have been isolated from domesticated cattle, only a small portion are considered clinically significant from a veterinary perspective (Yazwinski and Tucker, 2006). In the following discussion, GIN of veterinary importance will be presented and GIN will be grouped by the area of the GI tract that they primarily affect.

2.2.2.1 Abomasum. *Ostertagia ostertagi,* also known as the brown or medium stomach worm, is considered to be the most economically important parasite of cattle raised in temperate climates (Yawinski and Tucker, 2006; Irsik, 2012). This parasite is able to arrest its development which allows it to evade immune regulation by the host and lengthens the time of infection (Armour and Duncan, 1987; Klesius, 1988; Yazwinski and Tucker, 2006). Two clinical forms of *O. ostertagi* have been identified: type I disease and type II disease (Smith and Grenfell, 1985; Fox, 2016). Type I disease, typically found in in calves and yearlings, is caused by larvae that do not experience a developmental arrest period and occurs shortly after ingestion of larvae (Smith and Grenfell, 1985; Fox et al., 2016). Type II disease is caused by larvae that have experienced an arrest stage in their development and, therefore, most typically occurs in older cattle (Smith and Grenfell, 1985). Some research has indicated that arrested larvae will resume development in conditions when host immunity is compromised (Armour and Duncan, 1987). Clinical symptoms of both types of infection are by weight loss, reduced appetite, and diarrhea. Because symptoms are similar, the type of infection can only being distinguished by timing of outbreak following ingestion (Smith and Grenfell, 1985). As previously discussed, initial infection with *O. ostertagi,* as in other species of GIN, can suppress immune response in young animals (Klesius, 1988). While acquired immunity is eventually achieved, it may not be until an animal's second

Grazing season that they are able to effectively reduce worm burdens naturally and cattle may be susceptible to subclinical reinfection throughout their lifetime (Herlich, 1980; Klesius, 1988).

Another worm is the *Trichostrongylus axei,* also known as the stomach hairworm. While its prevalence is considerably less than other GIN discussed, being found in less than 10% of sampled populations, it remains of veterinary importance because it is not limited by age of host or previous exposure (Yazwinski and Tucker, 2006). Clinical symptoms of these GIN include gastritis, hyperemia, diarrhea, protein loss, and anorexia and weight loss (Fox, 2016).

Also known as the barber pole, large stomach worm, twisted stomach or wire worm, *Haemonchus contortus* are hematophagic parasites and are the largest, most pathogenic parasite of the ruminant species (Yazwinski and Tucker, 2006; Sutherland and Scott, 2010; Irsik, 2012). Contributing to their pathogenicity is their extensive genome with highly adaptive genotypic capabilities to selection, long generation time, and high rate of reproduction (Prichard, 2001; Yazwinski and Tucker, 2006). Also contributing to its pathogenic effect is its ability to arrest development in the early L_4 stage (Anderson, 2000). Not only does this stage of arrest allow for survival during suboptimal conditions, it has also been implicated as a mechanism of resistance to parasiticides (Anderson, 2000). Clinical signs of infection with *Haemonchus* spp. include poor body condition, stress, progressive anemia, pallor of the skin and mucus membranes, and submaxillary edema (bottle jaw) depending on the extent of blood lose and the severity of infection (Bowman, 1999).

2.2.2.2. Small Intestine. Of the phylum *Cooperia*, several species exist with *Cooperia oncophora, Cooperia punctate, and Cooperia pectinate* being the most predominant (Yazwinski and Tucker, 2006; Sutherland and Scott, 2010; Irsik, 2012). This parasite is found in the proximal region of the small intestine and is most burdensome to animals three years of age and younger, causing damage and inflammation to the lining of the GI tract resulting in leakage and loss of blood protein (Williams and Loyacano, 2001; Yazwinski and Tucker, 2006). Clinical signs in *Cooperia* are very similar to its abomasal counterpart *Trichostrongylus* (Bowman, 1999). While *Cooperia* have been considered less important compared to other nematodes due to low degree of pathogenicity as well as a rapid development of immunity against this parasite by the host by the second grazing season, recent observations of resistance to macrocyclic lactones have increased their attention and importance (Njue and Prichard, 2004; Yazwinski and Tucker, 2006)

Nematodirus helvetianus, generally termed the thread-necked worm, deviates from the previously discussed life cycle of nematodes because it remains inside the egg until it develops to the L_3 stage instead of hatching into the L_1 stage like other GIN (Yazwinski and Tucker, 2006; Sutherland and Scott, 2010). Development within the egg has been implicated in longevity of free-living *N. helventianus* through multiple grazing seasons in cooler regions (Gibbs, 1980). At doses of anthelmintic treatment below the label recommended dose, *N. helvetianus* are resistant to macrocyclic lactones, much like *Cooperia* and are thus called a dose-limiting species (Yazwinski and Tucker, 2006). However, unlike with *Cooperia*, hosts are able to mount a rapid immune response as yearlings, mitigating low efficacy of parasiticides with this species (Yazwinski and Tucker, 2006). The main clinical sign of infection is severe and debilitating diarrhea (Bowman, 1999).

2.2.2.3 Large Intestine. Fewer gastrointestinal nematodes reside in the large intestine. *Oesophagostomum radiatum*, sometimes referred to as the nodular worm, are mostly pathogenic in the larval stage (Sutherland and Scott, 2010). These GIN burrow into the mucosal layer of the distal small intestine and proximal large intestine and result in clinical signs of diarrhea at the time of worm emergence from the mucosal layer (Yazwinski and Tucker, 2006; Sutherland and Scott, 2010). These GINs are of veterinary importance because of a lack of acquired immunity by the host resulting in a constant, light infection (Yazwinski et al., 1999; Yazwinski and Tucker, 2006). While acquired immunity of the host may not be possible to control infections of this species, anthelmintic treatment is highly effective in eliminating infections of *O. radiatum* (Yazwinski et al., 1999).

2.2.3 Epidemiology

As previously expressed, a diverse population of GIN can infect hosts and exert equally diverse impacts in several locations throughout the gastrointestinal tract. As mentioned previously, parasitic infection is equal to the summation of all the species and stages of parasites present (Sutherland and Scott, 2010) and must be considered when determining epidemiology of parasitic infections. Epidemiology is an area of medicinal study that focuses on incidence, distribution, and possible control of disease. The study of parasite epidemiology is typically evaluated by population dynamics as suggested by Gordon (1948) because a threshold at which a worm burden becomes dangerous is not and cannot be defined in animals. This approach of population dynamics is also necessary because resulting infections are usually subclinical and have a less noticeable onset than other epidemics or diseases. Overriding determinants include climate, weather, season and region (Yazwinski and Tucker, 2006) where climate appears to determine the prevalence of parasites and weather appears to effect timing of parasitic outbreaks (Craig, 1979; Yazwinski and Tucker, 2006). Parasitic outbreaks are most common when the following conditions occur: large larval prevalence in the envrionment, poor host nutrition, and a poor immunological response to infestation (Roberts et al., 1952).

Outbreaks of parasitic disease can arise for the following reasons: 1) increase in parasite populations and therefore increased infecting mass, 2) an alteration in susceptibility of the host, 3) the introduction of susceptible stock to an already infested area, and 4) the introduction of infected stock into a clean environment (Gordon, 1948; Armour, 1980; Taylor et al., 2007). Integral to understanding parasitic infection and transmission in the these four scenarios is an understanding of a multitude of interactions and factors that play large roles into the epidemiological impact of parasites. These including parasite-pasture interactions (Armour, 1980; Stromberg and Gasbarre, 2006), parasite-host relationships (Armour, 1980; Stromberg and Gasbarre, 2006), environmental factors (Armour, 1980; Fox et al., 2013), pasture management (Armour, 1980; Stromberg, 1997; Fox et al., 2013), and host behavior (Armour, 1980; Stromberg and Gasbarre, 2006; Fox et al., 2013).

2.2.4 Parasite-host relationship

While all of the aforementioned factors influence epidemiological impact of parasites in beef cattle, producer concerns focus on parasite-host relationships and factors affecting worm-burden of individual animals as these are the primary source of economic loss in production settings (Stromberg and Gasbarre, 2006). Once infective larvae are ingested by the host, factors that impact the parasite's ability to cause disease can vary greatly between and within herds (Gasbarre et al., 2001).

Host immune status is one of the most important lines of defense against parasitic infection. It has been well defined that the immune response in cattle occurs via a Th2 response

(Svetic et al., 1993; Claerebout and Vercruysse, 2000; Gasbarre et al., 2001). This response releases helper-T cells in the wake of helminth infection stimulates a cascade release of a host of immune molecules including cytokine Interleukin 4 (IL4), IgG1, and IgE antibodies along with a large number of mast cells, but is not controlled by a single mechanism (Svetic et al., 1993; Gasbarre et al., 2001). The ability to mount an immune response to a helminth infection is dependent on a number of animal related factors.

Due to the location and pathogenic nature of GIN within the animal, a definite, established link has been made between parasite infections and nutritional status of the host (Armour, 1980; Coop and Kyrazakis, 1999; Sutherland and Scott, 2010). Nutritional status of the host during a parasitic infection can be evaluated from two perspectives: metabolic cost of disturbances caused by parasitism and the effect of nutritional status of host on ability to mount an immune response (Coop and Kyriazakis, 1999; Sutherland and Scott, 2010). The first perspective will be discussed in a subsequent section, whereas a discussion on the latter will be presented now. Gastrointestinal parasites can compromise the nutritional status of an animal. However, during a parasitic infection, infected animals are also mounting an immune response, further impacting nutrient requirements. In fact, Poppi et al. (1988) found that the nutritional penalty of parasitic infection was most severe during weeks 11 – 13 when animals appeared to be resisting larval challenge. The results from this study suggest that the nutritional cost of immunity to parasitic infections is greater than that associated with a primary infection.

Studies in sheep have demonstrated reduced production response of parasitized animals is associated with sequestration of protein in tissues of the gastrointestinal tract (Wang et al., 1998; Yu et al., 2000). These studies have implicated tissue repair as well as the production of acute phase proteins in gut mucosa as possible explanations for protein accumulation in the GI tract.

Symons and Jones (1975) noted increased liver protein synthesis in parasitized animals when compared to pair-fed controls, which is indicative of acute phase response to infections. Other studies have demonstrated competition for certain amino acids between immune function and wool growth in animals selected for high wool production (Miller et al., 1998) suggesting potential nutritional trade-offs between immunity and production. Other studies have demonstrated that carcasses of parasitized animals contain less protein than uninfected controls indicating a slower rate of muscle protein synthesis and a faster rate of whole-body protein catabolism (Symon and Jones, 1975; Sykes, 1983; Entrocasso et al., 1986).

While immunity may create high nutritional demand for parasitized animals, studies have shown that high levels of protein supplementation can impact response to a parasitic infection by improvement in clinical signs, reduction in fecal egg counts, enhanced onset of immunity and increased resistance to re-infection (Bown et al., 1986; Abbot et al., 1988; Houkijk et al., 2006).

Other factors that can impact host resilience to parasitic infection are sex, age, and previous infection of stock. Some work has demonstrated significantly higher egg counts in intact males than in their castrated or female counterparts (Copeman and Hutchinson, 1979; Herd et al., 1992) which can be considered when choosing parasite control programs. Exposure to infection for the purpose of acquired immunity and age of the animal go hand-in-hand. While young calves are impacted most severely by parasitic infection, acquired immunity to most GIN species is typically develops as the animal matures (Smith and Archibald, 1968; Yazinski and Tucker, 2006; Taylor et al., 2007). While difficult to quantify, research has suggested that a propensity for resistance to parasitic infection may be related to genetic differences between animals (Leighton et al., 1989; Gasbarre et al., 2001). Using fecal egg counts as a phenotypic indicator, genetic differences associated with these phenotypes are under current investigation (Gasbarre et al, 2001). Leighton et al. (1989) have indicated that sires can influence FEC of their offspring and have suggested that FEC have a heritability of 29%. Further investigation into genetic markers may one day provide producers an opportunity to help curb parasitic infection through targeted genetic selection

2.3 Anthelmintic treatment

As previously discussed, parasitic infections are multifactorial in nature. The pathology of disease is based on interactions between the host, environment, and the parasite and is highly influenced by individual management strategies (Charlier et al., 2015). While there is no one-size-fits-all treatment recommendation, strategic treatment programs are proposed in order to identify crucial interactions between environment and host in order to offer the best protection for all classes of cattle (Stromberg and Gasbarre, 2006). While past applications of deworming technologies have had a therapeutic focus, integrated programs today focus on utilizing biological and chemotherapeutic control methods simultaneously (Brundson, 1980; Williams and Loyacano, 2001). Such control methods put an emphasis on strategically-timed treatments which are designed to not only prevent clinical parasitic infections but also reduce pasture contamination and subsequently lower future risk of infection (Williams and Loyacano, 2001).

Crucial to implementing an effective chemotherapeutic control program is understanding regional climates and weather patterns (Williams, 1997; Williams and Loyacano, 2001; Stromberg and Gasbarre, 2006). Length of growing season, length of grazing season, and weather patterns optimal for nematode development and survival can impact risk of parasitic infection (Williams, 1997). The goal for strategic treatment methods is reduce larval contamination on pasture (Brundson, 1980). This strategically timed control method requires an understanding of climate/environment/parasite interactions in order to target periods where treatment will be most effective (Southcott et al., 1976; Brundson, 1980; Williams and Loyacano, 2001).

While climate and environment effect the timing of anthelmintic treatment, the class of livestock may affect frequency of treatment. Susceptibility of an animal varies with age (Smith and Archibald, 1968; Yazinski and Tucker, 2006; Taylor et al., 2007), sex (Copeman and Hutchinson, 1979; Herd et al., 1992), previous exposure to parasitic infection (acquired immune function), and stage of production, as it effects nutritional requirements (Armour, 1980; Coop and Kyrazakis, 1999; Sutherland and Scott, 2010). Especially in environments with extended periods of infection risk such as temperate climates, multiple treatments for more highly susceptible stock may be necessary to provide adequate protection from parasitic infections (Williams and Loyacano, 2001).

While these proposed strategic treatment regimens effectively optimize animal performance and provide clean pastures for grazing animals by removing parasites, there is mounting concern that continued, long-term use of existing anthelmintics will result in high proportions of resistant nematode populations and drastically reduce the efficacy of chemical compounds used to control internal parasitic diseases. A management strategy known as the refugia concept, has sparked high interest due to rising incidence of anthelmintic resistance, particularly in small ruminants (Besier, 2012). This concept will be discussed in depth later in this review.

Although recommended anthelmintic control programs aim to optimize efficiency, and subsequently, return on investment, based on environment and host variables, there are several other factors that may drive management strategies utilized by producers (Charlier et al., 2015). Although producers are business-minded, intrinsic factors such as management, tradition, attitude, and social norms can all play roles into the types of parasite control implemented into a production system (Charlier et al., 2015) and therefore, must be decided at the farm level.

2.4 Current anthelmintic treatments

As previously mentioned, anthelmintic treatment has an important role in a parasite control program and can be highly effective in conjunction with biological control methods. The physiological and biochemical differences between helminths and their host make the action of most commonly used anthelmintic drugs selectively toxic to the parasites without harming the host (Saz and Bueding, 1996; Kohler, 2001). Commonly, anthelmintic drugs effect three biochemical and physiological areas (Kohler, 2001). Target sites of these drugs are exclusively proteins including ion channels, enzymes, structural proteins and transport molecules (Kohler, 2001). The World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) defines a new anthelmintic drug as economically successful if the product has broad spectrum, effective activity on all major nematodes at all stages or fulfills a specific niche in parasites not controlled by current anthelmintic products (W.A.A.V.P., 1995). Great strides made from the 1960's to the 1990's have deemed it the 'golden age' of chemotherapeutic drugs including several novel anthelmintic products (Geary et al., 2004; Waller, 2006). With this pharmaceutical evolution came several new and improved anthelmintic products with increased efficacy at lower dose rates than the one before it (McKeller and Jackson, 2004; Waller, 2006).

Development of these new drugs allowed safe, easy and effective protection against a broad spectrum of parasites at an affordable cost and increased popularity and use of parasiticides worldwide (Waller, 2006). The following discussion is focused on two of the main classes of anthelmintic molecules: benzimidazoles and macrocyclic lactones. Although other classes do exist, their market share is relatively small compared to the benzimidazoles and macrocyclic lactones and therefore will not be discussed.

2.4.1 Benzimidazoles

The class of drugs known as the benzimidazoles consists of a large group of drugs (thiabendazole, parbendazole, oxibendazole, fenbendazole, oxfendazole, albendazole, traclabendazole, and ricobendazole) that are relatively insoluble and are most typically administered orally (Taylor et al., 2007). Through oral administration, the lowly soluble benzimidazole compounds are deposited directly into the rumen where low pH provides strong reducing conditions (Hennessy, 1993). The reduced metabolites that exit the rumen are more soluble than the parent compound and therefore have greater absorption (Hennessy, 1993). Another group called probenzimidazoles are metabolized to active benzimidazole metabolites, are included in this class (Taylor et al., 2007).

Benzimidazole drugs bind with high affinity to tubulin, the microtubule subunit protein, and disrupts microtubule structure and function (Friedman and Platzer, 1978; Kohler and Bachmann, 1981; Lacey, 1988). Movement of chromosomes during cell division, skeletal structure, movement of intracellular particles, specifically energy metabolites, and exocytosis are the main functions of microtubules (Stryer et al., 2002). This process of inhibition is known as “capping” because it binds to the positive pole of polymerization and results in a slow onset starvation due to inhibition of glucose uptake, protein secretion, and microtubule formation along with inhibition of egg production (Martin, 1997; Taylor et al., 2007). It also inhibits transportation of secretory granules within the cell cytoplasm, which results in cell lysis (Lacey, 1988). While microtubules are found in animals, plants, fungi, and some bacterial cells (Stryer et al., 2002), the mode of action of benzimidazole drugs has selective binding only to nematode β-tubulin (Martin, 1997).

Starting in 1960, the first lower dose, high efficacy drug was introduced in the form of thiabendazole, and became a staple in small ruminant production, especially in Australia and New Zealand (Waller, 2006; Sutherland and Scott, 2010). Throughout the 1970's, several more molecules in the benzimidazoles class were developed and released as novel anthelmintic products (McKellar and Jackson, 2004). Some of these drugs included fenbendazole (Safeguard® and Panacur®), albendazole (Valbazen®) and oxfendazole (Synanthic®). These products come in various forms including oral drenches, blocks, in-feed formulation, or intra-ruminal injection. All of these drugs have various withdrawal times and are effective on a range of parasites.

2.4.2 Macrocyclic lactones

Macrocyclic lactones consist of the avermectins (ivermectin, doramectin, eprinomectin) and milbemycins (moxidectin). Chemically, avermectins vary from each other in side chain substitutions on the lactone ring, while milbemycins vary from avermectins by the lack of a sugar moiety on the lactone skeleton (Taylor et al., 2007). This class of drugs is highly active at low dose rates and is highly lipophilic resulting in slower release (Taylor et al., 2007).

The mode of action of avermectins is not fully understood. While it was originally believed that avermectins cause paralysis by stimulating the release of γ-aminobutyric acid (GABA) from nerve endings resulting in enhanced binding to its receptor on an excitatory motor neuron (McKellar and Jackson, 2004; Taylor et al., 2007), it is now known to potentiate the effect of GABA (Kohler, 2001; Sutherland and Scott, 2010). This enhanced binding creates an increased flow of chloride ions resulting in hyperpolarization of the cell (Taylor et al., 2007). More recent studies have indicated that the main mode of action of avermectins are exerted on glutamate-gated chloride channels (Kohler, 2001; McKellar and Jackson, 2004; Sutherland and Scott, 2010). The effect of drugs such as ivermectin are irreversible, causing hyperpolarization of the cell membrane and muscle paralysis (Kohler, 2001). This paralysis blocks pharyngeal pumping and inhibits feeding, which disrupts ingestion and causes starvation of the parasite (Geary et al., 1993; Sangster and Gill, 1999). Muscle paralysis can also affect mobility and reproduction (Prichard, 2001) giving this group of drugs multiple targets to exert its effects. Similar to benzimidazole drugs, macrocyclic lactones are selectively toxic to nematodes because the molecules are too large to cross the blood-brain barrier in mammals (Taylor et al., 2007), however, since macrocyclic lactones are neurotransmitter agonists, the onset of their effects are much quicker than their benzimidazole counterparts (Martin, 1997).

The 1980's brought the release of the macrocyclic lactones, referred to as endoectocides for their dual treatment of both internal (endo) and external (ecto) parasites (Williams and Loyacano, 2001; Taylor et al., 2007). One of the most popular drugs, ivermectin (Ivomec®), was released in the early 1980's and is available as an injectable and a pour-on. Doramectin (Dectomax®), released in 1996 as a pour-on and injection as well as moxidectin (Cydectin®), released in 1998 as a pour-on are both products similar to Ivomec. In the late 1990's eprinomectin (Eprinex®) was released as a pour-on. All of these products range in length of effectiveness from 28 days to 35 days, making them short-range treatment options for parasite control. Recently, a long-acting eprinomectin injectable was released and has a length of effectiveness between 100 – 150 days.

2.5 Anthelmintic resistance

While anthelmintic treatment can be highly effective at reducing or removing worm burdens in animals, as previously discussed, there are some concerns with a loss of effectiveness of these drugs due to developing resistance in nematode populations. Parasite resistance to anthelmintic drugs acquired through genetic transmission of a loss of drug sensitivity in previously sensitive worm populations (Kohler, 2001; Wolstenholme et al., 2004). While anthelmintic resistance in small ruminants is a prevalent, world-wide problem, reports of resistance in large ruminants have been scarce (Waller, 1994; Waller, 1997; Geary et al., 1999; Coles, 2002; Kaplan, 2004; Wolstenholme et al., 2004). The absence of anthelmintic resistance in cattle is believed to be due to management, immunity differences, and a lack of investigation into resistance (Coles, 2002; Kaplan, 2004). While not a noted issue in North America, some strains of cattle GIN identified in other countries have demonstrated resistance to some broad-spectrum anthelmintic drugs (Vermunt et al., 1995; Hosking et al., 1996; Stafford and Coles, 1999; Mejia et al., 2003; Loveridge et al., 2003; Anziani et al., 2004; Gasbarre et al., 2009).

There are several genetic processes that can play a role in a parasite's ability to become resistant to certain anthelmintic drugs. Common genetic changes can either be caused by a mutation in a single gene or require a simultaneous mutation in many genes (Kohler, 2001; Wolstenholme et al., 2004; Sutherland and Scott, 2010) and can occur in circumstances of an appropriate, therapeutic dose or under-dosing (Sutherland and Scot, 2010). These genetic adaptations for anthelmintic resistance are heritable (Lacey, 1988; Taylor et al., 2007), can either occur naturally in a population, or develop after exposure to anthelmintic treatment (Sangster, 1999; Coles, 2002), and can result in a high number of resistant individuals with continued use of an anthelmintic (Taylor et al., 2007).

2.5.1 Genetic resistance to benzimidazoles

Mechanisms of resistance in GIN to the benzimidazoles has been studied extensively. As previously discussed, benzimidazoles selectively target nematodes by binding only to nematode β-tubulin (Martin, 1997). Two isotypes have been identified for nematode β-tubulin, type I and type II, each having separate genes (Kwa et al., 1993; Martin, 1997). Resistance to the benzimidazole drugs is the result of the loss of specific β-tubulin isotypes during selection resulting in alterations to β-tubulin isoforms (Prichard, 1994; Sangster and Gill, 1999). Alterations to the isoforms due to the mutation prevents the drugs from binding to their intended target receptor (Lacey, 1988; Roos et al., 1990; Martin, 1997; Kohler, 2001; Sutherland and Scott 2010) and is associated with a structurally changed tubulin within the population (Roos et al., 1990). Lubega and Prichard (1991) have demonstrated that in benzimidazole resistant nematodes, only β-tubulin isoforms are altered and α-tubulin isoforms are unchanged, suggesting selection effects specific to benzimidazole exposure. Resistance is magnified because selection for resistant phenotypes occurs even without continued exposure to benzimidazoles (Roos et al., 1990). Exacerbating the issue further is homozygous nature of the resistant genotype, which results in rapid, irreversible resistance (Roos et al., 1990).

2.5.2 Genetic resistance to macrocyclic lactones

The mechanism of resistance of GIN to macrocyclic lactones is complex and not fully understood. Because these drugs have multiple targets, it has been suggested that multiple genes are involved (Prichard, 2001; Wolstenholme et al., 2004; Sutherland and Scott, 2010). While patterns of resistance tend to vary both within and among species, common mechanisms of resistance include genes that encode specifically for pharyngeal and non-pharyngeal glutamate-gated chloride channel subunits and P-glycoproteins (Martin et al., 1997; Xu et al., 1998; Sutherland and Scott, 2010). Mixed reports have found resistance to be caused by either a single gene mutation or essential, simultaneous mutations in multiple genes (Gill and Lacey, 1998; Le Jambre et al., 2000). Because only isolated cases have been reported, it has been suggested a lack of wide-spread resistance is due to a necessary acquisition of multiple gene mutations in order to create a high level of resistance (Martin, 1997).

2.5.3 Resistant nematode strains

Resistance to anthelmintic products is often detected by the failure of treatment with an anthelmintic to reduce egg shedding to an appropriate level (Bliss et al., 2008). Detection of reduced efficacy is most commonly measured using fecal egg count reduction tests (FECRT), which compares fecal egg counts before and after treatment with an anthelmintic to measure the reduction in or elimination of fecal egg shedding (Taylor et al., 2002; Coles et al., 2006). While universally used, limitations to this test have been noted. In some species of GIN, there is not a good correlation between fecal egg counts and worm counts and may over- or underestimate actual worm burden (Taylor et al., 2002). Intermittent egg shedding and low egg output by adult nematodes and contribute to this low correlation (Taylor et al., 2002). Also, depending on the drug being studied, timing of fecal collection post-treatment may impact results (Taylor et al.,

2002) A study in goats found that treatment with ivermectin can suppress egg production from days 10-14 and produce a false negative result if fecal samples are collected during this time (Jackson, 1993). Also, FECRT is not reliable if the proportion of resistant worms is less than 25% (Coles et al., 2002). Despite noted limitations of this test (McKenna and Simpson, 1987; Coles et al., 1992; Waller, 1994; Taylor et al., 2002) it can be used for all classes of anthelmintics, is easy to execute, and feasible (Waller, 1994; Coles, 2006). In order to offset shortcomings of this test, guidelines have been recommended in order to standardize procedures universally (Coles et al., 1992). In 1982, the World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P) set efficacy standards and established that treatment efficacies of 90% or greater were very good (Powers et al., 1982). However, a revision of these guidelines in 1995, after the introduction of more highly effective drugs, was raised to 98% or greater (Woods et al., 1995). According to resistance detection guidelines as determined by Coles et al. (1992), resistance is suspected if percentage reduction in egg count (efficacy of a product) is less than 95%.

Using FECRT, several studies have reported anthelmintic resistance in several predominant and economically important strains of helminths. This resistance has been detected in several of the anthelmintic products currently used in cattle production. While the phenomenon is world-wide, it appears to be more widespread in countries in the southern hemisphere (Waller, 1997; Sutherland and Scott, 2010). Testing both macrocyclic lactones and bendimidazoles in the southeastern United States, Gasbarre et al. (2009) found varying degrees of reduced efficacies to moxidectin (82%), doramectin (62%), eprinomectin (42%), ivermectin (57%), and albendazole (69%) with a control group showing 54% reduction in egg counts. In this study, resistant strains were found in both *Haeomonchus contortus* with a smaller portion of resistant population in *Haemonchus placei*. Also, strong resistance was found in *Cooperia punctate* with a smaller degree of resistance in *Cooperia oncophore* and *Cooperia spatulata.* In a national survey in the United States, Bliss et al. (2008) found reduced efficacies in a number of both injectable and pour-on formulations. However, they did note that combination use of products from different classes improved efficacy to an acceptable level.

In a study conducted in the UK, Njue and Prichard (2004) found reduced efficacy of ivermectin (77%) and resistant strains of *Cooperia oncophora.* Studies in Argentina have indicated reduced efficacies to both injectable and oral formulations of macrocyclic lactones and benzimidazoles with resistance in *Haemoncus* spp., *Cooperia* spp. *Trichostrongylus* and *Ostertagia ostertagi* (Fiel et al., 2001; Mejia et al., 2003, and Anziani et al., 2004). Similar reports in New Zealand indicate reduced efficacies of topical macrocyclic lactones with resistance found in *C. oncophora* and *T. longispicularis* (Loveridge et al., 2003).

2.5.4 Management of nematode resistance

While resistance poses a threat to future ability of anthelmintics to be effective, there are management strategies that can be implemented in order to preserve anthelmintic efficacies. Refugia are a subpopulation of parasites that have not been exposed to, and therefore selected by, drug treatment (Van Wyk, 2001; Wolstenholme et al., 2004; McArthur and Reinemeyer, 2014). While refugia is comprised primarily of free-living nematodes, other conditions such as inhibited larvae or worms located in animals not treated can contribute to refugia within a population (Van Wyk, 2001; Wolsteholme et al., 2004; Sutherland and Scott, 2010). The refugia concept does not eliminate the chemical component of parasite control, but, by altering timing of dosing or reducing the number of animals treated, aims to dilute the number of resistant nematodes by maintaining or increasing non-resistant nematode populations (Besier, 2012). The goal is to mitigate production losses due to parasitic diseases while maintaining efficacy of commonly used anthelmintic drugs (Besier, 2012).

Current, effective applications of refugia control programs can be commonly found in small ruminant production. Selective treatment strategies have been shown to successfully control worm burden, increase refugia, and reduce resistant populations in sheep and goat production world-wide without compromising animal efficiency (Hoste et al., 2002; Cringoli et al., 2009 Greer at el., 2009; Besier, 2010). While effective, control strategies based on refugia may require different or more laborious management techniques (Besier, 2012). Identifying animals to treat can be done via production responses or parasite burden based on fecal egg counts (Besier, 2012). Another identifier that can be used in sheep and goats is the FAMACHA system for identifying, specifically, haemonchosis (van Wyk and Bath, 2002). By inspecting the ocular membranes for anemia, animals suffering from homonchosis can be identified and treated individually rather than treating the whole herd (van Wyk and Bath, 2002).

Success of these programs in small ruminants have demonstrated that refugia-based treatment strategies can reduce the amount of treatments, increase refugia, and help preserve efficacy of popular classes of anthelmintic drugs without negatively impacting production parameters including growth, milk, and wool production (Hoste et al., 2002; Cringoli et al., 2009; Greer at el., 2009; Besier, 2010; Besier, 2012). While anthelmintic resistance in cattle is less prevalent than that in small ruminants, implementation of these programs may one day be important to keeping resistance at bay and preserving efficacies of anthelmintics long-term.

Management of resistance is important. Consensus among the literature has concluded that reversion after a high degree of selection resistance is unlikely and thus, a permanent condition (Kwa et al., 1993; Shoop, 1993; Sangster, 1999; Kaplan, 2004; Wolstenholme, 2004; Taylor et al., 2007). This conclusion establishes the need for progressive action for the future of anthelmintic control.

Resistance is more prevalent in sheep and goats than in cattle and is most notably found in the southern hemispheres, specifically, Australia, New Zealand, South Africa, and South America (Taylor et al., 2007; Sutherland and Scott, 2010). A lack of ability for parasites to transfer between sheep and cattle is speculated to be the reason why the severity of resistance is less in cattle. However, it is uncertain as to why resistance in cattle parasites is delayed while resistance in sheep parasites has made sheep production impossible in certain regions of the southern hemisphere (Sutherland and Scott, 2010). Presently, there appears to be no short-term solutions to anthelmintic resistance in currently used chemicals (Kaplan, 2004). While future alternatives include vaccines, new compounds, and non-chemical methods, preserving efficacy of currently effective drugs for as long as possible is important (Kaplan, 2004; Wolstenholme et al., 2004).

2.6 Nutritional interactions

Even with concerns of resistance with current anti-parasitic drugs, anthelmintic treatment is still a highly effective method of mitigating the effects of parasitic infection in livestock. Essentially a ‘nutritional disease’, parasitic infections, if left unchecked, can create severe, long-term consequences in infected animals. Based on altered nutrient requirements created both directly and indirectly by parasitic infections, depression in performance of parasitized animals often ensues. Coop and Kyriazakis (1999) suggested a nutrition partitioning framework within a host animal, in a growing animal, and in a reproducing animal. This framework advises that nutritional allocation during a parasite challenge may not be prioritized favorably to meet production goals as well as mount an immune response. The authors propose that in a nutritionally limited environment, lowly prioritized physiological functions such as growth and reproduction along with immune acquisition and expression may be nutritionally limited, presenting trade-offs between parasitism and nutrition (Coop and Kyriazakis, 1999) thus effecting important production parameters. Other studies in cattle have also indicated a low priority of function for physiological processes, most notably reproductive activities such as estrous cycles and initiation of pregnancy (Short and Adams, 1988). It is reasonable to assume that in environments with impaired nutritional status, as is seen in parasitic infections, these important functions may be the first physiological processes to fail or be hindered in the wake of a parasitic infection. Because the presence of parasites in grazing animals is widespread and their eradication is extremely unlikely, understanding these interactions is of utmost importance and may play a large roll in implementing the best parasite control program in a herd.

2.6.1 Nutritional consequences of parasitic infection

Parasitic infections create nutritional inefficiencies in the hosts that they infect. These inefficiencies are the result of mechanisms that impact nutrient uptake and nutrient utilization within the host. One of the most notable symptoms of parasitized animals is reduced feed intake (Sykes and Coop, 1977; Fox et al., 1989). While the mechanisms for reduced feed intake are not thoroughly understood, changes in metabolic hormones (Gibbs et al., 1973; Fox et al., 1989) disruption of signaling to the central satiety center (Dynes et al., 1990), alterations in rumen pH (Leng, 1981), and decreased rumen motility (Gregory, 1985) have been implicated. Alterations to physiological optimal conditions within the animal ultimately contribute to decreased performance. However, studies in sheep have indicated that these physiological changes, specifically altered rumen pH, can act as a defense mechanism and prevent further establishment of parasites in a situation where an infection is already in progress and an immune response has not been mounted yet (Blanchard, 1985; Coop et al., 1986, 1988; Jackson, 1992,).

Parasitic infections can also impact nutrient absorption and utilization within the host. The most notable nutrient impacted by parasitic infections is protein. Parasitized animals have increased losses of endogenous protein into the gastrointestinal tract through plasma and erythrocytes (Holmes et al., 1968; Bremner, 1969; Holmes, et al., 1986) as well as sloughed epithelial cells and increased mucous secretions (Armour et al., 1966; Coop and Angus, 1975; MacDonald and Ferguson, 1978; Rowe et al., 1982). While lost endogenous protein has the potential to be reabsorbed in the distal end of the small intestine, there may be a reduction in the overall protein absorption (Poppi et al., 1986). Furthermore, lost protein leaving the abomasum from parasitized animals is often in the form of ammonia with increased urea synthesis and is unrecoverable by the animal (Rowe et al., 1982; Rowe, 1988). These studies suggest that parasitic infections result in a reduced availability of protein as well as increase the minimum amino acid requirement (Rowe, 1988).

Other nutritional impacts of parasitic infections include alterations in energy and mineral metabolism. Studies in both sheep and cattle have demonstrated reduced digestion of gross energy in diets in a range of helminth infection (Sykes and Coop, 1977; Randall and Gibbs, 1981; MacRae et al., 1982). However, results from these studies are variable and no correlation has yet been found between protein and energy metabolism during a parasitic infection. While limited literature exists, mineral metabolism, and thus, skeletal growth and mineralization, have also been found to be affected in the presence of gastrointestinal parasites. Most notably, calcium and phosphorus deposition have been found to be greatly reduced when compared to pair-fed counterparts (Sykes and Coop, 1977; Sykes et al., 1977). When evaluating trace mineral metabolism, Bang et al., (1990a) demonstrated a reduction in copper uptake by the liver during a parasitic infection as a result of elevated abomasal pH and a reduction of solubility of supplemented copper. Interestingly, follow-up studies (Bang et al., 1990b) indicated that copper administered in the form of copper oxide wire particles, when administered prior to infection, can reduce the establishment of certain parasite species in treated lambs. It should be noted that amounts of copper administered in this study were above normally recommended values to ensure sustained concentrations of abomasal soluble copper. Supplementation with molybdenum has been studied as well. Suttle et al. (1992a, 1992b) found that supplementation reduced worm burdens by 23% and 78%, respectively. Results from these studies have implicated a role of molybdenum in immune response as well as having a direct impact on parasites. Ferguson et al. (1989) found higher fecal egg counts as well as increased pepsinogen levels in lambs experimentally infected with *T. circumcincta* in the presence of a cobalt deficiency. While it is clear that mineral metabolism can be affected by parasitic infections, more studies are necessary to identify key minerals and supplementation recommendations.

2.7 Production responses following anthelmintic treatment

Numerous studies have shown that large portions of beef and dairy herds are parasitized. Abattoir and fecal egg count studies indicate that approximately 60 – 100% of cattle of various classes including beef cattle, beef calves, and dairy cattle have some level of parasite burden (Barth et al., 1981; Bairden and Armour, 1981; Vercruysse et al., 1986; Cox and Lemiski, 1989; Borgsteede et al., 2000; Drake et al., 2001; Murphy et al., 2006). Even low-level, subclinical infection can result in the depression of a number of production parameters among all classes of cattle. However, anthelmintic treatment has been shown to improve production parameters across all segments of the beef industry including increased weight gains, higher dry matter intake (DMI), improved feed efficiency, increased milk production, improved reproductive performance, improved carcass quality, higher (BCS), and a stronger immune system (Hawkins, 1993; Zajac, 1991; Purvis et al., 1994; Stromberg et al., 1997; Sanchez et al., 2002; Hersom et al., 2011; Clark et al., 2015).

2.7.1 Live performance and growth

2.7.7.1 Cow-calf. Anthelmintics used in cow/calf production have demonstrated positive effects on calf growth, dam weight gain and have been implicated in improving pregnancy rates. Results reporting the effect of anthelmintic treatment on cow weight are variable. Ciordia et al. (1982) reported weight advantages of 28.8 kg for treated cows compared to non-treated controls. Similarly, Stuedemann et al. (1989) reported weight gain advantages for treated cows compared to non-treated controls. However, Ciordia et al. (1984), Bumgarner et al. (1986) and DeRouen et al. (2009) saw no differences or trends in maintenance of treated cows when compared to cows that were not treated. Interestingly, Stromberg et al. (1997) reported lower weight gains for treated cows as well as a greater loss of BCS at time of weaning when compared to non-treated controls over a two-year study. When evaluating the effect of an extended-release anthelmintic, Backes (2016) saw no differences in BW between non-treated cows, cows treated with a short duration oral oxfendazole, and cows treated with extended-release eprinomectin. Meyers (1988) has suggested that increased milk production and/or improved reproductive success following anthelmintic treatment may confound cow weights so that weights may not be a meaningful production parameter when studying parasite control.

While cow results may vary, effect of anthelmintic treatment on calf gain are consistent in all trials with treated calves gaining more weight and having higher ADG than non-treated calves (Ciordia et al., 1982; Ciordia et al., 1987; Stuedemann et al., 1989; Wohlgemuth et al., 1990; Stromberg et al., 1997; Forbes et al., 2002; DeRouen et al., 2009; Hersom et al., 2011). Ciordia et al. (1982) speculate that improved weight gains in calves may be due to either a direct influence of anthelmintic treatment on calf parasites or indirectly through reduced parasitism in cows resulting in increased milk production. Stromberg et al. (1997) and Frechette and Lamothe (1981) both reported increases in milk production, which supports the latter hypothesis.

2.7.1.2 Heifers. Although not always statistically significant, dewormed heifers consistently gained more weight, and gained more quickly, than non-dewormed, control groups (Zajac et al., 1991; Bauck et al., 1992; Boyles et al., 1993; Larson et al., 1995; Mejita et al., 1998; Loyacano et al., 2002; Sanson et al., 2003). Mejita et al (1998) reported that female calves treated with ivermectin continuously from birth grew faster than untreated heifers and that weight differences were consistently significant at all time points past 6 months of age. Larson et al. (1995) noted that treated heifers had improved weight gain through summer grazing and pre-breeding, but not during the breeding season. It was also noted that most weight gained by treated heifers was gained in the first 28 days following anthelmintic treatment and that overall weight gain was correlated with an increase in BCS (Larson et al., 1995). Both Larson et al. (1995) and Mejia et al. (1998) noted significant increases in pelvic area of treated heifers compared to untreated heifers. Pelvic areas were increased by 7.5% in treated heifers (Larson et al., 1995). Pelvic areas were significantly increased by 8% and 11% at week 39 and 15 months of age, respectively, in treated heifers (Mejia et al., 1998).

Zajac et al. (1991) and Sanson et al. (2003) also reported consistently higher weight gains in treated, grazing heifers than un-treated cohorts. Boyles et al. (1993) reported faster drylot gains and more uniform gains during both drylot and pasture phases for treated heifers compared to non-treated heifers. Backes (2016) also reported greater post-weaning gains for heifers treated with either a short duration combination pour-on of moxidectin and oxfendazole or extended-release eprinomectin when compared to non-treated controls.

2.7.1.3 Stocker and feedlot. Benefits of deworming can be seen in both the stocker and feedlot sectors of the beef industry. Studies have indicated deworming not only results in higher body weights and ADG, but also improves carcass qualities along with reducing morbidity and mortality, resulting in economic benefits (Smith et al., 2000; Reinhardt et al., 2006; Clark et al., 2013; Clark et al., 2015).

In studies evaluating the effect of anthelmintic treatment on growth of stocker calves, Williams et al. (1995) saw 31 kg weight advantages for treated calves compared to un-medicated calves. Ballweber et al. (1997) also saw greater ADG for treated calves compared to non-treated calves in 3 out of 4 studies across the United States. Likewise, Skogerboe et al. (2000) saw greater ADG in treated stocker calves than un-medicated cohorts in three trials in three different states. Rickard et al. (1991) also noted advantages in ADG in grazing yearling steers administered ivermectin in a sustained release bolus. DeDonder et al. (2015) also saw greater end weight and greater ADG for stocker calves treated with extended-released eprinomectin compared to short duration doramectin.

Clark et al. (2013) noted greater change in BW and ADG over the stocker period for fall-born heifers treated with an extended release dewormer compared to a short duration dewormer.

However, difference in performance during the stocker phase did not translate into performance difference in the feedlot or difference in carcass quality.

Smith et al. (2000) studied the effect of strategic deworming during the stocker phase and/or subsequent treatment at the start of the feedlot phase. Treatments consisted of: 1) no treatment during either pasture or feedlot phase 2) treatment only during the pasture phase 3) treatment only during the feedlot phase, and 4) treatment at both pasture and feedlot phase. During the pasture phase, treated steers gained approximately 22 kg more than control steers. The study concluded that a two-time treatment, once during the stocker phase and once when entering the feedlot, significantly affected final weight, ADG, DMI, and feed to gain (F:G) conversions, however, a much greater effect on these parameters was seen in calves only treated at the time they entered the feedlot. On a live basis, calves treated only upon entering the feedlot saw the largest ADG, F:G, daily DMI and HCW along with an improved dressing percentage compared to all other treatment groups. Animals treated either once during the stocker phase or at both the stocker phase and feedlot also had improvements in performance. On a carcass adjusted basis, calves treated once upon entering the feedlot and calves treated at both phases had an even greater improvement on daily gain and F:G, which is attributed to improved dressing percentage (Smith et al., 2000). Utley et al. (1974) also noted advantages for heifers treated at the start of the feedlot phase for ADG and feed efficiency compared to un-medicated controls.

While Backes (2016) reported greater post-weaning gains in calves treated with either a short duration oral oxfendazole or extended-release eprinomectin compared to non-treated controls, there were no difference between HCW, 12^{th} rib fat thickness, or marbling. However, control calves had a lower YG and a greater Longissimus muscle area although there were no differences in quality grade between treatments. When comparing similar anthelmintic treatments, Watson (2016) saw no difference in BW or ADG of stocker calves. Vesco et al. (2015) saw a slight advantage in weight for heifers treated with an extended-release treatment compared to a conventional dewormer.

Clark et al. (2015) observed how the level of parasites upon arrival could affect feedlot performance. The study found that, while anthelmintic treatment at the beginning of the feeding phase helped to improve production parameters in all animals, animals with higher initial parasite burdens saw less improvement, having lower BW throughout the feeding phase and requiring more days on feed. This study also noted a trend for lesser 12th-rib backfat thickness, LM area and marbling scores at slaughter. This data suggests that long-term damage from parasite burdens acquired during the grazing phase prior to entering the feedlot can impact feedlot performance and carcass quality.

2.7.2 Health

While seldom reported in literature, parasite burdens can impair immune response in infected animals. Clark et al. (2015) noted that feedlot cattle with a lower parasite burden at the start of the feeding phase were treated for less health issues resulting in reduced cost of health treatments and increased income. Likewise, Smith et al. (2000) reported that steers not dewormed during the stocker phase arrived at the feedlot with a compromised immunocompetency status. While a limited number of feedlot trials have attempted to elucidate the effect of anthelmintic treatment on health parameters, no similar studies have been done in grazing cow/calf or stocker operations where exposure to parasites is heightened.

2.7.3 Reproduction

Anthelmintic treatment of yearling heifers has been shown to reduced age at onset of puberty and improve pregnancy rates (Boyles et al., 1993; Larson et al., 1995; Majia et al., 1998). A hastening of the onset of puberty was reported by Mejia et al. (1998) with treated heifers reaching pubertal status, based on serum progesterone concentrations, by 36 weeks of age, while untreated heifers did not reach puberty until 46 weeks of age. Larson et al. (1995) also observed a higher percentage of treated heifers reaching puberty before untreated heifers. Interestingly, both previously noted studies reported non-significant correlations between weight gain and onset of puberty for treated heifers, indicating that gain does not fully explain the differences in the onset of puberty (Larson et al., 1995; Mejia et al., 1998). However, correlations between weight gain and onset of puberty were significant (Mejia et al., 1998) or higher (Larson et al., 1995) for untreated heifers. Contrarily, Boyles et al. (1993) observed similar onsets of puberty across treated and untreated groups.

Similarly, Purvis and Whittier (1996) conducted a two-year study to determine the effects of treatment with an ionophore, an anthelmintic, or a combination of the two would impact age at puberty when compared to control heifers. Because diets were adjusted regularly to achieve equal weights across all four treatments, there was no correlation between onset of puberty and weight. The authors also found an increase in first-service conception rate, although no differences in overall pregnancy rates were noted. The study determined that animals treated with an ionophore, an anthelmintic, or a combination were 10 kg lighter and 8.8 days younger at puberty than controls. It is noteworthy that the combination of treatments was not different than single treatments of either an ionophore or an anthelmintic suggesting there was no additive effect when the treatments were administered simultaneously.

Larson et al. (1995) observed a 56.4% average pregnancy rate for treated heifers compared to a 25.6% average pregnancy rate for untreated heifers, however higher pregnancy rates were not attributed to treatment, but to a higher number of treated heifers reaching attaining puberty before the end of the breeding season. Boyles et al. (1993) observed no difference across treatments of conception to AI with both groups achieving 65% conception rates. Backes (2016) found heifer cyclicity, estrous detection, natural service, and overall pregnancy rates were greater for heifers treated with either a short duration or extended-release dewormer compared to control heifers.

While few studies have evaluated the effect of anthelmintic treatments on reproduction in mature cows, studies have found anthelmintic treatment improves reproductive performance of treated cows when compared to non-treated controls. Studemann et al. (1989) reported an average pregnancy rate of 97.5% for treated cows while untreated cows had an average pregnancy rate of 75%. While they reported no change in calving interval, calving rates for treated cows were higher with an average calving rate of 90% compared to an average rate of 67.5% for untreated cows (Studemann et al., 1989). Correspondingly, Stromberg et al. (1997) found significant improvement reproductive with an 11.8% and 12.4%, respectively during a two-year period with an average pregnancy rate of 94.2% for treated cows and 82.1% for untreated cows over the two-year trial. Conversely, Backes (2016) found no differences in pregnancy rate between control cows, and cows treated with either a short duration oral oxfendazole or an extended-release eprinomectin.

2.8 Economics of parasitism

It is undisputed that GIN infections in cattle impact economics by decreasing animal performance via a variety of physiological mechanisms (Hawkins, 1993; Morris and Marsh, 1994; Perry and Randolph, 1999; Stromberg and Gasbarre, 2006; Charlier et al., 2012; Charlier et al., 2014). Estimations for economic losses from parasitic infection of livestock in the United States alone are over $3 billion annually (Bagley et al., 1998). However, due to the subclinical nature of many parasitic diseases, identification of economic losses is difficult (Vercruysse and Claerebout, 2001; Charlier et al., 2014) and therefore little data exists.

While decreased production parameters have been clearly demonstrated in response to parasitic infection, growth and production advantages following the use of deworming products have been established in all phases of beef production ranging from pregnancy rates through the feedlot phase (Zajac, 1991; Purvis et al., 1994; Stromberg et al., 1997; Sanchez et al., 2002; Hersom et al., 2011; Clarke et al., 2015). Eradication of parasites and parasitic diseases is unlikely even under the most optimal of conditions (Perry and Randolph, 1999; Le Jambre, 2006) and parasitic infections can have long-term effects on production even after successful removal from their host (Perry and Randolph, 1999; van der Voort et al., 2013). Since the disease cannot be avoided, assessment of the economic impact of parasitic infections should focus on the recoverable portion of production through anthelmintic intervention (Perry and Randolph, 1999; van der Voort et al., 2013).

Lawrence and Ibarburu (2007) assessed the how elimination of current pharmaceutical technologies would impact break-even prices in all segments of the beef industry. The study evaluated the value of certain pharmaceutical technologies and identified deworming as the most important technology available to beef producers. The authors reported that deworming in the cow/calf sector greatly impacted weaning rate, which encompasses pregnancy rate and survival rate of calves, and weaning weight. Elimination of this technology in this sector would result in a $165/pair loss to producers. Likewise, removal of this technology in the stocker segment would result in a $21/head/year loss due to reduced ADG. Exclusion of de-worming technologies in the feedlot would result in a loss of $22/head/year based on reduced feed intake and ADG. Overall, the cost of eliminating deworming technologies in the beef industry is $190 per head annually. This study identified a significant impact of parasite control on production and cost to beef system, making its impact significant over all three segments of beef production.

While cost-benefit analysis may be more appropriate for elucidating the economic impact of parasitic infections, they can be very difficult to determine (Perry and Randolph, 1999 van der Voort et al., 2013). Accounting for highly variable management strategies, treatment techniques, environmental conditions, and cost differences between farms can present challenges to economic analysis of parasitic diseases (Charlier et al., 2014; Charlier et al., 2016).

2.9 Conclusion

According to the National Animal Health Monitoring System (NAHMS), approximately 62% of producers deworm unweaned calves, 75% deworm developing replacement heifers, 59% deworm weaned stocker calves, 87% treat mature cows, and 90% treat all classes of cattle at least occasionally (NAHMS, 2008). From the same survey, 85% of operations indicated that cattle were dewormed on a regular schedule regardless of appearance or any other diagnostic tool. Deworming is a common practice for beef producers around the country and can help mitigate nutritional inefficiencies and decreased performance created by parasitic infections. Performance improvements can clearly be demonstrated on a number of parameters including calf growth, stocker calf growth, replacement heifer development, feedlot performance and carcass characteristics. Thus, the practice of implementing parasite control within a herd, or not implementing parasite control, has economic implications for producers and has the potential to strongly impact break-even prices, most notably in the cow/calf sector. However, relatively few studies have focused on its effect on mature, grazing beef cow herds, which is surprising considering it is the largest group of cattle to receive regular anthelmintic treatment. It is clear from aforementioned impacts of parasites on production parameters in parasitized animals that performance of grazing, reproducing, lactating cattle may be greatly impacted by a parasitic infection. Therefore, understanding how herd health programs, such as deworming strategies, may help improve reproductive performance and performance parameters in beef cow herds is important and can have economic implications for cow/calf producers.

CHAPTER 3.
EFFECTS OF EXTENDED-RELEASE EPRINOMECTIN ON COW/CALF PERFORMANCE AND REPRODUCTIVE SUCCESS IN A FALL-CALVING BEEF HERD

3.1 Abstract

A fall-calving Angus herd was utilized to elucidate the effects of extended-release eprinomectin compared to a conventional deworming product on cow performance and reproductive success as well as performance of progeny. In Exp. 1, 119 fall-calving cows were treated with either a conventional, short duration injectable ivermectin (n=53; **CONV**) or an injectable extended-release eprinomectin (n=66; **EPR**) in August 2015 prior to calving. Cow BW were collected at time of treatment and at pregnancy diagnosis in April of 2016 after a 90-d natural breeding season. Calving data from both 2015 and 2016 calving seasons were collected. Performance and reproductive success of cows following treatment was evaluated. Calving interval between the 2015 and 2016 calving season as well as calving distribution in 2016, the year following initial treatment, were evaluated. Performance results were analyzed using PROC mixed of SAS and reproductive endpoints were analyzed using the GLIMMIX in SAS. Change in BW and average daily gain were greater in EPR cows compared to CONV cows ($P \leq 0.01$). Pregnancy rates tended to be greater for EPR than CONV cows ($P = 0.15$). Calves from dams treated with EPR were younger at weaning, but had greater weaning weights than calves from CONV dams ($P < 0.01$). In Exp. 2, 74 yearling fall replacement heifers were treated with a conventional, short duration injectable ivermectin (n=33; CONV) or an injectable extended-release eprinomectin (n=44; EPR) in August of 2015 and BW were taken. In December, heifers were AI if standing heat was observed followed by a 45-day natural breeding season. Pregnancy diagnosis was conducted and BW were taken in April of 2016. Final BW were collected in August of 2016.

Performance, cyclicity, conception to AI, and overall breeding season pregnancy rates were evaluated. Calving data was collected during the first calving season in the fall of 2016 to evaluate calving distribution. Data were analyzed in an identical manner to Exp. 1. Weights taken 7 months and 12-months post-treatment demonstrated heavier BW ($P < 0.01$; $P = 0.10$), greater overall weight gain ($P \leq 0.01$) and a greater ADG ($P < 0.01$) for heifers treated with EPR. Heifers treated with EPR had greater yearling pregnancy rates to AI ($P = 0.03$) and greater overall pregnancy rates ($P = 0.02$) compared to CONV. Also, a greater proportion of EPR heifers calved in the first 21 days of the subsequent calving season ($P = 0.04$). Results from this study indicate improved performance and greater reproductive success for replacement heifers and mature cows treated with extended-release eprinomectin as well as performance advantages for their subsequent offspring compared to animals treated with ivermectin.

Key words: anthelmintic, cow-calf, dewormer, pregnancy

3.2 Introduction

Parasitic infections in cattle are known to negatively impact cattle performance by depressing a number of production variables including weight gain, milk production, reproductive efficiency, and carcass quality (Hawkins, 1993). It has been demonstrated that anthelmintic treatment which reduces or eliminates gastrointestinal worm burdens can positively influence cattle productivity by improving the aforementioned parameters (Stromberg et al., 1997; Hersom et al., 2011; Clark et al., 2015). Anthelmintic drugs have long been used in commercial cattle production as a means to prevent internal parasitic infection and improve production in all classes of the beef industry. Specifically in cow/calf production, anthelmintic treatment has been shown to improve growth, hasten onset of puberty in developing heifers and improve first breeding season pregnancy rates (Larson et al., 1995; Mejia et al., 1999; Loyacano et al., 2002). Similarly, in mature cows, anthelmintic treatment can improve or help BCS, improve overall breeding season pregnancy rates, and impact progeny performance (Stuedemann et al., 1989; Wohlgemuth et al., 1990; Stromberg et al., 1997; Hersom et al., 2011).

In 2012, Merial, Inc. (Duluth, GA) introduced the extended-release version of their injectable anthelmintic drug, eprinomectin. This product label claims 100 to 150 days of parasite protection with one injection. Research evaluating plasma concentration of eprinomectin over the extended-release period showed effective plasma concentrations up to 150 d post-administration (Solls et al., 2013). Although this anthelmintic has shown to reduce worm burdens and increase weight gains in stocker cattle (Rehbein et al., 2013a, 2013b; Clark et al., 2014) little research has been published regarding the effects of extended-release eprinomectin on reproductive performance in beef cows and heifers compared to a traditional, short duration anthelmintic. Therefore, the goal of this study was to assess performance parameters and reproductive success of fall-calving replacement heifers and mature cows treated with extended-release eprinomectin compared to a conventional, short duration injectable ivermectin. We hypothesized that treatment of cows and replacement heifers with extended-release eprinomectin would improve cow performance and reproductive success in fall-calving herds and positively impact progeny performance compared to a short duration, conventional anthelmintic.

3.3 Materials and Methods

Data were collected under the supervision of trained Merial personnel and all procedures and protocols were in compliance with Merial Institutional Care and Use Committee approvals.

In both experiments, all treatments were administered subcutaneously at 1 ml/50 kg of BW. Needles on the treatment syringes were changed as needed to ensure proper delivery of the product. Observation of cattle following treatment indicated no abscesses at the injection site.

3.3.1 *Experiment 1*

A herd of 119 fall-calving Angus cows were managed in two groups separated by age (first-calf heifers [n = 38]; and ≥ 3 years of age [n = 81]) at a cooperator farm in northwest Missouri. Each age group was managed on a singular, but separate pasture. In August of 2015, before calving season, cows were individually weighed and assigned to either: 1) injectable ivermectin (Vetrimec™; VetOne, Boise, Idaho; n=53 [n = 19 primiparous; n = 34 multiparous cows]; CONV) or 2) injectable extended-release eprinomectin (LongRange™; Merial, Duluth, GA; n = 66 [n = 18 primiparous; n = 47 multiparous]; EPR; Figure 1). Cows were randomly allocated to treatment within age group, thus both treatments were represented in each pasture. Following treatment in August, a 76-day calving season began in early September and continued through late November (Figure 1). Breeding was accomplished using non-synchronized natural service with two herd sires for the first calf heifers and three herd sires for the mature cows. The 90-d breeding season began in late November of 2015. In April of 2016, all cows were weighed and palpated to determine overall breeding season pregnancy rates.

Animals continued to be managed by age on separate pastures and were monitored through the subsequent calving season. Dam BW, performance, overall pregnancy rates, calving interval between 2015 and 2016 calving seasons, as well as performance data from the 2015 calf crop were evaluated. Because animals were randomly assigned to treatment and not stratified by initial BW, treatment effects on performance were primarily evaluated based on change in BW and ADG.

3.3.2 *Experiment 2*

In August of 2015, before to their first breeding season, a herd of 74 fall-calving replacement heifers at a cooperator farm in northwest Missouri were allocated to one of two anthelmintic treatments. Heifers were individually weighed and treated with either an injectable ivermectin (Vetrimec™, VetOne, Boise, Idaho; n=33; CONV) or injectable extended-release eprinomectin (LongRange™, Merial, Duluth, GA; n = 41; EPR) before initiation of their first breeding season (Figure 2).

Following treatment, groups were kept on separate- but like-pastures (one treatment per pasture; 2 total pastures). In December, all yearling heifers were monitored for estrus over a 25-day period and artificially inseminated if a standing heat was observed. Following this period, all heifers were exposed to a bull for a 47-day natural service breeding season with two herd sires turned out with each group. Forty-five days after the bulls were removed, heifers were individually weighed and evaluated for both pregnancy to AI and overall breeding season pregnancy rates.

In August 2016, heifers were individually weighed, and all animals were dewormed with injectable extended-release eprinomectin prior to their first calving season. Body weights, ADG, AI pregnancy rates, overall pregnancy rates, and calving distribution were evaluated.

3.3.3 *Statistical Analysis*

3.3.3.1 ***Experiment 1.*** For all analyses, SAS 9.4 (SAS Institute, Inc., Cary, NC) was utilized with an experimental unit of cow or calf, when appropriate, and a fixed effect of treatment. Cow performance variables also included a fixed effect of age and a covariate of BW at treatment to account for differences in initial weight. The main effects of treatment and age (primiparous or multiparous) were tested as well as the appropriate interaction. The interaction was removed if not significant ($P > 0.10$). Performance data were analyzed using the MIXED procedure of SAS. Pregnancy data, calving interval and calving distribution were analyzed using GLIMMIX of SAS. A first-calf heifer in the EPR group died during the calving season to issues unrelated to treatment and was removed from analysis (final number of experimental units: CONV n=53; EPR n = 65). For calf data calf sex, was utilized as a main effect when analyzing weaning weights.

3.3.3.2 ***Experiment 2.*** For analyses, SAS 9.4 was utilized with an experimental unit of heifer and a fixed effect of treatment. Performance data were analyzed using the MIXED procedure. Pregnancy data, calving interval and calving distribution were analyzed using GLIMMIX in SAS.

For all analysis, significance was declared at $P \leq 0.05$ and tendencies $0.05 < P \leq 0.15$.

3.4 Results and Discussion

3.4.1 *Experiment 1*

Dam performance results and reproductive measurements are reported in Table 1. There was a treatment × age interaction for treatment BW ($P \leq 0.01$; Figure 3). Specifically, multiparous EPR dams were significantly heavier at treatment ($P < 0.001$) than primiparous cows and multiparous CONV dams. Furthermore, multiparous CONV cows were heavier than primiparous cows. This initial weight difference did translate to significant weight differences at time of pregnancy checks where multiparous EPR cows were heavier compared to the other treatment groups, although there was no treatment × age interaction. This is a reflection of study design as animals were randomly allocated to treatment and were not stratified by weight, age, parity, or expected calving date. There was a treatment × age interaction for ADG and change in BW. In multiparous cows, EPR lost less BW and had a higher ADG over the course of the grazing season, whereas no differences in weight loss were observed due to treatment in primiparous females.

Cows treated with EPR tended to have greater overall pregnancy rates ($P = 0.10$; Table 1) than CONV ($P = 0.15$; Table 1), which could result in significant economic impact at the producer level. Although not comparable to the present study, previous literature has shown greater pregnancy rates for cows given anthelmintic treatment than cows not given anthelmintic treatment (Stuedemann et al., 1989; Stromberg et al., 1997). The studies of Studemann et al., (1989) and Stromberg et al (1997) compared non-treated controls to those administered anthelmintic treatment, whereas the current study compares two anthelmintic treatments with different lengths of protection. The extended protection against gastrointestinal parasites claimed by EPR (100 – 150 d; Solls et al., 2013) compared to CONV (14 – 28 d) may have allowed for re-infection of CONV while EPR were not re-infected again over the grazing season. This extended protection appears to have led to differences in performance and may have impacted reproductive success. It is plausible that improved ability of EPR cows to maintain BW during early lactation for an extended period over the course of the grazing season, may have contributed to reproductive success (Short et al., 1990; Hess et al., 2005). It is well known that energy is crucial to beef cow reproduction (Hess et al., 2005). Therefore, maintaining BW and BCS during this nutritionally demanding stage of production, may have maintained or increased energy balance, and may have positively influence reproductive performance (Hess et al., 2005)

Furthermore, cows treated with EPR had a 10 d shorter calving interval than CONV (P = 0.03; Table 1). A shorter calving interval may provide economic benefits through both increased calf weaning weight and increased post-partum recovery before initiation of the breeding season and is negatively correlated with nutritional status of the animal (Bridges and Lemenager, 2007).

Calf performance for the 2015 calf crop are reported in Table 2. Calves from EPR dams were younger at weaning ($P = 0.007$), tended to have a greater actual weaning weight ($P = 0.09$), and thus had greater age-adjusted weaning weights ($P < 0.001$) when compared to calves from CONV dams. As expected, calves from older cows had greater weaning weights ($P < 0.001$; data not shown) when compared to first-calf heifers although there was no treatment × age interaction ($P = 0.84$). Increased performance in pre-weaned calves following anthelmintic administration could be a result of direct action of anthelmintic treatment on the calf parasites (Ciordia et al., 1982). However, calves in this study were not directly dewormed. Based on previous studies, we may infer that by treating dams and reducing parasite load on the pastures, calves were indirectly protected through dam treatment, thus improving calf performance. A corresponding increase in cow milk production following dam anthelmintic treatment could also result in improvements in calf growth (Ciordia et al., 1982). Previous studies have reported increased milk production (Frechette and Lamothe, 1981; Stromberg and Corwin, 1993), providing support to this hypothesis. It is possible that better maintenance of BW for EPR cows may have increased milk production compared to CONV cows and thus calf weaning weights, although milk production was not directly measured in the present study. Furthermore, because cows were treated during the last trimester, an improved nutritional status of the EPR dam during crucial points of fetal development following treatment may have positively impacted both pre- and post-natal development and productivity (Wu et al., 2004).

3.4.2 *Experiment 2*

Performance results for Exp. 2 are reported in Table 3. Initial BW did not differ between groups ($P = 0.98$). However, EPR heifers were heavier at spring pregnancy evaluation ($P < 0.001$) than CONV and tended to weigh more a year after initial treatment ($P = 0.10$) than CONV. Moreover, when compared to CONV, EPR also had a greater overall change in BW and higher ADG ($P < 0.001$) from the time of initial treatment to the time of pregnancy evaluation the following spring. Similarly, Backes (2016) found that EPR treated fall replacement heifers were heavier and grew faster than cohorts treated with a combination of pour-on moxidectin and oral oxfendazole.

During the 25-day AI period where animals were monitored for estrus prior to bull turn-out, there was no difference in the number of CONV or EPR heifers noted cycling ($P = 0.31$; Table 4). However, conception to AI ($P = 0.03$; Table 4) and overall breeding season pregnancy rates ($P = 0.03$) were greater for EPR compared to CONV. These results agree with Backes (2016) who noted no difference in cyclicity at the start of the grazing season between treatment groups, but saw greater conception rates for heifers treated with extended-release eprinomectin compared to heifers treated with combination of pour-on moxidectin and oral oxfendazole. In the year following treatment, EPR heifers in the current study began calving 10 days sooner and had an average Julian calving date that was 12 days earlier ($P = 0.06$) than CONV. Moreover, EPR had a larger percentage of calves born in the first 21 days of the calving season compared to CONV (17% CONV; 44% EPR; $P = 0.04$).

Data from the US Meat Animal Research Center have illustrated that heifers that breed earlier in the breeding season and calve earlier the subsequent year have greater reproductive success in their second breeding season, wean heavier calves, and have greater longevity in the herd (Kill et al., 2012). Although more validation is needed, these data implicate economically-relevant immediate and long-term production advantages for fall-bred heifers treated with extended-release eprinomectin compared to a conventional ivermectin injectable dewormer.

3.5 Implications

It is important to acknowledge that because fecal samples were not collected in this trial, little is known about the level of parasitic infection of these cattle, therefore, caution should be taken when extrapolating these data to larger populations or alternative environments. However, the results of this study indicate that treatment with extended-release eprinomectin may result in performance and reproductive advantages for both replacement heifers and mature cows when compared to a conventional, short duration injectable ivermectin. Dam treatment with extended-release eprinomectin may also have an indirect impact on growth and performance of their offspring.

3.6 Acknowledgements

The authors thank Norman Kanak from Grant City, Missouri for providing the animals used in this study and his contribution to data collection and Merial and Jerry Sorenson, for facilitating the study and providing data for analysis.

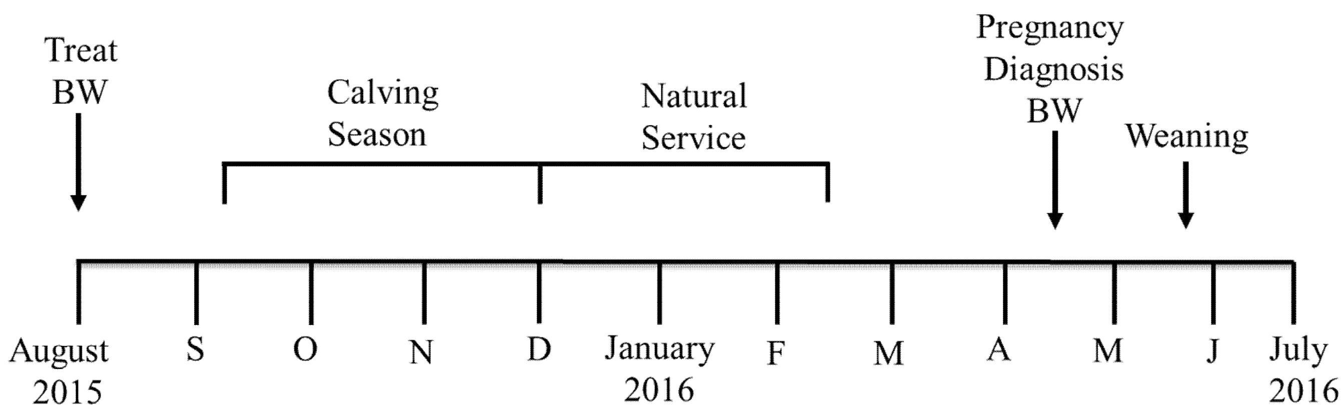

Figure 1: Experimental timeline for Exp. 1.

.
.
.

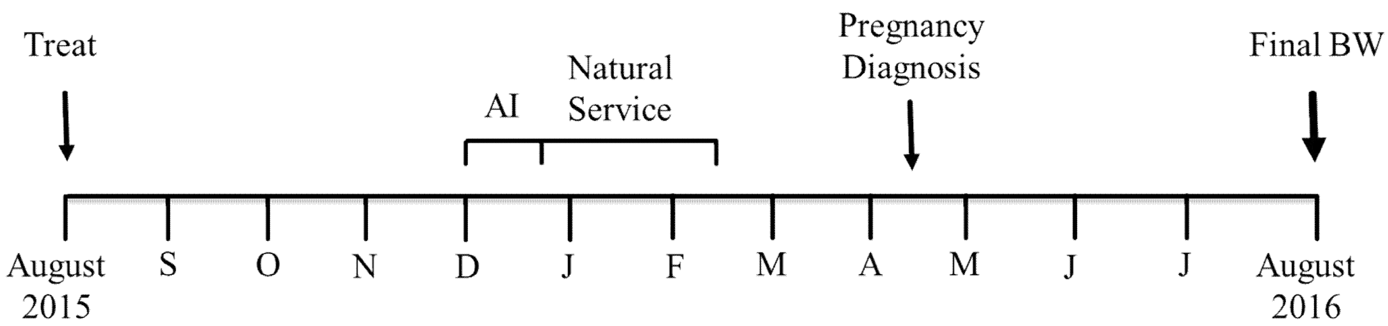

Figure 2: Experimental timeline for Exp. 2.

Table 1: Performance of fall-calving cows treated with different anthelmintic treatments during the grazing season (Exp. 1).

	Treatment							
	CONV[1]		EPR[1]			P-Value[3]		
Item	Primiparous[2]	Multiparous[2]	Primiparous[2]	Multiparous[2]	SEM[4]	Treatment	Age	Treatment × Age
Body weight, kg								
Treatment, August 2015	487	521	481	569	10.8	0.02	<0.01	<0.01
Pregnancy diagnosis, April 2016	432	446	433	483	15.2	0.04	0.04	NS
Body weight change[5]								
Total, kg	-91	-82	-88	-42	9.9	0.01	<0.01	0.02
Percent change, %	-17.7	-15.2	-16.7	-8.0	2.0	0.01	<0.01	0.05
ADG, kg	-0.35	-0.33	-0.34	-0.17	0.04	<0.01	0.01	0.02
Reproduction								
Pregnancy rate[6], % (no./no.)	89.5 (17/19)	88.2 (30/34)	94.4 (17/18)	97.9(46/47)	---	0.15	0.82	NS
Calving interval[7], days	376	365	365	355	5.9	0.03	0.05	NS

[1]Treatment: CONV = ivermectin (Vetrimec 1%; VetOne, Boise, Idaho; n = 53); EPR = extended release eprinomectin (LongRange; Merial, Duluth, GA; n = 65).
[2]Age: primiparous (n = 38); multiparous (n = 81).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Larger SEM presented.
[5]Calculations based on weight changes from August 2015 to April 2016.
[6]Pregnancy rate for 2016; natural service only; only one pregnancy diagnosis.
[7]Calving interval from 2015 calving to 2016 calving.

Table 2: Performance of fall calves whose dams were treated with different anthelmintic treatments during the grazing season (Exp. 1).

	Treatment[1]			
Item	CONV	EPR	SEM[2]	*P*-Value[3]
Weaning weight[4], kg, actual	223	235	5.1	0.09
Weaning weight[5] kg, adjusted	217	238	4.6	<0.001
Age at weaning, days	235	229	1.8	0.007

[1]Treatment: CONV = ivermectin (Vetrimec 1%; VetOne, Boise, Idaho); EPR = extended release eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 53 CONV; n = 66 EPR).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Actual weaning weight.
[5]Adjusted statistically for age difference at weaning.

Table 3: Performance of fall-calving replacement heifers treated with different anthelmintic treatments during their yearling grazing season (Exp. 2).

	Treatment[1]			
Item	CONV	EPR	SEM[2]	P-Value[3]
Body weight, kg				
Treatment, August 2015	274	274	5.0	0.98
Pregnancy diagnosis, April 2016	349	374	5.2	<0.001
Deworming, August 2016	429	442	5.8	0.10
Body weight change[4]				
Total, kg	75	102	5.0	<0.001
Percent change	27.9	38.8	3.13	0.01
ADG, kg	0.30	0.41	0.02	<0.001

[1]Treatment: CONV = ivermectin (Vetrimec 1%; VetOne, Boise, Idaho); EPR = extended release eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 33 CONV; n = 41 EPR).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Calculations based on weight changes from August 2015 to April 2016.

Table 4: Reproductive success of fall-calving replacement heifers treated with different anthelmintic treatments during their yearling grazing season (Exp. 2).

	Treatment[1]			
Item	CONV	EPR	SEM[2]	P-Value[3]
Reproductive Success, % (no./no)				
Cyclicity, % (no./no.)	52 (17/33)	63 (26/41)	---	0.31
Artificial insemination	47 (8/17)	77 (20/26)	---	0.03
Entire breeding season	73 (24/33)	95 (39/41)	---	0.02
Average calving date, Julian	285	273	4.8	0.06
Cumulative calving distribution,[4] %				
21 days	16.7	44.4	---	0.04
42 days	58.3	72.2	---	0.27
63 days	79.2	86.1	---	0.48
84 days	100	100	---	0.99

[1]Treatment: CONV = ivermectin (Vetrimec 1%; VetOne, Boise, Idaho); EPR = extended release eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 33 CONV; n = 41 EPR).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Of heifers that became pregnant in 2015, cumulative proportion of total that calved by the end of each 21-d period during the 2016 calving season.

CHAPTER 4.
EFFECTS OF EXTENDED-RELEASE EPRINOMECTIN ON PRODUCTIVITY MEASURES IN COW/CALF SYSTEMS AND SUBSEQUENT FEEDLOT PERFORMANCE AND CARCASS CHARACTERISTICS OF PROGENY

4.1 Abstract

The objective of this study was to elucidate the effects of a single injection of extended-release eprinomectin on economically relevant production variables in beef cows and calves as well as subsequent feedlot health, performance and carcass traits of calves. Animals from 13 cooperator herds across 7 states were stratified within herd by cow age, calf birth date, calf birth BW, and calf sex and assigned to 1 of 2 treatments; injectable doramectin (DOR; Dectomax™, Zoetis, Animal Health, Parsippany, NJ; n=828) or injectable eprinomection (EPR; Longrange™, Merial, Duluth, GA; n=832) at a rate of 1cc/50 kg. Average duration between treatment and the end of the grazing season was 133 ± 36 d. Fecal samples were randomly collected from 20 cows from five cooperator herds and consisted of both spring- and fall-calving herds. Fecal samples were collected at treatment and again at the end of the grazing season to evaluate fecal egg count (FEC). Continuous and categorical data were analyzed using the MIXED and GLIMMIX procedures of SAS, respectively. Cow treatment BW and end of grazing season BW were not different (P=0.40) between treatments. There was also no difference in change in BW or ADG over the course of the grazing season ($P \geq 0.12$). Initial and final BCS did not differ between treatments (P=0.76). While FEC at treatment did not differ (DOR=2.07; EPR=2.97; P=0.18), cows treated with EPR had a lesser FEC at the end of the treatment period (DOR=1.76; EPR=0.71; P=0.02) and had a greater reduction of FEC over the course of the grazing season (P = 0.01). Calf treatment BW, weaning BW, and ADG did not differ between treatments ($P \geq$ 0.34). There was no difference in incidence of pinkeye for calves (P = 0.43). Incidence of

pinkeye tended to be less ($P = 0.06$) for cows treated with EPR. Fly counts were not different between treatments ($P = 0.14$). Conception to AI, overall breeding season pregnancy rates, and calving interval were not different between treatments ($P \geq 0.45$). Following weaning, a subset of calves from each herd selected at the discretion of the cooperator were shipped to TCSCF feedlot for the finishing phase. Calf BW did not differ at initiation of the feedlot phase ($P = 0.20$). While EPR calves tended to be heavier at re-implantation ($P = 0.07$) final BW as well as overall ADG were not different between treatments ($P \geq 0.13$). Health records indicated lower morbidity for EPR calves ($P = 0.05$) resulting in lower health costs during the feeding phase. Carcass performance including HCW, dressing percent, backfat, KPH, REA, YG, and marbling score were not different between treatment groups ($P \geq 0.12$). Analysis of quality grade indicated higher average quality grade for EPR calves ($P < 0.01$) as well higher percentage of calves that graded average choice or higher ($P = 0.03$). There were no differences in the percentage of steers that graded low choice or lower ($P \geq 0.37$). Economic analysis indicates an opportunity for producers working on a retained ownership platform who treated with EPR to realize a profit above the initial cost of treatment through improved health status during the feeding phase. A lack of performance differences observed in the current study may likely be a function of low initial fecal egg counts in participating herds.

Keywords: anthelmintic, deworm, economics, fecal egg count, feedlot, pregnancy

4.2 Introduction

It has been well documented that gastrointestinal parasites can be detrimental to cattle health and performance. Production parameters impacted by parasitic infection include weight gain, reproductive efficiency, health, feedlot performance, and carcass quality (Hawkins, 1993). Since the 1960's, anthelmintic treatment has been a staple in ruminant production systems to mitigate production losses caused by helminth infection. In cow-calf production, anthelmintic treatment has been shown to improve cow BW and BCS, increase overall breeding season pregnancy rates, and improve calf performance (Stuedemann et al., 1989; Wohlgemuth et al., 1990; Stromberg et al., 1997; Hersom et al., 2011). The effects of anthelmintic treatment during the feeding phase have been shown to improvements in ADG, feed to gain (F:G), daily dry matter intake (DMI), and final BW (Smith et al., 2000). Furthermore, studies have linked calfhood deworming treatment to improved lifetime performance including growth, reproduction, and health (Mejia et al., 1999; Stacey et al., 1999; Clark et al., 2015).

In 2012, Merial, Inc. released the extended-release version of their injectable anthelmintic drug, eprinomectin. This product label claims 100-150 days of parasite protection with one injection. Evaluation of concentration of eprinomectin shows effective plasma concentrations up to 150 days post-administration (Solls et al., 2013). Studies with stocker cattle have proven extended-release eprinomectin effectively reduces worm burdens and improves weight gains in this class of cattle (Rehbein et al., 2013a; Rehben et al., 2013b, Clark et al., 2014). However, to date, little research has been published regarding the effects of extended-release eprinomectin on cow-calf performance. Therefore, the objective of this study was to assess economically relevant performance parameters in cow herds following administration of extended-release eprinomectin at the start of the grazing season and to assess subsequent feedlot performance of progeny. We hypothesized that treatment of cows and calves with extended-release eprinomectin would improve cow performance and reproductive success and positively impact progeny performance compared to a short-duration anthelmintic.

4.3 Materials and Methods

All procedures and protocols were approved by the Iowa State University Institutional Animal Care and Use Committee (3-16-8209-B).

4.3.1 Survey

Because one of the study goals was to follow progeny through the feedlot phase to assess health and performance, Tri-County Steer Carcass Futurity (TCSCF) cooperators were identified as cooperators for this study because of the retained ownership platform (Reinhardt et al., 2009).

In May 2015, a Qualtrics survey (Qualtrics, Provo, UT) was administered by TCSCF and Iowa State University to screen potential cooperator herds. Survey questions were aimed at identifying management styles, record keeping, and herd health protocols. Questions inquired about current parasite control programs including if a parasite control program was in place, what type of wormer was used (i.e. pour-on or injectable), which classes of cattle were commonly dewormed in the operation (i.e. cows, calves or both), and post-weaning parasite management of calves. Other questions identified common production practices such as if and when body weights were typically recorded, if and when body condition scores (BCS) were recorded, when calving season typically began and ended, if calving data were recorded, and if pregnancy checks were conducted.

In order to qualify for participation in the study, producers must have had a parasite control program in place as part of a herd health protocol and be able to provide accurate visual ID records for both cows and calves. Birth records, including birth date, sex, and birth weight, for both the year of initial treatment (2016) and the subsequent calving season (2017) must have been available. Producers must have had the ability to collect timely and accurate measurements including cow and calf BW and cow BCS at time of treatment and at weaning. Necessary reproduction data included pregnancy checks for both spring- and fall-calving herds with fetal aging if possible, AI dates (if applicable) as well as length of bull exposure. Producers that met minimum requirements (Table 1) were then selected for participation in the study. It is important to note that producers participating in this study were not required to have any history of parasitic infection within their herd nor were they required to identify the level of parasitic infection prior to the initiation of the study.

4.3.2 Experimental Design

Twelve cooperator herds located in seven states (Iowa, Missouri, Indiana, Kentucky, Tennessee, Ohio, and Georgia) participated in the study. The total number of animals enrolled in the trial was 1,768 cow-calf pairs and included both spring- and fall-calving herds. Animals were stratified within herd by cow age, calf birth date, calf birth BW, and calf sex and assigned to 1 of 2 treatments; injectable doramectin (DOR; Dectomax™, Zoetis, Animal Health, Parsippany, NJ; n=879) or injectable eprinomection (EPR; LongRange™, Merial, Duluth, GA; n=889) at a rate of 1cc/50 kg. Treatments were administered in the spring of 2016 during pasture turnout (Table 2). Average pasture turn-out date for participating herds was May 16, 2016. On average, treatments were administered on May 9th, 2016 with a treatment range of March 23rd to June 15th.

Individual and overall herd characteristics at time of treatment are presented in Table 2. Overall, at treatment administration, cows averaged 5 ± 3.0 years of age, weighed 568 ± 92 kg with an average BCS of 5.4 ± 0.9, and were 69 ± 33 days post-partum (DPP). One hundred and eight pairs (n = 51 DOR; n = 57 EPR) were removed from the trial due to nontreatment-related issues including mortality, morbidity, or culling during the grazing season.

The study consisted of two different treatment tiers. In tier one, only cows were treated. Following treatment, EPR cows were managed on similar but separate pastures from DOR cows and treatments were not co-mingled at any time between treatment and weaning. Moreover, cows were not grazed in pastures where the opposite treatment had grazed previously during the grazing season. In tier two, EPR cows and DOR cows were co-mingled from the start of the trial. At approximately 90 days of age, per label instructions, calves were treated with the identical product as their dams. The two-tier design implemented in this study allowed for unique evaluation of both parasite burden and performance response. In order to maintain separate parasite burdens relative to treatment, tier one was implemented. This design prevents EPR cows from potentially diminishing parasite loads that DOR may otherwise have been exposed to. However, because reproductive variables were of interest in this study, tier two was implemented in order to evenly apply variables, such as natural service sires, between treatment groups. In addition, tier two allowed for mitigation of forage type and quality variables that often confound results in replicated grazing studies. It is important to note that previous studies have successfully detected performance and parasite load differences between anthelmintic treatments that were comingled in a grazing environment (Clark et al., 2013; Watson, 2016).

4.3.3 Production Measures

4.3.3.1 Performance. Cow body weights (BW) and body condition scores (BCS; 1–9; Wagner et al., 1988) were taken at time of treatment and again at the end of the trial. The end of the trial was determined as time of weaning for spring-calving herds and at that time cows were removed from pasture for fall-calving herds. Calves that were in tier two of the trial were weighed at time of treatment (n=543 DOR; n=543). All calves in the study were weighed at time of weaning (n=807 DOR; n=809 EPR). Birth weights of fall calves (n=79 DOR; 73 EPR) were evaluated as a response variable to anthelmintic treatment. It is well established that nutritional status during gestation plays a crucial role in fetal development and postnatal progeny performance. Undernutrition, such as often seen during a parasitic infection, can be detrimental to development and lifetime performance of an animal by decreasing birth weight, impacting development during gestation, and ultimately altering post-natal metabolism and performance (Funston et al., 2009; Canton and Hess, 2010).

4.3.3.2 Fecal Samples. Fecal samples were taken from a subset of five herds. Approximately 15 cows per treatment at each location were sampled at the start (n=75 DOR; n=69 EPR) and end (n=70 DOR; n=65 EPR) of the trial to measure initial and final fecal egg counts. Samples collected included both spring- and fall-calving herds as well as herds from both experimental tiers. All fecal samples were shipped to Texas A&M Diagnostic Lab for analysis of fecal egg counts (FEC) as well as coproculture if warranted.

4.3.3.3 Health Outcomes. Available herd health records were used to analyze incidence of pinkeye over the course of the grazing season. Health records were submitted from two herds and both indicated treatment records for pinkeye for cows (n=323 DOR; n=325 EPR) and calves (n=312 DOR; n=308 EPR). In July, fly counts were conducted on a subset of five herds to evaluate fly burden. Herds included in the analysis consisted of both experimental tiers as well as both spring- and fall-calving herds. Live fly counts were evaluated in the pastures (n=151 DOR; 150 EPR) in mid-July. Within a pasture, animals were selected at random and fly burdens were estimated from a single side of the animal and included face, shoulders, back, and legs. Flies were counted individually until the number exceeded 25, and then counted in groups of 5 (Steelman et al., 1997). Estimations from a single side were then doubled to obtain a full body estimate of fly burden. At the time of live evaluation, pictures (n=133 DOR; n=134 EPR) were taken of the side used in the live analysis for fly count confirmation.

4.3.3.4 Reproduction End Points. For all herds, overall breeding season pregnancy rates were collected for both spring and fall herds (n=828 DOR; n=832 EPR). Of participating herds, six producers implemented AI protocol. Where applicable, conception rates to AI were analyzed (n=334 DOR; n=327 EPR). Calving distribution for the 2017 calving season was evaluated as well as calving interval between 2016 and 2017 calving for all spring-calving herds (n=610 DOR; n=611 EPR).

4.3.3.5 Feedlot and Carcass Data. After weaning, calves were managed at individual cooperating locations per the standard operating procedure of each farm. A subset of calves from each herd at the discretion of the cooperator were then sent to a TCSCF feedlot for the finishing phase. Calves arrived at the feedlot between October 16 and December 22, 2016 (n=238 DOR; n=259 EPR). While at TCSCF, feedlot performance and health were monitored. Finished cattle were harvested between March 21 and July 6 of 2017. Following slaughter, carcass data were collected. Thus, feedlot performance, morbidity, and carcass parameters were analyzed.

4.3.3.6 Economic Analysis

Extended-release eprinomectin (EPR) is marketed as offering novel performance response and has a label-claim for lengthened protection. However, the cost of this product is in an added out-of-pocket expense to producers compared to conventional parasite control products. Therefore, an economic analysis evaluating production responses to anthelmintic treatment and thus, economic impact on producers, was conducted. The goal of this analysis was to evaluate the initial cost of treatment and the differential performance needed for producers to make-up the increased cost of EPR compared to a conventional parasite control product like DOR.

The economic model used for the cow-calf enterprise analysis was a partial budget (Texas Cooperative Extension, 2002). For this analysis, a treatment herd was standardized to 100 cow-calf pairs. Margin over cost was set at 0% to determine breakeven prices and labor was considered equal between the two treatment groups. A standard weaned calf percentage of 90% was used for both treatments. An average weaning weight of 238 kg, was used for both treatments. In addition to the baseline analysis, alternative scenarios were analyzed by increasing or decreasing calf prices by 20% while holding all other variables constant.

An enterprise budget was used for analysis of the feedlot data (Ag Decision Maker, 2017). Budgets for each treatment group were created using actual records and prices reported by TCSCF.

4.3.4 Statistical Analysis

4.3.4.1 Cow/calf analysis. Performance data and calving interval were analyzed using the MIXED procedure of SAS 9.4. Conception to AI, overall breeding season pregnancy rates, calving distribution, and health outcomes were analyzed using the GLIMMIX procedure of SAS 9.4. Cow, or calf when appropriate, was the experimental unit for the analysis. The model included fixed effects of treatment, calf sex when appropriate, and included the random effect of pasture nested within location to account for variation within and across herds relative to management and weather.

4.3.4.2 Feedlot performance and carcass quality analysis. Feedlot and carcass performance were analyzed using the MIXED procedure of SAS 9.4. Quality grade distribution and morbidity was analyzed using the GLIMMIX procedure of SAS 9.4. Calf was the experimental unit for the analysis. The model included fixed effect of treatment, a covariate of calf sex, and included the random effect of producer to account for variation in management.

Tier and season were tested as main effects for interaction and removed if no interaction was detected. Significance was declared at $P \leq 0.05$ and tendencies $0.05 < P \leq 0.10$.

4.4 RESULTS AND DISCUSSION

The objective of the study was to measure a multitude of standard, economically relevant production variables of beef cows and calves as well as subsequent feedlot health, performance, and carcass traits of those calves from herds that were administered extended-release eprinomectin compared to dectomax 1% injectable at the labeled dose rate.

.

4.4.1 Cow Performance

Cow performance data is presented in Table 3. Initial and final BW did not differ due to treatment ($P \geq 0.32$). In addition, change in BW over the course of the trial was not different and there was no difference in change in BW as a percent of initial BW which correlated into no differences in ADG ($P \geq 0.12$). Subsequently, there were no differences in either initial or final BCS ($P \geq 0.23$) as a result of treatment. While previous literature has found weight differences (Ciordia et al. 1982 and Stuedemann et al. 1989), comparisons have predominately been made between dewormed groups and non-treated controls. However, the present study compares differences between two groups treated with anthelmintics that differ in duration of efficacy. Results from a similar study (Backes et al., 2016) have reached comparable conclusions showing no overall weight difference between groups treated with a conventional short duration oral oxfendazole or extended-release eprinomectin. However, Meyers (1988) has suggested that increased performance in the form of improved milk production or reproductive success following anthelmintic treatment may confound cow weights so that weights may not be a meaningful production parameter when studying parasite control in cow-calf production.

4.4.2 Health Outcomes

Previous studies have indicated some level of fly control associated with treatment with extended-release eprinomectin in grazing environments (Vesco et al., 2015; Trehal et al., 2017). Anecdotal evidence has found reduced fly burdens with lower incidence of pinkeye in grazing cattle that were treated with extended-release eprinomectin. While extended-release eprinomectin is not labeled for fly control, one of the objectives of the current study was to evaluate claims of reduced fly burden and incidence of pinkeye. An evaluation of fly burden in the current study indicated no differences between EPR and DOR treated cows (*P* ≥ 0.62; Table 4). These results are similar to those reported by Watson (2016), where there were no differences in fly counts between control, combination treatment of oxfendazole and moxidectin, or extended-release eprinomectin treated calves comingled during a 100-day stocker period. Interestingly, EPR cows in the current study tended to have a lower incidence of pinkeye as reported by treatment records (*P* = 0.06), however, this reduction is not explained by differences in fly burden. When evaluating incidence of pinkeye in calves, there was no difference in pinkeye treatment between treatment groups (*P* = 0.43).

There has been speculation that the fly control associated with extended-release eprinomectin is correlated with the reduction in pinkeye within treated herds. Fly control following treatment with extended-release eprinomectin is believed to be a result of residue in manure pats that disrupt egg and larval development of fly species who use the manure to procreate, in a manner similar to an insect-growth regulator (IGR). While treatment with extended-release eprinomectin has been shown to reduce horn fly burdens in grazing stocker cattle (Trehal et al., 2017), there is no data on its effectiveness on face flies, the main transmitters of pinkeye within a grazing herd. Furthermore, face flies can travel long distances and spend minimal time on an animal, making control of these pests difficult with products such as IGR (Antonelli and Ramsay, 2014). Therefore, it is hard to identify a causal relationship between fly control and pinkeye with this product. More research is necessary to verify and determine the relationship, if one exists, between these two variables.

4.4.3 Reproduction

Marked improvement in reproductive success of both mature cow herds and developing heifers have been noted following administration of anthelmintic treatment when compared to non-treated controls (Stuedemann et al., 1989; Larson et al., 1995; Stromberg et al., 1997; Loyacano et al., 2002; Andresen et al., 2017). Improved conception rates that have been previously reported have frequently been in conjunction with increases in BW and BCS indicating an improvement in the nutritional status of the animal. Given the low priority of function of reproductive processes such as cyclicity and initiation of pregnancy (Short and Adams, 1988), it is plausible that the improved nutritional status often associated with anthelmintic treatment could improve reproductive function, especially during early lactation when nutritional demands are increased. The extended days of parasite protection claimed by extended-release eprinomectin allows the possibility to improve nutritional status for a longer period before reinfection with GIN during a critical time when a cow is nursing and trying to conceive. When evaluating reproductive success of cow herds in the current study (Table 4), there were no difference in conception to AI (DOR = 47%; EPR = 50%; $P = 0.51$) or overall breeding season pregnancy rates (DOR = 88%; EPR = 88%; $P = 0.45$). Contrarily, Backes (2016) reported dams treated with oral oxfendazole tended to have higher overall conception rates when compared to cows treated with EPR. However, neither the current study nor Backes (2016) reported differences in ADG or BW over the course of the grazing season, indicating nutritional status was not greatly improved between the short duration group and the extended protection groups in these studies. Evaluation of calving distribution in the calving season following treatment indicated no differences in the number of calves born in the first 21 days as a result of treatment ($P = 0.98$). Analysis of subsequent 21-day intervals showed no differences between treatment in the number of calves born in each interval ($P \geq 0.33$). As expected, with no differences in calving distribution, there was also no difference in calving interval between the 2016 and 2017 calving season (DOR = 371 d; EPR = 370 d; $P = 0.72$).

4.4.4 Fecal Egg Counts

Fecal samples were collected from a subset of five cooperator herds at the start and end of the grazing season for evaluation of FEC as well as coproculture if warranted. Of the five herds sampled, two DOR and four EPR groups warranted coprocultures from samples collected at the start of the grazing season. Species identified in DOR groups were predominantly comprised of *Cooperia* (100%, 81% and 76%) and *Haemonchus* (19% and 24%). Similarly, EPR groups consisted primarily of *Cooperia* (100%, 100%, 82% and 55%) followed by *Haemonchus* (18% and 12%). Other species detected in the EPR group were *Oesophagostomum* (12%) and 18% of larvae cultured were too damaged to identify. No coprocultures were warranted for fecal samples taken at the end of the grazing season.

Fecal egg count data is reported in Table 4. Efficacy is most commonly measured using fecal egg reduction tests (FECRT), which compares fecal egg counts before and after treatment with an anthelmintic to measure the reduction in or elimination of fecal egg shedding (Taylor et al., 2002; Coles et al., 2006). While initial FEC were not different between treatment groups in this study ($P = 0.89$), final FEC were lower ($P = 0.02$) in EPR cows compared to DOR cows. Subsequently, EPR cows had a greater overall reduction in FEC compared to DOR cows ($P = 0.01$). However, FEC of both treatments at both treatment and at final performance measurement were far below a threshold that would be indicative of clinical parasitism (Bagley et al., 1998). We believe that a lack of parasitic infection during the grazing season may have resulted in a lack of performance differences in this study. Low FEC may be a reflection of the types of herds that were selected to participate in this study. Because of the stringent requirements to qualify for participation, herds selected were uncommonly well-managed which likely contributed to low overall FEC. In similar studies, consisting of treatments that included positive control groups and comingled treatments, both Pfeifer et al. (1999) and Ward et al. (1991) saw similar FEC during the course of the respective trials and reported no performance differences following anthelmintic treatment. This indicates, in agreeance with previous work, the level of parasitic infection in the current study may not have been high enough to elicit a production response. However, it should be noted that Clark et al. (2013) was able to detect significant differences in performance between commingled ivermectin and extended release eprinomectin treated stocker calved that had FEC of 5.14 and 0.90, respectively.

4.4.5 Calf Performance

Results for calf growth and performance are reported in Table 5. There were no differences in birth BW for calves regardless of tier or calving season ($P = 0.57$). Because fall-calving herds were treated in the spring while cows were pregnant, birth weights of fall calves were analyzed as possible fetal programing response to treatment. However, analysis of birth weights of fall calves indicated no difference between treatments ($P = 0.43$; data not shown). Calf BW at time of treatment for calves in tier two was not different ($P = 0.50$). Likewise, weaning weights were not different between the two treatment groups regardless of tier or calving season ($P = 0.75$), although as expected there was a season effect ($P \leq 0.01$) where fall calves were lighter at weaning than spring calves. Subsequently, ADG between time of treatment and weaning was not different ($P = 0.28$), and overall pre-weaning ADG did not differ due to treatment ($P = 0.57$).

While little comparable literature exists for evaluation of a short duration and extended release anthelmintic, Backes (2016) found increased WW for calves from dams treated with oral oxfendazole compared to calves from dams treated with extended-release eprinomectin. While milk production has been previously implicated in improved performance of pre-weaned calves (Frechette and Lamothe, 1981; Ciordia et al., 1982; Stromberg et al., 1997), a lack of performance differences in cows makes it an unlikely mechanism in the present study. Likewise, low FEC found in cows suggest low worm burdens, possibly a result of well managed pastures, which may have correlated to low levels of parasitic infection in calves. However, pre-weaning anthelmintic treatment may have implications for improved performance later in both stocker and feedlot phases. Stacey et al. (1999) found that pre-weaning treatment with a sustained-release ivermectin bolus improved stocker weight gains compared to calves treated with a conventional ivermectin pour-on. Clark et al. (2015) found that calves entering the feedlot with a higher worm burden had reduced growth, compromised immunocompetency, and altered carcass composition compared to steers with low fecal egg counts even though both groups were treated upon feedlot arrival. Furthermore, Clark et al. (2015) suggest that not only do calves with a lesser parasite burden have improved pre-weaning performance, but that early parasite protection may improve lifetime production.

4.4.6 Feedlot Performance and Carcass Characteristics

Feedlot performance and carcass measurements are presented in Table 6. There was no difference in BW between DOR and EPR calves at initiation of the feeding period ($P = 0.20$). Subsequent BW taken at re-implantation approximately 50 days after initiation of feeding showed a tendency for EPR treated calves to weigh more ($P = 0.07$). While not statistically different ($P = 0.13$), EPR treated calves did finish with a slight weight advantage compared to DOR calves. Although EPR calves finished with slightly heavier weights throughout the feeding period, this did not correlate into differences in ADG ($P \geq 0.31$) between treatments. However, when evaluating health of calves in the feedlot, EPR calves were treated for various health issues fewer times compared to DOR calves ($P = 0.05$) indicating improved health status. While all essential components of the immune system are present at birth, full functionality of immunity is not possibly until 2-4 weeks of age and may continue to develop through puberty (Wilson et al., 1996; Chase et al., 2008). Because DOR calves were protected from parasitic infection for a shorter period of the grazing season, as were their dams, exposure to parasites may have occurred. Because parasites can impair or even inhibit immune response (Gomez-Munoz et al., 2004), an infection during this critical stage of development may have resulted in impaired development of the immune system thus impacting lifetime immunocompetency. Although FEC in this study were low, calves are more susceptible to parasites, and although immediate performance was not impacted, disruption of immune development may have been occurred resulting in higher feedlot morbidity.

Subsequent carcass measurements showed no differences due to treatment including HCW, KPH, or backfat (BF; $P \geq 0.22$). Likewise, REA and YG were similar ($P \geq 0.60$) between treatments. Calves treated with EPR had a higher marbling score as well as higher average quality grade ($P \leq 0.01$). This resulted in difference in quality grade distribution where EPR calves have a greater percentage of carcasses grade average choice or higher compared to DOR (38.4% DOR; 49.7% EPR; $P = 0.03$). However, there were no differences in the number of carcasses that graded low choice or select and lower ($P \geq 0.37$). Gardner et al. (1999) reported that feedlot morbidity results in a reduction in quality grade, with a higher percentage of steers identified as sick grading Standard. Therefore, reduced morbidity and improved quality grade create potential for a greater return on initial anthelmintic treatment. The results of this study are in agreeance with those of Gardner et al. (1999) where DOR calves had a higher incidence of morbidity, resulting in an increased health cost, and had a lower average quality grade as well as fewer calves grading average choice or higher compared to healthier EPR calves.

These results are in line with previous studies. Clark et al., 2013 found that while calves treated with extended-release eprinomectin performed better than calves treated with injectable ivermectin during the stocker phase, this did not translate into improved feedlot performance or carcass characteristics. Likewise, Backes (2016) noted improved growth during the stocker phase, but saw no difference in HCW, marbling score, backfat, KPH, YG, or quality grade distribution between calves treated with extended-release eprinomectin or oral oxfendazole at weaning. Again, low FEC at initiation of the present study may have resulted in a lack of performance throughout all phases of production.

4.5 Economic Impact

4.5.1 Cow/Calf

Performance responses were evaluated for differences in economic value between treatment groups. Variables considered as economically relevant in the cow-calf analysis include cow BW, overall breeding season pregnancy rates, calving interval, calving distribution, and calf weaning BW. As seen by production measurements presented in Tables 1 and 2, little variation exists between treatment groups. Overall breeding season pregnancy rates were not different indicating a lack of evidence for increased return on investment through increased calf crop.

Likewise, calving interval and calving distribution were not different, and there were no differences in calf performance.

A lack of differences in the current study provides little opportunity for EPR cows to recoup the increased cost of treatment during the pre-weaning phase. Therefore, the cow-calf analysis sought to determine increased production, in kilograms of calf weaned, necessary for the respective treatments to be indifferent. Because treating with DOR is considered a conventional practice, the improved performance needed by EPR calves in order to negate the cost difference between treatments was also evaluated.

The partial budget for this analysis is organized into two categories—expenses and income associated with the change. In the present study, this considers a change from DOR to EPR treatment.

4.5.1.1 Expenses. Because expenses such as forage, feed, labor, and reproduction were the same irrespective of treatment, only costs associated with differences in anthelmintic treatment were considered. Based on drug prices at the time of treatment, DOR costs $0.32/cc and EPR costs $1.38/cc. The average amount of medicine administered for cows and calves was 12cc and 3cc, respectively, for both treatments. This resulted in a cost of $5.01 per cow-calf pair treated with DOR and a cost of $21.39 per cow-calf pair treated with EPR. Cost difference between EPR and DOR treatments was $16.38/pair.

4.5.1.2 Income. Income was determined by evaluating pounds of calf weaned at the market price on the average date of weaning for cooperating herds. A market price of $3.40/kg (Iowa auction average for Sept. 2016) was used (USDA-AMS, 2016).

Results from the economic analysis are reported in Table 7. This analysis indicates that EPR cows would need to wean calves with a 4.8 kg weight advantage over DOR calves in order to eliminate the difference in cost between treatments. For producers to recoup the cost of the specific anthelmintic in cow-calf production, DOR and EPR calves would need to add 1.5 kg and 6.3 kg by weaning, respectively. The sensitivity of kilograms of weaned calf required to pay for the cost of anthelmintic treatment at alternative calf prices are reported in Table 7. Results of the sensitivity analysis indicate, as expected, that the added weight necessary for a producer to recoup the cost of anthelmintic treatment was highly variable depending on the market price.

While it may not be efficient to retain open females in a herd, attention to management and marketing of cull cows can impact profitability. Cull cows can represent up to 10-20% of total revenue within the cow-calf enterprise (Peel and Doye, 2008). While marketing is important, management strategies alone can increase cull cow value by 25 to 45% (Peel and Doye, 2008). Increase pounds of animal sold can result in increased revenue at comparable prices. Therefore, the use of a specific anthelmintic could improve cow-calf returns through increased cull cow values. While there were no differences in cow BW at weaning, evaluation of BW differences between open cows in each treatment group were analyzed for opportunities for increased cull cow value. Analysis shows a slight weight advantage for open DOR cows compared to open EPR cows (577 kg DOR; 571 kg EPR; data not shown) (Table 5). This slight weight advantages creates an opportunity for producers to realize a greater return, on average, from cull animals treated with DOR. With an average cull cow price of $1.56/kg from October 2016 (Sioux Fall, SD) (USDA-AMS, 2016), DOR cows had the potential to have an increased return of $9.23/head (Table 7). It is also important to note the reduction in incidence of pinkeye in EPR cows. This also provides an opportunity, through reduced health and labor costs, to increase returns on the initial cost of anthelmintic treatment. Thus, improved performance in the form of added weight for either weaned calves or cull cows and improved herd health have the potential to improve return on investment for pre-weaning anthelmintic treatment for the cow-calf enterprise.

While not evident in the current study, performance increases necessary to offset cost of treatment during the pre-weaning phase may be possible in alternative environments such as those with higher levels of parasitic infections. Data evaluating the use of extended-release eprinomectin compared to a conventional ivermectin injectable in fall-calving beef herds has shown improvements in conception to AI as well as overall breeding season pregnancy rates (Andresen et al., 2017). Therefore, improvements in reproductive efficiency manifested as greater overall season pregnancy rates following anthelmintic treatment may provide opportunities for a greater return on investment.

The same study also found reduced calving interval and a shift in calving distribution in the calving season following initial anthelmintic treatment for cows treated with EPR, as well as increased weaning weights for their calves. Thus, a reduced calving interval and a shift in calving distribution following anthelmintic administration may improve the probability of weaning heavier calves. Data from Funston et al. (2012) shows that steers and heifers born in the first 21-day calving period perform better than cohorts born in later calving periods. Shifting calving distribution may also improve cow pregnancy rates by increasing the post-partum recovery time. This may result in a larger calf crop as well as increased pounds of calf weaned per cow. These data indicate alternative conditions to the ones in the current study have the potential to generate a greater return on investment following treatment with EPR. However, it is important to note that improvements in returns based on improved performance will be highly dependent on the economic conditions at the time calves are marketed.

It is also important to note that estimates from this analysis are likely conservative. The comparison in the current study was made between extended-release eprinomectin and a single treatment of a short duration anthelmintic. Because the goal of this study was not to compare the effectiveness of deworming, no comparison was made using a short duration anthelmintic multiple times throughout the grazing season to create an equal number of protected days as EPR, which would have increased initial treatment costs for DOR. The goal of the current study was to evaluate extended-release eprinomectin compared to conventional dewormers in common production settings where deworming typically occurs once during the grazing season which was also the basis of the economic analysis conducted.

4.5.2 Feedlot

The enterprise budget for this analysis used actual income and expense records for each treatment group and prices reported by TCSCF.

4.5.2.1 Expense. Costs including feed, interest, death loss, and yardage were assumed equal between treatment groups as these costs were accrued regardless of anthelmintic treatment. Because there were no differences in WW, placement cost at time of delivery was the same for each group ($2.60/kg) based off reported market price at time of delivery by TCSCF. Records obtained through TCSCF allowed for individual animal health records including how many times a calf was treated and the cost of health treatments throughout the feeding period. Calves treated with DOR pre-weaning had a greater number of health issues (Table 6) throughout the feedlot phase resulting in higher health costs of $6.00 per animal.

4.5.2.2 Income. Fed cattle prices used were the average price received by producers in this study as reported by TCSCF. Average final BW was used to determine the live value of animals within each treatment group. This price accounted for premiums and discounts that were paid for various quality, yield, and weight characteristics. Although quality grade distribution presented in Table 6 indicates a larger number of carcasses grading average choice or greater for EPR treated calves, premiums for YG, CAB, and prime were consistent between the two treatment groups. This may have been a result of variability in marketing time as market dates for finished cattle ranged from March 21, 2017 to July 18, 2017. While fed cattle price was not different between treatment groups ($2.87/kg), EPR calves did finish the feedlot phase with a slight weight advantage over DOR calves (550 kg DOR; 557 kg EPR) resulting in a slight increase in income on a live weight basis.

Results of the feedlot budget analysis are reported in Table 6. The culminating effect of both healthier and heavier EPR calves resulted in a lower breakeven price ($1.10 DOR vs. $1.08 EPR) and an opportunity for slightly higher profits ($200.11 DOR; $227.22 EPR) per animal.

4.5.3 Retained Ownership

As seen by slightly higher returns for EPR calves in the feedlot, administering EPR pre-weaning may be able to make up the cost difference between the two anthelmintic treatments.

For producers operating on a retained ownership platform, like cooperating herds in this study, opportunities to capitalize on a higher calf-hood deworming investment are much greater.

While a lack of differences in the cow-calf portion of this study indicated little potential for improved returns for cow-calf production alone, improved immunocompetency and higher final BW of EPR calves may allow producers to realize a return on investment of the original treatment given pre-weaning.

While, on average, participating cooperator herds anecdotally noted returns on the added cost of extended-release eprinomectin, variability in market conditions over time will greatly impact economic outcomes for environments outside of the current study. Returns realized by implementing a value-added practice will be highly impacted by differences in cattle prices at key marketing times including weaning, backgrounding, or finishing. While retained ownership may increase price risk due to delayed marketing and potentially added price volatility, cow-calf producers have opportunities to mitigate some production risk through value added practices such as preventative health protocols that reduce performance variability (White et al., 2007).

4.6 Conclusion

To our knowledge, this is one of two studies published to date that evaluates the effect of extended-release eprinomectin on cow-calf production and feedlot performance of progeny compared to a conventional, short duration anthelmintic. The results of this study show no difference in cow performance or reproductive success over the course of the grazing season. Likewise, there were no improvements in calf pre-weaning performance or feedlot performance. While carcass characteristics were largely unchanged due to treatment, there was an improvement in quality grade for EPR treated calves. Improved immunocompetency via extended parasite protection during the preweaning phase may have had long-term impacts on feedlot morbidity resulting in improved quality grade measurements. This was evident by a lower percent of illness during the feeding phase, increased marbling score, a higher average quality grade, and a higher percent of EPR calves grading average choice or higher, presenting a chance to increased returns to producers by have more animals qualify for value-added programs.

It is important to note that FEC counts were very low in this study and may have provided very little opportunity for performance improvement following anthelmintic treatment in both treatment groups. Thus, more research is needed in populations carrying greater parasitic burdens to evaluate the effect of extended-release eprinomectin on cow-calf production.

Table 1: Requirements for cooperator herds to participate.

Cow Response Variables of Interest	Calf Response Variables of Interest
Body weight • Treatment • Off-study	Body weight • Treatment • Weaning
BCS • Treatment • Off-study	
Health outcomes • Pinkeye • Fly burden	Health outcomes • Pinkeye • Fly burden • BRD treatments in feedlot
Fecal egg counts • Initial • Final	Feedlot performance • Feedlot ADG • Health • Carcass characteristics • Carcass value/income
Reproduction end points • Conception to AI • Overall breeding season pregnancy rates • Calving distribution 2017 • Calving Interval between 2016 and 2017	

Table 2: Age, calving date, birth weight, treatment date, days postpartum, BW, and BCS of cows from cooperating herds enrolled in the study.

Herd[1]	n	Mean age, yr (range)	Julian calving date, mean and range	Calf birth weight, mean and range	Dam treatment date[2], mean and range	Days postpartum[3], mean and range	Mean BW, kg (range)	Mean BCS[4], (range)
1	75	5.4	56	36	160	104	576	5.5
		(2 to 13)	(16 to 97)	(25 to 49)	(160 to 161)	(63 to 144)	(431 to 750)	(4.0 to 9.0)
2	51	4.8	58	---	124	69	582	6.0
		(2 to 11)	(23 to 101)		(121 to 128)	(27 to 105)	(452 to 716)	(4.0 to 8.0)
3	40	5.1	90	---	91	0.6	591	6.2
		(3 to 10)	(12 to 201)		(---)	(-110 to 79)	(448 to 740)	(4.0 to 8.0
4	164	4.9	23	33	89	67	541	5.81
		(2 to 13)	(-2 to 57)	(21 to 49)	(81 to 104)	(26 to 93)	(350 to 769)	(4.0 to 8.0)
5	194	4.8	18	---	139	120	621	4.3
		(2 to 12)	(-18 to 109)		(122 to 153)	(44 to 166)	(376 to 858)	(3.0 to 6.0)
6	67	4.2	72	---	128	56	658	4.3
		(2.0 to 11)	(125 to 136)		(125 to 136)	(19 to 91)	(372 to 803)	(3.0 to 6.0)
7	402	5.7	127	37	150	69	522	5.7
		(2 to 14)	(16 to 290)	(18 to 52)	(116 to 166)	(31 to 143)	(306 to 796)	(3.3 to 8.0)
8	129	5.2	142	39	140	60	621	5.4
		(2 to 15)	(19 to 291)	(23 to 56)	(126 to 147)	(14 to 128)	(495 to 782)	(4.0 to 7.3)
9	188	6.2	109	37	131	49	602	5.4
		(2 to 14)	(51 to 268)	(27 to 45)	(130 to 133)	(7 to 79)	(413 to 759)	(4.3 to 7.3)
10	118	4.3	85	34	127	43	566	5.5
		(2 to 16)	(45 to 148)	(20 to 49)	(126 to 132)	(-22 to 87)	(395 to 744)	(4.0 to 7.5)
11	90	3.9	81	33	126	45	537	5.7
		(2 to 10)	(57 to 112)	(21 to 43)	(---)	(14 to 69)	(372 to 779)	(4.0 to 8.0)
12	248	5.8	110	35	---	---	---	---
		(2 to 15)	(79 to 167)	(16 to 51)				
Overall	1,766	5.3	89	36	133	70	568	5.4
		(2 to 16)	(-19 to 291)	(16 to 56)	(81 to 166)	(-110 to 166)	(306 to 858)	(2.0 to 9.0)

[1]Herds were located in seven different states.
[2]Julian date of treatment within a herd.
[3]Days postpartum at anthelmintic administration.
[4]Body condition score on 1 to 9 scale (1 = emaciated and 9 = obese; Wagner et al., 1988)

Table 3: Performance of cows treated with different anthelmintic treatments during the grazing season.

Item	Treatment[1]		SEM	P-Value[3]
	DOR	EPR		
BW, kg				
Treatment	577	578	11.4	0.85
Weaning	587	590	10.8	0.40
Change in[4], kg	9	12	4.7	0.13
Change in[4], %	1.95	2.67	0.81	0.12
Performance				
ADG[4], kg	0.05	0.08	0.04	0.23
BCS				
Treatment	5.57	5.57	0.07	0.99
Weaning	5.58	5.60	0.09	0.59
Change in	0.00	0.02	0.08	0.67

[1]Treatment: DOR = doramectin (Dectomax; Zoetis Animal Health, Parsippany); EPR = eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 828 DOR; n = 832 EPR).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Calculations based on weight changes from treatment to weaning/end of grazing season.

Table 4: Health and reproductive success of cows treated with different anthelmintic treatments during the grazing season.

Item	Treatment[1] DOR	EPR	SEM	P-Value[3]
FEC				
Initial	2.07	2.97	0.49	0.18
Final	1.76	0.71	0.34	0.02
Change in	-0.30	-2.12	0.60	0.01
Health				
Cow Pinkeye, %	8.4	4.6	---	0.06
Calf Pinkeye	19.5	21.1	---	0.43
Live Fly Counts	62	60	11.3	0.62
Picture Fly Counts	50	58	11.8	0.69
Reproduction, % (no./no.)				
Conception to AI	47 (157/334)	50 (164/327)	---	0.51
Pregnancy Rate[4]	88 (729/828)	88 (733/832)	---	0.45
Calving Interval[5], d	371	370	2.1	0.72

[1]Treatment: DOR = doramectin (Dectomax; Zoetis Animal Health, Parsippany); EPR = eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 828 DOR; n = 832 EPR).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Pregnancy rate for 2016.
[5]Calving interval from 2016 to 2017 calving.

Table 5: Performance and health of calves who were treated with different anthelmintic treatments during the grazing season.

	Treatment[1]			
Item	DOR	EPR	SEM	P-Value
BW, kg				
Birth	35	35	0.6	0.57
Treatment	142	141	7.4	0.50
Weaning[4]	231	232	5.5	0.75
Performance, kg				
Treatment ADG[5]	1.02	1.04	0.04	0.34
Weaning ADG[6]	1.05	1.05	0.02	0.66
Health, %				
Pinkeye	18.6	21.1	---	0.43

[1]Treatment: DOR = doramectin (Dectomax; Zoetis Animal Health, Parsippany); EPR = eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 828 DOR; n = 832 EPR).
[3]P-value: Tendency $0.05 < P \leq 0.10$.
[4]Actual weaning weight.
[5]Calculation based on weight change from time of anthelmintic treatment to weaning.
[6]Calculation based on weight change from birth to weaning.

Table 6: Feedlot and carcass characteristics of calves who were treated with different, pre-weaning anthelmintic treatments.

	Treatment[1]			
Item	DOR	EPR	SEM[2]	P-Value[3]
BW, kg				
Initial	367	374	14.5	0.20
Re-Implant	442	453	11.1	0.07
Final	555	560	9.6	0.13
Performance, kg				
ADG	1.62	1.60	0.15	0.33
Health				
Treated, %	22.4	13.6	---	0.05
Carcass Quality				
HCW[5], kg	345	348	5.9	0.22
Dress[6], %	61.7	61.9	0.00	0.24
Backfat, cm.	1.39	1.37	0.07	0.55
KPH[7], %	2.28	2.23	0.08	0.12
Ribeye area[8], cm.^{2}	81.90	82.25	1.14	0.58
Yield grade[9]	2.55	2.58	0.11	0.61
Marbling score[10]	1081	1101	12.6	0.01
Quality grade[11]	12.27	12.56	0.14	<0.01
% QG Distribution[12]				
Avg choice or Higher	40.38	51.43	---	0.03
Low choice	47.31	41.43	---	0.63
Select and lower	12.31	7.14	---	0.37

[1]Treatment: DOR = doramectin (Dectomax; Zoetis Animal Health, Parsippany); EPR = eprinomectin (LongRange; Merial, Duluth, GA).
[2]Larger SEM presented (n = 238 DOR; n = 259 EPR).
[3]*P*-value: Significant $P \leq 0.05$; Tendency $0.05 < P \leq 0.10$.
[4]Hot carcass weight.
[5]Dressing percent.
[6]Kidney, pelvic, heart fat.
[7]Marbling score: small: $1{,}000^0$, modest: $1{,}100^0$, moderate: $1{,}200^0$, etc.
[8]USDA quality grade: 12: Choice$^-$, 13: Choice^0, 14: Choice$^+$, etc.
[9]Percentage of steers in each treatment by quality grade, within treatment total is 100%.

Table 7. Economic analysis and break-even weight for calves and cull cows treated with different anthelmintic treatments during pre-weaning.

	Treatment[1]		
	DOR	EPR	Difference[2]
Herd size[3]	100	100	---
Cost of Treatment	$5.01	$21.39	$16.38
Average WW, kg	238	238	---
Breakeven weight needed[4], kg			
$2.73/kg	1.8	7.9	6.0
$3.40/kg[5]	1.5	6.3	4.8
$4.06/kg	1.2	5.3	4.0
Average cull cow weight, kg.	577	571	6
Cull cow value[6], $/hd	$902.41	$893.78	$9.23

[1]Treatment: DOR = doramectin; EPR = eprinomectin.
[2]Cost difference that must be made up by EPR calves in order to breakeven with a conventional treatment.
[3]Budget utilized from Texas Extension Cooperative (2002).
[4]Added weaning weight necessary above average WW for treatments to breakeven at various market prices.
[5]Weighted average market price of medium to large, frame 1, 227-249 kg fed calves for Iowa auctions on September 2016.
[6]Value calculated based on October 2016 Boning cow 544-907 kg prices reported from Sioux Falls, SD.

Table 8. Economic analysis and break-even prices for feedlot animals treated with different anthelmintic treatments pre-weaning.

	Treatment[1]		
$/steer[2]	DOR	EPR	Difference[2]
Total costs	$1,375.49	$1,369.18	$6.31
Income	$1,576	$1,596	$21
Profit	$200.11	$227.19	$27.08
Breakeven selling price, ($/kg)			
For variable costs	$2.43	$2.38	$0.05
For all costs	$2.49	$2.45	$0.04

[1]Treatment: DOR = doramectin; EPR = eprinomectin
[2]Budget utilized from Iowa State University Extension and Outreach (Ag Decision Maker, B1-21). All market prices were average of actual market values obtained through Tri-County Steer Carcass Futurity (TCSCF) records.

CHAPTER 5.

GENERAL DISCUSSION

Gastrointestinal parasites create nutritional inefficiencies in the host they infect. This is accomplished through reduced feed intake and altered protein metabolism. These inefficiencies can alter nutrient partitioning and impact lower priority functions such as growth and reproduction. These alterations can be especially detrimental in growing, developing, or reproducing animals that may be highly impacted by nutritional deficiencies as well as hard to identify. Anthelmintic treatment has been shown to reduce worm burdens and improve efficiency in parasitized animals, thus improving measurable performance parameters. Deworming has long been utilized in agriculture production settings, but development of new products has been stagnant for the last decade. A recent introduction of a novel anthelmintic drug has given producers new option in parasite protection

While introduction of this novel anthelmintic, extended-release eprinomectin, has provided a unique alternative, it comes with an increased out of pocket cost and a number of unknowns. Conventional anthelmintic treatment has long been proven to improve performance compared to non-treated controls across all sectors of the beef industry. However, extended-exposure to anthelmintic compounds such as extended-release eprinomectin has not been studied. Impacts on performance, particularly reproduction in cows and bulls are of interest as these parameters have not been largely studied, with either an extended-release or short duration anthelmintic. While there has been a great interest in the use of extended-release eprinomectin due to its extended length of protection throughout the grazing season, anecdotal evidence of both fly control and reduced incidence of pinkeye, assumed to have a cause and effect relationship, have caught the attention producers throughout all phases of beef production. The experiments conducted in this thesis were aimed at elucidating the effects of extended-release eprinomectin on economically relevant production parameters in cow/calf production, particularly, reproductive success as well as evaluating anecdotal evidence of added benefits. Additionally, lifetime performance of progeny was assessed.

As reported in Chapter 3, growth and reproductive success were greatly improved in both mature cows and replacement heifers following administration of extended-release eprinomectin compared to a conventional, short duration dewormer. The improvement in overall breeding season pregnancy rates, shortened calving interval, and calving interval coupled with improved maintenance of body condition and weight indicate improved nutritional status of the animals following anthelmintic treatment. Furthermore, weaning BW of their offspring, who were younger than cohorts whose dams were treated with a conventional dewormer, may be indicative of increased milk production.

Results from Chapter 4 indicate little difference in performance between extended-release eprinomectin and conventionally treated cattle. It is interesting to note that health parameters seemed to be the most improved, noted by both a decreased in pinkeye in EPR treated cows and reduced feedlot morbidity in EPR treated calves. While FEC were low throughout the study, subtle improvements in immunocompetence were noted. This is interesting, as nutrient allocation theories have suggested expression of immunity may be prioritized beneath growth and reproduction during a parasitic infection. The fly control properties that have been associated with extended-release eprinomectin have thought to be the cause for reduced incidence of pinkeye. Although this relationship is conceivable, there was no correlation between the two in this study. It is possible that improved immunity following deworming may be correlated to the reduced health issues, as feedlot morbidity was reduced for calves treated with extended-release eprinomectin. Perhaps infections were low enough that performance was not impaired, but high enough to impede immune response. However, improved immunocompetence of EPR animals provides opportunities to increase return on the cost of initial treatment and was most evident for producers who retained ownership through the feedlot phase.

While the results of the studies presented in Chapter 2 and 3 are inconsistent, they demonstrate the variability in performance responses to anthelmintic treatment in different environments. Because of the subclinical nature of most parasitic infections, production responses following anthelmintic treatment can be unpredictable and may depend on several factors including level of infection, management practices, nutrition and overall health of the herd.

While variable, the results presented in this thesis indicate possible production responses following administration of extended-release eprinomectin. Furthermore, opportunities may exist to capitalize on initial treatment through improved performance and retained ownership. However, implementation of extended-release eprinomectin into herd health protocols warrants more research, particularly into environments with varying parasitic infections to the ones noted in these studies.

LITERATURE CITED

Abbott, E.M., J.J. Parkins, and P.H. Holmes. 1988. Influence of dietary protein on the pathophysiology of haemonchosis in lambs given continuous infections. Res. Vet. Sci. 45:41-49.

Ag Decision Maker. 2017. Feedlot Enterprise Budget B1-21. Iowa State University Extension and Outreach.

Amaradasa, B.S, R.A. Lane, and A. Manage. 2010. Vertical migration of Haemonchus contortus infective larvae on Cynodon dactylon and paspalum notatum pastures in response to climate change. Vet. Parasitol. 170:78-87. doi:10.1016/j.vetpar.2010.01.026

Anderson, R. 2000. Nematode Parasites of Vertebrates Their Development and Transmission (2nd ed.). Wallingford: CAB International.

Andresen, C.E., D.L. Loy, T.A. Brick, and P.J. Gunn. 2017. Effects of extended-release eprinomectin on cow/calf performance and reproductive success in a fall-calving beef herd. Prof. Anim. Sci. (Accepted).

Anziani, O.S., V. Suarez, A.A., Guglielmone, O. Warnke, H. Grande, and G.C. Coles. 2004. Resistance to bendimidazole and macrocyclic lactone anthelmintics in cattle nematodes in Argentina. Vet. Parasitol. 122L303-306. doi:10.1016/j.vetpar.2004.05.018

Armour, J. 1980. The epidemiology of helminth disease in farm animals. Vet. Parasitol. 6:7-46. doi:10.1016/0304-4017(80)90037-0

Armour, J. and M. Duncan. 1987. Arrested larval development in cattle nematodes. Parasitol. Today. 3(6):171-176. doi:10.1016/0169-4758(87)90173-6

Armour, J., W.F.H. Jarrett, and F.W. Jennings. 1966. Experimental Ostertagia circumcincta infections in sheep: development and pathogenesis of a single infection. Am. J. of Vet. Res. 27:1267-1278.

Backes, E.A. 2016. Evaluation of long-acting eprinomectin compared to conventional anthelmintics in cow-calf production. Doctoral dissertation. University of Arkansas. 1677.

Bagley, C., M.C. Healey, and D. Hansen. 1998. Internal parasites in cattle. Beef Cattle Handbook. BCH-3305.

Bairden, K. and J. Armour. 1981. A survey of abomasal parasitism in dairy and beef cows in south-west Scotland. The Veterinary record 109(8): 153-155. doi:10.1136/vr.109.8.153

Ballweber, L.R. 2014. Gastrointestinal nematode infections in cattle. pp 1503-1506 in: Large animal internal medicine, 5th edition. B. Smith. ed. Elsevier Mosby, St. Louis, Missouri.

Ballweber, L.R., L.L. Smith, J.A. Stuedemann, T.A. Yazwinski and T.L. Skogerboe. 1997. The effectiveness of a single treatment with doramectin or ivermectin in the control of gastrointestinal nematodes in grazing yearling stocker cattle. Vet. Parasitol. 72:53-68. doi:10.1016/S0304-4017(97)00078-2

Bang K.S., A.S. Familton, and A.R. Sykes. 1990a. Effect of ostertagiasis on copper status in sheep: a study involving use of copper oxide wire particles. Res. Vet. Sci. 49:306-314.

Bang K.S., A.S. Familton, and A.R. Sykes. 1990b. Effect of copper oxide wire particle treatment on establishment of major gastrointestinal nematodes in lambs. Res. Vet. Sci. 49:132-137.

Barth, D., D. Bernhard, and J. Lamina. 1981. The prevalence of gastro-intestinal nematodes in dairy cows. in Epidemiology and Control of Nematodiasis in Cattle. Springer Netherlands. Pp 117-130.

Bauk, S.W., C.A. Piche and K.M. Newcomb. 1992. Effect of antiparasitic treatment in beef replacement heifers. Can. Vet J. 33:394-396.

Beef Cattle Decision Aids. 2002. Economic Analysis of Select Health and Production Management Practices. Texas Cooperative Extension.

Behnke, J.M., J. Hannah, and D.I. Pritchard. 1983. Evidence that adult Nematospiroides dubiusimpair the immune response to a challenge infection. Parasite Immunology, 5:397–408.

Besier, R.B., R.J. Love, J. Lyon, A.J. van Burgel. 2010. A targeted selective treatment approach for effective and sustainable sheep worm management: investigations in Western Australia. Anim. Prod. Sci. 50:1034–1042. doi:10.1071/AN10123

Besier, R.B. 2012. Refugia-based strategies for sustainable worm control: factors affecting the acceptability to sheep and goat owners. Vet. Parasitol. 186:2-9 doi:10.1016/j.vetpar.2011.11.057

Blanchard, J.L. 1985. Interaction of Ostertagia circumcincta and Haemonchus contortus in sheep. Diss. Abstr. Internat. 45:2067.

Bliss, D.H., R.D. Moore, W.G. Kvaskicka. 2008. Parasite resistance in US cattle. AABP Proceedings. 41: 109-114.

Borgsteede, F.H.M., J. Tibben, J.B.W.J. Cornelissen, J. Agneessens, and C.P.H. Gaasenbeek. 2000. Nematodes of adult dairy cattle in the Netherlands. Vet. Parasitol. 89:287-296. doi:10.1016/S0304-4017(00)00219-3

Bowman, D. D. 1999. Helminths. Pp 109-234 in: Georgis parasitologi for veterinarians, 7th edition. W.B Saunders Company, Philadelphia, Pennsylvania.

Bown, M.D., D.P. Poppi, and A.R. Sykes. 1986. The effect of postruminal infusion of protein or energy on the pathology of Trichostrongylus colubriformis infection and body composition in lambs. Proceedings of the New Zealand Society of Animal Production. 46:27-30.

Boyles, S.L., L.J. Johnson, W.D. Slanger, B.J. Kreft, and J.D. Kirsch. 1993. The effect of deworming naturally infected heifers on liveweight gain reproductive performance and fecal egg counts. Can. J. Anim. Sci. 73:287-293. doi:10.4141/cjas93-031

Bremner, K. C. 1969. Pathogenetic factors in experimental bovine oesophagostomosis. III. Demonstration of protein-losing enteropathy with 51Cr-albumin. Exp. Parasitol. 24:364-374.

Bridges, A. and L. Lemenager. 2007. Impact of body condition at calving on reproductive productivity in beef cattle. Dept. Anim. Sci., Purdue University.

Brundson, R.V. 1980. Principles of helminth control. Vet Parasitol. 6:185-215. doi:10.1016/0014-4894(69)90174-X

Bumgarner, S.C., M.A. Brauer, R.M. Corwin, E.A. Thomas, and G.H. Meyers. 1986. Strategic deworming for spring-calving beef cow/calf herds. J. Am. Vet. Med. Assoc. 189:427-431.

Canton, J.S. and B.W. Hess. 2010. Maternal plane of nutrition: Impacts on fetal outcomes and postnatal offspring responses. Pages 104 – 122 in 4th Grazing Livestock Nutrition Conference. B. W. Hess, T. DelCurto, J.G.P. Bowman, and R.C. Waterman eds. West. Sect. Am. Soc. Anim. Sci., Champaign, IL.

Charlier, J., E. Claerebout, E. De Muelenaere, and J. Vercruysse. 2005. Associations between dairy herd management factors and bulk tank milk antibody levels against Ostertagia ostertagi. Vet. Parastiol. 133:91-100. doi:10.1016/j.vetpar.2005.05.030

Charlier, J., F. Vande Velde, M. van der Voort, J. Van Meensel, L. Lauwers, V. Cauberghe, J. Vercruysse, E. Claerebout. 2015. ECONOHEALTH: Placeing helmingh infections of livestock in an economic and social context. Vet. Parasitol. 212:62-67. doi:10.1016/j.vetpar.2005.05.030

Charlier, J., M. van der Voort, F. Kenyon, P. Skuce, and J. Vercruysse. 2014. Chasing helminths and their economic impact on farmed ruminants. Trends in Parasitol. 30(7):361-367. doi:10.1016/j.pt.2014.04.009

Charlier, J., M. van der Voort, H. Hogeveen, and J. Vercruysse. 2012. ParaCalc®—A novel tool to evaluate the economic importance of worm infections on the dairy farm. Vet. Parasitol. 184:204-211. doi:10.1016/j.vetpar.2011.09.008

Charlier, J., V. De Waele, E. Ducheyne, M. van der Voort, F. Vande Velde, and E. Claerebout. 2016. Decision making on helminths in cattle: diagnostics, economics and human behavior. Irish. Vet. J. 69:14-19. doi:10.1186/s13620-016-0073-6

Chase, C.C.L., D.J. Hurley, and D.J. Reber. 2008. Neonatal immune development in the calf and its impact on vaccine response. Vet. Clin. Food. Anim. 24:87-104. doi:10.1016/j.cvfa.2007.11.001

Chaudary, F.R., M. Qayyum, and J.E. Miller. 2008. Development and survival of Haemonchus contortus infective larvae derived from sheep feces under sub-tropical condition in the Potohar region of Pakistan. Trop. Anim. Health. Prod. 40:85-92. doi:10.1007/s11250-007-9037-x

Ciordia, H. and W.E. Bizzell. 1963. The effects of various constant temperatures on the development of the free living-stages of some nematodes parasites in cattle. J. Parasitol. 49(1):60-63. doi:10.2307/3275675

Ciordia, H., G.V. Calvert, and H.C. McCampbell. 1982. Effect of an anthelmintic program with morantel tartrate on the performance of beef cattle. J. Anim. Sci. 54:1111-1114. doi:10.2527/jas1982.5461111x

Ciordia, H., H.C. McCampbell, G.V. Calvert, and R.E. Plue. 1984. Effect of ivermectin on performance of beef cattle on Georgia pastures. Am. J. Vet. Res. 45(11)2455-2457.

Ciordia, H., R.E. Plue, G.V. Calvert, and H.C. McCampbell. 1987. Evaluation of the parasitological and production response of a cow/calf operation to an anthelmintic program with ivermectin. Vet Parasitol. 23:265-271.

Claerebout, E. and J. Vercruysse. 2000. The immune response and the evaluation of acquired immunity against gastrointestinal nematodes in cattle: a review. Parasitol. 120 Suppl:S25-42. doi:10.1016/0304-4017(87)90012-4

Clark, C. A., P.J. Gunn, J. Dedrickson, and J. Sorenson. 2013. Comparison of ivermectin and extended-release eprinomectin deworming treatment on stocker and subsequent feedlot performance and carcass characteristics of fall-born angus heifers. Iowa State Research Farm Progress Reports. Paper 2103.

Clark, C.A., W.D. Busby, and P.J. Gunn. 2015. Effects of internal infection at feedlot arrival on performance and carcass characteristics of beef steers. Prof. Anim. Sci. b31:412-416. doi:10.15232/pas.2014-01381

Coles, G.C., C. Bauer, F.H.M. Borgsteede, S. Geerts, T.R. Klei, M.A. Taylor, and P.J. Waller. 1992. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) methods for the detection of anthelmintic resistance in nematodes of veterinary importance. Vet. Parasitol. 44:35-44. doi:10.1016/0304-4017(92)90141-U

Coles, G.C., F. Jackson, W.E. Pomroy, R.K. Prichard, G. von Samson-Himmelstjerna, A. Silvestre, M.A. Taylor, and J. Vercruysse. 2006. The detection of anthelmintic resistance in nematodes of veterinary importance. Vet. Parasitol. 136:167-185. doi:10.1016/j.vetpar.2005.11.019

Coles. G.C. 2002. Cattle nematodes resistant to anthelmintics: why so few cases? Vet Res. 33:481-489. doi:10.1051/vetres:2002034

Coop, R. L. and K.W. Angus. 1975. The effect of continuous doses of Trichostrongylus colubriformis larvae on the intestinal mucosa of sheep and on liver vitamin A concentration. Parasitol 70:1-9. doi:10.1017/S0031182000048800

Coop, R.L, A.C. Field, R.B. Graham, K.W. Angus, and F. Jackson. 1986. Effect of concurrent infection with Ostertagia circumcincta and Trichostrongylus vitrinus on the performance of lambs. Res. Vet. Sci. 40:241-245. doi:10.1017/S0021859600082113

Coop, R.L., F. Jackson, R.B. Graham, and K.W. Angus. 1988. The influence of two levels of concurrent infection with Ostertagia circumcincta and Trichostrongylus vitrinus on the growth performance of lambs. Res. Vet. Sci.45:275-280.

Coop, R.L., I. Kyriazakis. 1999. Nutrition-parasite interactions. Vet. Parasitol. 84:187-204. doi:10.1016/S0304-4017(99)00070-9

Copeman, D.B., G.W. Hutchinson. 1979. The economic significance of bovine gastrointestinal nematode parasitism in north Queensland. Proceedings of the Second International Symposium on Veterinary Epidemiology and Economics, Australian Government Publishing Service, Canberra, pp. 383–387

Cox, W.R. and D. Lemiski. 1989. Prevelance of gastrointestinal nematodes in dairy heifers in western Canada. Can. Vet. J. 30:666-668.

Craig, T.M. 1979. Seasonal transmission of bovine gastrointestinal nematodes in the Texas Gulf Coast. J. Am. Vet. Med. Assoc. 174(8), 844-847.

Cringoli, G., L. Rinaldia, V. Veneziano, L. Mezzino, J. Vercruysse, F. Jackson. 2009. Evaluation of targeted selective treatments in sheep in Italy: effects on faecal worm egg count and milk production in four case studies. Vet. Parasitol. 164:36–43. doi:10.1016/j.vetpar.2009.04.010

DeDonder, K.D., D.J. Rezac, K. Lechtenberg, S. Parimi and V. Singu. 2015. Comparison of the effects of Longrange™ and Dectomax™ on grazing performance and parasite burden in stocker cattle. Intern. J. Appl. Res. Vet. Med. 13(2):150-157.

DeRoun, S.M., J.E. Miller, L.D. Foil and G.T. Gentry. 2009. Control of horn flies (Haematobia irritansI) and gastrointestinal parasites and its relation with cow-calf performance. Vet. Parasitol. 162:320-326. doi:10.1016/j.vetpar.2009.03.021

Drake, D.J., E.R. Atwill, R. Phillips and E. Johnson. 2001. Internal parasites prevalent in California's beef cattle. Calif. Agricult. 55(2):28-32. doi:10.3733/ca.v055n02p28

Dynes, R.A., A.E.L. Ankersmit, D.P. Poppi, G.K. Barrell, A.R. Sykes. 1990. Studies on the physiological basis of appetite depression in nematode infection in sheep. Proc. NZ Soc. Anim: Prod. 50:249-253.

Entrocasso C.M., J.J Parkins, J. Armour, K. Bairden and P.N. McWilliam. 1986. Production, parasitological and carcass evaluation studies in steers exposed to tri-chostrongyle infection and treated with a morantel bolus or fenbendazole in two consecutive grazing seasons. Res. Vet. Sci. 40:76-85.

Ferguson, E.G.W., G.B.B. Mitchell, and A. MacPherson. 1989. Cobalt deficiency and Oslertagia circumcincta infection in lambs. Vet. Rec. 124:20.

Fiel. C.A., C.A. Saumell, P.E. Steffan, and E.M. Rodriguez. 2001. Resistance to Cooperia to ivermectin treatments in grazing cattle of the Humid Pampa, Argentina. Vet. Parasitol. 97(3): 213-219. doi:10.1016/S0304-4017(01)00407-1

Fitzpatrick, J.L. 2013. Global food security: the impact of veterinary parasites and parasitologists. Vet. Parasitol. 195:233-248. doi:10.1016/j.vetpar.2013.04.005

Forbes, A.B., K.L. Cutler and B.J. Rice. 2002. Sub-clinical parasitism in spring-born, beef suckler calves: epidemiology and impact on growth and performance during the first grazing season. Vet. Parasitol. 104:339-344. doi:10.1016/S0304-4017(01)00640-9

Fox N.J., G. Marion, R.S. Davidson, P.C.L. White, and M.R. Hutchings. 2013. Modelling parasite transmission in a grazing system: the importance of host behavior and immunity. PLoS ONE 8(11):e77996. doi:10.1371/journal.pone.0077996

Fox, M.T. 2016. Gastrointestinal parasites of cattle. in: The Merck veterinary manual, 11th edition. S.E. Aiello and M.A. Moses. ed. Merck & Co., Inc, Kenilworth, NJ.

Fox, M.T., D. Gerreili, S.R. Pitt, D.E. Jacobs, M. Gill, and D.L. Gale. 1989. Ostertagia ostertagi infection in the calf: effects of a trickle challenge on appetite, digestibility, rate of passage of digesta and liveweight gain. Res. Vet. Sci. 47:294-298.

Frechette, J. L., and P. Lamothe. 1981. Milk production effect of a morantel tartrate treatment at calving in dairy cows with subclinical parasitism. Can. Vet. J. 22:252-254.

Freidman, P.A., E.G., Platzer. 1978. Interaction of anthelmintic benzimidazoles and benzimidazole derivatives with bovine brain tubulin. Biochem Biophys Acta 44:605-614. doi:10.1016/0304-4165(78)90334-3

Funston, R.N., D.M. Larson, and K.A. Vonnahme. 2009. Effects of maternal nutrition on conceptus growth and offspring performance: Implications for beef cattle production. J.

Anim. Sci. 88(E. Suppl.):E205-E215. doi:10.2527/jas.2009-2351. doi:10.2527/jas.2009-2351

Gardner, B.A., H.G. Dolezal, L.K. Bryant, F.N. Owens. And R.A. Smith. 1999. Health of finishing steers: Effects on performance, carcass traits, and meat tenderness. J. Anim. Sci. 77:3168-3175 doi:10.2527/1999.77123168x.

Gasbarre, L.C., E.A. Leighton, and T. Sonstegard. 2001. Role of the bovine immune system and genome in resistance to gastrointestinal nematodes. Vet. Parasitol. 98:51-64. doi:10.1016/S0304-4017(01)00423-X

Gasbarre, L.C., L.L. Smith, J.R Lichtenfels, and P.A. Pilitt. 2009. The identification of cattle nematode parasites resistant to multiple classes of anthelmintics in a commercial cattle population in the US. Vet. Parasiol. 166:281-285. doi:10.1016/j.vetpar.2009.08.018

Geary, T. G., Conder, G. A., & Bishop, B. 2004. The changing landscape of antiparasitic drug discovery for veterinary medicine. Trends in Parastiol. 20(10):449-455. doi:10.1016/j.pt.2004.08.003

Geary, T. G., S. M. Sims, E. M. Thomas, L. Vanover, J.P. Davis, C.A. Winterrowd, R.D. Klein, N.F.H Ho, and D.P. Thompson. 1993. Haemonchus contortus: ivermectin-induced paralysis of the pharynx. Exp. Parasitol. 77:88-96. doi:10.1006/expr.1993.1064

Geary, T.G., N.C. Sangster, and D.P. Thompson. 1999. Frontiers in anthelmintic pharmacology. Vet. Parasitol. 84:275-295. doi:10.1016/S0304-4017(99)00042-4

Gibbs, H.C. 1980. Persistence on pasture of the infective larvae of nematodes parasitizing Maine dairy cattle. Am. J. Vet. Res. 41(10):1694-1695

Gibbs, J., R.C. Young, G.P. Smith. 1973. Cholecystokinin decreases food intake in rats. J. Comp. Physiol. Psychol. 84:488-495. doi:10.1002/j.1550-8528.1997.tb00305.x

Gill, J.H. and E. Lacey. 1998. Avermectin resistance to trichostrongyloid nematodes. Int. J. Parastiol. 28:863-877. doi:10.1016/S0020-7519(98)00068-X

Gordon, H.M. 1948. The epidemiology of parasitic diseases, with special reference to studies with nematode parasites of sheep. Aus. Vet. J. 45:17-45. doi:10.1111/j.1751-0813.1948.tb01569.x

Greer, A.W., F. Kenyon, D.J. Bartley, E.B. Jackson, Y. Gordon, A.A. Donnan, D.W. McBean, and F. Jackson. 2009. Development and field evaluation of a decision support model for anthelmintic treatments as part of a targeted selective treatment (TST) regime in lambs. Vet. Parasitol. 164:12–20. doi:10.1016/j.vetpar.2009.04.017

Gregory, P.C. 1985. Parasitic infection and stomach motility: relation to intestinal motility and food intake. Vet. Res. Commun. 1:267-286.

Hawkins, J.A. 1993. Economic benefits of parasite control in cattle. Vet. Parasitol. 46:159-173. doi:10.1016/0304-4017(93)90056-S

Herd, R.P., W.G. Queen, G.A. Majewski. 1992. Sex-related susceptibility of bulls to gastrointestinal parasites. Vet. Parasitol. 44:119-125. doi:10.1016/0304-4017(92)90150-8

Herlich, H. 1980. Ostertagia ostertagi infection and reinfection in cattle of different ages. Am. J. Vet. Res. 41:259-261.

Hersom, M.J., R.O. Meyer, and J.N. Carter. 2011. Influence on weaning weights of nursing beef cattle calves de-wormed 90 days prior to weaning. Livestock Science 136:270-272. doi:10.1016/j.livsci.2010.07.024.

Hess, B.W., S.L. Lake, E.J. Scholljegerdes, T.R. Weston, V. Nayigihugu, J.D.C. Molle, and G.E. Moss. 2005. Nutritional controls of beef cow reproduction. J. Anim. Sci. 83L(E.Suppl.):E90-E106. doi:10.2527/2005.8313_supplE90x

Holmes, P. H. 1986. Pathophysiology of nematode infections. In Proceedings of The Sixth International Congress of Parasitology, Ed. M. J. Howell. Canberra: Australian Academy of Science.

Holmes, P. H., J.D. Dargie, J.M. Maclean, and W. Mulligan. 1968. The anaemia in fascioliasis: experiments with 51Cr-labelled red cells. J. Comp. Pathol. 78:415-420. doi:10.1016/0021-9975(68)90039-X

Hosking, B.C., T.G. Watson, D.M. Leathwick. 1996. Multigeneric resistance to oxfendazole by nematodes in cattle. Vet. Rec. 138:67-68.

Houdijk, J.G.M., F. Jackson, R.L. Coop, and I. Kyriazakis. 2006. Rapid improvement of immunity to Teladorsagia circumcincta is achieved through a reduction in the demand for protein in lactating ewes. Int. J. Parasitol. 36:219-227. doi:10.1016/j.ijpara.2005.09.014

Irsik, M. 2012. Gastrointestinal Parasites of Beef Cattle. University of Florida College of Veterinary Medicine.

Jackson, F. 1993. Anthelmintic resistance—the state of play. Brit. Vet. J. 149:123–138. doi:10.1016/S0007-1935(05)80083-1

Jackson, F., E. Jackson, R.L. Coop, and J. Huntley. 1992. Interactions between Teladorsagia circumcincta and Trichostrongylus vitrinus infections in young lambs. Res. Vet. Sci. 53:363-370.

Kaminsky, R. L. Rufener, J. Bouvier, R. Lizundia, S. Schorderet, and H. Sager. 2013. Worms – A ‘license to kill”. Vet. Parasitol. 195:286-291. doi:10.1016/0034-5288(92)90141-N

Kaplan, R.M. 2004. Drug resistance in nematodes of veterinary importance: a status report. Trends in Parasitol. 20(10):477-481. doi:10.1016/j.pt.2004.08.001

Keymer, A.E. and Hiorns, R.W. 1986. Heligmosomoides polygyrus (Nematoda): the dynamics of primary and repeated infection in outbred mice. Proceedings of the Royal Society of London. 229:47–67. doi:10.1098/rspb.1986.0074

Kill, L.K., E.M. Mousel, R.A. Cushman, and G.A. Perry. 2012. Effect of heifer calving date on longevity and life time productivity. J. Anim. Sci. 95(Suppl. 2):131(Abstr.).

Klass, M.R. 1977. Aging in the nematode Caenorhabditis Elegans: major biological and environmental factors influencing life span. Mech. Ageing. Dev. 6:413-429. doi:10.1016/0047-6374(77)90043-4

Klesius, P.H. 1988. Immunity to Ostertagia ostertagi. Vet. Parasitol. 27:159-167. doi:10.1016/0304-4017(88)90071-4

Kohler, P. 2001. The biochemical basis of anthelmintic action and resistance. Int. J. Parasitol. 31:336-345 doi:10.1016/S0020-7519(01)00131-X

Kohler, P. and R. Bachmann. 1981. Intestinal tubulin as possible target for the chemotherapeutic action of mebendazole in parasitic nematodes. Mol. Biochem. Parasitol. 4:325-336. doi:10.1016/0166-6851(81)90064-5

Krecek, R.C., R. Hartman, H.T. Groeneveld, and A. Thorne. 1995. Microclimate effect on vertical migration of Haemonchus contortus and Haemonchus placei third-stage larvae on irrigated Kikuyu pasture. Onderstepoort J. Vet. Res. 62:117-122.

Kwa, M.S.G., J.G. Veenstra, and M.H. Roos. 1993. Molecular characterization of β-tubulin genes present in benzimidazole-resistant population of Haemonchus contortus. Mol. Biochem. Parasitol. 60:133-144. doi:10.1016/0166-6851(93)90036-W

Lacey, E. 1988. The role of the cytoskeletal protein, tubulin, in the mode of action and mechanism of drug resistance to benzimidazoles. Int. J. Parasitol. 18:885-936. doi:10.1016/0020-7519(88)90175-0

Larson, R.L., L.R. Corah, M.F. Spire, and R.C. Cochran. 1995. Effect of treatment with ivermectin on reproductive performance of yearling beef heifers. Theriogenology. 44:189-197. doi:10.1016/0093-691X(95)00168-8

Lawrence, J.D. and M.A. Ibarburu. 2007. Economic analysis of pharmaceutical technologies in modern beef production. Proceeding of the NCCC-134 Conference on Applied Commodity Price Analysis, Forecasting, and Market Risk Management. Chicago, IL.

Le Jambre, L.F. 2006. Eradication of targeted species of internal parasites. Vet. Parasitol. 139:360-370. doi:10.1016/j.vetpar.2006.04.034

Le Jambre, L.F., J.H. Gill, I.J. Lenane, and P.Baker. 2000. Inheritance of avermectin resistance in Haemonchus contortus. Int. J. Parasitol. 30:105-111. doi:10.1016/S0020-7519(99)00172-1

Leighton, E.A., K.D. Murrell, and L.C. Gasbarre. 1989. Evidence for genetic control of nematode egg-shedding. J. Parsitol. 75(4):498-504.

Leng, R.A. 1981. Nutrition and metabolism of parasitized and non-parasitized ruminants. Some approaches for studying mode of action of parasites. In: Isotopes and Radiation in Parasitology 4. International Atomic Energy Agency, Viennca. pp. 191-206.

Loveridge, B., M. McArthur, P.B. McKenna, and B. Mariadass. 2003. Probably multigeneric resistance to macrocyclic lactone anthelmitics in cattle in New Zealand. N. Z. Vet. J. 51(3):139-141. doi:10.1080/00480169.2003.36353

Loyacano, A.F., J.C. Williams, J. Gurie and A.A. DeRosa. 2002. Effect of gastrointestinal nematode and liver fluke infections on weight gain and reproductive performance of beef heifers. Vet. Parasitol. 107:227-234. doi:10.1016/S0304-4017(02)00130-9

MacDonald, T.T. and A. Ferguson. 1978. Small intestinal epithelial cell kinetics and protozoal infection in mice. J. Gastroenterol. 74:496-500. doi:00165085/78/7403-0496

MacRae, J.C., J.S. Smith, G.A.M. Sharman, W. Corrigall, and R.L. Coop. 1982. Energy metabolism of lambs infected with Trichostrongylus colubriformis. In: A. Ekern and F. Sundstel, Energy Metabolism of Farm Animals, European Association of Animal Production Publication no. 29. Ed. Aas, Norway: The Agricultural University of Norway. pp. 112-115.

Martin, R.J. 1997. Modes of Action of Anthelmintic Drugs. Vet. J. 154:11-34. doi:10.1016/S1090-0233(05)80005-X

McArthur, M.J. and C.R. Reinemeyer. 2014. Herding the U.S. cattle industry toward a paradigm shift in parasite control. Vet. Parasitol. 204:34-43. doi:10.1016/j.vetpar.2013.12.021

McKellar, Q.A., F. Jackson. 2004. Veterinary anthelmintics: old and new. Trends Parastiol. 20:456-461. doi:10.1016/j.pt.2004.08.002

McKenna, B.P. and B.H. Simpson. 1987. The estimation of gastrointestinal stronglyle worm burdens in young sheep flocks: a new approach to the interpretation of faecal egg counts II. evaluation. N. Z. Vet. J. 35(6):98-100.

Mejia, M., A. Gonzalez-Iglasias, G.S. Diaz-Torga, P. Villafane, N. Formia, C. Libertun, D. Becu-Villalobos, and I.M. Lacau- Mengido. 1999. Effects of continuous ivermectin treatment from birth to puberty on growth and reproduction in dairy heifers. J. Anim. Sci. 77:1329-1334. doi:10.2527/1999.7761329x

Mejia, M.E., B.M. Fernandez Igartua, E.E. Schmidt, and J. Cabaret. 2003. Multispecies and multiple anthelmintic resistance on cattle nematodes in a farm in Argentina: the beginning of high resistance? Vet. Res. 34:461-467. doi:10.1051/vetres:2003018

Michel, J.F. 1976. The epidemiology and control of some nematode infections in grazing animals. Adv. Parasitol. 14:355-- 387. doi:10.1016/S0065-308X(08)60517-5

Miller, F.M., H.T. Blair, G.W. Reynolds, D.K. Revell. 1998. The role of cysteine in the increased parasite susceptibility of Romney sheep selected for hogget fleece-weight. Proc. N.Z. Soc. Anim. Prod. 58:150-153.

Morely, F.H.W. and A.D. Donald. 1980. Farm management and systems of helminth control. Vet. Parasitol. 6:105-134. doi:10.1016/0304-4017(80)90040-0

Morris, R.S. and W.E. Marsh. 1994. The relationship between infections, diseases and their economic effects. In: Perry, B.D., Hansen, J.W., (Eds.), Modelling vector borne and other parasitic diseases. Proc. Workshop organized by ILRAD in collaboration with FAO, Nairobi, Kenya, 23–27 November 1992, International Laboratory for Research on Animal Diseases, pp. 199–213.

Murphy, T.M., K.N. Fahy, A. McAuliffe, A.B. Forbes, T.A. Clegg and D.J. O'Brien. 2006. A study of helminth parasites in culled cows from Ireland. Prevent. Vet. Med. 76:1-10. doi:10.1016/j.prevetmed.2006.04.005

Myers, G.H. 1988. Strategies to control internal parasites in cattle and swine. J. Anim. Sci. 66:1555–1564. doi:10.2527/jas1988.6661555x

Niezen, J.H., W.A.G. Charleston, J. Hodgson, C.M. Miller, T.S. Waghorn, and H.A. Robertson. 1998. Effect of plant species on the larvae of gastrointestinal nematodes which parasitize sheep. I. J. Parasitol. 28:791-803. doi:10.1016/S0020-7519(98)00019-8

Njue, A.I, and R.K. Prichard. 2004. Efficacy of ivermectin in calves against a resistant Cooperia oncophora field isolate. Parastiol. Res. 93:419-422.

O'Connor, L.J., S.W. Walkden-Brown, L.P. Kahn. Ecology of the free-living stages of major trichostrongylid parasites of sheep. Vet. Parasitol. 142:1-15. doi:10.1016/j.vetpar.2006.08.035

Peel D.S. and D. Doye. 2008. Cull cow grazing and marketing opportunities. Oklahoma Cooperative Extension Service Fact Sheet. AGEC 613.

Perry, B.D. and T.F. Randolph. 1999. Improving the assessment of the economic impact of parasitic diseases and their control in production animals. Vet. Parasitol. 84:145-168. doi:10.1016/S0304-4017(99)00040-0

Pfeifer, M.L., J.C. Baker, J.T. Seeger, D.A. Blasi, and G.E. Jr. Newdigger. 1999. Evaluation of springtime deworming strategies for beef cow/calf pairs. Kansas Agricultural Experiment Station Research Reports: Vol. 0:Iss. 1.

Poppi, D.P., J.C. Macrae, A. Brewer, and R.L. Coop. 1986. Nitrogen transactions in the digestive tract of lambs exposed to the intestinal parasite Trichostrongylus colubriformis. Brit. J. of Nut. 55:593-602. doi:10.1079/BJN19860064

Powers, K.G., I.B. Woods, J. Eckert, T. Gibson, and H.J. Smith. 1982. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) guidelines for evaluating the efficacy of anthelmintics in ruminants (bovine and ovine). Vet. Parasitol. 10:265-284. doi:10.1016/0304-4017(82)90078-4

Prichard, R.K. 2001. Genetic variability following selection of Haemonchus contortus with anthelmintics. Trends in Parastiol. 17:445-453. doi:10.1016/S1471-4922(01)01983-3

Purvis, H.T. and J.C. Whittier. 1996. Effects of ionophore feeding and anthelmintic administration on age and weight at puberty in spring-born beef heifers. J. Anim. Sci. 74:736-744. doi:10.2527/1996.744736x

Purvis, H.T., J.C. Whittier, S.L. Boyles, L.J. Johnson, H.D. Ritchie, S.R. Rust D.B. Faulkner, R.P. Lemenager, and K.S. Hendrix. 1994. Weight gain and reproductive performance of spring-born beef heifer calves intraruminally administered Oxfedazole. J. Anim Sci. 72:817-823. doi:10.2527/1994.724817x

Randall, R.W. and H.C. Gibbs. 1981. Effect of clinical and sub-clinical gastrointestinal helminthiasis on digestion and energy metabolism in calves. Am. J. of Vet. Res. 42: 173C-1734.

Rehbein, S., D.G. Baggot, E.G. Johnson, B.N. Kunkle, T.A. Yazwinski, S. Yoon, L.G. Cramer and M.D. Soll. 2013a. Nematode burdens of pastured cattle treated once at turnout with eprinomectin extended-release injection. Vet. Parastiol. 192:321-331. doi:10.1016/j.vetpar.2012.11.038

Rehbein, S., D.G. Baggot, G.C. Royer, S. Yoon, L.G. Cramer, M.D. Soll. 2013b. The efficacy of eprinomectin extended-release injection against induced infection of developing (fourth-stage larvae) and adult nematode parasites of cattle. Vet. Parasitol. 192:338-345. doi:10.1016/j.vetpar.2012.11.041

Reinhardt, C. D., J. P. Hutcheson, and W. T. Nichols. 2006. A fenbendazole oral drench in addition to an ivermectin pour-on reduces parasite burden and improves feedlot and carcass performance of finishing heifers compared with endectocides alone. J. Anim. Sci. 84:2243-2250. doi:10.2527/jas.2005-598

Reinhardt, C. D., W. D. Busby, and L. R. Corah. 2009. Relationship of various incoming cattle traits with feedlot performance and carcass traits. J. Anim. Sci. 87(9):3030-3042. doi:10.2527/jas.2008-1293

Rickard, L.G., G.L. Zimmerman, E.P. Hoberg and D.H. Wallace. 1991. Effect of ivermectin delivered from a sustained-release bolus on the productivity of beef cattle in Oregon. Vet. Parasitol. 39:267-277. doi:10.1016/0304-4017(91)90043-U

Roberts, F.H.S., P.J. O'Sullivan, and R.F. Riek. 1952. The epidemiology of parasitic gastro-enteritis of cattle. Aust. J. of Agric. Research. 3(2):197-226. doi:10.1071/AR9520187

Roos, M.H., J.A. Boersema, F.H.M. Borgsteede, J. Cornelissen, M. Taylor, and E.J. Ruitenberg. 1990. Molecular analysis of selection for benzimidazole resistance in the sheep parasite Haemonchus contortus. Mol. Biochem. Parasitol. 43:77-88. doi:10.1016/0166-6851(90)90132-6

Rowe, J.B., E.M. Abbott, J.D. Dargie, and P.H. Holmes. 1982. The effect of haemonchosis and blood loss into the abomasum on nitrogen digestion in sheep. Proceedings of the Nutrition Society 41:74A. doi:10.1079/BJN19880016

Rowe, J.B., J.V. Nolan, G. de Chaneet, E. Teleni, and P.H. Holmes. 1988. The effect of haemonchosis and blood loss into the abomasum on digestion in sheep. Brit. J. of Nut. 59:125-139. doi:10.1079/BJN19880016

Sanchez, J., A. Nødtvedt, I. Dohoo, & L. DesCoteaux. 2002. The effect of eprinomectin treatment at calving on reproduction parameters in adult dairy cows in Canada. Prev. Vet. Med. 56:165-177. doi:10.1016/S0167-5877(02)00118-6

Sangster, N. C., & Gill, J. 1999. Pharmacology of anthelmintic resistance. Parasitol Today 154:141-146. doi:10.1016/S0169-4758(99)01413-1

Sangster, N.C. 1999. Anthelmintic resistance: past, present and future. Int. J. Parasitol. 29:115-124. doi:10.1016/S0020-7519(98)00188-X

Sanson, D.W., A.A. DeRosa, G.R. Oremus and L.D. Foil. 2003. Effect of horn fly and internal parasite control on growth of beef heifers. Vet. Parasitol. 117:291-300. doi:10.1016/j.vetpar.2003.09.005

Saz, H.J., E. Bueding. 1966. Relationship between anthelmintic effects and biochemical and physiological mechanisms. Pharmacol. Rev. 18:871-894.

Schad, G.A. 1977. The role of arrested development in the regulation of nematode populations. In: Regulations of Parasite Populations. Academic Press, New York, San Francisco, London, pp. 111-67.

Shoop, W.L. 1993. Ivermectin resistance. Parsitol. Today. 9(5):154-159. doi:10.1016/0169-4758(93)90136-4

Short, R.E. and D.C. Adams. 1988. Nutritional and hormonal interrelationships in beef cattle reproduction. Can. J. Anim. Sci. 68:29-39. doi:10.4141/cjas88-003

Silva, B.F., M.R.V. Amarante, S.M. Kadri, J.R. Carrijo-Maud, and A.F.T. Amarante. 2008. Vertical migration of Haemonchus contortus third stage larvae on Brachiaria decumbens grass. Vet. Parasitol. 158:85-92. doi:10.1016/j.vetpar.2008.08.009

Skogerboe, T.L., L. Thompson, J.M. Cunningham, A.C. Brake and V.K. Karle. 2000. The effectiveness of a single dose of doramectin pour-on in the control of gastrointestinal nematodes in yearling stocker cattle. Vet. Parasitol. 87:173-181. doi:10.1016/S0304-4017(99)00162-4

Smith, G. and B.T. Grengell. 1985. The population biology of Ostertagia ostertagi. Parasitol. Today. 1(3):76-81. doi:10.1016/0169-4758(85)90047-X

Smith, H.J. and R.M. Archibald. 1968. The effects of age and previous infection on the development of gastrointestinal parasitism in cattle. Can. J. Comp. Med. 32:511-517.

Smith, R. A., K. C. Rogers, S. Huse, M. I. Wray, R. T. Brandt Jr, J. P. Hutcheson, W. T. Nichols, R. F. Taylor, J. R. Rains, and C. T. McCauley. 2000. Pasture deworming and (or) subsequent feedlot deworming with fenbendazole. I. Effects on grazing performance, feedlot performance and carcass traits of yearling steers. Bovine Practitioner 104-114.

Solls, M.D., B.N. Kunkle, G.C. Royer, T.A. Yazwinski, D.G. Baggot, T.A. Wehner, S. Yoon, L.G. Cramer and S. Rehbein. 2013. An eprinomectin extended-release injection formulation providing nematode control in cattle for up to 150 days. Vet. Parasitol. 192:313-320. doi:10.1016/j.vetpar.2012.11.037

Southcott, W.H., G.W. Major, and I.A. Barger. 1976. Seasonal pasture contamination and availability of nematodes for grazing sheep. Aust. J. Agric. Res. 27:277-286. doi:10.1071/AR9760277

Stacey, B.R., K.C. Barnes, and D.L. Lalman. 1999. Performance of calves deowmred with Ivomec SR Bolus® compared with Ivomec Pour-on®. Oklahoma State University Animal Science Research Report. p. 225-257.

Stafford, K. and G.C. Coles. 1999. Nematodes control practices and anthelmintic resistance in ddairy calves in the southwest of England. Vet. Rec. 144:659-661. doi:10.1136/vr.144.24.659

Steelman, C.D., M.A. Brown, E.E. Gbur, and G. Tolley. The effects of hair density of beef cattle on Haematobia irritans horn fly populations. Vet. Med. Entomol. 11:257-264. doi:10.1111/j.1365-2915.1997.tb00404.x

Stromberg, B.E. 1997. Environmental factors influencing transmission. Vet Parasitol. 72:247-264. doi:10.1016/S0304-4017(97)00100-3

Stromberg, B.E. and L.C. Gasbarre. 2006. Gastrointestinal nematode control programs with an emphasis on cattle. Vet. Clin. Food. Anim. 22:543-565. doi:10.1016/j.cvfa.2006.08.003

Stromberg, B.E., and R.M. Corwin. 1993. Epizootiology of Ostertagia ostertagi in cow-calf production systems in the American Midwest. Vet. Parasitol. 46:297-302. doi:10.1016/0304-4017(93)90067-W

Stromberg, B.E., R.J. Vatthauer, J.C. Schlotthauer, G.H. Meyers, D.L. Haggard, V.L. King, and H. Hanke. 1997. Production responses following strategic parasite control in beef cow/calf herd. Vet. Parasitol. 68:315-322. doi:10.1016/S0304-4017(96)01081-3

Stryer, L., J.L. Tymoczko, J.M. Berg. Biochemistry. 2002. 5th edition. ed. W.H. Freeman, New York, New York.

Stuedemann, J.A., H. Ciordia, G.H. Meyers, H.C. McCampbell. 1989. Effect of a single strategically timed dose of fenbendazole in cow and calf performance. Vet. Parasitol. 34:77-86. doi:10.1016/0304-4017(89)90167-2

Sutherland, I., and I., Scott. 2009. Gastrointestinal nematodes of sheep and cattle: biology and control. ed. Wiley-Blackwell, West Sussex, UK.

Sutphin, G.L. and M. Kaeberlein. Dietary restriction by bacterial deprivation increases life span in wild-derived nematodes. Expe. Geront. 43:130-135. doi:10.1016/j.exger.2007.10.019

Suttle N.F., D.P. Knox, F. Jackson, R.L. Coop, and K.W. Angus. 1992b. Effects of dietary molybdenum on nematode and host during *Trichostrongylus vitrinus* infection in lambs. Res. Vet. Sci. 52:224-229. doi:10.1016/0034-5288(92)90014-S

Suttle N.F., D.P. Knox, K.W. Angus, F. Jackson, and R.L. Coop. 1992a. Effects of dietary molybdenum on nematode and host during *Haemonchus contortus* infection in lambs. Res. Vet. Sci. 52:23-235. doi:10.1016/0034-5288(92)90015-T

Svetic, A., Madden, K.B., Zhou, X., Lu, P., Katona, I.M., Finkelman, F.D., Urban Jr., J.F., Gause, W.C., 1993. A primary intestinal helminth infection rapidly induces a gut-associated elevation of Th2-associated cytokinesand IL-3. J. Immunol. 150:3434–3441.

Sykes A.R. 1983. Effects of parasitism on metabolism in the sheep. In: The Sheep Production. Nottingham Easter School of Agricultural Science. Ed. W. Haresign. London: Butterworths. No 35. pp. 317 -334.

Sykes, A.R. and R.L. Coop. 1976. Intake and utilization of food by growing lambs with parasitic damage to the small intestine caused by daily dosing with Trichostrongylus colubriformis larvae. J. Ag. Sci., Cambridge. 86:507-515. doi:10.1017/S0021859600061049

Sykes, A.R., R.L. Coop, and K.W. Angus. 1977. The influence of chronic Ostertagia circumcincta infection on the skeleton of growing sheep. J. Comp. Pathol. 87:521-529. doi:10.1016/0021-9975(77)90058-5

Symons, L.E.A. and W.O. Jones. 1975. Skeletal muscle, liver, and wool protein synthesis by sheep infected by the nematode Trichostrongylus colubriformis. Aust. J. Agric. Res. 26:1063-1072. doi:10.1071/AR9751063

Taylor, M.A., K.R. Hunt, and K.L. Goodyear. 2002. Anthelmintic resistance detection methods. Vet. Parasitol. 103:183-194. doi:10.1016/S0304-4017(01)00604-5

Taylor, M.A., R.L. Coop, R.L. Wall. 2007. Veterinary parasitology. ed. Blackwell Publishing, Oxford, UK.

Trehal, S. S., J.L. Talley, D.K. Sherrill, T. Spore, R.N. Wahl, W.R. Hollenbeck, and D. Blasi. 2017. Horn fly control and growth implants are effective strategies for heifers grazing Flint Hills pasture. Kansas Agricultural Experiment Station Research Reports: Vol. 3:Iss. 1. https://doi.org/10.4148/2378-5977.1337

USDA NAHMS. 2010. 2007-08 Beef Cow-calf Studies, Part IV: Reference of Beef Cow-calf Management Practices in the United States.

Utley, P.R., T.B. Stewart, H. Ciordia and W.C. McCormick. 1974. Effect of anthelmintic treatment on feedlot performance of growing and finishing heifers. J. Anim. Sci. 38(5):984-990. doi:10.2527/jas1974.385984x

van Wyk, J.A. and G.F. Bath. 2002. The FAMACHA system for managing haemonchosis in sheep and goats by clinically identifying individual animals for treatment. Vet. Res. 33:509–529. doi:10.1051/vetres:2002036

van der Voort, M., J. Charlier, L. Lauwers, J. Vercruysse, G. Van Huylenbroeck, and J. Van Meensel. Conceptual framework for analysis farm-specific economic effects of helminth infections in ruminants and control strategies. Prev. Vet. Med. 109:228-235. doi:10.1016/j.prevetmed.2012.10.017

Van Wyk, J.A. 2001. Refugia-overlooked as perhaps the most potent factor concerning the development of anthelmintic resistance. Onderstepoort J. Vet. Res. 68:55-67.

Vercruysse, J. and E. Claerebout. 2001. Treatment vs non-treatment of helminth infections in cattle: defining the threshold. Vet. Parasitol. 98:195-214. doi:10.1016/S0304-4017(01)00431-9

Vercruysse, J., P. Dorny, P. Berghen, and J. Geeraerts. 1986. Abomasal parasites in dairy cows in Belgium. Vet. Parasitol. 22:285-291. doi:10.1016/S0304-4017(00)00232-6

Vermunt, J.J., D.M. West, W.E. Pomroy. 1995. Multiple resistances to ivermectin and oxfendazole in Cooperia species of cattle in New Zealand. Vet. Rec. 137:43-45. doi:10.1136/vr.137.2.43

Vesco, A.C., A.K. Sexten, C.S. Weibert and B.E. Oleen. 2015. Evaluation of the productivity of a single subcutaneous injection of LongRange in stocker calves compared with a positive

(Dectomax) and negative (Saline) control. Kansas Agricultural Experiment Station Research Reports. Vol 1:Iss 1. doi:10.4148/2378-5977.1018

Waller, P. J. 2006. From discovery to development: current industry perspectives for the development of novel methods of helminth control in livestock. Vet. Parasitol. 139(1):1-14. doi:10.1016/j.vetpar.2006.02.036

Waller, P.J. 1994. The development of anthelmintic resistance in ruminant livestock. Acta Trop. 56:233-243. doi:10.1016/0001-706X(94)90065-5

Waller, P.J. 1997. Anthelmintic resistance. Vet. Parastiol. 72:391-412. doi:10.1016/S0304-4017(97)00107-6

Wang, Q., T.A. Meyer, S.T. Boyce, J.J. Wang, X.Y. Sun, G. Tiao, J.E. Fischer, and P.O. Hasselgren. 1998. Endotoxemia in mice stimulates production of complement C3 and serum amyloid in mucosa of small intestine Am. J. Physiol. Regul. Integr. Comp. Physiol. 44:R1584-R1592.

Ward, J.K., D.L. Ferguson, A.M. Parkhurst, J. Berthelsen, and M.J. Nelson. 1991. Internal parasite levels and response to anthelmintic treatment by beef cows and calves. J. Anim. Sci. 69:917-922. doi:10.2527/1991.693917x

Watson, E.A. 2016. Effects of anthelmintic treatments on performance indicators in stocker calves. Honors College Thesis 9.

White, B.J., J.D. Anderson, R.L. Larson, K.C. Olson, and D.U. Thompson. 2007. The cow-calf operation retained ownership decision. Prof. Anim. Sci. 23:18-28. doi:10.1532/S1080-7446(15)30932-3

Williams JC, A.F., Loyacano. 2001. Internal parasites of cattle in Louisiana and other southern states. LSU Research and Extension Research Information Sheet #104, p. 1–20.

Williams, J.C. 1997. Anthelmintic treatment strategies: current status and future. Vet. Parasitol. 72:461-477. doi:10.1016/S0304-4017(97)00111-8

Williams, J.C. and F.R. Bilkovich. 1971. Development and survival of infective larve of the cattle nematode, Ostertagia ostertagi. J. Parastiol. 57(2):327-338. doi:10.2307/3278037

Williams, J.C., A.F. Loyacano, S.D. Broussard and D.F. Coombs. 1995. Effect of treatment with an ivermectin sustained-bolus on productivity of stocker beef calves. Vet. Parasitol. 58:75-82. doi:10.1016/0304-4017(94)00707-J

Wilson, R.A.. A. Zolnai, P. Rudas, and L.V. Frenyo. 1996. T-cell subsets in blood and lymphoid tissues obtained from fetal calves, maturing calves, and adult bovine. Vet. Immunol. Immunopathol. 53:49-60. doi:10.1016/0165-2427(95)05543-6

Wiltbank, J. N. 1970. Research needs in beef cattle reproduction. J. Anim. Sci. 31(4):755-762. doi:10.2527/jas1970.314755x

Wohlgemuth, K., M. Biondini, A. Misek, and L. Anderson. 1990. Deworming beef cows and calves with Fenbendazole: effect on weaning weight of calves. Farm. Res. 48(4):27-30.

Wolstenholme, A.J., I. Fairweather, R. Prichard, G. von Samsom-Himmelstjerna, and N.C. Sangster. 2004. Drug resistance in veterinary helminths. Trends in Parasitol. 20:469-476. doi:10.1016/j.pt.2004.07.010

Wood, I.B., N.K. Amaral, K. Bairden, J.L. Duncan, T. Kassai, J.B. Malone Jr., J.A. Pankavich, R.K. Reinecke, O. Slocombe, S.M. Taylor, and J. Vercruysse. 1995. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) second edition of guidelines for evaluating the efficacy of anthelmintics in ruminants (bovine, ovine, caprine). Vet. Parasitol. 58:181-213. doi:10.1016/0304-4017(95)00806-2

Wu, G., F.W. Bazer, T.A. Cudd, C.J. Meininger, and T.E. Spencer. 2004. Maternal nutrition and fetal development. J. Nutr. 134(9):2169-2172

Xu, M. M. Molento, W. Blackhall, P. Ribeiro, R. Beech, and R. Prichard. 1998. Ivermectin resistance in nematodes may be caused by alteration of P-glycoprotein homolog. Mol. Biochem. Parsiol. 91:327-335. doi:10.1016/S0166-6851(97)00215-6

Yazwinski, T.A. and C.A. Tucker. 2006. A sampling of factors relative to the epidemiology of gastrointestinal nematode parasites of cattle in the United States. Vet. Clin. Food. Anim. 22:501-527. doi:10.1016/j.cvfa.2006.07.005

Yazwinski, T.A., C. Tucker, S. Copeland, T. Yazwinski, and F. Guerino. 1999. Dose confirmation of moxidectin pour-on against natural nematode infections in lactating dairy cows. Vet. Parasitol. 86:223-228. doi:10.1016/S0304-4017(99)00153-3

Yu, F., L.A. Bruce, A.G. Calder, E. Milne, R.L. Coop, F. Jackson, G.W. Horgan, and J.C. Macrae. 2000. Subclinical infection with the nematode Trichostrongylus colubriformis increases gastrointestinal tract leucine metabolism and reduces availability of leucine for other tissues. J. Anim. Sci. 78:380-390. doi:10.2527/2000.782380x

Zajac, A.M. 2006. Gastrointestinal nematodes of small ruminants: life cycle, anthelmintics, and diagnosis. Vet. Clin. Food Animal. 22:529-541. doi:10.1016/j.cvfa.2006.07.006

Zajac, A.M., J.W. Hansen, W.D. Whittier, and D.E. Eversole. 1991. The effect of parasite control on fertility in beef heifers. Vet. Parasitol. 40:281-291. doi:10.1016/0304-4017(91)90108-8