ABSTRACT

GENIAC, VICTORIA MARIE. Effect of Copper Oxide Wire Particles on Parasitism and Growth in Katahdin Lambs Divergently Selected for Fecal Egg Count Estimated Breeding Value (Under the direction of Dr. Andrew Weaver).

Gastrointestinal nematodes (GIN) pose a significant threat to the small ruminant industry in the United States. A history of anthelmintic misuse has enabled the development of anthelmintic resistance (AR) to the detriment of producers. This necessitates research into further mitigation strategies for GIN. Copper oxide wire particles (COWP) have been shown to have negative effects on the adult *Haemonchus contortus* (Bang et al., 1990; Burke and Miller, 2020). Selection for low fecal egg count (FEC) estimated breeding values (EBV) in Katahdin sheep has led to improved resistance to GIN within the breed. The objective here was to evaluate the interaction between COWP and selection for low FEC EBV over two years. Katahdin ram lambs in both years [Year 1(Y1; n = 51) and Year 2 (Y2; n = 39)] were three-way dewormed with fenbendazole, moxidectin and levamisole at weaning and rested for a minimum of three weeks. Lambs were classified by genotype, either high (HFEC) or low (LFEC), and were randomly assigned to the control (Con) or COWP treatment within genotype. For Y1, designated lambs received their 2-gram COWP bolus in Week 0. Lambs in Y2 received 5,000 L3 *H. contortus* orally to ensure GIN exposure and designated lambs received 2-gram COWP at Weeks 4, 8, and 12. Lambs were raised as a single contemporary group on pasture each year. Fecal samples, blood for packed cell volume (PCV), body weights, FAMACHA scores and forage samples were collected every two weeks throughout both years. Additional fecal samples were collected in Weeks 4, 8, and 12 in Y2 for coproculture. The interaction between COWP treatment and selection for genotype had no effect either year. Lambs selected for low FEC EBV had lower FEC, body weights and PCV than their counterparts in Y1, while average daily gain (ADG), and

FAMACHA score were unaffected. Treatment with COWP had no effect on any metric for Y1. Lambs selected for low FEC in Y2 had lower FEC than the high FEC lambs, but no effects on any other parasite or growth metrics. Lambs treated with COWP had lower PCV than the Con lambs. No lambs required deworming in Y1, but 30% of HFEC-Con and 20% of LFEC-COWP lambs required deworming in Y2. Coproculture indicated that only 5% of larvae were *H. contortus* across all treatment groups, which could explain the lack of efficacy of the COWP, even with multiple treatments. Selection for low FEC, regardless of treatment with COWP, can lessen GIN burden and should be combined with other mitigation strategies to control parasite burden in small ruminants.

Effect of Copper Oxide Wire Particles on Parasitism and Growth in Katahdin Lambs Divergently Selected for Fecal Egg Count Estimated Breeding Value

by
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DEDICATION

Dedication of this thesis goes to God, my Mom, Dad, and Peter, the Almy, Slack, and Almy-Pagan families, and to Isaac. You have all supported me and loved me no matter what and for that I can never thank you enough! I love you all!

BIOGRAPHY

Born and raised in Greensboro, NC, Victoria Geniac had little interaction with the agricultural industry. In high school, she was employed by the local pet store where she cultivated her love for animals. Attending NC State University to pursue a bachelor's degree in animal science offered her the opportunity to explore livestock production up close. In October of her sophomore year, she began volunteering at the Small Ruminant Educational Unit and quickly discovered a passion for small ruminants. The volunteer position became an employed position, which led to a job at a goat dairy in Washington State upon graduation. After a year learning about dairy goats and working with the meat sheep flock, she returned home to North Carolina to pursue her master's in animal science under the direction of Dr. Andrew Weaver. After the completion of her degree, Victoria plans to teach agriculture in a high school to share her passion for livestock with the new generation of animal scientists.

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TABLE OF CONTENTS

Chapter II: Effect of Copper Oxide Wire Particles and Selection for Fecal Egg Count Estimated Breeding Value in Katahdin Ram Lambs

LIST OF TABLES

LIST OF FIGURES

CHAPTER I: LITERATURE REVIEW

Introduction

The biggest challenge faced by small ruminant producers in the Southeastern United States (US) is gastrointestinal nematodes (GIN). Historically, chemical anthelmintics have been used, but improper and overuse has supported the development of anthelmintic resistance (Kassai, 1999). Consequently, new tools for combatting GIN have been investigated, including using genetic selection for resistance to GIN infection and copper oxide wire particles (COWP) as an alternative deworming method. This review will explore how fecal egg count (FEC) estimated breeding values (EBV) provided by the National Sheep Improvement Program (NSIP) can be used in tandem with COWP to mitigate the effects of GIN in Katahdin (KT) sheep. This will include discussion of the GIN lifecycle, production loss caused by GIN, and the significant threat of anthelmintic resistance (AR). Lastly, the various tools that are available to prevent and control effects of GIN infections are explored. This background will highlight the impact of GIN on sheep and should provide insight on ways to better manage GIN.

Katahdin Sheep

The climate of the southeastern region of the US favors hair sheep over wool breeds. Hair sheep do not require shearing or tail docking and are more heat tolerant and GIN resistant than most wool breeds (Burke and Miller, 2002; Barton, 2014). Due to evolving in a native habitat dominated by poorer quality tropical forages coupled with higher ambient temperatures, increased relative humidity, and an increased availability of GIN, Caribbean hair breeds are considered highly adaptable and better suited to thrive in this region (Wildeus, 1997).

The KT breed was developed from crosses between the Virgin Island White and several British breeds, in particular, the Wiltshire Horn and Suffolk. Developed in the 1950s in Maine, the KT breed is a composite hair breed selected for fast growth, prolificacy, carcass quality, mothering ability and a polled phenotype. Ewes range from 55 to 73 kg on average while rams are heavier, ranging from 68 to 90 kg (Wildeus, 1997). In a well-managed flock, KT have a tendency to raise twins (Barton, 2014). It has been well documented that hair breeds such as the St. Croix, KT and even Dorpers are more resistant to GIN than wool breeds, such as Hampshires or Dorsets (Courtney et al., 1985, Burke and Miller, 2002; 2004, Vanimisetti et al., 2004). However, when compared to Caribbean hair breeds such as the St. Croix, the KT tends to have higher fecal egg counts (FEC), lower packed cell volume (PCV) and requires deworming sooner (Burke and Miller, 2002; Vanimisetti et al., 2004b; Palomo-Couoh et al., 2017, Ngere et al., 2018). Although St. Croix are more resistant than KT, the improved carcass qualities of the KT make them desirable to producers (Burke et al., 2003). Overall, the KT is well suited for the stressful conditions of the southeastern region of the U.S. and requires less intensive management practices than wool breeds, making them a favorable choice for sheep producers.

National Sheep Improvement Program

The National Sheep Improvement Program (NSIP) was established in 1987 with the goal of providing American sheep producers with genetic evaluation tools (Notter, 1998). The program was originally only capable of evaluating single traits for animals within-flocks until 1993 when breeders of Targhee, Polypay and Suffolk sheep inquired if it were possible to establish an across-flock evaluation similar to those available for the beef and dairy industries. Sufficient genetic linkage or connectedness is required amongst flocks to allow for comparisons between flocks for an accurate across-flock analysis (Huisman et al., 2006). It was determined there was sufficient linkage due to collaborative sire usage and increased popularity of artificial insemination (Notter, 1998). This led to a reassessment of the program that resulted in multi-trait estimated progeny differences (EPD) available for use between flocks for the Targhee, Polypay and Suffolk breeds.

Estimated breeding values provide a tool that quantifies the genetic merit of livestock and can help improve the accuracy of breeding decisions and flock genetic improvement. These EBVs differ from EPDs, which predict the genetic merit for the progeny of the individual (Newton et al., 2013). These EBVs are calculated by removing known sources of variation caused by the environment to accurately predict the genetic contribution for a given trait (Burke et al., 2022). As a predictive value, EBVs must be at least 70% accurate to be reliable and even still, are not as accurate as raw phenotypic data.. To determine the EBV for a trait in an animal, data are collected and adjusted for the known environmental influences and then compared to the average of the individual's contemporary group. A contemporary group is a group of animals of similar age (within 45 days of one another) and managed in the same manner. This value is then combined and weighted with performance data from known relatives and how closely related they are, before the final adjustment for trait heritability. Heritability describes the amount of influence that genetics have in the phenotypic expression of a trait in comparison to the environmental influence (Newton et al., 2013). Heritability for a trait is typically between 10 and 30%, indicating that environment and management play a larger (70-90%) role in trait expression (Bielek and Newton, 2018). Increasing the accuracy of EBV can be done through increasing the number of progeny records or by increasing the number of flocks where a sire is utilized (Newton et al., 2013). The NSIP converts performance data into a predictable, economically valuable selection tool that allows for improved genetic progress (NSIP.org).

Producers can use EBVs to select traits of economic relevance to their operation. Of the 22 traits that are measured, FEC both for weaning (WFEC) and post-weaning (PFEC) are a focus for sheep breeders interested in improving parasite resistance. Fecal egg count relates to an individual's ability to resist GIN infection. For the majority of EBVs, a higher value indicates the preferred trait, with a few exceptions, such as the FEC EBVs, which are expressed as a percent change on a scale of -100% to + ∞ (EAPK Fact Sheet #3, 2020). A lower number indicates a lower FEC and thus higher resistance to GIN infection, so negative values are preferred (Newton et al., 2013; Notter and Lewis, 2018). Selection for low FEC EBVs can be used to make rapid genetic progress for parasite resistance due to improved selection accuracy. For example, selecting a ram with a PFEC EBV of -60% predicts a 30% reduction in FEC in his offspring compared to progeny of a ram with a PFEC EBV of 0% (EAPK Fact Sheet #3, 2020). These EBVs are being used to improve resistance to GIN within breeds, such as with the KT. The current NSIP breed average PFEC for the KT breed is -29.12%, with the top 1% of the KT breed at -99.99% and the least resistant at 373.76% (NSIP Katahdin Percentile Report, 2024). Although this is a wide range, the breed average is below 0%, which indicates genetic progress towards parasite resistance.

Parasite Biology

Parasites

Gastrointestinal nematodes infect the gastrointestinal tracts of animals. These GIN infections have severe ramifications for the livestock industry, not only through death loss, but also through the less quantifiable, but still impactful, production losses. Helminths exist all over the world and vary in life cycle, infection pathway, and effects on their host, as determined by their environment (Dobson et al. 1996). Within the Nematoda class, the Trichostrongyloidea superfamily contains bursate worms responsible for considerable mortality and morbidity in ruminant animals worldwide. *Cooperia*, *Haemonchus*, *Nematodirus*, *Teladorsagia* and

Trichostrongylus are some of the most impactful genera within the gastrointestinal nematodes. *Cooperia* is found in the small intestine (SI) and is associated with loss of appetite and decreased weight gain. *Nematodirus*, or the thread-necked worm, is also found in the SI, where it causes damage to the villi and mucosa, causing diarrhea that leads to rapid dehydration of the host. *Teladorsagia*, or the brown stomach worm, is found in the abomasum of small ruminants and causes weight loss by interfering with the post-absorptive metabolism of protein by breaking down the junctions between cells and inducing loss of appetite (Holmes, 1987; Stear et al., 2003; Cortés et al., 2020). *Trichostrongylus* are discovered in the SI, where villi are atrophied and fused to intestinal crypts that are elongated and dilated, causing dark colored diarrhea and a decrease in weight (Taylor et al., 2007).

Although these other nematodes negatively impact small ruminants, they are not as common in the United States as *Haemonchus contortus*, especially in the southeast region. *H. contortus* is the major GIN found in small ruminants residing in warm, humid climates. *H. contortus* has been deemed the nematode that is the most detrimental in terms of small ruminant health and contributions to economic losses and represents 75-80% of the worm burden found in the southeastern U.S. (Miller et al.,1998, Mortensen et al., 2003, Burke et al., 2004). Not only does it consume blood from the host, but *H. contortus* have developed resistance to the available chemical anthelmintics, whereas the other aforementioned genera still tend to have some susceptibility to anthelmintics (Taylor et al., 2007; Howell et al., 2009).

<u>Lifecycle</u>

Haemonchus contortus are members of the trichostongylidae family which have a direct life cycle that consists of two phases, the pre-parasitic and parasitic phases (Taylor et al., 2007). The parasitic phase occurs within the abomasum of the host, while the pre-parasitic phase is free living in the environment. Eggs are deposited in the feces and hatch into the first larval stage (L1) assuming proper environmental conditions are met. These factors include the proper moisture, 80-100% relative humidity is preferred, and temperatures between 18 – 26ºC. The larva itself will also control further development as it will secrete enzymes that help break down the inner layer of the egg. Once the inner layer is gone, water can be absorbed until the rest of the layers burst and allow the larva to escape (Taylor et al. 2007). Veglia (1915) identified a tendency for the eggs to hatch in the 19th hour post excretion, with the majority hatching by hour 22 post-excretion in the feces.

The L1 larvae consumes bacteria and organic matter found in the soil until they shed their sheath and molt into the second larval stage, L2. The L2 continues to consume bacteria and organic material until molting into the third larval stage, L3, where the cuticle, or outer sheath, is retained from the L2 (Taylor et al., 2007). The time from L1 to L3 stages is approximately 7-14 days, depending on environmental conditions.

At the L1 and L2 stages, the larvae are very susceptible to extreme temperatures and desiccation (Craig, 1986). The sheath protects the larva from unfavorable environmental conditions until it is consumed by the host. Higher temperatures accelerate larvae development, but this leads to a faster depletion of the energy stores and a shorter survival period outside the host. Cooler temperatures are more ideal for long-term survival as the rate of development and metabolism slows and can even stop below 10ºC. The movement and metabolism of the L3 larva slows even further below 5ºC, conserving the energy stores and supporting extended larval survival. The larvae can remain in this stage for several months if the conditions are right. This is the only infective stage of the larva, as consumption of L1 or L2 will not result in establishment in the host. Larval survival will be shortest in dry, hot conditions where desiccation or UV exposure will result in death (Taylor et al. 2007).

To increase the likelihood of host consumption, larvae will use water droplets (dew) to travel up the plant to be available for consumption during the periods when ruminants are most actively grazing, such as during the evening, overnight, and morning hours. Although sheep, goats, and cattle can all host *Haemonchus contortus* and other GIN, other hosts will not provide the desired environment for the exsheathement of the larvae following ingestion of the L3 larva (Kassai, 1999). There is some discussion on whether or not *Haemonchus contortus* and *Haemonchus placei* truly correspond to two separate hosts (sheep and cattle respectively) or if they are the same organism (Zarlenga et al., 2016). If they are not consumed, the larvae will seek shelter at the base of the roots of the plant to receive further protection from the environment. Once inside the host, L3 larva will exsheath and molt into the fourth larval stage in the abomasum (Taylor et al., 2007). L4 larva will burrow into the upper layer of the mucosa in the abomasum and begin to feed on host blood before undergoing two further molts (Al-Zubaidy et al., 1987; El-Ashram et al., 2017; Flay et al., 2022). The larva will then molt into the L5 stage where it develops a lancet-like tooth in its buccal cavity. The L5 will burrow further though the mucosa into the gastric pits, where it will cause hemorrhages in the tissue via slices made with the lancet-like tooth (El-Ashram et al., 2017, Flay et al., 2022). Before the final transformation into the adult worm stage, the larvae will return to the lumen of the abomasum (Kassai, 1999).

The adult worm is the only stage that is sexually mature and can therefore reproduce. These worms do not attach to the mucosa and can freely move as they consume blood. The common name for *H. contortus* is the Barber Pole Worm, named for the red and white candy stripe appearance of the red blood-filled digestive tract wrapped around the white reproductive tract of the females. Males do not have the barber pole appearance and are less distinctive. The females tend to be longer, measuring 18-30 mm in length and have a vulvar flap. The males measure 10-20 mm in length and have a dorsal ray of bursa that are asymmetric (Taylor et al. 2007). Although the L4 and L5 stages cannot yet reproduce, they still consume blood and contribute to the anemia and deterioration of the health of the host.

Anemia

Each individual adult female worm can consume up to 0.05 mL a day. An infection of 5000 worms alone can cost the host 250 mL of blood daily (Urquhart et al., 1996). Anemia is the condition associated with a low concentration of red blood cells. Anemia can be quantified using the packed cell volume (PCV) measurement. The larvae and adult worms burrow into the gastric pits via the mucous layer of the abomasum where the lancet-like tooth in their oral cavity is used to slice the tissue which hemorrhages, allowing for consumption of the blood (Dargie and Allonby, 1975; Taylor et al., 2007; El-Ashram et al., 2017, Flay et al., 2022). The body of the host has to use proteins from other sources to repair the damage to the epithelium and replenish the red blood cells (Knox et al., 2006). The number of worms and the ability of the host to replace the lost blood are two factors that contribute to the degree of anemia (Dargie and Allonby, 1975).

Dargie and Allonby define three stages of anemia development. These are characterized by an initial fall in PCV that is stabilized by an increase of erythropoiesis in the bone marrow where 65-75% of the body's iron stores are used to produce hemoglobin, the protein found in red blood cells (RBC; Andrews, 2000; Rittasse, 2020). This is followed by a period of continued hemorrhage and erythropoiesis, which depletes iron stores of the host. Finally, the bone marrow is depleted and a significant decline in hematocrit and serum iron concentrations indicates the failure of the host to keep up with the blood loss (Dargie and Allonby, 1975, Taylor et al., 2007).

Identifying infection

There are various ways to quantify a GIN infection. A tool that can be used to diagnose and quantify GIN infections is FEC, which is an indirect indicator of infection level and can be used to quantify an animal's GIN resistance. For a modified McMasters fecal float, 2 grams of fecal sample are collected directly from the rectum and then suspended in 28 ml of a supersaturated solution with a specific gravity of 1.18 - 1.20 to float eggs. The number of strongyle eggs counted for both chambers is then multiplied by 50 to determine the eggs per gram (EPG) (Whitlock, 1948). A caveat to using FEC as a diagnostic tool is that the parasite eggs observed only represent the infection level from roughly three weeks or more prior and will not include any newer worms due to the prepatent period. Only the adult stage of *H. contortus* lays eggs, but L4 and L5 larvae still consume blood and can contribute to anemia.

Another method is the FAMACHA score, which was originally developed in South Africa and is named after the creator, Dr. Francois "Faffa" Malan: FAffa MAlan CHArt (Bath et al, 1996, Malan et al., 2001). FAMACHA scoring is a management practice that requires looking at the ocular mucosal membrane to determine anemia status on a scale of one to five; where a score of one is a bright, healthy red mucosal membrane, and a score of five is a white, anemic membrane. Based on a targeted selection treatment protocol, FAMACHA scores of one and two do not require deworming, a score of three allows the producer to determine whether or not to treat based on other indicators such as body condition score (BCS), and scores of four and five require deworming (Kaplan et al., 2004). Once trained, producers can easily use this tool to identify and treat anemic, unthrifty animals.

Packed cell volume (PCV) is another anemia-based tool used to identify animals with decreased packed cell volume which can be indicative of *H. contortus* infection. This is done by collecting a blood sample, centrifuging it to separate the red blood cells (RBC) from the serum, and measuring the percentage RBCs to determine anemia status. The normal range for sheep is 27 – 45% and a PCV below 20% is considered anemic (Wiley textbook 2002; Flay et al., 2022). While FAMACHA scores and PCV do not definitively diagnose a GIN infection, they do estimate anemia level, which is indicative of *H. contortus.*

Production loss

Internal parasites have a significant impact on the sheep industry in the United States and globally. Allonby (1975) reported an estimate of $26 million in loss annually due to *H. contortus* in sheep and goats. According to the 2022 report released by Animal and Plant Health Inspection Service (APHIS), GINs are the second greatest cause of non-predatory death loss in both sheep and lambs, behind age-related deaths for adult sheep and weather-related death for lambs. The primary pathogenic effects are caused by the blood feeding activity of worms, which results in anemia and usually becomes apparent after approximately two weeks of infection (Baker et al., 1959, Roeber et al., 2013). Acute disease depends on the intensity of the infection and is associated with dark fecal matter, submandibular edema (more commonly known as bottle-jaw), decreased wool production, reduced muscle yield, and can be fatal. Chronic disease can present as a loss of appetite, weight loss, and anemia (Kassai, 1999, Roeber et al., 2013, Mavrot et al., 2015). A systematic review of 88 studies concluded that infected sheep weighed 15% less and produced only 90% of the wool and 78% of the milk as compared to parasite-free animals (Mavrot et al., 2015). Field trials conducted in Western Australia indicate a potential for 10% in hidden production losses when dewormers were used in production systems with developed anthelmintic resistance in comparison to programs using a fully effective anthelmintic (Besier, 2007).

Anthelmintic Resistance

A major threat to global parasite control is the development of anthelmintic resistance (AR) in parasite populations (Waller 1994, Dobson et al., 1996). Resistance to anthelmintics is heritable and is observed when a greater number of individuals within a parasite population can persist or are no longer negatively affected by a fatal dose of anthelmintic, or when a higher dose is required to produce negative effects (Prichard, 1980, Kassai, 1999; Wolstenholme et al., 2004, Kaplan et al., 2020). Anthelmintic resistance increases when individuals within the parasite population no longer susceptible to anthelmintics pass on their resistant genetics. In the past, chemical dewormers were relatively cheap and were marketed as broad spectrum, possibly contributing to a culture of excessive use that supported the development of AR (Kassai, 1999). Anthelmintic dosage is weight-based. However, producers may not weigh the animal prior to treatment, which leads to both under and overdosing. Underdosing can reduce the efficacy of the anthelmintic and contribute to AR, whereas overdosing is not only expensive, but does not necessarily increase the efficacy of the treatment, and may lead to toxicity. Additional practices that have contributed to the development of AR consist of deworming too frequently, continuing to use a dewormer once it has lost efficacy, and deworming the entire herd instead of just the individuals that require it (Kassai, 1999; Taylor et al., 2007)

Resistance to thiabendazole, the original broad spectrum anthelmintic, was first reported in 1963 (Drudge et al., 1963; Waller, 1994). Blouin et al. reported in a 1995 study on the interaction between host movement and genetic structure in five different populations of nematodes a great opportunity for the dissemination of the rare alleles for resistance. This is due to the high rate of gene flow (the speed with which genetic potential can be passed between generations) within the trichostrongyloid populations that are infecting cattle and small ruminants in the U.S. Although Blouin acknowledged that alleles for resistance are considered rare, the high rate of gene flow supported by the rapid reproduction rates of the parasites increases the chances of these alleles being passed on to the next generation. *H. contortus* are sexually reproductive with high gene flow, supported by the short prepatent period of 15 - 21 days and by the female's ability to produce between 5,000 - 15,000 eggs daily, indicating that once given the opportunity to develop, resistance is developed rapidly (Emery et al., 2016).

The rapid development of anthelmintic resistance is supported by Kates et al. (1973) and Egerton et al. (1988), who showed that *H. contortus* could develop resistance to anthelmintics within four to seven generations if the host receives less than the recommended anthelmintic dose. To retain a minimum of 95% efficacy in the 8th generation required almost four times the original dose (Egerton et al., 1988). Recently, 46 farms in the southeastern region of the United States were evaluated for the development of AR. 44 of 46 farms had GIN populations consisting mostly of *H. contortus* (>50%), none of which were susceptible to all three classes of anthelmintics. Seventeen percent of the farms evaluated contained *H. contortus* that were resistant to all three classes, including moxidectin (Howell et al., 2009). Currently, there are records of resistance to every available anthelmintic on the market, along with reports of multidrug resistance (MDR) globally (Howell et al., 2009; Kaplan, 2009)).

Conclusions

In summary, GIN are detrimental to the sheep industry by causing production losses and death in severe infections. The challenge of AR was first reported in the 1960's, and has continued to grow, despite continued mitigation efforts. There is now documented resistance to every chemical dewormer available on the market, along with MDR, indicating other tools need to be examined and used in conjunction with one another as a part of an integrated parasite management (IPM) plan to minimize continued losses in the small ruminant industry. As more resistance develops, researchers and producers need to determine better strategies for parasite control in small ruminants to mitigate further losses.

Methods of parasite control

Introduction

Due to the significant impact of GIN infection on small ruminant production, many tools have become available to combat these nematodes. The most utilized tool is chemical dewormers, but there are many other management practices that can help reduce parasite burden. These other tools include proper nutritional management, genetic selection for resistant animals, pasture management, and non-chemical forms of dewormers such as copper oxide wire particles.

One study comparing different strategies for parasite control found a reduction in FEC due to genetic selection (69%), supplementation of protein (35%), and by drenching with anthelmintics (28%), along with insignificant effects from two experimental vaccines that contained either secretory or excretory *Haemonchus contortus* antigens (Eady et al., 2003). According to van Wyk et al. (2006), no singular approach is capable of mitigating the increase in anthelmintic resistance. Thus, Integrated Parasite Management (IPM) was developed. This is the practice of utilizing multiple strategies for parasite control in a concentrated effort to reduce the availability of GIN, while improving the flock's response to infection. The methods used in this practice may be unique to each production system and no singular combination of practices work all of the time. Wells (1999) highlighted the importance of studying the farm in its entirety to identify which parts can be better managed to decrease parasite burden and the corresponding negative effects on livestock.

Chemical dewormers

There are three major classes of chemical dewormers used in the United States: the macrocyclic lactones, the benzimidazoles, and the imidazothiazoles. These three classes contain broad spectrum nematicides, but certain anthelmintics target certain helminths better than others (Kaplan, 2009**).** Side resistance is a term describing the phenomenon where resistance to a particular anthelmintic in a class indicates resistance to that entire class due to the presence of a gene within the parasite population that codes for a mechanism of action to disrupt the toxic activity of the drug (Prichard et al., 1980; Kassai, 1999; Kaplan, 2009).

The benzimidazoles are ovicidal and act on the worms by binding to cytoplasmic β-tubulin in microtubules, creating a cap that inhibits the dynamic depolymerization/ polymerization behavior (Cooper, 2000). This prevents the further development of microtubules, which prevents uptake of glucose and induces protein secretion. Additionally, some enzyme activity is reduced. This interferes with the mitochondrial metabolism of the worms, the pathway that generates energy, which causes worm death and expulsion 2-3 days after treatment (Kassai, 1999; Taylor et al., 2007).

Imidothiazoles are also short acting similar to benzimidazoles but are not ovicidal. Imidothiazoles act as cholinergic agonists to paralyze the worms (Taylor et al., 2007; Kaplan, 2009). Imidothiazoles bind to the acetylcholinesterase receptor, causing spastic muscle contraction, or paralysis and rapid expulsion of the worm (Kassai, 1999). Levamisole is an imidothiazoles that is safe to administer during gestation. However, it is the most potent of the imidothiazoles and has a low safety index. Due to the low safety index, it is important to administer the proper dosage to prevent lethal effects (Vercruysse and Claerebout, 2014).

Macrocyclic lactones have two sub-classes, avermectins and milbemycins. The difference being the lack of a disaccharide substituent for the milbemycins (Kassai, 1999). Macrocyclic lactones cause non-spastic paralysis and parasite death by binding to specific channels, permanently opening them, and allowing for an influx of chloride ions with hyperpolarization of the muscle or nerve cells (Kassai, 1999). Macrocyclic lactones are also very lipophilic and can provide longer lasting protection against potential reinfection, depending on the specific anthelmintic and parasite species (Kaplan, 2009).

There is some indication that the side resistance phenomenon is not quite accurate for macrocyclic lactones, as resistance in other macrocyclic lactones, such as ivermectin, does not necessarily translate to moxidectin (Kaplan, 2009). The general review of chemical control of parasites in livestock indicated the need for an integration of chemical and non-chemical parasite control methods (Strong and Wall, 1990, Barnes et al., 1995). It is also indicated that the combination of dewormers should help to reduce the development of AR, especially after resistance to individual anthelmintics has been established (Barnes et al., 1995, Papadopoulos, 2008). Combining dewormers refers to using two to three dewormers from distinct classes which are given as individual doses, not mixed into one syringe. The mathematical model designed by Barnes et al. (1995) indicated that combination deworming contributes minimally to anthelmintic resistance, less so than four variations of grazing practices. This is supported by the additive effects of dewormer efficacy which indicate that an efficacy of 90% in dewormer A combined with an efficacy of 80% in dewormer B, would result in 98% removal of targeted parasites. This practice works when the anthelmintics are still over 50% effective against the worms. However, in the event that the individual anthelmintics are less than 50% effective, even the use of 3 dewormers (one from each class allowed in the U.S.) will yield less than 90% efficacy against parasites and not be of benefit (Leathwick et al., 2015; Kaplan, [ACSRPC] 2017). Thus, the American Consortium for Small Ruminant Parasite Control (ACSRPC) recommends using combination treatments before dewormer efficacy is lost.

Refugia

Although the initial efficacy of anthelmintics was originally greater than 99%, this has since dropped (Kaplan, 2024). Even when administered correctly, anthelmintics with 90% efficacy (< 95% is considered the efficacy threshold) will still leave 10% of worms behind, which can pass on alleles for resistance to the following generations (Howell et al., 2009). When parasites are able to avoid exposure to anthelmintics, either due to living freely in the environment or as adults existing in untreated animals, they can pass on their genetics that are more susceptible to anthelmintic treatment and dilute the opportunity for resistance (van Wyk, 2006). This practice of leaving susceptible worms in the population is called refugia and it can be used to slow the development of AR (Martin et al., 1981; Kenyon et al., 2009).

Regular and frequent deworming treatments result in selection of worms with resistance genes as it allows for mutations on the receptor sites that are acted upon by the anthelmintics (Coles, 2005). Repeated, unnecessary exposure to dewormers allows for increased opportunity for resistance to develop unless the treatment is 100% effective. Strategic deworming supports a refugia population by using management tools to determine which animals within a flock need treatment, instead of treating the entire flock at regular intervals.

The 5-point check is an on-farm assessment that involves inspection of the eyes, nose, jaw, back, and tail for symptoms of parasite infection (Bath and van Wyk, 2009). The

FAMACHA score (ranges 1-5) system is an on-farm tool that can help identify the animals within a flock that require treatment for GIN infection by inspecting the color of the ocular mucosal membrane to determine anemia status (van Wyk et al., 2006). It is a simple choice on whether to deworm or not when the FAMACHA is at either extreme (1 = healthy, or 5 = severely anemic), but producers can use the rest of the 5-point check to determine if an animal with FAMACHA score 3 should be dewormed to retain refugia. Therefore, strategic deworming practices that maintain refugia to allow subsequent generation to evolve from untreated worms will help to delay the development of anthelmintic resistance (Martin et al., 1981; Coles, 2005).

Genetics

Phenotypes can be defined as observable traits possessed by an individual due to the interaction of the environment and their genotype (Oxford Languages). As previously stated, heritability refers to the proportion of phenotypic variation that can be explained by genetics (Newton et al., 2013). Phenotypic traits are categorized as low (less than 20%), moderately (between 20 to 30%), or highly heritable (greater than 30%) (Aaron, 2014). Resistance to GIN, quantified by FEC, is a heritable trait that can be used for genetic selection (Prichard, 1980, Eady et al., 2002, Kaplan et al., 2021).

The NSIP has contributed to progress in identifying animals more resistant to GIN, based on FEC EBVs (Notter, 1998, Burke et al., 2022). Variation in heritability estimates for FEC exist both between and within breeds, but generally ranges between 0.2 and 0.4 (Windon, 1996). Safari et al. (2005) analyzed 165 studies, 16 of which showed a weighted heritability of 0.27±0.02. Ngere et al. (2018) found that their estimates of heritability based on sire models in KT were higher than estimates from animal models with ranges 0.18 – 0.26 for WFEC and 0.23 – 0.46 for PFEC. The moderate heritability of FEC, along with the correlation between FEC and related worm burden, indicates that FEC can be used as a tool to improve parasite resistance in sheep through genetic selection for low FEC (Preston and Allonby, 1979; Boareki et al., 2021). Weaver et al. (2021) indicated that while a direct relationship between presence of the adult worm and FEC exists in Suffolk sheep due to delayed recognition of *H. contortus*, the immune response in Texel sheep targets the adult stage, indicating that worm presence doesn't always directly influence FEC. Although there is not a direct relationship between worm count and FEC across all breeds, the necropsy findings by Preston and Allonby (1979) demonstrate that FEC can be used as a reflection of worm burden. Vanimisetti et al. (2004b) reported the possibility of improving resistance in both lambs and ewes via genetic selection but suggested that focusing on lamb selection is best due to different mechanisms that control the response in non-lactating ewes as compared to lambs. Lower PCV and higher FEC were reported for yearling ewes compared to mature ewes and differences in heritabilities between the two for PCV were 0.39 vs 0.15, respectively, and for FEC, 0.10 and 0.31, respectively; (Vanimisetti et al., 2004b). Additionally, genetic progress for parasite resistance in Katahdin lambs can be made without sacrificing body weight, as shown by the additive genetic correlation between PWFEC and PWWT of 0.01 ± 0.17 (Ngere et al., 2018).

Preston and Allonby (1979) studied the relative resistance between the Red Masai, Blackhead Persian, Merino, Dorper, Corriedale and Hampshire sheep breeds to *H. contortus* over the course of 27 months. The Hampshire breed was the most susceptible to GIN as indicated by a mortality rate of 100% by week 26 of exposure to the infected pasture due to acute haemonchosis. Fecal egg counts at death ranged from 15,000 to 25,000 epg. The Red Masai had 0% mortality and only three cases where FEC for an individual exceeded 300 epg. The other four breeds experienced 16 sporadic deaths over the course of the study. Six Red Massai and six merinos were autopsied for worm collection and identification. 99% of the collected worms were identified as *Haemonchus contortus*, with mean egg counts of 83.3 epg for Red Massai and 5,300 epg for Merinos (Preston and Allonby, 1979). Smith and Christie (1978) showed an association between resistance to GIN and high levels of specific anti-larval IgA in the abosomal mucosa, of which the Red Masai had higher mean levels.

Burke and Miller (2002) determined that the relative resistance of Dorper crossbred ewes was higher than Hampshires, as shown by lower FEC and higher PCV in the hair breed. The Dorper sheep showed a slightly increased FEC and slightly decreased PCV in comparison to the KT and St. Croix sheep from July to September but had similar FEC and PCVs for the remainder of the first and for the entire second year (Burke and Miller, 2002). Vanimisetti et al. (2004) compared KT ewes to Dorset, Dorper crosses, and St. Croix. On average, Dorsets had the highest FEC and the Dorper crosses had the lowest PCV, while the KT and St. Croix maintained lower FEC and higher PCV. A contributing factor for improved resistance in hair breeds, such as St. Croix and KT, in comparison to wool breeds, are the speed and intensity of immune response. Bowdridge et al. (2013) reported both greater and more rapid humoral immune response in St. Croix over a composite wool breed, observable through elevated IgA concentrations. The hair sheep began with higher IgA concentrations and were able to rapidly increase levels upon infection. Although the IgA of the wool breed followed a similar pattern, it failed to meet the concentration level of the hair sheep (Bowdridge et al., 2013).

There are differences in resistance to GIN within breeds as well. Katahdins, for example, currently have a post-weaning fecal egg count (PFEC) EBV range of -99.99% to 373.76% with a breed average of -29.12%. Polypay sheep have a range of -90.90% to 214.89% with a breed average of 0%.

A study on the response to GIN by Romney sheep divergently bred for high or low FEC indicated that selective breeding could alter the degree of resistance or susceptibility over generations. By 1992, the divergence of the high and low FEC selected lines was up to 0.17 units, or 0.46 genetic standard deviations of divergence (Morris et al., 1997). A 20 year-long study in Merino sheep found a divergence of 0.36 to 0.46 phenotypic standard deviations between the lines selected for high or low FEC (Woolastont and Windon, 2001). A much shorter, 3-year study conducted on Scottish Blackface determined that genetic variation exists for acquired resistance, but not innate resistance (Bishop et al., 1996). Further work by Bentley et al. (2024) indicated that ewes divergently bred for low FEC EBV produced 2.5 times more IgG in their colostrum than the ewes selected for high FEC EBV. Additionally, Weaver et al. (2023) indicated increased survivability for lambs divergently bred for low FEC EBV when compared to those selected for high FEC EBV.

These studies demonstrate that not only are certain breeds more resistant to GIN, but individual animals within the same breed respond differently than one another due to different immune responses. This is important information when using genetic selection to produce more genetically resistant animals.

Pasture management

Pasture management practices could be beneficial in disruption of the environmental portion of the GIN lifecycle, reducing GIN exposure. Allowing livestock to overgraze forage increases the opportunity for GIN infection by increasing exposure to infective larvae (Besier et al., 2016). Preventing overgrazing of forage can be managed with rotational grazing and appropriate stock density. Rotational grazing is a practice that can disrupt the GIN lifecycle and reduce the need for anthelmintic treatment by moving the potential host to a new grazing allocation before larvae reach the infective L3 stage (Waller, 2006). Barger et al. (1994) established a 10-paddock rotational grazing system where animals were moved every 3.5 days. Mean FEC for rotationally grazed goats tended to be less than 1000 epg, whereas the continuous grazed goats required 3 treatments due to infections over 2,000 epg. Stocking rate is another grazing tool that has demonstrated a direct relationship to parasite availability on pasture. The stocking rate, or the density of livestock on a given area, affects the intensity of available GIN on pasture (Waller, 2006). Higher stocking rates lead to intense competition, forcing livestock to eat closer to the roots of the forages, where the larvae are more concentrated (Santos et al., 2012).. Downey (1969) highlighted the negative effects of high stocking rates via decreased growth in untreated lambs when compared to untreated lambs in lower stocking rates. Overall, proper pasture management can contribute to a successful integrated parasite management system.

Nutrition

Nutrient supplementation is another tool to reduce FEC by supporting the host's natural immune response (Bowdridge et al., 2013). When nutritional needs are not met, many functions, such as growth or immune response against GIN, can be penalized (Houdijk, 2011). A study investigating the efficacy of different methods for parasite control compared genetic selection (using divergently bred lines), deworming (3 separate doses of dewormer consisting of 6 ml of closantel plus 7.5 mL of ivermectin in March, 10 mL of ivermectin in April, and a final 12 mL dose of ivermectin in August of the same year), vaccination (two experimental antigen-based vaccines), protein supplementation and sex differences. Supplementation with 100 g of a commercially available protected pellet (31% protein) per head per day given twice a week for 32 weeks reduced FEC by 35%, 7% more than the strategic drenching (Eady et al., 2003). Another study focused on reducing the periparturient rise (PPR), a phenomenon where ewes experience a temporary decline in worm resistance during the periparturient period that leads to a rise in FEC, showed that ewes supplemented with 250 g of cottonseed meal (CSM) had a mean reduction of 66% in FEC post-partum, whether bred for resistance or not (Kahn, et al., 2003). Providing supplementation increased the metabolizable protein available, which in turn aided in the ewe's response to GIN (Kahn et al., 2003).

Infection with GIN can cause significant gastroenteric losses of protein in the form of blood, plasma, sloughed epithelial cells, and mucus. Additionally, there can be an impact on mineral absorption and retention which are vital for the growth and development of young animals. The damage caused to the wall of the abomasum by *H. Contortus* requires protein synthesis for repair, which drains the stores that would otherwise contribute to production, such as growth, lactation, or wool (Knox et al., 2006). Van Houtert et al. (1995) reported increased stimulation of lymphocytes and decreased FEC in sheep supplemented with 100 g of fishmeal, which averages 80% undegraded protein post-microbial proteolysis in the rumen (Satter,1986). These studies show the benefits of supplementing protein to support the host when infected with GIN, but ensuring the protein can be delivered and used by the host is key. The rumen can degrade a considerable amount of dietary protein to produce microbial protein. This leaves little protein available for the host as only 63% of rumen degradable protein will yield metabolizable protein (AFRC, 1993, Houdijk, 2011). In contrast, rumen undegradable protein (RUP) contributes directly (1:1 ratio of RUP to metabolizable protein), which is much more efficient to feed and is more accessible to the host (Houdijk, 2011).

The supplementation of RUP has been shown to improve host response through increased body weight and PCV in tandem with decreased FAMACHA scores and FEC (Crawford et al., 2020). Rumen undegradable protein are proteins that have been bound such that they are protected against the microbial degradation of the rumen and can pass into the lower portion of the tract (Hoste et al., 2006). One of the first studies on the effects of RUP on GIN in sheep indicated that the sheep supplemented with the protected protein were able to overcome the negative effects caused by a moderate trichostrongyloid infection (van Houtert et al., 1994).

There are a few different methods to protect proteins, but forages (either fresh or cut for hay) that contain tannin do this naturally. The two kinds of tannins are hydrolysable, a more readily accessible and therefore toxic form, and condensed tannins, which have the ability to form both soluble and insoluble complexes with proteins, which "protects" the protein from the rumen (Hoste et al., 2006). Supplementation of 3-6% dry matter (DM) of the diet of condensed tannins have shown antiparasitic effects, such as reduced FEC by negatively impacting the fecundity of the female worm, but feeding over 7% DM in the diet can lead to reduction in feed intake, inhibition of growth, and can interfere with the rumen microbes (Min et al., 2003, Waghorn and McNabb, 2003, Hoste et al., 2006).

Copper Supplementation

Copper is a mineral required by sheep for several functions, such as supporting enzymatic activity (Harris, 1997), maintaining proper function of the central nervous system through myelin formation, synthesizing melanins, and metabolizing iron (Wang et al., 1996; NRC, 2007). The recommended copper requirements for sheep are 7-11 mg/kg dry matter (DM), where <5 mg/kg DM indicates a copper deficiency and 15 mg/kg DM is the maximum amount tolerable to avoid copper toxicity when a normal amount of molybdenum (1-2 mg/kg DM) is included in the diet (NRC, 2007). Molybdenum and sulfur react to form thiomolybdates (TM) that bind available copper in the rumen, forming an unabsorbable complex that helps to control excess copper and prevent toxicity (Gould and Kendall, 2011; Suttle, 2012). The small margin between required and toxic levels of copper have led to copper concerns within the sheep industry, even though it's known to have negative effects on the adult stage of *H. contortus* (American Consortium for Small Ruminant Parasite Control [ACSRPC], 2018; Yin et al., 2019).

First developed for anthelmintic use by Hutcheon in 1892, copper sulfate (CS) was then further studied by Hall and Foster in 1918 and found to have effects against *H. contortus* (Hutcheon, 1892; Hall and Foster, 1918; Bang et al., 1990). When comparing a CS drench to powdered CS in a capsule, the drench performed better with an efficacy of 93% compared to the 0.3% efficacy of the capsule against stomach worms (Hall and Foster, 1918). As efficient as the drench is, care must be taken to administer the correct dose and reduce stress events as much as possible as this combination can lead to copper toxicity.

Another form of copper started becoming popular in the 1980s called copper oxide wire particles (COWP; Dewey, 1977; Suttle, 1981; Judson et al., 1982; 1984; Langlands et al. 1983; Bang et al., 1990). Similar to bypass protein, this form of copper bypasses the rumen to the abomasum where the higher acidity helps dissolve the capsule to release the copper oxide (Hale et al., 2007).

In a study conducted in 1990, COWP were 96% effective against *H. contortus*, 56% effective against *Ostertagia circumcincta*, and had no effect on *Trichostrongylus colubriformis* (Bang et al, 1990). Another study looked at the effects of 2, 4, and 6 g COWP boluses on 6-month-old lambs artificially infected with 10,000 L3 (97% *H. contortus*). At each treatment level, FEC was reduced, which did take 7 days longer in the group treated with 2 g. Those treated with 4 and 6 g had elevated levels of copper, which would predispose the lambs to toxicity (Burke et al., 2004). Further investigations were conducted to determine the lowest effective dose in order to reduce the risk of toxicity. Miller et al. (2005) found evidence that doses as low as 0.5 and 1 g are effective for controlling *H. contortus.* Considering past evidence of efficacy, multiple, low doses of COWP were then compared to the efficacy of levamisole. It was determined that low (0.5 or 1 g) doses of COWP every 6 weeks for a total of 4 treatments were as effective as levamisole in young, weaned lambs, with the effectiveness of the low doses dropping off as they mature (Burke and Miller, 2006). With the threat of anthelmintic resistance, COWP could be a viable option for producers, especially as new regulations make anthelmintics more expensive and harder to obtain. More research is needed on effects of COWP in naturally infected sheep, efficacy between breeds, and the mechanism of action copper has on GIN. Although the effects of copper against GIN have been studied for over 30 years, the mechanism of action is still unclear. Additionally, effects and interactions of copper oxide and genetic selection for FEC EBVs need to be studied further.

Conclusion

Gastrointestinal nematodes, specifically *H. contortus*, pose a significant challenge to the sheep industry. Their blood sucking feeding behavior contributes to anemia, which translates to production losses and even death in certain situations. Due to improper use of chemical dewormers, AR has developed to most chemical dewormers. However, there are a number of proven tools available to address both GIN and AR, such as the selection for GIN resistant sheep, supplemental protein, using selective deworming (FAMACHA scoring, etc.) to maintain refugia in the GIN population, and COWPs. When several tools are used cohesively in a production system through an integrated parasite management plan, the GIN exposure and burden can be reduced, improving sheep well-being and performance.

Summary

Katahdin sheep work well in the southeast region of the U.S. as they require less intensive management, have good mothering ability, and are relatively adapted to this region. Gastrointestinal nematodes have caused negative impacts on economic viability and animal wellbeing and will continue to do so unless better management practices are implemented. Given the development of AR, selecting sheep for parasite resistance, improving nutrition, and using other treatment options such as COWP will help producers better control GIN burden in their flock, reducing loss and further supporting the sustainability of the sheep industry.

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CHAPTER II: Effect of copper oxide wire particles and selection for fecal egg count estimated breeding value on parasitism and growth in Katahdin ram lambs

Introduction

Gastrointestinal nematodes (GIN) have a significant negative impact on the sheep industry in the United States as GIN infections are the greatest cause of non-predator related death loss, second only to age-related death (APHIS report, 2022). Although many species of GIN exist, *Haemonchus contortus* is the most detrimental and the most commonly represented (75-80%) in the Southeast region of the U.S. (Miller et al.,1998, Mortensen et al., 2003, Burke et al., 2004). Anthelmintics have historically been used to control GIN infection. However, repeated misuse (treating the entire flock, routine scheduled treatments, and underdosing) have led to the development of anthelmintic resistance (AR; Kassai, 1999). As a result, an integrated parasite management plan (IPM) should be developed to slow the progression of AR and mitigate effects of GIN infection in the sheep industry. There are various methods to mitigate effects of GIN in small ruminants, such as rotational grazing, supplementation of rumen bypass protein, development of refugia through targeted selective treatment, and alternative dewormer methods – such as tannin containing plants. Genetic selection for resistant sheep and copper oxide wire particles (COWP) are two additional tools that are being investigated for use in tandem with others in IPM plans.

While resilient or tolerant animals can handle a GIN infection with less impact on their production, they are still supporting the GIN lifecycle and depositing eggs for the more susceptible animals to consume. Resistance is preferred over resilience for the fact that resistant animals can eliminate the GIN infection and break up the lifecycle.

Katahdin sheep are a composite sheep breed that originated in Maine and have shown to have increased resistance to GIN parasites (Wildeus, 1997). Although the Katahdin breed tends to be more parasite resistant than wool breeds and even dorpers, there is significant variation within breeds. EBVs are calculated by the National Sheep Improvement Program (NSIP) based on phenotypic data collected and submitted by producers around the U.S. The fecal egg count (FEC) EBV describes an individual animal's susceptibility to GIN infection in relation to other animals within the breed. Heritability for EBVs indicates how effective selection for a specific trait will be, which is moderate (0.2 - 0.4) for the FEC EBV (Windon, 1996; Newton et al., 2013). Selection for both extremes of FEC EBV has been used to breed a divergent Katahdin population at the Southwest Virginia Agricultural Research and Extension Center (SWAREC, Glade Spring, VA) to further explore effects of genetic selection for parasite resistance. Weaver et al. (2023b) determined that FEC EBV could be used to predict resistance to GIN through reduced FEC and improved survival in lambs. Additionally, Bentley et al. (2023) added to these findings that lambs selected for low FEC EBV generate a greater immune response when vaccinated with *clostridium perfringens* types C and D. This indicates that EBVs can be used to select for low FEC to increase parasite resistance in sheep (Newton et al., 2013).

Another tool is copper supplementation through COWP. These COWP have been shown to eliminate the adult *H. contortus* worm from sheep (Bang et al., 1990). According to the NRC (2007) lambs postweaning have a copper requirement of 7-11 mg/kg dry matter (DM), when assuming normal levels (1-2 mg/kg DM) of molybdenum are available. This range is dependent on the level of molybdenum (Mo) available in the forage as it binds with sulfur (S) to form a thiomolybdate that binds the copper and makes it less bioavailable. Low levels of molybdenum can lead to copper toxicity if too much copper is provided in the diet and high levels of molybdenum can cause copper deficiency. Although copper toxicity is more of a concern in sheep due to low tolerance levels, COWP are less readily absorbed and thus a safer variation when given at low (0.5-1.0g for lambs, 1.0-2.0 g for mature ewes, per the ACSRPC) doses.

Additionally, COWP has demonstrated the ability to improve the efficacy of anthelmintics against GIN (Burke and Miller, 2020). However, literature on incorporating COWP with other IMP tools is lacking.

Therefore, the objective of this study was to evaluate the interaction of COWP and selection for FEC EBV on GIN infection and growth in spring-born Katahdin ram lambs. The hypothesis was that supplementation of COWP to lambs post-weaning would negatively impact a naturally achieved *H. contortus* infection and allow lambs genetically less resistant to GIN infection to respond as their more resistant counterparts would, demonstrated by a reduction in FEC and anemia.

Year 1

All animal procedures were approved by the Institutional Animal Care and Use Committee (No. 23-138) of Virginia Tech. This study was conducted from late June to mid-October 2023 and repeated from early July to early November 2024 at the Southwest Virginia Agricultural Research and Extension Center (SWAREC) in Glade Spring, VA.

Breeding Scheme

The SWAREC began a breeding program in October of 2017 to establish a Katahdin flock selected for either extremely high or extremely low fecal egg count (FEC) estimated breeding value (EBV). The first two years focused on divergently selecting sires based on FEC EBV. For Year 1 (2017) of the breeding program, two High FEC (HFEC) sires and two Low FEC (LFEC) sires were randomly bred to Katahdin ewes. The second year (2018), a total of eight sires (HFEC, n = 4; LFEC, n = 4), including two used the previous year for connectedness, were randomly bred to Katahdin ewes (Weaver et al., 2023). Beginning Year 3 (2019), ewes were also divergently selected for high or low FEC EBV and were mated to three sires of the corresponding genotype (Bentley et al., 2023). For years 4 (2020) and 5 (2021), LFEC ewes were randomly bred to three LFEC sires and HFEC ewes were randomly bred to three HFEC sires each year, with one LFEC sire and two HFEC breeding both years for connectedness (Valliere et al., 2023).

This breeding scheme established the divergent breeding lines used for this study (Table 2.1). For year 1 (Y1), HFEC ewes (n = 18; average PFEC = +38.11%, accuracy > 63%) were bred to HFEC sires (n = 3; average PFEC = +195.37%, accuracy > 90%) and LFEC ewes (n = 23; average PFEC = -51.47%, accuracy > 63%) were bred to LFEC sires (n = 4; average PFEC = -88%, accuracy > 82%) in October 2022. Sires were 5 years old on average and ewes averaged 3 years. These pairings resulted in 51 Katahdin (KT) ram lambs born between March 20 and April 16, 2023. Lambs remained with their dams on fescue-based pasture as one contemporary group until weaning.

Materials and Methods

Weaning for lambs in Y1 occurred on June 29, 2023, at an average age of 74 days (Figure 2.1). Ram lambs were used for sex consistency and only rams heavier than 13.6 kg were utilized. At weaning, fecal samples, FAMACHA scores, and weights were collected, and all lambs were dewormed with fenbendazole, moxidectin and levamisole according. Lambs were rested for three weeks on pasture. Lambs (HFEC, n = 22; LFEC, n = 29) were then randomly sorted into either the control (Con) or copper oxide wire particle (COWP) treatment groups with equal representation of genotype. Genotype by treatment groups consisted of HFEC-Con (n = 11), HFEC-COWP (n = 11), LFEC-Con (n = 15), and LFEC-COWP (n = 14). The lambs were raised as one contemporary group on fescue-based pasture (Figure 2.1) to attain a natural GIN infection and were supplemented with at 2% of their bodyweight with a 16% crude protein (CP), 76% total digestible nutrients (TDN) pellet made locally (Table 2.2).

Lambs selected to receive the copper oxide wire particle (COWP) bolus treatment were administered a 2-gram Copasure bolus at Week 0. Blood for packed cell volume (PCV), fecal samples, body weights, FAMACHA scores, and forage samples were collected at Week 0 and every two weeks until the conclusion of the study 12 weeks later. Blood was used to determine packed cell volume (PCV). The fecal egg counts (FEC) were conducted via the Modified McMaster's method (Whitlock, 1948). Forage samples were sent to the North Carolina Department of Agriculture (NCDA) lab in Raleigh, North Carolina for nutritional analysis. Lambs with a FAMACHA score ≥ 3 were dewormed with levamisole. Over the 12-week trial, one lamb in the HFEC-COWP group died due to suspected pneumonia, a second from the LFEC-COWP group was dewormed with levamisole on Week 11. Data from lambs requiring deworming treatment was removed from subsequent analysis.

Packed Cell Volume

Blood was collected from the jugular vein via venipuncture every two weeks via a 20-gauge needle into a vacutainer and purple top tube containing Ethylenediamine tetraacetic acid (EDTA). The blood tubes were kept in a cooler with ice until processing within the subsequent 12 hours post-collection. For processing, blood tubes were inverted by hand to mix the components, the top was removed, and a micro-capillary tube was filled two thirds of the way with blood via capillary action. The micro-capillary tubes were then centrifuged in a Stat-Spin MP centrifuge at a rate of 16,000 RPM for 120 seconds. After centrifugation, packed cell volume was determined as the proportion of red blood cells in the blood using a micro-capillary reader.

Modified McMasters Fecal Egg Counts

Fecal samples were collected directly from the rectum. Fecal samples were refrigerated until they were processed within the subsequent two weeks.

Fecal samples were run using the modified McMasters method as described by Whitlock (1948). Two grams of fecal matter were added to 28 ml of McMasters solution (1.18 SG). The mixed, homogenous solution was filtered and pipetted into a two-chambered McMasters slide. The solution was allowed to rest on the slide for a minimum of five minutes. The number of strongyle eggs were recorded and fecal egg count in eggs per gram (EPG) were determined by multiplying 50 by the number of eggs counted. A minimum of 0.6 g of fecal material was required for sample processing and FEC calculation was adjusted by weight.

Forage samples

Forage samples were collected every two weeks and consisted of cutting a 30.5cm by 30.5cm square area of forage at a height of 5.08cm above the ground to simulate what would be consumed by lambs. A minimum of 20 samples were taken per pasture at each sampling day. The forage samples were mixed and a random subsample selected and submitted to the forage lab in the North Carolina Department of Agriculture (Raleigh, NC) every two weeks. In Y1, lambs remained in the same 2.06-hectare pasture that consisted of fescue, orchard grass, and clover. Copper levels in the soil were 0.2 ppm (Soil Test Report, 2022).

Statistics

Statistical analyses were performed using SAS (SAS Institute, Cary, NC). Statistical significance was determined at $P \leq 0.05$ and a tendency was determined at $0.05 < P \leq 0.10$. Fecal egg count data were log transformed (lnFEC = log (FEC+100)) for normality. PROC Mixed with repeated measures was used to analyze data to account for fixed effects of genotype (HFEC or LFEC), treatment (COWP or Con), time, and their interaction on FAMACHA score, PCV, FEC, and body weight. PROC Mixed was also used to analyze effects of genotype, treatment, and their interaction on ADG, which was calculated as weight gained over the trial length of 84 days. PROC GLM was used to analyze fixed effects of genotype, treatment, and their interaction by time.

Results

Parasitological data

There was no interaction between the FEC EBV genotype and treatment with a single 2g COWP bolus three weeks post-weaning. Treatment with COWP had no effect on the FEC for the single dose in Y1 ($P = 0.16$) (Figure 2.3). Additionally, COWP treatment had no effect on PCV or FAMACHA in Y1 ($P = 0.60$ and $P = 0.35$, respectively) (Figure 2.4)

Although there was an interaction of genotype by treatment on change in FEC ($P = 0.05$) in Y1, there was no effect on PCV ($P = 0.66$).

Fecal samples were collected and run on lambs at weaning in both years to determine if the breeding scheme worked prior to the study (Figure 2.2). The LFEC lambs in Y1 had lower FEC than HFEC lambs (284 epg vs 758 epg, respectively; $P < 0.01$) and higher PCV than lambs selected for high FEC EBV (30.1% vs 29.7%, respectively; $P < 0.05$). Lambs selected for low FEC tended to have higher FAMACHA scores than those selected for high FEC in Y1 (1.3 vs 1.2, respectively; $P = 0.10$). No lambs required deworming for Y1.

Growth Data

The forage analysis for Y1 showed an average crude protein (CP) of 20.8%, average total digestible nutrients (TDN) of 73.9% and an average copper concentration of 3.6ppm. In combination with the 8.44 ppm copper concentration in the pellet, these lambs received enough copper to satisfy their nutritional requirement. The interaction between selection for genotype and treatment had no effect on body weight (Y1, $P = 0.87$) or on ADG ($P = 0.65$ and $P = 0.58$, Figure 2.4). Treatment with COWP alone had no effect on body weight for Y1 or Y2 ($P = 0.24$, Figure 2.4), or for ADG ($P = 0.78$). Lambs selected for HFEC had higher body weights than the LFEC lambs in Y1 (31.7 kg vs 28 kg, respectively; $P < 0.05$; Figure 2.4). Average daily gain was also greater for HFEC lambs in Y1 (0.15 vs 0.12 kg, $P < 0.01$; Figure 2.3).

Discussion

This study investigated the effects and interaction of two GIN mitigation strategies, COWP and selection FEC EBV on GIN infection and growth in Katahdin ram lambs. The original objective was to determine if giving a single 2g COWP bolus to lambs with high FEC EBV would allow the lambs to tolerate a natural GIN infection comparably to low FEC EBV lambs. The first year (Y1) of the study consisted of a 12-week study where lambs were randomly selected within each genotype to receive a single dose of COWP at the start of the study and samples to determine anemia level, GIN infection level and growth were collected every two weeks. Results indicated that lambs selected for low FEC EBV had lower FEC, PCV, ADG and body weights. Low FEC EBV lambs also tended to have higher PCV than the high FEC EBV lambs, while treatment with COWP had no effect on any variable. Bang et al. (1990) found that the COWP is most effective against the adult *H. contortus* (96%) and less effective against other nematode species, such as *Ostertagia* (56%). As the pre-patent period for *H. contortus* is 21 days and lambs only had three weeks post three-way deworming to get infected in the pasture, the lambs may not have had enough of an adult population of *H. contortus* to show an effect of the COWP treatment in Y1. COWP has been shown to be effective against *H. contortus* for up to 14 days and then again after day 35 (Galindo-Barboza et al., 2011). This encouraged a new objective, which was to evaluate the effects of multiple doses of COWP on GIN infection and growth of Katahdin lambs divergently selected for FEC EBV.

Year 2

Breeding Scheme

Year 2 (Y2) consisted of HFEC ewes (n = 17; average PFEC = +96%, accuracy > 62%) bred to HFEC sires (n = 2; average PFEC = +183.82%, accuracy > 74%) and LFEC ewes (n = 18; average PFEC = -50.8%, accuracy > 62%) bred to LFEC sires (n = 2; average PFEC = -90.99%, accuracy > 83%) in October 2023. Some sires (n = 3) from Y1 were used again in Y2 for connectedness. On average, the sires were 2 years old, and the ewes were 3 years old. The pairings for Y2 resulted in 39 ram lambs born from March 14 to April 1, 2024. Lambs remained with their dams on fescue-based pasture as one contemporary group until weaning.

Materials and Methods

Weaning in Year 2 (Y2) occurred on June 13, 2024 (Figure 2.1) and ram lambs heavier than 13.6 kg were selected for the study. Average lamb age at weaning was 85 days. Lambs were sired by one of four sires (HFEC sires, n = 2; LFEC sires, n = 2). Fecal samples, FAMACHA scores, body weights, and forage samples were collected and analyzed at weaning, along with all lambs receiving a three-way deworming with fenbendazole, moxidectin, and levamisole. Lambs were rested for five weeks after which fecal samples, blood for PCV, FAMACHA scores, weights, and forage samples were collected every two weeks until the conclusion of the study 16 weeks later. All samples were collected and analyzed in the same manner as in year one (Y1), with the addition of coproculture.

Lambs were randomly assigned to Con or COWP groups with equal representation of genotype. The four treatment groups consisted of HFEC-Con (n = 9), HFEC-COWP (n = 10), LFEC-Con (n = 10), and LFEC-COWP (n = 10). To ensure *H. contortus* challenge in Y2, at Week 0, all lambs were orally administered 5,000 L3 *H. contortus* larvae. Larvae were cultured as described by Bowdridge et al. (2015). At Week 4, 2 g Copasure COWP boluses were administered orally via bolus gun to the lambs in the two COWP groups and again in weeks 8 and 12. Additional fecal samples were collected each time the COWP boluses were administered to allow for larval identification through coproculture. The coproculture from Week 4 was a random sample from the entire group, but separate samples were collected for Weeks 8 and 12 by treatment group.

Lambs were raised on fescue-based pasture as a single contemporary group allowing for a natural GIN infection and were supplemented at 2% of their bodyweight with a 16% CP, 76% TDN pellet (Table 2.1). Lambs in Y2 were managed on a 0.53-hectare pasture initially and moved to a new 0.77-hectare pasture on Week 8 due to insufficient forage availability. Both pastures in Y2 were used for tall fescue but also contained a mix of other forages, such as orchard grass and white clover (Nutrient Management Plan Identification, 2022). The reported soil copper concentration was 0.2 ppm (Soil Test Report, 2022). Lambs were dewormed as needed (FAMACHA ≥3) and lambs requiring deworming treatment were removed from subsequent data analysis. Three lambs, one from the HFEC-COWP group and two from the LFEC-COWP group, died during the study.

Coproculture

Additional fecal samples were collected for coproculture in Weeks 4, 8, and 12. The samples collected in Week 4 were pooled from a random selection of at least 10 animals within the entire group to be used as a baseline as no treatment had been administered prior to this point. Fecal collection occurred before the administration of COWP boluses each time. For Weeks 8 and 12, samples were randomly collected from both the control animals and those treated with COWP but kept separate to identify potential treatment differences. Samples collected for coproculture were not kept in the cooler post collection to allow the eggs to hatch and begin the larvation process. For Week 4, there were 3 pooled 10 g samples weighed out as the group could be treated as the control, as fecals were collected prior to administration of the COWP. Weeks 8 and 12 had two 10 g samples per treatment, per sample week, for comparison between treatment groups.

A simple Baermann's apparatus was derived using two plastic cups (one large, one small), cheese cloth cut into 10.2cm x 20.3cm sections, and a rubber band. The small cup had holes punched in the bottom to allow oxygen and the larger cup was filled ¼ full of water. The 10 g fecal sample was placed into the smaller cup and the double folded cheese cloth was pulled tautly over the top of the cup and secured with the rubber band. The small cup was inverted and pushed down into the larger cup until the cheese cloth and fecal ball were just over the water, but not touching. Samples remained at room temperature (20ºC) and out of the sun for 14 days to allow the larvae to hatch and develop into the third larval stage (L3).

After the 14-day period, enough water was added to submerge the fecal matter for 8-12 hours. The fecal solution was allowed to sit for an additional 4-8 hours to allow the larvae to sink to the bottom, after which the supernatant was removed until only 20 mL remained. The remaining 20 mL was refrigerated until larval identification.

A P100 pipette was used to dispense drops of solution onto a slide. Lugol's iodine (5%) was added to each drop to kill and straighten out larvae. A 10x lens on the microscope was then used to count and identify individual larvae. The first 120 larvae found were counted and measured for the baseline (Week 4) samples. 100 larvae were counted and measured for each treatment (Con and COWP) for identification for Weeks 8 and 12 (Table 2.3). Larvae were identified by measuring the anus to tip of sheath, end of tail to tip of sheath, and overall morphology (Zajac and Conboy, 2012).

Statistics

Statistical analyses were performed in the same manner as for year 1 using SAS (SAS Institute, Cary, NC). Data on lambs requiring anthelmintic treatment were removed from analyses in the subsequent weeks after treatment. PROC Mixed with repeated measures was used to analyze data to account for fixed effects of genotype (HFEC or LFEC), treatment (COWP or Con), time, and their interaction on FAMACHA score, PCV, FEC, and body weight. PROC Mixed was also used to analyze effects of genotype, treatment, and their interaction on ADG over the 113 days of the trial. PROC GLM was used to analyze fixed effects of genotype, treatment, and their interaction by time. These data were analyzed using PROC GENMOD to evaluate the effects of genotype, treatment, and their interaction on deworming.

Results

Parasitological data

The only interaction between FEC EBV genotype and treatment with COWP was reduced PCV for the HFEC-COWP lambs in comparison to the HFEC-Con lambs (29.3% vs 30.0%, respectively; $P < 0.05$) for Y2. Although statistically significant, this is not biologically so. There were no other interactions between genotype and treatment for Y2. Treatment with COWP had no effect on FEC for multiple doses in Y2 ($P = 0.23$, Figure 2.5). Lambs treated with COWP in Y2 showed no difference from the control lambs for FAMACHA score ($P = 0.91$), but had a decreased PCV (29.1% vs 30.7%, $P < 0.05$) (Figure 2.6).

There was a significant increase in FEC for the HFEC lambs in comparison to the LFEC lambs following the first treatment (1256 epg vs 718 epg, respectively; $P < 0.01$) (Figure 2.7) in Y2. Following the second treatment administered in Week 8, there was no effect of treatment on either FEC or PCV (Figure 2.8), but LFEC lambs continued to have a smaller increase in FEC (162 epg vs 462 epg; $P < 0.01$) (Figure 2.7). Following the third treatment in Week 12, there was a smaller increase in FEC in lambs dosed with COWP treatment than the control lambs (102 epg vs 290 epg, respectively; $P < 0.05$) (Figure 2.7).

Fecal samples were collected and run on lambs at weaning in both years to determine if the breeding scheme worked prior to the study (Figure 2.2). The LFEC lambs in Y2 also had lower FEC than the HFEC lambs (648 vs 1177 epg, respectively; $P < 0.01$), but selection for genotype had no effect on PCV ($P = 0.94$). Lambs selected for low FEC had no effect on FAMACHA score in Y2 ($P = 0.16$). Anthelmintic treatment was required to treat 30% of the

HFEC-Con and 20% of the LFEC-COWP lambs in Y2 due to FAMACHA scores equal or greater than 3, which led to their removal from the data post-treatment.

Growth Data

The forage analysis for pasture 1 (P1) in Y2 showed an average CP of 20.6%, average TDN of 73.6% and an average copper concentration of 3.5ppm. Pasture 2 (P2) had an average CP of 20.7%, average TDN of 73.7% and an average copper concentration of 3.6ppm. Combined with the pellet's copper concentration of 8.44ppm, these lambs were receiving adequate copper to meet their nutritional requirements. The interaction between selection for genotype and treatment had no effect on body weight ($P = 0.36$) or on ADG ($P = 0.58$, Figure 2.6). Treatment with COWP alone had no effect on body weight for Y2 ($P = 0.65$, Figure 2.4), or for ADG ($P = 0.78$). Selection for FEC EBV had no effect on either body weight (P = 0.87) or ADG for the lambs in Y2 (P = 0.42).

Discussion

For the second year (Y2) of the study, lambs were given 5 weeks post-weaning on pasture and were orally dosed with 5,000 L3 *H. contortus* at the start of the project, a month before receiving the first COWP bolus to ensure infection. Burke and Miller (2006) have demonstrated multiple low doses of COWP to be as effective as levamisole in reducing FEC but the Y2 study with lambs exposed to both natural and artificial GIN infection did not support this.

There are many possible explanations for this. According to the forage analysis and the nutritional analysis of the supplemented pellet, the lambs were provided with sufficient copper if the normal levels of molybdenum were present. There is no historical evidence of copper deficiency at SWAREC in Glade Spring, however the range between deficiency, satisfactory and toxic is very small. The symptoms for copper deficiency can present as loss of pigment, diarrhea, anemia and ataxia, which can also be symptoms of copper toxicity (Veterinary handbook for cattle, sheep and goats). Without a necropsy, it could be difficult to determine which is the cause of death. Liver biopsies were not performed on these lambs, but it is most probable that the lambs were not copper deficient. Had they been, there might have been a more drastic response against the GIN as the body would have had the necessary tools to respond better.

An important consideration when using COWP is the location of degradation. According to Copasure, the gel capsule degrades as it passes through the rumen, allowing the particles to settle in the reticulum, omasum and abomasum. The location of the *H. contortus* within the abomasum could explain why they are one of the few GIN negatively impacted by COWP. If the boluses were made such that they degraded later in the digestive tract, or lasted for longer, there might be a longer-term effect against the GIN.

A possible explanation for this could be the antagonistic relationship of *H. contortus* with other GIN species as discussed by Evans et al. (2023) where the blood feeding activity of *H. contortus* allows for improved establishment of other GIN that induce immune responses that are, in turn, harmful to the *H. contortus.* This is supported by the findings of Lello et al. (2018) where *Trichostrongylus colubriformis* (*T. colubriformis*) were used and found to have negative impacts on the establishment of *H. contortus* in Merino sheep.

Selection for low FEC EBV works as a strategy to mitigate the effects of *H. contortus*. The lambs in Y2 treatment groups were smaller than Y1, which could have contributed to the reduction in significant findings. In Y2, lambs had two weeks longer to adapt to the natural infection from pasture in addition to being nine days older at weaning. It would be expected that they were heavier on average than the lambs in Y1. Despite being older, lambs in Y2 were lighter at the start of the project than lambs in Y1. The lower weights could be related to the drought experienced in Virginia at this time that impacted forage yield, or it could be related to the lambs being managed on a much smaller pasture in Y2 than in Y1 (0.53 hectares to 2.06 hectares, respectively). Regardless, genetic selection is a tool that has been proven to reduce FEC, while COWP still requires further research to determine the mechanism of action, persistence within the abomasum and efficacy in various breeds.

Table 2.1 Average estimated breeding values (EBV) for sires and dams used in this study.

Year 1							Year 2						
	n	WWT[3] (kg)	PWWT[3] (kg)	WFEC (%)	PFEC[2] (%)	Mat. Hair index[4]		n	WWT[3] (kg)	PWWT[3] (kg)	WFEC (%)	PFEC[2] (%)	Mat. Hair index[4]
HFEC Dam Average[1]	18	1.5	3.3	16.3	36.3	102.2	HFEC Dam Average[1]	17	1.2	1.8	47.1	96.0	102.2
LFEC Dam Average[1]	23	1.2	1.8	-33.8	-55.0	101.7	LFEC Dam Average[1]	18	1.5	2.1	-43.1	-61.0	102.1
HFEC Sires Average[1]	3	1.0	1.8	109.8	195.4	103.2	HFEC Sire Average[1]	2	1.1	2.3	142.0	183.8	103.1
LFEC Sires Average[1]	4	1.8	1.6	-76.5	-88.0	102.8	LFEC Sire Average[1]	2	2.0	2.6	-88.4	-91.0	102.9

[1] Dams and sires were selected for either low (LFEC) or high (HFEC) fecal egg count estimated breeding value (EBV)
[2] Selection for either low or high FEC EBV was based on post-weaning fecal egg count EBV (PFEC)
[3] Weaning and post-weaning weight EBVs (WWT and PWWT, respectively) were similar across groups
[4] Maternal Hair Index (Mat. Hair Index) predicts lamb weight weaned per lambing ewe by combining weaning weight (WWT), maternal weaning weight (MWWT), number of lambs born (NLB) and number of lambs weaned (NLW) was similar across groups

Table 2.2 Nutrient table for pellet supplemented at 2% body weight in both years

Nutrient	Dry Matter (%)
Dry Matter	89.43
Protein	16.48
TDN	76.27
Fat	3.95
Fiber	17.05
Calcium	1.03
Phosphorus	0.56
Cu, ppm	8.44

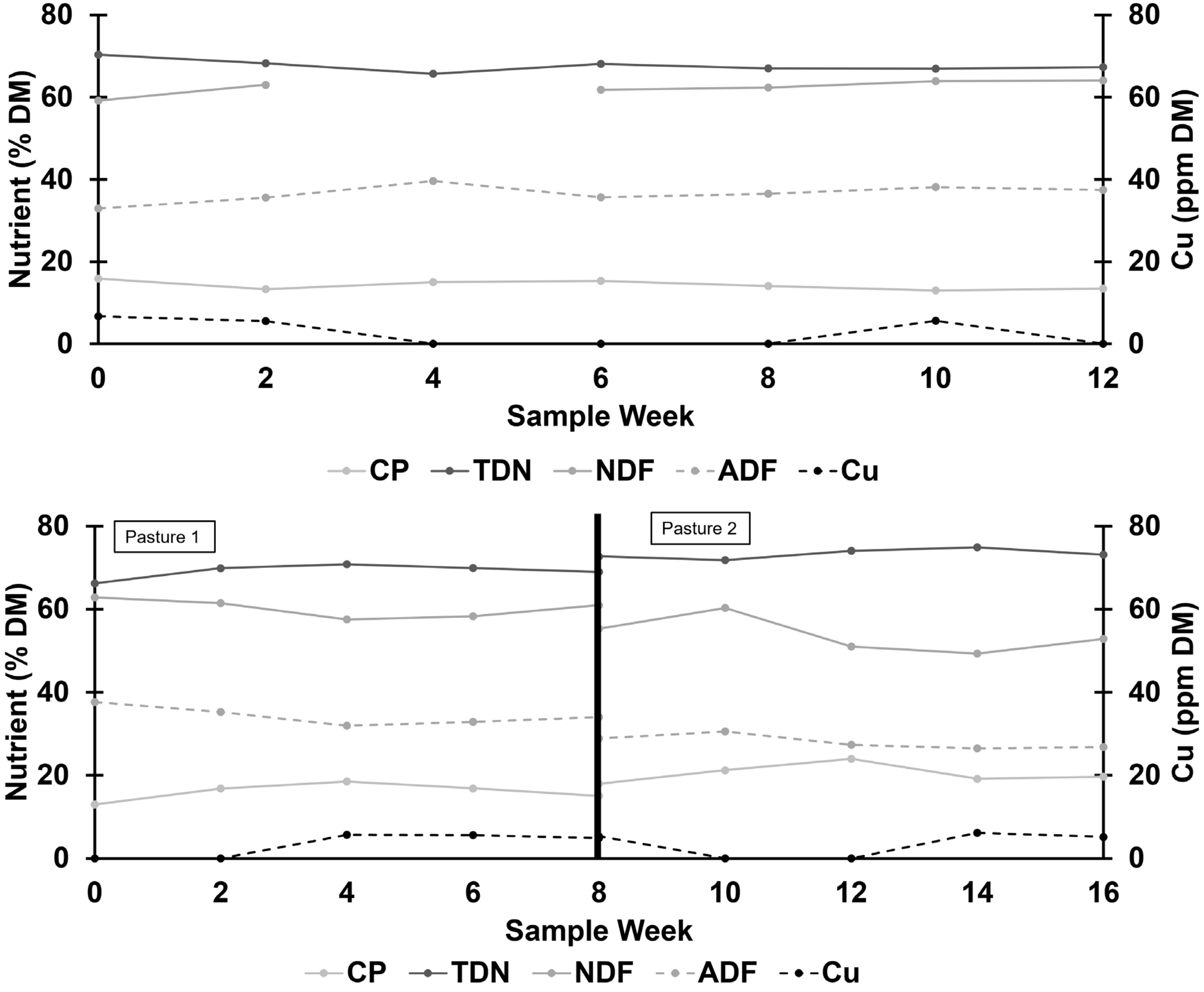

Figure 2.1 Forage analysis both Year 1 (Y1) and Year 2 (Y2)

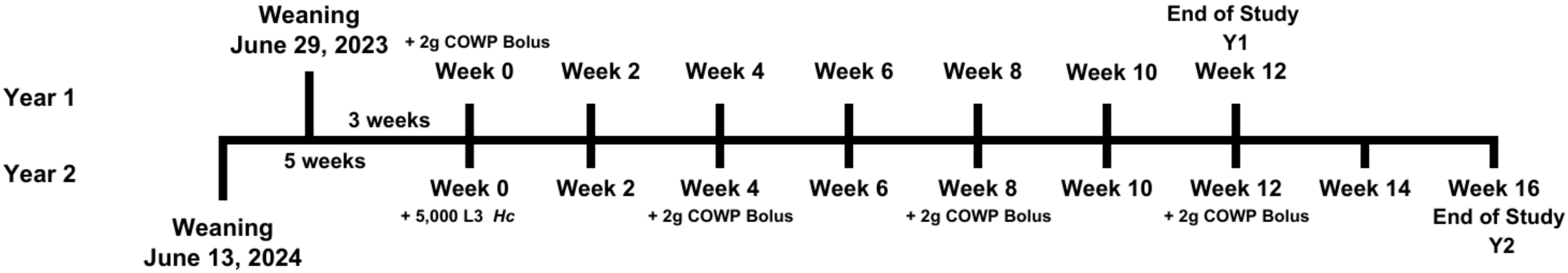

Figure 2.2 Timeline for Year 1 (Y1) and Year 2 (Y2)
Lambs in Y1 were weaned on June 29, 2023, at an average lamb age of 74 days. At weaning, lambs were dewormed with fenbendazole, moxidectin and levamisole. Lambs were rested for three weeks post-weaning to account for the withdrawal period of moxidectin (21 days). Lambs within each genotype, high (HFEC) or low (LFEC), were randomly assigned to either the control (Con) or copper oxide wire particle (COWP) groups. At Week 0, COWP groups were administered a 2g Copasure® COWP bolus orally. Fecal egg counts (FEC), packed cell volume (PCV), weights, and FAMACHA scores were collected every two weeks until the end of the study. Lambs in Y2 were weaned on June 13, 2024, at an average of 85 days of age. Lambs were dewormed with the same dewormers as in Y1 and rested for five weeks. All lambs were dosed with 5,000 L3 *Haemonchus contortus* at Week 0. Lambs were randomly assigned to either Con or COWP treatment within each genotype (LFEC or HFEC). COWP lambs were dosed with 2 g Copasure® COWP bolus in Weeks 4, 8, and 12. Fecal egg count, PCV, weights and FAMACHA scores were collected every two weeks until the conclusion of the study in Week 16.

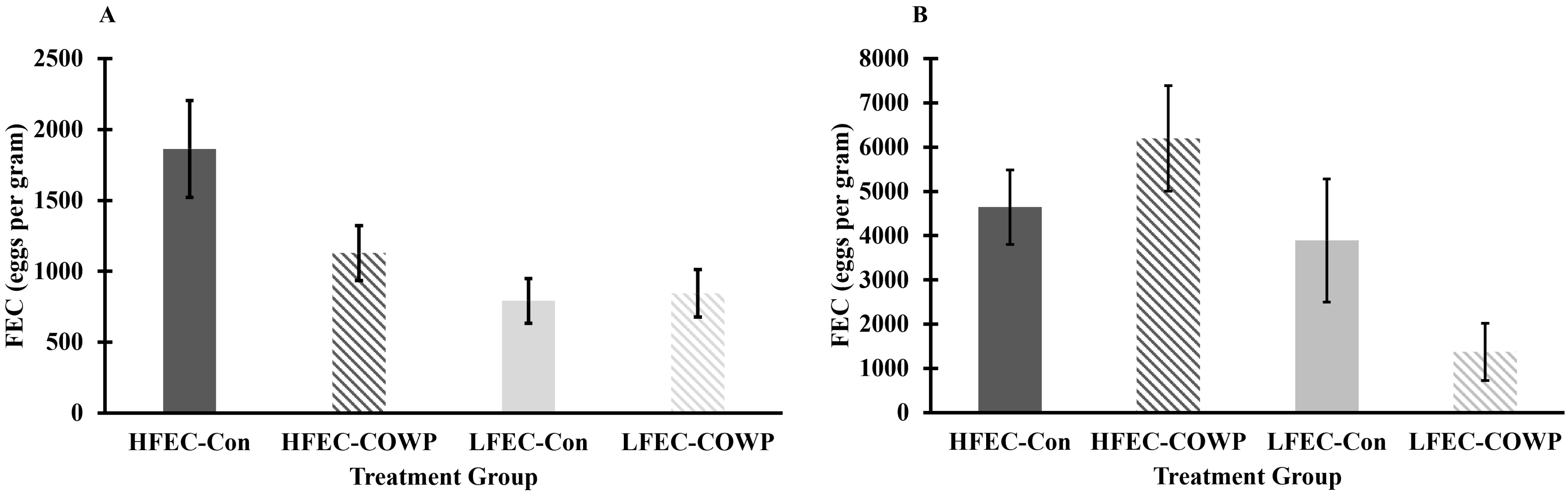

Figure 2.3 Weaning fecal egg counts (WFEC) by treatment group for Year 1 (Y1) and Year 2 (Y2) Weaning fecal samples were collected in both years. Lambs were, on average, 74 days old in Y1 (A) and 85 days old in Y2 (B). Lambs in Y2 had higher WFEC than lambs in Y1.

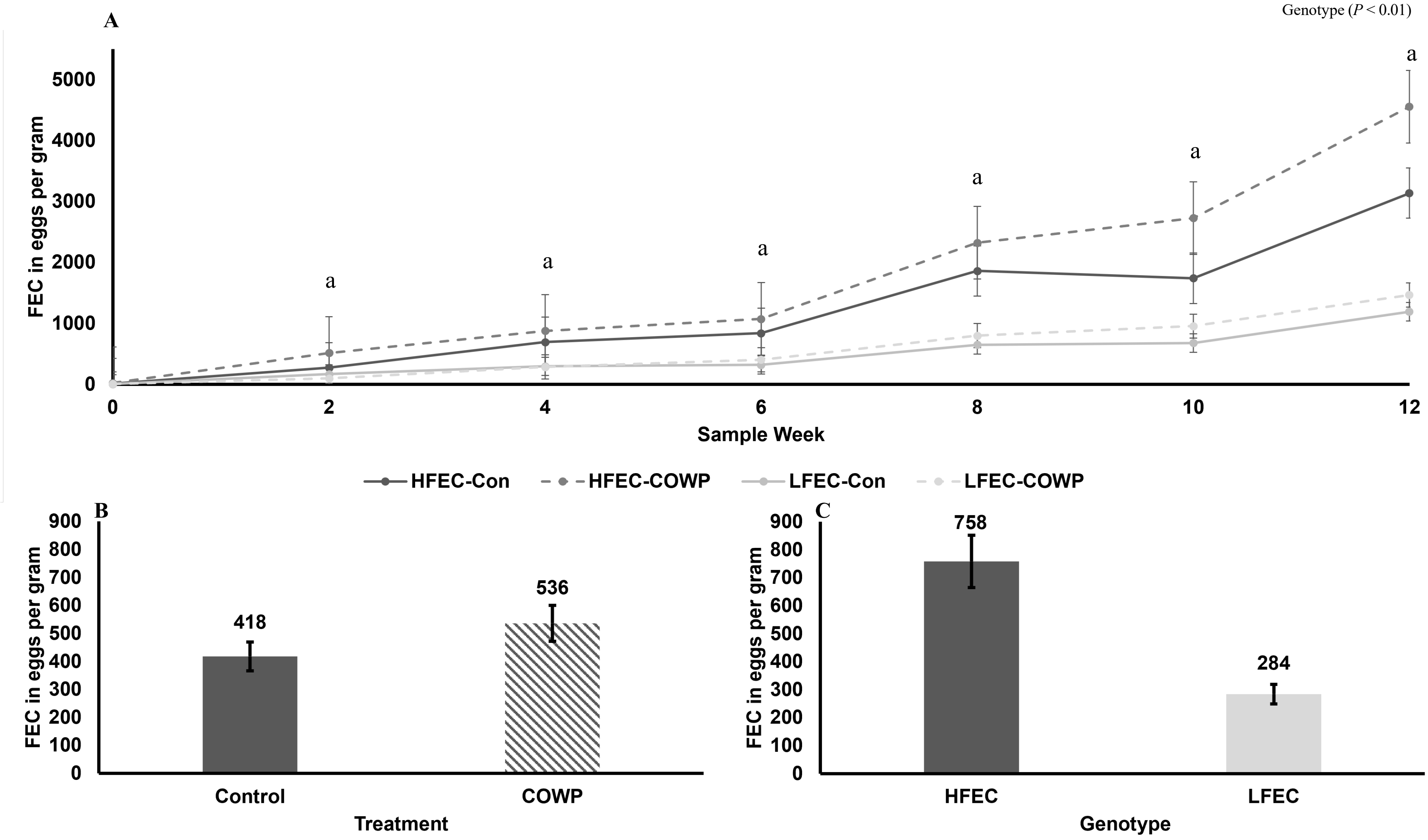

Figure 2.4 Fecal egg counts between treatment status and genotype in Year 1 (Y1)
Ram lambs were divergently selected for either high (HFEC) or low (LFEC) fecal egg count estimated breeding values (FEC EBV) and further divided into the control (Con) or copper oxide wire particle bolus treated (COWP) groups. COWP was administered at Week 0. Fecal samples were collected every two weeks from Week 0 to Week 12 (C) to compare between treatments (A) and between genotype (B). (a) denotes when genotype had an effect on FEC.

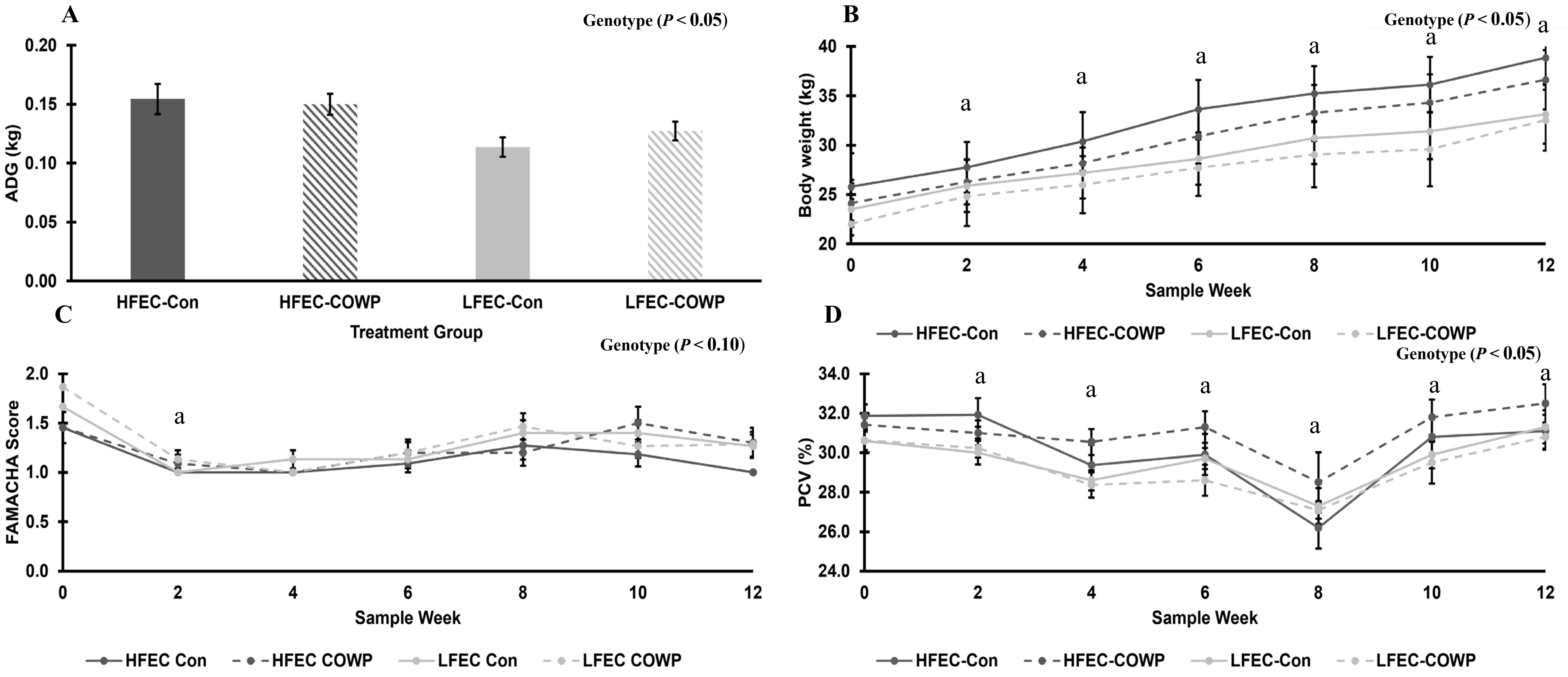

Figure 2.5 Growth performance and GIN infection levels in Year 1 (Y1)

Lamb weight (B), FAMACHA score (C), and packed cell volume (PCV) (D) were measured every two weeks, from the start of the project (Week 0) to the end of the project (Week 12). Overall average daily gain (ADG) was calculated by subtracting end weight from start weight and dividing by the number of study days (84).

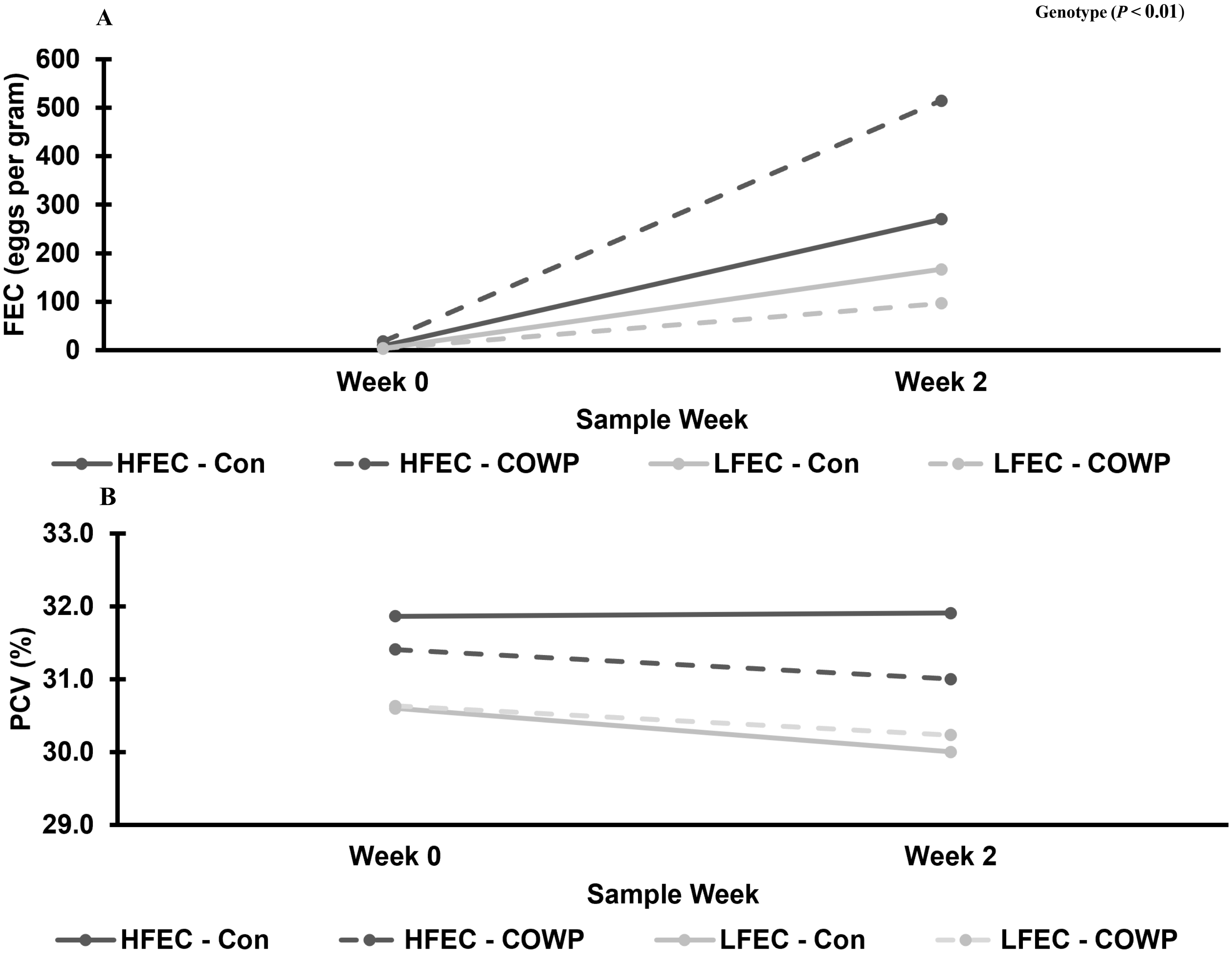

Figure 2.6 Changes in fecal egg count (FEC; A) and packed cell volume (PCV;B) two weeks post copper oxide wire particle treatment in Year 1 (Y1)

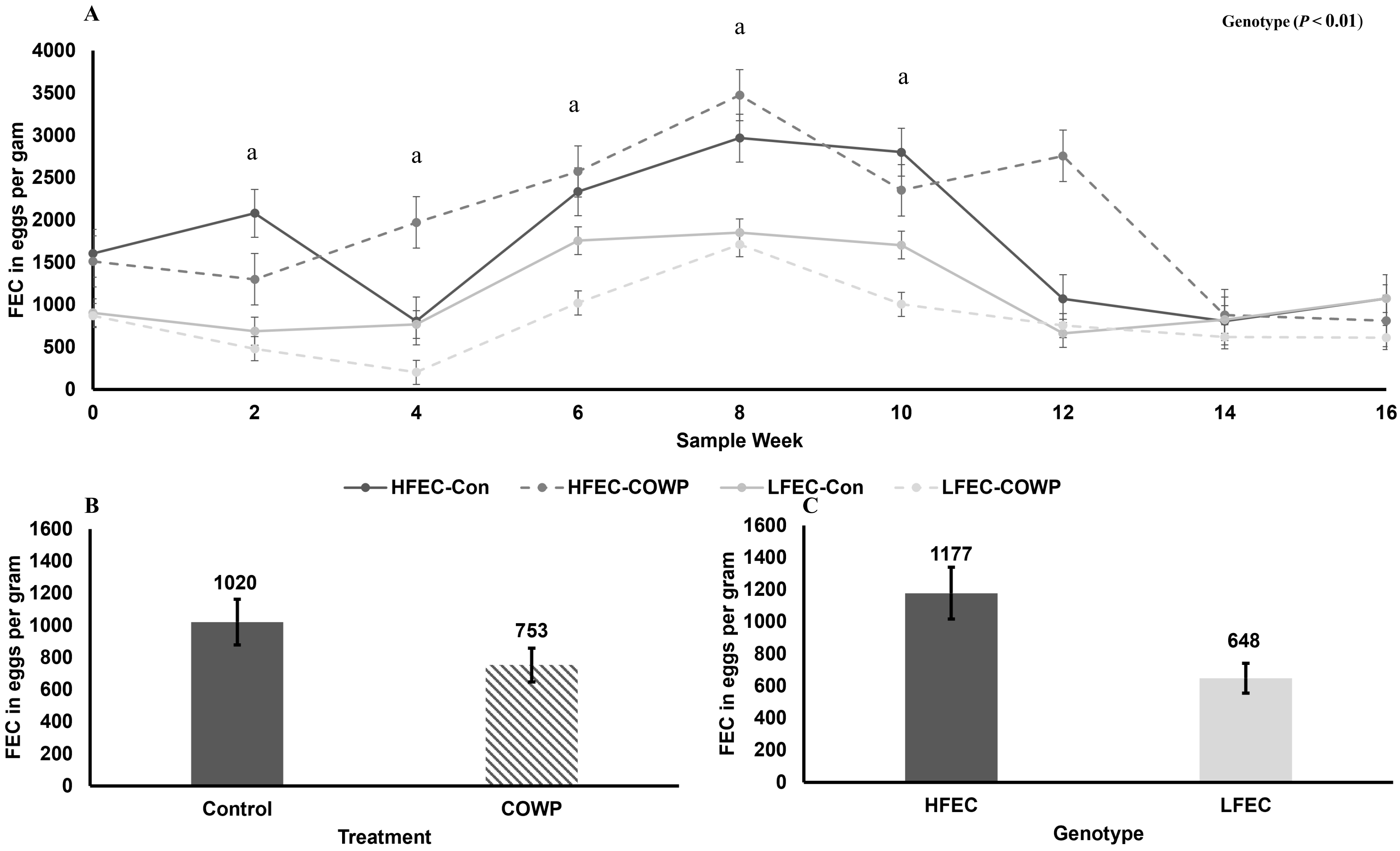

Figure 2.7 Fecal egg counts between treatment status and genotype in Year 2 (Y2)
Ram lambs were divergently selected for either high (HFEC) or low (LFEC) fecal egg count estimated breeding values (FEC EBV) and further divided into the control (Con) or copper oxide wire particle bolus treated (COWP) groups. The COWP was administered in weeks 4, 8 and 12. Fecal samples were collected every two weeks from week 0 to week 16 (C) to compare treatments (A) and between genotype (B). (a) denotes times when genotype had an effect on FEC.

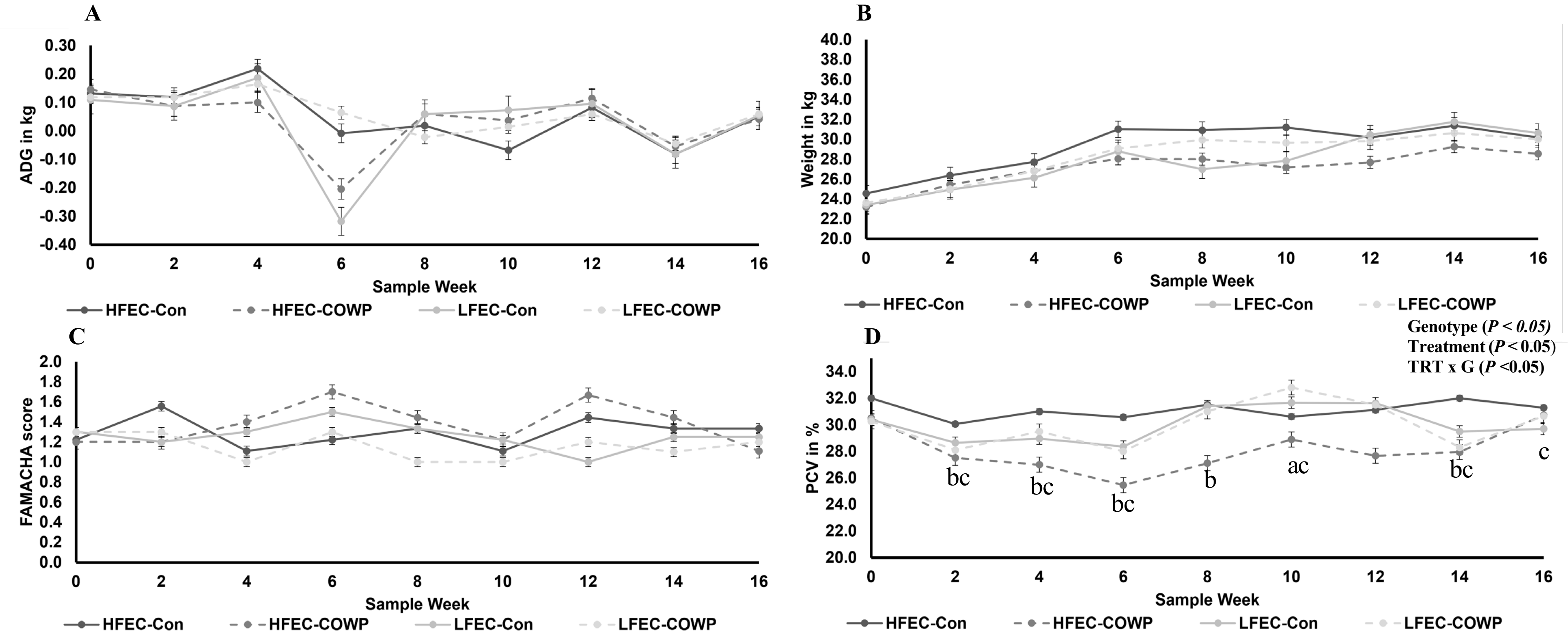

Figure 2.8 Growth performance and GIN infection levels in Year 2 (Y2)

Lamb weight (B), FAMACHA score (C), and packed cell volume (PCV) (D) were measured every two weeks, from the start of the project (week 0) to the end of the project (week 16). Overall average daily gain (ADG) was calculated by subtracting end weight from start weight and dividing by the number of study days (113). (a) denotes times when genotype had an effect, (b) denotes when treatment had an effect, and (c) denotes times when the interaction between genotype and treatment had an effect.

Table 2.3 Larval analysis from coprocultures for Weeks 4, 8 and 12 in Year 2

	Week 4	Week 8		Week 12	
	Con	**Con**	**COWP**	**Con**	**COWP**
Trichostrongylus	16%	15%	17%	14%	33%
Teladorsagia	12%	29%	44%	20%	10%
Haemonchus	**1%**	**5%**	**6%**	**5%**	**5%**
Cooperia	15%	51%	32%	61%	52%
Strongyloides	56%	0%	0%	0%	0%
Oesophagostomun	0%	0%	1%	0%	0%

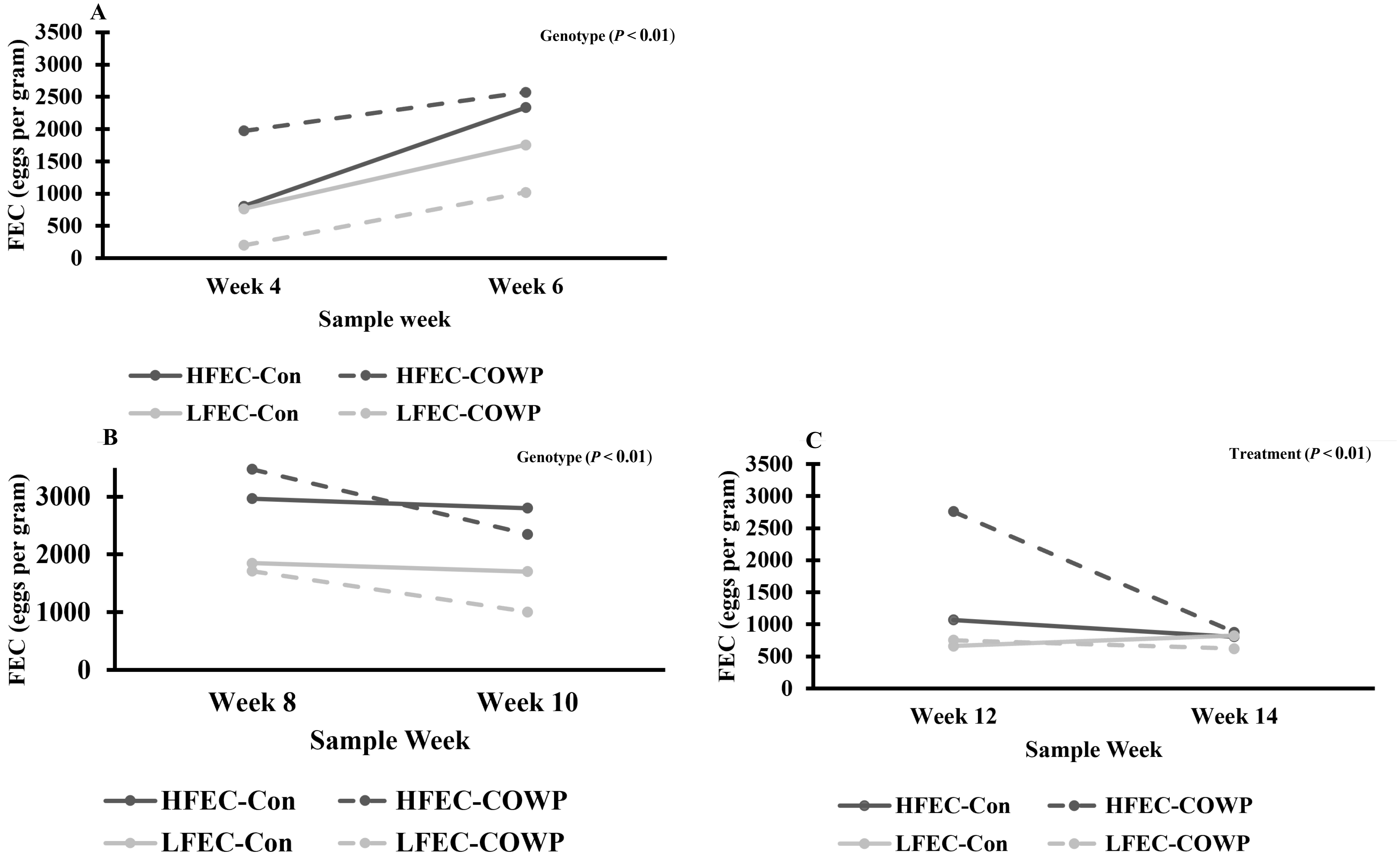

Figure 2.9 Changes in fecal egg count (FEC) two weeks post copper oxide wire particle treatment in Year 2 (Y2)
Changes in FEC two weeks post treatment with COWP for Week 4 (A), Week 8 (B), and Week 12 (C

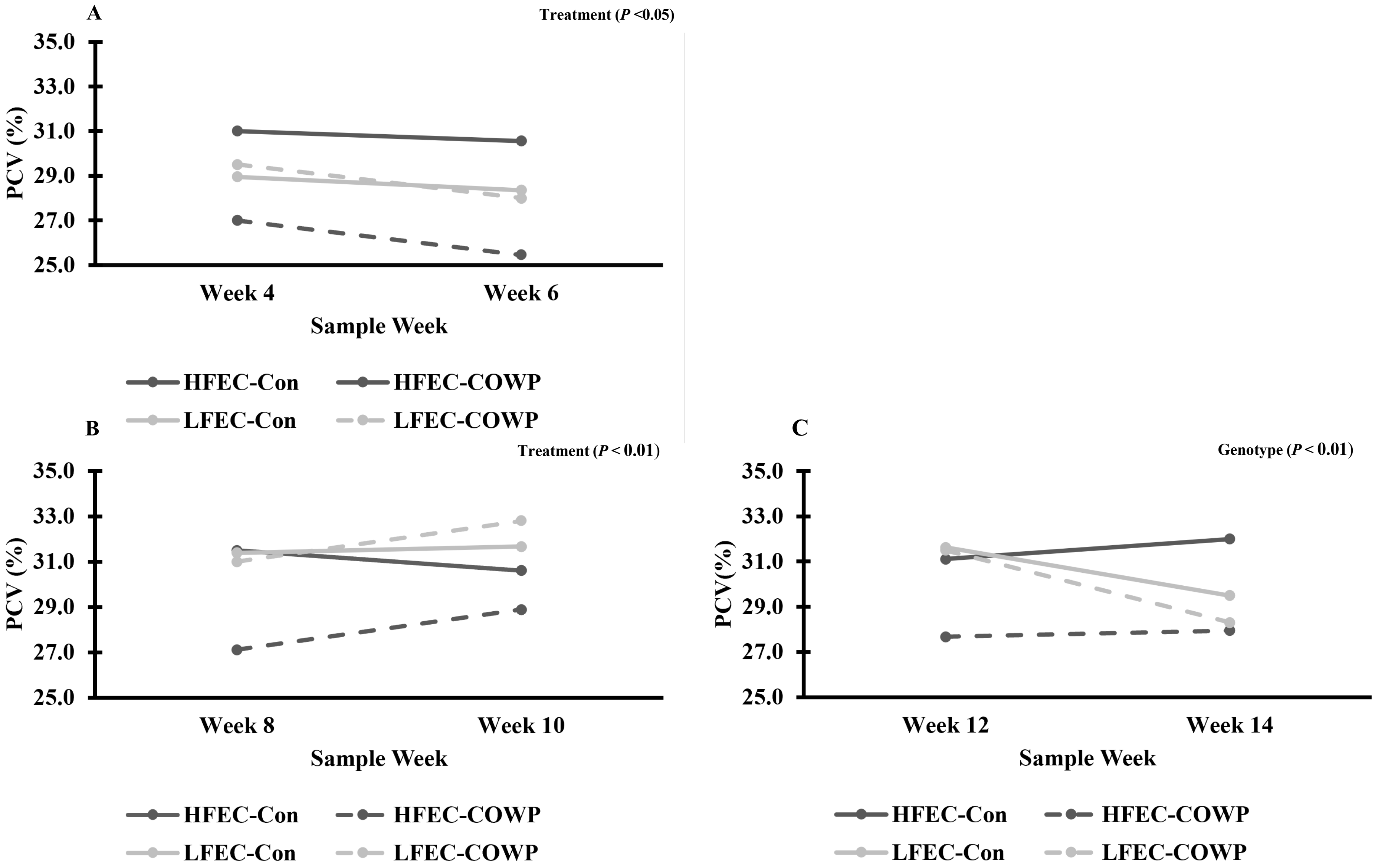

Figure 2.10 Changes in packed cell volume (PCV) two weeks post copper oxide wire particle (COWP) treatment in Year 2 (Y2)
Changes in PCV two weeks post treatment with COWP for Week 4 (A), Week 8 (B), and Week 12 (C)

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CHAPTER III: IMPLICATIONS

The threat posed by gastrointestinal nematodes (GIN) to the sheep industry in the United States is significant. The development of anthelmintic resistance within parasite populations necessitates further mitigation strategies outside of chemical anthelmintics. *Haemonchus contortus* is especially detrimental to the southeastern region of the United States so it was our nematode of focus. This study investigated the effects and interaction of two GIN mitigation strategies, copper oxide wire particles (COWP) and selection for fecal egg count (FEC) estimated breeding values (EBV) on parasitism and growth in Katahdin ram lambs. Year 1 indicated that lambs selected for Low FEC EBV had lower FEC, PCV, ADG and weight gain. Low FEC EBV lambs also tended to have higher PCV than the high FEC EBV lambs, while treatment with COWP had no effect on any variable. Bang et al. (1990) found COWP to be 96% effective against the adult *H. contortus,* 56% effective against Ostertagia and ineffective against *Trichostrongylus.* It remains unknown why COWP negatively impacts the blood feeding *H. contortus* specifically, especially since the mechanism of action is not fully understood. Further research could be done to better understand why COWP affects *H. contortus* so much more than other species.

In the second year of the study, lambs naturally attained an infection on a contaminated pasture in addition to receiving an oral dose of 5,000 L3 *H. contortus* at the start of the project, 4 weeks prior to the first treatment with COWP. Burke and Miller (2006) indicated that multiple low doses of COWP are as effective as levamisole in reducing FEC but the Y2 study with lambs exposed to both natural and artificial GIN infection did not support this. Results indicated that only selection for FEC EBV had any effect on FEC, but the COWP treated lambs did have reduced PCV. This contradicts the findings of Spickett et al. (2012), where goats treated with

COWP had increased PCV for the two weeks post-treatment in comparison to the control group. Could this be due to sheep having lower tolerance for copper than goats? It would be interesting to explore further to determine if a correlation or causation exists between the two.

If this study were to be repeated, increasing the number of subjects would be needed, along with increasing the frequency of sample collection. Sampling weekly or even daily might have shown a clearer picture of the effects due to COWP treatment. Additionally, other breeds, especially wool breeds, could be used to determine the interaction between selection for FEC EBV and treatment with COWP and to further explore different sensitivities to COWP.

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