ABSTRACT

NEWSOME, McKAYLA ASHTON. Effects of Grazing Novel or Toxic Endophyte-Infected Tall Fescue during Mid-Gestation on Cow Performance and Subsequent Heifer Calf Performance. (Under the direction of Dr. Daniel H. Poole).

Consumption of toxic endophyte-infected tall fescue results in poor reproductive performance. The objective of this two-year study was to examine physiological changes in pregnant cows grazing tall fescue to develop a better understanding of the factors that contribute to the poor reproductive performance attributed to fescue toxicosis. The second objective was to then evaluate the birth weights and placental characteristics of the heifer calves from those cows that grazed tall fescue during their second trimester of gestation. Pregnant Angus and Simmental-Angus cows were blocked by age (2-3, 4-7, and >7 y), body weight (BW), and breed; and then randomly assigned to graze either novel (EN; <5% infection rate; n=27 Year 1, n=16 Year 2) or toxic endophyte-infected tall fescue (E+; 99% infection rate; n=27 Year 1, n=17 Year 2). Weekly BW, body condition scores (BCS), hair coat scores (HCS), and hair shedding scores (HSS) were collected from mid-April through July of 2017 (Year 1) and 2018 (Year 2) when ergot alkaloid concentrations are greatest in the forage. Blood samples were collected to measure progesterone and prolactin concentrations. Forage samples were taken every 2 weeks to determine forage quality and composition. Data were analyzed using the MIXED procedure of SAS with repeated measures examined for effects of age, treatment (novel EN or toxic E+) and time. Statistical significance was determined at $P<0.05$ and a tendency at $0.05 \leq P \leq 0.10$. Year 1 pastures consisted of 69% and 67.5% available fescue for the novel and toxic endophyte-infected pastures, respectively, and Year 2 pastures consisted of 90.3% and 86.9% available fescue for novel and toxic endophyte-infected pastures, respectively. Average daily gain tended to be higher in EN cows than E+ for Year 1 (0.16, 0.01 kg/d, respectively; $P=0.09$). Year 2 cattle grazing EN

pastures had higher average daily gain than those cows grazing E+ pastures (0.73, 0.27 kg/d, respectively; P <0.0001). Cows on EN pastures had greater BCS compared to cows on E+ pastures for both Year 1 (6.09, 5.77, respectively; *P*<0.05) and Year 2 (5.98, 5.92, respectively; P=0.009). Similarly, an age effect was observed with mature (4-7 and >7 y) cows having higher scores when compared to younger cows for Year 1 (6.0, 6.1, and 5.7, respectively; *P*<0.05) and Year 2 (6.06, 6.13, and 5.67, respectively; P=.0013). The HCS and HSS were greater in cows on E+ pastures compared to cows on EN pastures for Year 1 (*P*<0.05), but not for Year 2 (HCS: P=0.06 and HSS: P=0.83). The HSS were greater in the >7 y cows in Year 1 (2.69) compared to other age groups (2.40, 2.51, for 2-3 and 4-7 y, respectively, *P*<0.05) on E+ pastures, whereas no age differences in HSS were observed in cows on EN pastures. By d21 of Year 1 of the grazing period, cows on EN pastures displayed a greater ability to shed hair compared to cattle on E+ pastures (*P*<0.0001), which continued throughout the remainder of the grazing period. Progesterone concentrations in E+ cows in Year 1 (3.75 ng/mL) and Year 2 (3.80 ng/mL) were decreased throughout the grazing period compared to EN cows in Year 1 (6.53 ng/mL, *P*<0.05) and Year 2 (5.25 ng/mL, P<.0001). Once the cows calved, several measurements were taken including gestation length, birth weight, placenta weight, and cotyledon weight. There were numerical differences between the treatment groups, however there were no significant values. Future studies will follow the production life of the heifers to see the effects that their intrauterine environment during the second trimester had on their reproductive performance.

Effects of Grazing Novel or Toxic Endophyte-Infected Tall Fescue during Mid-Gestation on Cow Performance and Subsequent Heifer Calf Performance

by
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DEDICATION

This thesis is dedicated to the numerous individuals who have supported me throughout my life and college career. Without my family, I would never have had the courage to leave my comfort zone and the only home I have ever known to pursue my dreams of working in the animal agriculture industry. Their constant support and encouragement has helped me stay strong and learn to appreciate the opportunities that I have been blessed with in life.

To my parents, who taught me that hard work, determination, and standing up for myself will allow me to achieve my goals and give me the strength to overcome obstacles by living as examples of that for me.

This thesis is also dedicated to my fiancé, Jacob, who I met within my first few weeks of my undergraduate career and became best friends with. Your constant love, support, listening skills, pep talks, and understanding has done more than you can ever imagine getting me through these last five and half years of college. I cannot wait to marry you and start a life together.

BIOGRAPHY

McKayla Ashton Newsome was born in Winston-Salem, North Carolina to parents Brad and Vickie Newsome, but grew up in King, North Carolina along with her two younger sisters; Madeline and Meredith Newsome. McKayla developed an interest in agriculture from an early age by growing up on a poultry breeder operation and commercial cow-calf farm. Her love of animals began with her dogs, cats, horses, and pet goat as a toddler and then grew to several other livestock species as she was exposed to others that her father would often bring home unexpectantly. McKayla was involved in 4-H as a child and exhibited sheep, goats, and cattle in the local fairs. Her true interest for cattle began in middle school when her family decided to re-enter the cattle business after taking a break for a couple of years to focus on other farming aspects. McKayla enjoyed learning new management strategies and techniques for the herd and developed the identification system, record keeping system, and vaccination protocol that they still use today; and also orders any supplies that is needed on the farm for the various species of livestock.

McKayla graduated from West Stokes High School as the Valedictorian in May 2013 and then continued on to NC State University to pursue a bachelor's degree in Animal Science with a minor in Agribusiness Management. Her interest in furthering her knowledge and education in the livestock industry and reproductive physiology led her to pursue a master's degree at NC State University in January 2017. During her time in graduate school, McKayla studied fescue toxicosis and its effects on reproduction and fetal programming in beef cattle. She also assisted with several other projects in the beef research groups of NC State where she diversified herself in several areas of research. After completing her master's degree in December 2018, McKayla will marry her best friend and college sweetheart, Jacob, in April 2019 and will work in the animal production and research industry near her home in western North Carolina.

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The graduate and undergraduate students that I have had the pleasure of working with have by far been one of the best parts of my graduate experience. I have made friends that I will have for a lifetime. Kyle Mayberry and Becky Poole have been the best lab mates that I could have asked for and have helped me immensely during my project and time here. I can honestly say that my graduate school experience would have not been nearly as enjoyable without their willingness to work together on projects and the constant supply of laughs along the way. I also would not have accomplished nearly as much in my research if it were not for the outstanding jobs of several undergraduate students, including Ruby Monn, Garrett Williams, and Anna Smith, who were always willing to help with tasks. Several other graduate students including Sam Ingram, Caitlyn Armstrong-Price, Jeffrey Wiegert, Jennifer Moore, Jordan Cox-O'Neil, Grace Ott, and James Quick have made my graduate school experience and membership of the Polk 208 office one that I will forever remember and be thankful for. I can only hope that I will get to experience as great of a work family in my future career as I have during my time in Polk Hall.

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Without such an extensive support system I would not have accomplished near the amount that I have today. The saying “it takes a village” is so true, and luckily, I have a strong village.

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INTRODUCTION

The Southeast United States has several successful agriculture commodities that support the population and farm families, including beef cattle production. Cow-calf herds comprise the majority of the beef cattle production in the area since 70% of the calves being produced are sold at weaning instead of being kept for replacements or finished out for meat (McBride and Mathews, 2011). Cow-calf production dominates the area because of the moderate climate and opportunity for forage growth and production for a large portion of the year. The majority of the producers have smaller herds with the average size being around 25 cows for each producer. Land is mostly utilized for crops or in forest land, so there are many producers who utilize smaller pieces of land in close proximity for their cattle operations. Many producers use cattle as a supplemental income or part-time position while they have full time careers elsewhere, so the cheapest and most time efficient methods are usually conducted for this reason, especially when it comes to pasture management.

The most abundant and popular forage that is used on beef cattle farms in the Southeast United States is a cool season, perennial forage called endophyte-infected tall fescue (Lolium arundinaceum [Schreb.] Darbysh), with the most common variety called 'Kentucky-31' (KY-31). It is estimated that the United States has over 8.5 million cattle grazing tall fescue pastures (Hoveland, 1993). The forage is economically important and occupies more than 35 million acres across the United States and can be found in various locations including parks, playgrounds, athletic fields, lawns, along highways, waterways, and in fields that are used for hay production or pasture. The forage has many positive characteristics which include the ease of establishment, long grazing season, its ability to survive harsher conditions such as drought, insect damage, and overgrazing, which has made it the popular and most commonly used forage throughout the Southeast United States. The forage, however, has a downside to its popularity and use because of its toxic properties to the animals that depend on it for grazing. The plant has a symbiotic relationship with an endophytic fungus (*Epichoë coenophiala*) that can be found in the plant that produces toxic ergot alkaloids. These toxic properties can induce a syndrome in cattle that is referred to as fescue toxicosis. The symptoms of fescue toxicosis include overall reduced reproductive performance, reduced hair shedding and the appearance of rough hair coats, reduced average daily gains, reduced calf growth and performance, disruption of hormone profiles, and decreases in overall cattle productivity.

There have been new cultivars of fescue introduced to the market to help remedy the issue of fescue toxicosis and reduce the negative effects in cattle. The cultivars are either endophyte-free tall fescue or novel endophyte-infected tall fescue. The endophyte-free version does not contain the toxin-producing endophyte; therefore ergot alkaloid toxins are not produced. The issue is that the plant does not contain the symbiotic relationship with an endophyte that helps it survive. The novel endophyte-infected tall fescue version contains an endophyte, yet the endophyte does not produce the toxins so that the forage is safe for animal consumption and does not cause the syndrome. Novel endophyte has become the next best option to endophyte-infected tall fescue when considering the different varieties of tall fescue to plant. The possible issue is pasture renovation and the extra steps that it may take to have a successful, non-toxic stand without the toxic version invading the field.

There are still questions about comparing the performance of cattle on each forage to see if renovating pastures with novel fescue is worth the risk, money investment, and time investment. The purpose of this study was to look into the concept of fetal programming when referring to novel versus toxic endophyte-infected tall fescue to see if future generations can be improved reproductively by grazing novel endophyte-infected tall fescue rather than toxic endophyte-infected tall fescue. The majority of beef cattle herds in the Southeast United States utilize a fall calving system. This means that the cows are pregnant during one of the peak periods during the year for ergot alkaloid toxins, which is in the late spring and early summer. It has been proven that the dam's nutrition and environmental factors during pregnancy can determine the health and performance of the offspring (Duckett et al., 2014). This study used the second trimester of gestation, when heifer calf fetuses experience the majority of muscle and ovary development, as the treatment period to see how the dams respond to different forages and then how the calves perform based on their *in utero* exposure to either toxic endophyte-infected tall fescue or novel endophyte-infected tall fescue.

CHAPTER 1

LITERATURE REVIEW

Brief History of Beef Cattle

With the thousands of cattle that are present in the United States today, it is hard to believe that they are not native to the North American continent. Cattle were introduced to the Caribbean islands by Christopher Columbus during the 1490's. As colonists continued to come to America to make a home, they brought cattle from different areas including Great Britain, continental Europe, and some from Africa. The majority of the cattle were from Great Britain (Herring, 2014). The first breed to be considered improved or modified that was brought to the United States was the Durham, otherwise known as the Shorthorn (ASA, 2012). The U.S. herd book for the breed was started in 1846. There was an influx of many new cattle breeds into the United States in the late 1960's and early 1970's (Herring, 2014). There are differences between breeds in the same area or county, but there are similarities between breeds that come from the same country of origin. For example, British breeds are known for their good fertility, reaching puberty at an early age, good fat deposition and body reserves, and desirable longevity. The breed that is recognized as being native to America or an American breed is Brahman or any Brahman-influenced composites. These animals are known for their maternal ability, longevity, and resistance to heat and parasites. The Brahman breed was developed from Zebu (Bos indicus) cattle in Texas and Louisiana so that they would be able to handle the environment (Herring, 2014).

Beef Cattle Breeds and History

There are around 1,000 breeds of cattle that exist throughout the world that have been developed for the area or a specific purpose. Breeds are defined as different populations of cattle that share similar phenotypic and production characteristics. Examples of these characteristics consists of hair color, presence of horns, shape and size of horns, presence or absence of a hump, plus many other characteristics (Herring, 2014). Domesticated cattle can be classified into two different sub-species: *Bos taurus* and *Bos indicus*. *Bos taurus* breeds are classified as those that do not have humps on their necks and breeds that are originally from the Middle East domestication event. *Bos indicus* cattle are classified as having a shoulder hump and the breeds originate from the Indian subcontinent of Asia and are considered to be adapted to tropical conditions. These cattle are typically known as zebu. Domesticated cattle are also classified based off of geography. British breeds originated from the British Islands off of the European continent and were developed for meat production. Continental European breeds originated from Western and Central Europe and were developed for meat production with some being dual purpose for meat and milk. Many had ancestors that were used for draft (Herring, 2014).

In the case of Butner Beef Cattle Field Labs where this study was conducted, Angus and Simmental-Angus crosses are utilized in the herd. The Angus breed is British and originated in Aberdeenshire and Angushire of Scotland and was imported to the United States in 1873. The Angus breed is phenotypically identified by its black color and not possessing horns, or being naturally polled (Taylor et al., 1999). British-based breeds are known for their meat traits such as tenderness, marbling, and muscle deposition. These differences in meat can also affect other aspects such as the time of slaughter, growth patterns, amount of feed needed to reach slaughter, and size at slaughter (Herring, 2014). Angus beef is often recognized for its tenderness and good meat quality.

The Simmental breed is a Continental-European breed that is prominent in Switzerland and France. The first bull arrived in Canada in 1967. The breed was originally developed for their meat and milk production but is commonly classified as a beef breed in the United States today (Taylor et al., 1999). The phenotypic classifications are broader than those for the Angus breed. Simmental cattle can be classified as having yellow to red and white color patterns and can be seen polled or horned (Taylor et al., 1999). Unlike British breeds, Continental European breeds tend to be taller, take longer to reach a slaughtering condition, and do not have the higher amount of marbling and tenderness as British breeds such as Angus (Herring, 2014).

The Angus and Simmental breeds were crossed due to wanting to take the traits from both and add hybrid vigor to produce an animal that could yield greater production and have genetics that complement each other. Simmental and Angus crosses, more commonly denoted as SimAngus, are classified as being at least one fourth Simmental and one fourth Angus or Red Angus, but not more than three fourths Simmental, Angus, or Red Angus (American Simmental Association, 2018). Angus is a British breed, while Simmental is a Continental breed, which means traits from two different countries have been combined to bring out the best of both (Nadarajah et al., 1985). Both Angus and Simmental are among the top ten most popular breeds in the Southeast United States and in the United States as a whole (Top 10 most popular cattle breeds in the United States, 2018). These breeds are heavily studied for the effects that fescue toxicosis has on them because of their popularity among cattle producers.

Cow-Calf Operations

Any producer who has the goal of maintaining a cow herd for breeding and to produce calves for a profit is considered a cow-calf producer (Herring, 2014). Cow-calf producers can be further classified into commercial or seedstock, otherwise known as purebred breeders. The difference between the two categories is that commercial producers often raise non-registered animals that supply a great deal of the beef market (Herring, 2014). The heifer calves can be retained for replacement animals in the herd or sold to another farmer who needs a replacement animal if they are considered to be desirable for breeding purposes. Steer calves can be sold to be used for meat or grown out by the farmer for meat, along with any heifers that are not desirable for breeding. Some purebred breeders use their cow-calf herds to produce seedstock, so they are considered to be involved in the cow-calf industry but be specialized in the seedstock industry. These seedstock producers have the goal of improving the genetics of the beef industry and can be considered the genetic engineers of the beef industry (Taylor et al., 1999). The seedstock farmers will usually register their animals with their specific breed association so that detailed records of the animals can be maintained and used to determine the outcome of progeny later on. These producers often times raise the purebred, registered bulls that will be sold to commercial cow-calf producers to breed with their crossbred cows (Herring, 2014).

Cow-calf producers expect each cow to raise one calf each year that they will sell shortly after weaning. Cows are expected to be bred back after calving in 60-90 days so that each calf crop can be born in a certain time frame, which helps the marketing of the animals once they are weaned. Some producers choose to keep their best heifers as replacement animals to add to their herd if some cows need to be culled. The most common sector of the cow-calf system in the United States is commercial producers (Herring, 2014). The calves are the main source of revenue for commercial cow-calf farmers, so utilizing the proper genetics that have been improved by the seedstock producers and selling their animals in the proper condition at the right time are imperative to making a profit. The majority of cow-calf producers are smaller with around 41 brood cows (Herring, 2014). Almost eighty percent of the beef cattle operations in the United States have less than 100 head of cattle, but nearly three-quarters of the beef cow population resides in herds of more than 100 cows (Taylor et al., 1999). These figures are not surprising since many cow-calf farmers do not use their beef cattle operation as a primary source of income for their family. Many beef cattle are owned by individuals who are part-time farmers, many of whom own fifty acres or less (Taylor et al., 1999). There are many of these smaller farms that then make up the large beef industry in North Carolina.

The mid-western United States has farms that have a larger volume of cattle because of the prime location of being near or in the corn-belt. This high-volume area is comprised of the states from North Dakota down to Texas and then the eastern parts of New Mexico, Colorado, Wyoming, and Montana and can be known as the Great Plains or beef belt. This area accounts for fifty percent of the total United States beef cattle population (Taylor et al., 1999). The benefits of utilizing both crops and livestock on a farming operation have convinced many producers in the Great Plains to use the method. Livestock integration into crop systems has four benefits which are: feeding costs of animals can be reduced since the crops can be used, the manure produced by the animals can be used as fertilizer for the crops, livestock can be used to recycle or get rid of byproducts from crops that cannot be used, and ruminants establish the need to have pastures and fields with perennial forages and legumes (Randall, 2003). The close proximity to a plethora of crops to feed the beef cattle and the financial benefits of the farmers who have a crop-livestock integrated operation make the Great Plains and corn-belt an extremely popular area for cow-calf producers and for feedlots that the calves from all over the United States are transported to be fed out for human consumption. This area is extremely important to cow-calf production, including production in North Carolina since many of the cattle from the Southeast United States are sold to the area.

Financial. The beef industry operates in an internationally competitive environment and the prices or profits that people make is heavily dependent on the price of other meats, animal feedstuff costs, and the consumer preference (Cottle and Pitchford, 2014). As for the smaller producer who has one hundred head of brood cows or less, they need to be weary of the overall industry condition and expectations if they want to make a profit. Determining the inputs and outputs on a cow-calf beef cattle farm can be difficult for many producers. The larger issue is that producers have to take the price changes and the amount being paid for cattle at that time, but cannot make them (Taylor et al., 1999). One of the key factors to be a successful cow-calf producer is to maximize the production efficiency and use resources correctly. There are multiple parts in an operation that include feedstuffs, forages, and then figuring out what the animals need of each of these. Six grazing principles that should be put into place by producers include: ensure forages have adequate resting time, observe stocking capacity of pastures, effectively manage grazing, manage livestock effectively, use the maximum stocking density for the minimum time, and manage for biodiversity of forages (Cottle and Pitchford, 2014). The animal components that need to be observed, specifically in reproduction include the following: cows should remain in healthy body condition with a minimum body condition score of a three, cows should calve in a sixty-day window, replacement heifers should be healthy and large enough to be bred, cows should be nutritionally flushed before mating, bulls should receive a breeding soundness exam before each breeding season, make sure genetic selection makes a positive impact on offspring, and breeding season should correlate with a time when there is sufficient quality and quantity of feedstuffs available (Cottle and Pitchford, 2014). It is important to think of all aspects of an operation and try to keep everything within a recommended range so that production and income do not suffer.

Calving Seasons. Among the many business decisions that cow-calf producers must make in their operation, they must pick the time of the year that their cows will calve.

Reproduction is a large part of any operation because without reproduction, there will be no product (Dargatz et al., 2004). Timing of a calving season determines when the calves can be weaned and then sold. Prices fluctuate in the beef system and certain months can be better to sell than others. The popular calving seasons include the fall and winter. Fall is considered to be the months of September through November and winter is considered to be January through March. Dargatz et al. (2004) conducted a study in which they found national averages and frequencies of calving management practices in beef cattle herds so that they could then develop educational and research programs to help producers improve their operations. During this study, producers were asked when their calving season was and why. Fifty-three point six percent of the producers surveyed did not have a set breeding season, so bulls were not removed from the cows for at least one month during the year and had a yearlong calving season. March was the most popular month for calving with 27.2% of the calves being born in this time frame. The majority of the calves that were born in the United States were born within the months of February, March, and April, which are considered to be late winter and spring calves. When beef cattle producers were asked why they chose their calving season, the majority (39.4%) responded with the weather conditions at the time, second determining factor was tradition (29.7%), third was forage availability (9.3%), and the factors that were considered the least consisted of weaning weights, market, labor availability, time of moving herds, and other (Dargatz et al., 2004). There are several factors that must be taken into consideration, but each area can have a different factor that may have more weight on how these decisions are made.

Body Condition Scores. In order to properly evaluate a cattle herd and ensure that the cattle can achieve maximum production, body condition scores need to be evaluated to help a producer figure out what may need improvements and what works. Body condition scores (BCS) are subjective measurements to evaluate the physical appearance of cattle (Randel et al., 1990). Beef cattle are evaluated using a 1-9 scale with 1 being completely emaciated and 9 being obese. The ideal BCS is a 5 or 6, depending on the stage of production and age of animal. Body condition scores are one of the most important evaluation criteria to monitor in a cow-calf herd because of the effects they can have on reproduction (Herring, 2014). In order to properly and accurately body condition score a cow, there are several points on the body that need to be observed. The best areas to evaluate are where there is little muscle coverage between the skin and bone. These areas consist of the rib cage, around the tail head, across the back or vertebrae, the sides of the vertebrae, loin region, and brisket area of the chest. The ideal score for a cow being bred is a 5 and the indications should be a moderate overall body condition score where the twelfth and thirteenth ribs are not visible to the eye, vertebrae are not noticeable to the eye, and areas around the tail head are not mounded, but well filled. Cows with a body condition score of 6 possess good condition overall with their ribs fully covered, plump and full hindquarters, spongy covering on each side of the tail head and last few ribs, and firm pressure is needed to feel the transverse processes (Herring, 2014). Cows who have extremes of low or high body condition scores can experience many issues that can harm the profitability of an operation. Cattle who possess a low body condition score are likely to have reduced reproduction and be more apt to injury or sickness because of the lack of body reserves. Cattle with a low BCS may also have decreased milk production and raise calves that do not gain weight quickly. Cattle who have high body condition scores and have more fat coverage than normal might also have reproduction difficulties and reduced milk production because of fat deposits taking up space in the mammary gland. Cattle who have higher body condition scores may also be costing more money and not producing a profit if they are unable get pregnant or do not produce enough milk to raise a calf properly. These cattle may eat more than other cows and then not have a monetary return. Cow-calf operations have to take all of this into consideration when deciding how to manage their herd, so using the body condition scoring system is an important tool that should be learned and utilized.

Tall Fescue Plant

Tall fescue (Lolium arundinaceum [Schreb.] Darbysh) is a cool season, perennial plant and one of the most abundant forages in the United States with over 8.5 million cattle grazing tall fescue pastures (Hoveland, 1993). It was originally introduced into the United States from Europe in the late 1800's. Speculation is that the forage was brought over on accident as a contaminant in hay or packing materials. Tall fescue has since become the most important and utilized forage in the country (Ball et al., 1993; Hoveland, 1993). Farmers gave the forage a great opportunity to flourish and invade the native species by converting the native grasslands to pasture and arable lands for farming (Saikkonen et al., 2016). Today, the commercialized and most popular version of the tall fescue is called 'Kentucky-31' (KY-31). The seed was introduced to the market when E. N. Fergus, an agronomy professor from the University of Kentucky, visited a farm in 1931 in Menifee County, Kentucky and found a hardy, resilient tall-fescue ecotype that he then collected. Up until the release of Kentucky-31 by the University of Kentucky in 1943, the use of the forage to develop pastures and hay land was slow (Ball, 1993). Kentucky-31 has been used for a wide variety of reasons including animal feed in the form of grazing and hay, lawns and turf, soil stabilization, and wildlife food plots. In 1977, approximately 97% of all the tall fescue turf in the United States was KY-31 tall fescue (Murray et al., 1979).

Tall fescue has deep roots and grows in an upright fashion with course leaves (Jennings, 2008). The forage has an annual root system, which means that the majority of the roots are replaced each year during the spring flush growth period (Cook). The leaves are long and dark-green with distinct veins and rough edges. The forage is considered a bunch grass but can look more uniform in situations where it is kept mowed or grazed lower. Mature tall fescue will be 2 to 4 feet tall and can yield anywhere from 2 to 4 tons of dry matter per acre. Since tall fescue is a cool season forage, the two main growing periods are in the spring and fall. Around two thirds of the yearly growth occurs in the spring, while the other one third of growth occurs in the summer and fall months. The optimum growth temperature is between 68 degrees Fahrenheit (20 degrees Celsius) and 77 degrees Fahrenheit (25 degrees Celsius) (Jennings, 2008).

Nutrient Composition of KY-31. Kentucky-31 Tall Fescue is capable of producing high-quality forage that contains high levels of digestible energy, protein, minerals, and has the capability to accumulate high levels of usable carbohydrate in the spring and fall (Hannaway, 1999). An animal's daily performance is dependent on the nutritive value of forage, which includes digestible energy, crude protein, minerals, and vitamins (Burns, 2009). The forage is the best adapted of the cool season grasses to stockpile, which means that the growth is accumulated so that animals can graze throughout the fall and winter. Tall fescue is also usually higher quality than other cool-season forages in the fall because of the greater leaf retention (Hall, 2008). The forage also remains greener and at an acceptable quality into the fall and winter throughout the eastern adaptation range (Hannaway et al., 1999). Like all forages, the exact nutrient composition of tall fescue depends on the stage of maturity. The stages of the forage can range from fresh, early vegetative to hay, full bloom. The level of nutrients decrease as the forage matures. The total digestible nutrients (TDN) on a dry matter basis range from 73% at the fresh, early vegetative stage to 58% at the hay, full bloom stage. The digestible energy (DE) can range from 2.56-3.22 Mcal/kg, the metabolizable energy (ME) can range from 2.10-2.64 Mcal/kg, net energy for maintenance (NEm) can range from 1.24-1.73 Mcal/kg, net energy for gain can range 0.68-1.11 Mcal/kg, crude protein (CP) can range from 12.1-22.1%, calcium (Ca) can range 0.41-0.51%, and phosphorus (P) can range 0.30-0.37% (Hannaway et al., 1999). All values are determined on a dry matter basis.

Kentucky-31 is utilized by many farmers in the United States, but it is most common in the transition zone of the eastern and central part of the country (Strickland et al., 2009). With the abundance and high utilization of the forage, it is economically important to the producers of the United States and covers about 15 million ha (Buckner et al., 1979). The reason that the forage is so popular with cattle producers is its survivability and hardiness through differing conditions. The forage is fairly easy to establish, persistent, can adapt to conditions even though it is a cool season grass, can be grazed a longer length of time than other forages, is pest resistant, and is tolerant to poor management (Stuedemann and Hoveland, 1988). Tall fescue can tolerate continuous stocking or grazing better than other cool season grasses, but there is potential for a greater forage production and animal gains if there is intensified management of grazing (Hannaway et al., 1999)

Epichoë coenophiala. Kentucky-31 tall fescue's survivability is attributed to its symbiotic relationship with a microscopic, endophytic fungus called *Epichoë coenophiala* that grows within the plant (Roberts and Andrae, 2004). The toxic properties of the plant that are produced by the endophytic fungus are believed to be ergot alkaloids, which include clavine alkaloids, lysergic acid amides, and ergopeptines (Bacon et al., 1977), which are bioactive secondary metabolites (Young et al., 2014). Some other bioactive secondary metabolites that are produced by the fungus include the alkaloid classes of indole-diterpenes, lolines, and peramine (Siegel et al., 1990). Ergot alkaloids and the indole-diterpene, lolitrem B, have been shown to cause fescue toxicosis (Bacon et al., 1977) and ryegrass staggers (Fletcher and Harvey, 1981) through its anti-mammalian activity. The alkaloid class, peramine, is considered to be an insect deterrent (Johnson et al., 1985; Rowan and Latch, 1994) and lolines have been documented as being a potent insecticide for tall fescue (Bush et al., 1997). Ergopeptine alkaloids are considered to be the primary agent in causing KY-31 to be toxic (Smith et al., 2012). Past literature has suggested that the mutualism between Kentucky-31 and *Epichoë coenophiala* is highest in areas where there is a high nutrient agro-environment (Saikkonen et al., 2006; Saikkonen et al., 2010; Saikkonen et al., 1998; Saikkonen et al., 2016). The toxins that are produced during this fungal and plant mutualism benefit the plant yet harm the ungulates that eat them and causes what has become to be known as fescue toxicosis, which has been considered to be the major grass-induced toxicity in the United States (Cheeke, 1995).

Epichoë coenophiala is the endophytic fungus that actually produces the toxic properties, so it is of great interest to researchers and those who want to measure the presence of toxin in pastures. The fungus is only spread through the seed of the plant (Bacon and Siegal, 1988; Welty et al., 1986), but is present is other areas of the plant once it grows. The fungus can move from the germinating seed into the seedling and then colonizes leaf sheaths, meristems, and internodes of elongating stems. The roots, however, are not colonized (Hoveland, 2009). The spreading of the endophyte in plants from the meristem to the leaves is not fully understood, but it is thought that as the leaves grow, the endophyte is carried from the meristem into the leaves. When rapid growth occurs of the fescue plant in the spring, the fungal hyphae, grow rapidly so that the endophyte is not as concentrated towards the end of the leaf of the plant. This means that the fungus is more concentrated towards the base of the plant. Saikkonen et al. (2016) hypothesized that Kentucky-31 tall fescue would reap more benefits from *Epichoë coenophiala* than wild types of the forage because grazed or maintained land would be fertilized and the soil would be more appropriate for growing forages (Saikkonen et al., 2016). When tests are completed to determine the endophyte mass or ergovaline concentration, the portion of the plant that is used must be specified since there are different concentrations depending on the height above ground level that the sample was taken. It is recommended that forage tillers are taken because they are a portion near the base of the plant that are the most reliable portion of the plant to qualitatively document the presence of fungus (Barker et al., 2009).

The issue with the detection of the endophyte is that there are no distinct physical differences in a plant that has the endophyte, and one that does not. The clue that there is infected endophyte present is the poor performance of the animals, poor forage utilization, lack of insect presence, and the forage will stay greener than others during drought. In order to determine endophyte presence, a microscope or laboratory test can be used (Barker et al., 2009). The most common method of endophyte detection is a microscope (Clark et al, 1983). Endophyte infection can be measured by the presence or absence of fungal hyphae, which are filaments within the tall fescue seed or tiller (Barker et al., 2009). The hyphae are present within the intercellular spaces of grass pseudostems and also in the leaves, but to a lesser extent (Shelby and Dalrymple, 1987; Hiatt et al., 1999; Hill et al., 2002a). The seedheads are what propagate and then spread the fungal endophyte, so that is where the most concentrated portion of toxin can be found. The time that is more harmful to graze animals on tall fescue is when the seedheads are prevalent, which is in the flowering stage of late spring and after the formation of the seedhead in early summer (Barker et al., 2009). Since the stage of the seedheads can determine the toxicity, there are certain times that are better for sampling than others to determine the fungal endophyte and toxic alkaloid levels of the forage to get a more accurate result. The endophyte infection of a pasture is not static and changes throughout a year, but then remains on a cycle each year with the levels aligning year by year, depending on the month that the pastures are sampled. It has been proven that the ability to find the endophyte in an infected plant is reduced during the winter months and spring months of January through April, so it is not advised to sample during February, March, or April (Barker et al., 2009).

Ergot Alkaloids. Ergot alkaloids are indole compounds that are biosynthetically derived from L-tryptophan. They are nitrogenous fungal metabolites and make up the largest group found in nature. There have been over 80 different ergot alkaloids isolated (Schiff, 2006). Ergot alkaloids fall into a class of compounds that are produced by fungi, which are referred to as secondary metabolites, meaning that they are not necessary for the survival and life processes of the organism that they are produced by and reside in. However, ergot alkaloids can have substantial impact on the other organisms in the environment that may ingest or come into contact with them (Flieger et al, 1997). The fungi that produce ergot alkaloids are within the *Hypocreales* and *Eurotiales* orders (Strickland et al., 2011). All of the species within *Hypocreales* parasitize more than 600 plants, which include many economically important cereal grains and forages (Bové, 1970; Groger, 1972). The fescue seed is invaded by Claviceps purpurea, which is an ergot fungus. The fungal mycelia then form an ergot alkaloid-contaminating body called the sclerotium (Strickland et al., 2011). Consumption of the sclerotium, which includes ergot alkaloids, can cause ergotism. The rate of fungal growth depends on environmental conditions. The favored fungal conditions include warm temperatures, high rainfall and humidity, and high soil fertility (Craig and Hignight, 1991)

Ergot alkaloids were discovered thousands of years ago when humans would use them in obstetrics. The earliest authenticated reports of their use date back to 1100 BC. Ergots and their effects were referred to as grain diseases that came from infected grain that could be determined by damp grain becoming a red color. Written evidence of grain diseases has been found in books of the Old Testament in the Bible, which spanned from 850-550 BC. Ergots became extremely troublesome to humans during an epidemic called 'St. Anthony's Fire' where humans were experiencing horrible, gangrenous symptoms. The form of ergot was called *Ergotismus gangraenosus* and was most prevalent in France. The condition was characterized by people having peripheral vasoconstriction of their extremities, which included swelling of hands, feet, and entire limbs. The limbs would turn red and have a burning pain that would eventually lead to the separation of the limb since there was so much vasoconstriction, causing the tissue to become gangrenous. The condition would eventually lead to a complete separation of the limb without the loss of blood or much pain because of the severity of vasoconstriction. Another type of ergotism, called the convulsive form (*Ergotismus* convulsivus) that was more common in Germany, caused humans to develop delirium and hallucinations that were accompanied by involuntary muscle spasms, convulsions, severe diarrhea, and extremely painful limbs that were flexed all of the time (Schiff, 2006).

Ergopeptine alkaloids: Ergovaline. Ergopeptine alkaloids are one of the three major classes of ergot alkaloids and are of the greatest concern for causing fescue toxicosis or ergotism (Strickland et al., 2011). Within the ergopeptine class is a compound named ergovaline (Klotz and Nicol, 2016). Like the ergot alkaloids that ergovaline is derived from, it is a secondary metabolite, meaning that it is not essential for the life of the plant. The ergopeptine class of ergot alkaloids can be identified by its tricyclic peptide moiety that is attached to the 8-carbon of the tetracyclic ergoline ring or lysergic acid structure. The structure of ergopeptines are so similar to that of biogenic amines, which include serotonin, norepinephrine, and dopamine, that ergopeptines can actually interact with their receptors (Berde, 1980). Rowan and Shaw (1987) found that ergovaline makes up 40% of the ergot alkaloids that are detected. The remaining portion of the ergot alkaloids are comprised of ergotamine, ergosine, ergoptine, ergocryptine, and ergocornine. The percentages and the amounts of ergot alkaloids present are dependent on the cultivar, environment, and time of year interactions (Klotz and Nicol, 2016). Since the findings of Rowan and Shaw (1987), it has been reported that the ergovaline concentrations for tall fescue are substantially higher in the United States (Yates et al., 1985; Lyons et al., 1986), which may be due to Rowan and Shaw (1987) using data from New Zealand (Klotz and Nicol, 2016).

There are several delivery methods of ergovaline to cattle which include, pasture, ground seed, whole seed, and seed extracts. There has been much speculation about the rate or amount of toxin absorbance by the digestive systems of animals based on the method of delivery of ergovaline in tall fescue. Previous studies demonstrated the toxicity level of a seed with ergovaline by incubating it in rumen fluid, then feeding it to a rat. The studies found that feeding a whole seed that had been incubated in rumen fluid resulted in less toxicity than feeding a seed that had not been incubated, which suggested that the rumen microflora reduced the concentration of toxic compounds (Westendorf et al., 1992). Moyer et al. (1993) found that in the liquid phase, there is metabolism and conversion of ergovaline to another compound. One factor that can affect the metabolism of ergovaline is the seed head maturity. Goff et al. (2012) reported that 100% of ergovaline was released from an immature seedhead, but then dropped to 95.9% being released once the seedhead matured. Several *in vitro* studies have looked at the percentage of ergovaline that is released from digested plant tissues. De Lorme et al. (2007) reported that 64% of ergovaline was released in an *in vivo* study with sheep.

Ergot alkaloid absorbance. In order for an animal to display a physiological response from a toxin, there must be a sufficient concentration of the toxin through an effective route for a period of time before the molecular concentration is sufficient at the target site (Strickland et al., 2011). The most common way that cattle are exposed to the ergot alkaloid toxins is by ingesting them. Once ergovaline is ingested, it has been hypothesized that it can take one of several different paths which include digestive system, lymphatic system, blood/circulation, and then the various steps after committing to those paths (Klotz and Nicol, 2016). The gastrointestinal absorption of toxic ergot alkaloids, such as ergovaline, involves the passage of the substance either passively or by facilitated/active mechanisms across the gastrointestinal epithelium (Eckert et al., 1978). The rumen has been the speculated site of a majority of the toxin absorption because of the near neutral pH and the lack of a thick, protective mucosal layer like other parts of the gastrointestinal system possess (Russell and Rychlik, 2001). Ergovaline is speculated to be absorbed at a slow amount of one percent of the daily dose ingested (Klotz and Nicol, 2016). Since the absorption in the rumen is so slow and at a low amount, it is also speculated that ergovaline absorption may also occur in the small intestine. The ergopeptine alkaloids are charged at a low pH, so it is assumed that they are unable to be absorbed in the abomasum (Eckert et al., 1978) of ruminants, therefore they would not be able to be absorbed in the stomachs of monogastrics. The absorption of ergopeptine alkaloids such as ergovaline appears to be limited to the small intestine (Rothlin, 1933) and forestomach (Westendorf et al., 1992; Hill et al., 2001) of nonruminants, but can occur in conjunction with the rumen absorption in ruminants (Strickland et al., 2011). Since ergot alkaloids can be absorbed by the gastrointestinal system and enter the bloodstream, there is a concern with evidence of the toxins in animal products that are consumed by humans. So far, there has not been any published evidence that there is an accumulation of ergovaline in edible animal tissues that consumed tall fescue or perennial ryegrass (Klotz and Nicol, 2016).

Issues Associated with Fescue Toxicosis

As mentioned earlier, ergot alkaloids can elicit a response that is referred to as fescue toxicosis. The response can have a range of severity with the least severe symptoms being slight physiological and physical debilitations, to severe symptoms that could lead to animal death. The symptoms can include reduced reproductive performance, reduced weight gain, and overall poor performance despite the forage's sufficient quality analysis which includes digestible dry matter, crude protein, cell wall content, and minerals (Schmidt and Osborn, 1993).

Reproduction. One of the direst financial consequences that results from fescue toxicosis is reduced reproductive efficiency (Hoveland, 1992). The annual economic loss to the cattle industry for reproductive reasons that are due to fescue toxicosis was more than three hundred million dollars in 1993. The losses were attributed to the 20% decrease in calving rate for twenty-one states that were grazing endophyte-infected tall fescue. Other factors that could have caused a decrease in calving rate could have been climate, environment, and management (Hoveland, 1993). Several species have been discovered to have reproductive issues that are caused by endophyte-infected tall fescue. The species affected include mice, rabbits, horses, sheep, and cattle (Daniels et al., 1984; Boling, 1985; Zavos et al., 1987; Bond et al., 1988; Monroe et al., 1988; Porter and Thompson, 1992; Jones et al., 2003; Schuenemann et al., 2005). The species that have the greatest effects of dystocia and abortion are monogastrics and hindgut fermenters, which include horses. Mares in the later portion of pregnancy have been the most severely affected animals found to date (Strickland et al., 1993). Mares can suffer from a wide range of symptoms which include prolonged gestation, dystocia, retained and thickened placentas, poor milk production, and reduced colostrum (Monroe et al., 1988). Unfortunately, the foal, and sometimes the mare and foal, are lost during parturition (Cross et al., 1995). Ruminants do not have as severe of reproductive symptoms and most often suffer from low conception rates, which results in lower production and profits for producers (Strickland et al., 1993). As a result of low conception rates, the calving rates will also be reduced. Boling (1985) conducted a study that compared the calving rates of cows grazing low endophyte-infected fescue versus cows grazing high endophyte-infected fescue. The cows grazing low-endophyte fescue had calving rates of 86%, whereas the cows grazing high-endophyte fescue had calving rates of 67%. For each 10% increase in fungal infection, there is a 3.5% decrease in conception rates.

Another reported reproductive effect of fescue toxicosis is delayed puberty (Washburn and Green, 1991). Puberty in cattle is defined as the first sustained increase in serum progesterone. Washburn et al. (1989, 1991) studied Angus heifers that had been raised on endophyte-infected fescue to see how many of them reached puberty before the breeding season at 15 months of age. It was concluded that puberty was delayed by looking at the progesterone concentrations of the heifers. During the first year, 0% of the heifers on high endophyte pastures reached puberty by the breeding time, while 32% of the heifers on low endophyte reached puberty by fifteen months of age. Year two had 26% versus 53% and year three at 5% versus 26% of heifers on high versus low endophyte, respectively, that reached puberty by fifteen months of age. The goal of cow-calf producers is to have heifers calve for the first time at two years of age, therefore they should reach puberty prior to 14 months of age. The first estrous cycle of a heifer is usually not as fertile as the subsequent estrous cycles, so it is pertinent that heifers have at least one or two complete estrous cycles prior to breeding (Taylor et al., 1999).

Impaired ovary and corpus luteum (CL) function has also been determined to be a side effect of fescue toxicosis (Ahmed et al., 1990; Estienne et al., 1990; Mahmood et al., 1994). Heifers on toxic endophyte-infected tall fescue have been observed to have fewer nuclei on the CL and there was a greater number of large luteal cells with increased diameters. Upon ultrasound examination of the large luteal cells, it was discovered that the cells had increased cellularity with a greater number of mitochondria, lipid droplets, and secretory granules (Estienne et al., 1990). Heat stress in conjunction with endophyte-infected tall fescue has been found to have an impact on the endocrine system of beef heifers. Burke et al. (2001) conducted a study that looked at the interaction between endophyte-infected tall fescue and heat stress on the ovarian function of beef heifers. They found that the combination of the toxic forage and hot environmental temperatures caused the diameter of preovulatory follicles to be reduced, but the factors alone did not cause any change. Progesterone, which is released by the corpus luteum, was reduced in serum concentrations when heat stress and ergot alkaloid consumption were each a factor. The serum progesterone concentrations did not change, however, when heat stress was not a factor.

Many studies have proven the adverse effects of endophyte-infected tall fescue on beef cattle reproduction however, some studies have not shown any reproductive performance differences when comparing cows or heifers that graze endophyte-infected versus endophyte free tall fescue. Drewnoski et al. (2009) explains that this could be due to differences in experimental design such as breeding season, environmental temperature, or the amount of ergot alkaloid consumed. An elevated ambient temperature exacerbates the negative effects of ergot alkaloids in tall fescue and is a key to how severe of symptoms that an animal may experience. Jones et al. (2003) reported that beef heifers that are consuming endophyte-infected tall fescue during heat stress have shortened estrous cycles and decreased mid-cycle progesterone levels. Mid-cycle progesterone concentrations are dependent on the corpus luteum function, which was mentioned earlier.

Average Daily Gain (ADG). Along with reduced reproductive efficiency, reduced average daily gain (ADG) is a consequence of fescue toxicosis (Hoveland, 1992). Average daily gain is the amount of weight that an animal gains daily and is dependent on the feedstuffs provided, stage of production, age, and physiological composition of the animal. This number can be positive or negative, depending on the condition and circumstances.

One important factor of the average daily gain of an animal is their daily dry matter intake, which can be highly dependent on the ambient temperature and if heat stress is a factor. Research has shown that livestock that consume endophyte-infected tall fescue tend to have reduced feed intake, which results in a lower average daily gain than what is expected or preferred (Strickland et al., 2009). The reduced feed intake could be from the animal not feeling completely well with a reduced gut motility and heat stress contributing to the issue. Studies have looked at the possibility of ergovaline affecting rumen and gut motility, thus affecting feed digestion, feed passage rate, and nutrient availability (Klotz and Nicol, 2016). As discussed previously, ergovaline interacts with biogenic amines to reduce blood flow and contract the smooth muscle of blood vessels, which reduces the amount of blood flow, otherwise known as vasoconstriction. The digestive system is made up of smooth muscle, so the vasoconstriction can affect how well the gut is able to digest the feed intake. It has been reported by McLeay and Smith (2006) that the baseline tonus of the reticulum and rumen increased, as well as the amplitude of the reticular contractions when ergovaline was introduced intravenously. The smooth muscle of the digestive system associated with motility or peristalsis may be affected by ergovaline, which can negatively affect digestion (Klotz and Nicol, 2016). McLeay and Smith (2006) conducted a study where they looked at the effects of intravenous infusion of ergovaline on the rumen and reticulum. The conclusion was that disruption of digestion may occur in livestock that are grazing endophyte-infected pastures with a high ergovaline content. Little is known about the effects of ergovaline on the small intestine, but a study conducted by Dalziel et al. (2013) studied the effect of ergotamine, which is related to ergovaline, on isolated distal rat colon. The study demonstrated that there was in increase in the contractile tension and a momentary increase in the contractile frequency. Studies that looked at the actual passage rate of feed have differing opinions of the effects of ergovaline. The difficulty is establishing a control and a treatment and then monitoring gut fill. Although there are differing opinions on the passage rate and gut fill, it is clear that ergovaline has an effect on the smooth muscle of the digestive tract (Klotz and Nicol, 2016).

Studies have suggested that altered feed passage rate can be due to gut fill. If rumen fill increases or does not change as quickly, then intake will be reduced. In two separate studies using steers, Koontz et al. (2013) and Foote et al. (2013) controlled the intake of the animals so that each treatment group of endophyte-infected and endophyte-free animals would have the same feed intake with ruminally dosed seed at 0.051 mg ergovaline/kg$^{0.75}$ liveweight per day (Koontz et al. 2013) or at 0.059 mg ergovaline/kg$^{0.75}$ liveweight per day (Foote et al. 2013). Both studies saw a significant increase in the total amount of ruminal dry matter in animals consuming endophyte-infected seed, which suggested that the reduced average daily gain of animals on an endophyte-infected diet is not correlated with the dry matter intake amount but is more likely due to reduced ruminal motility. Ergovaline had the possibility of altering the passage rate of the feedstuff in the steers that were exposed to ergovaline in the endophyte-infected seed. There is an obvious effect of endophyte-infected feedstuff on the passage rate and gut fill in livestock, but the actual mechanics of the situation have yet to be fully understood (Klotz and Nicol, 2016).

Heat stress has been proven to exacerbate the reduction in average daily gain and overall health of an animal grazing endophyte-infected tall fescue, but symptoms of fescue toxicosis can remain year-round and effect animals differently during different times of the year. Hoveland et al. (1984) found that poor weight gains can occur throughout the year and with each season when animals graze endophyte-infected tall fescue, not just during the summer and hot weather. The average daily gain can even almost be reduced as much in the cool-season months as in the warm-season months. The effects on the cattle and the potency of the ergot alkaloids depend on the infection rate (or frequencies) of the pastures. Crawford et al. (1989) utilized pastures that had endophyte infection frequencies that ranged from 3% to 83%. The researchers reported that there was seasonal variation because spring and summer average daily gain was decreased by 0.068 kg day^{-1} for each 10% increase in endophyte infection, but there was no relationship for the autumn grazing time period between average daily gain and endophyte infection.

The early grazing trials looked at the difference in animal performance between those grazing high infestation or low infestation tall fescue. These earlier studies found that there was a negative linear relationship between the amount of endophyte infestation and the amount of weight gain by steers that were grazed on pastures with very high or very low infestation rates. This meant that as the infestation rate increased, the amount of weight gain decreased in the steers. It was suggested that the average daily gain of the steers decreased approximately 0.045 kg for each 10% increase in infection rate (Garner et al., 1984; Williams et al., 1984;

Stuedemann et al., 1985b; Pedersen et al., 1986). Several studies have looked at switching cattle from endophyte-infected tall fescue to a non-toxic version of tall fescue such as endophyte-free or novel endophyte-infected tall fescue, or vice versa. Stuedemann et al. (1989a) found that the forage intake remained decreased for at least 10 days for a group of steers that was switched from endophyte-infected tall fescue to endophyte-free tall fescue, but then was normal by 28 days after the switch. The steers also showed compensatory gains during the 112 days after the pasture switch. Another group of steers was switched from endophyte-free tall fescue to endophyte-infected tall fescue and had depressed forage intake within one week of the pasture change, then had reduced gains during the period after the change.

The amount of fescue that is in a pasture greatly determines that level of infection and the opportunities that cattle have to consume the toxic forage. Garner and Cornell (1987) conducted a study that looked at the selectivity of bulls with endophyte-free versus endophyte-infected seed. Twelve bulls that had no prior exposure to fescue were put on a diet of endophyte-free seeds, then switched to endophyte-infected seeds. Once the bulls were switched to the toxic variety of fescue seed, three of them refused to eat for 48 hours, seven ate amounts of 0.9 to 1.8 kg daily, and two ate approximately 5 kg daily. When the bulls were on the endophyte-free fescue seed, consumption was 6.3 to 9.1 kg daily, so there was quite a difference in consumption between days.

Vasoconstriction and Heat Stress. Exposure to ergot alkaloids in conjunction with heat stress have been proven to cause vasoconstriction, which can then lead to many other physiological issues. Elevated body temperature has been proven to be a result of fescue toxicosis because of the binding of ergot alkaloid toxins to the biogenic amine receptors that then restrict blood flow through the peripheral vasculature (Oliver, 2005). This then impairs the animal's ability to dissipate body heat (Aiken et al., 2013). The symptoms become apparent in hot, humid conditions that are often found in the summers of the Southeastern United States. The average body temperature for cattle is between 38 degrees Celsius (101 degrees Fahrenheit) and 39 degrees Celsius (102 degrees Fahrenheit) with a normal range of 38 degrees Celsius to 39.5 degrees Celsius (100.4 to 103.1 degrees Fahrenheit) (Taylor and Field, 1999), therefore the normal core body temperature remains almost constant within $\pm$ 1 degree Celsius (Guyton, 1986). Normal fluctuations in body temperature occur with the difference in the time of day and the amount of physical activity that the animal experiences (Taylor and Field, 1999). It is important that body temperature stays within a normal range for the sake of the normal metabolic processes. If an animal experiences sickness or something to cause a spike in temperatures, this can cause them to suffer from heat stress, irregular bodily functions and behavior. Signs of heat stress due to fescue toxicosis are more prevalent when the ambient temperatures are high (Hemken et al., 1981; Osborn, 1988). The toxins in endophyte-infected tall fescue have the ability to cause neurotransmitter and endocrine imbalances within the brain (Marple et al., 1988; Schillo et al., 1988) because of the ability of the hypothalamus to receive impulses from the thermosensitive cells throughout the body and then adjust the body temperature based on the signals (Curtis, 1983; Guyton, 1986). It has been concluded that if areas of the brain are being affected by endophyte-infected tall fescue toxins and then causing the neural disfunction and issues with the thermoregulatory center, that this may be the cause of irregular temperature, hyperthermia, and heat stress on cattle grazing the forage.

Hemken et al. (1981) found that cattle consuming endophyte-infected tall fescue had the most detrimental effects when the ambient temperature exceeded 31 degrees Celsius (87.8 degrees Fahrenheit). In a study designed to examine the carryover effects of cattle who were grazing endophyte-infected tall fescue to endophyte-free tall fescue, it was noted that the steers had different grazing patterns based off of the type of forage that they were exposed to. The steers that were on the endophyte-free pastures spent 60% of their time between the hours of 12:00 and 18:00 grazing, whereas the steers on endophyte-infected pastures spent only 4-6% of that time period grazing (Stuedemann et al. 1985). The time period between the hours of 12:00 and 18:00 are in the afternoon and late afternoon when the temperature would normally be the hottest, so the cattle on endophyte-infected pastures were too hot to graze during this time period.

Several recent studies by Klotz et al. (2006, 2007, 2008, 2010) have studied the differences in the constriction of the bovine lateral saphenous vein in vitro. As discussed before, ergovaline has been proven to be the most potent of the ergopeptines. Klotz et al, (2006, 2007) found that ergovaline is approximately 1,000-fold more potent and 5-fold more effective in causing vasoconstriction than lysergic acid, and that ergotamine has a similar contractile dose response curve to ergovaline. Dryer (1993) found that ergovaline induced the contraction of bovine uterine and umbilical cord arteries in vitro via $5HT_{2A}$ serotonergic receptors but did not restrict the arteries via α_1-adrenergic receptors.

Studies have shown that there is decreased vasoactivity in the peripheral (Klotz et al., 2012; Klotz et al., 2013) and gastrointestinal beds (Egert et al., 2014) in animals who have been exposed to ergot alkaloids. These symptoms, however, have not been observed in animals that have been removed from grazing tall fescue and finished on an ergot alkaloid-free diet for up to 103 days prior to slaughter (Klotz et al., 2012). As mentioned previously, ergot alkaloids and the subsequent vasoconstriction can affect many tissues of the body. This includes the cardiovascular system, which plays a large role in temperature regulation, nutrient transportation, and waste elimination (Strickland et al., 2011). The vascular tone and the possible alterations that can occur in morphology contribute to reduced and restricted blood flow to many tissues within the animal (Rhodes et al., 1991; Aiken et al., 2007; Strickland et al., 2009a,b).

Animals that consume a large amount of ergot alkaloids lose their ability to effectively dissipate heat, so they experience excessive panting, spend excessive time in the shade, and are often times covered in mud from standing in ponds or sources of water. Animals who are transported to feed yards often times become extremely stressed and their physiological systems suffer from consuming endophyte-infected tall fescue. The combined physiological effects, transportation stress, and environmental temperatures can cause negative responses which include sickness and even death (Aiken et al., 2001). Along with struggling in the heat with trying to keep cool, animals affected by fescue toxicosis can experience a loss in their ability to regulate body temperature in colder weather as well. Cattle especially have difficulty in regulating their body temperature in the peripheral areas of their bodies, which can lead to frostbite and the loss of ears, hooves, and tail switches. All of these symptoms occur because of the decrease in blood flow to certain areas of the body (Jacobson et al., 1963).

Given the reports of biogenic amines having interactions with ergot alkaloids, it is not surprising that the alkaloids have so many effects on many parts of the body, including the cardiovascular system. The challenge is being able to identify the specific biogenic amines that the ergot alkaloids interact with and how to mediate the issue in the various vascular beds (Strickland et al., 2011). The further complication and issue is that once there has been long-term irreversible damage, the animal can suffer from vascular congestion and long-term morphological changes in the blood vessels. Past research has reported that there is thickening of the intimal layer of small peripheral blood vessels after livestock have been exposed to ergot alkaloids by grazing endophyte-infected tall fescue (Julien et al., 1974; Williams et al., 1975; Garner and Cornell, 1978). Strickland et al (2011) proposes that artery congestion is due to the vasoconstriction and thrombosis that is within the compromised blood vessels. Blood flow could be reduced further by the thickening of the intimal layer and the constant vasospasm that is induced by ergot alkaloid exposure. Strickland et al. (1996) observed that the growth was inhibited in bovine smooth muscle cells when the cells were incubated in ergovaline, but growth was stimulated when cells were incubated in ergonovine and α-ergocryptine. Another contribution to the vascular pathology and decreased blood flow may be endothelial cell death (Shappell, 2003) induced by ergot alkaloids.

Since ergovaline is only one portion of the class of ergot alkaloids, there can be differing effects depending on which one is most prevalent in a forage. Each individual alkaloid can elicit a variety of responses, so it can be difficult to deduce conclusions about the overall class of ergot alkaloids. Different ergot alkaloids can also have different effects within various tissues of the body, which include the differing rate of contraction that was previously discussed (Strickland et al., 2011).

Prolactin in relation to hair shedding and milk production. Hormone profiles have been shown to become abnormal when an animal is grazing endophyte-infected tall fescue. One hormone in particular that is infamous for being affected in animals grazing the toxic forage is prolactin. Other hormones have been shown to be affected, but prolactin is known for having conclusive studies showing the effects on the levels based on type of forage utilized (Schmidt and Osborn, 1993). Numerous studies have shown that plasma prolactin concentrations are reduced in animals that are grazing endophyte-infected tall fescue (Hurley et al., 1981; Bolt et al., 1982, 1983; Bond and Bolt, 1986; Thompson et al., 1987a). Prolactin is a polypeptide protein hormone that is synthesized and secreted from specialized cells in the anterior pituitary gland, central nervous system, the immune system, the uterus and other reproductive organs, and the mammary gland. The hormone was originally named for its known ability to produce milk in mammals. Over time, more has been discovered about the protein hormone and there is now a plethora of knowledge and known parts of the body that can produce prolactin and be affected. Prolactin stimulates over 300 biological activities that are not denoted by its name (Freeman et al., 2000). Other than lactation, some of the other biological activities that the hormone has been linked to include hair shedding, hair follicle cyclicity, maintaining homeostasis and many reproductive mechanisms (Houedebine et al., 1985; Poindexter et al., 1979; Lebedeva et al., 2004).

The suppression of prolactin by ergot alkaloids is caused by the similarity of dopamine to the ergoline ring portion of the ergot alkaloids, which allows them to interact with the D2 dopamine receptors (Pertz et al., 1999). Dopamine is an antagonist to prolactin, which means that it causes the suppression of prolactin. Less dopamine will allow a greater amount of prolactin, while a higher amount of dopamine will cause a suppression of prolactin. In a study where steers were grazing endophyte-infected fescue and were determined to have reduced prolactin levels, metoclopramide, which is a dopamine antagonist, was administered. This caused an increase in serum prolactin and average daily gains (Lipham et al., 1989), which further solidified that prolactin plays a role in the overall well-being of the animals and an increase in the hormone can begin to reverse some of the fescue toxicosis burdens. Since serum concentrations of prolactin have become known to be good indicators of animals who are suffering from fescue toxicosis, they can be used to determine the possible severity of ergot alkaloid infection in pastures and amount of animal exposure (Klotz, 2015). Hurley et al. (1981) was the first group that was able to associate the suppressed prolactin with the endophyte that causes fescue toxicosis. The group also found that the temperature-induced increase in prolactin was inhibited. Reports indicate that serum prolactin can be reduced in sheep and mares within 2 to 3 days of grazing endophyte-infected tall fescue (Bolt et al., 1982; McCann et al., 1989). Recovery of prolactin levels can occur in approximately the same amount of time when livestock are removed from the forage. There are, however, differences in the amount of a suppressive effect that ergot alkaloids have on prolactin. Thompson et al. (1987b) found that there are differences in the level of prolactin suppression between Zebu and Angus breeds when grazing endophyte-infected tall fescue. The Zebu steers had a reduced amount of suppression compared to the Angus steers, therefore breed differences can be taken into consideration when looking at the physical signs of fescue toxicosis. Some factors that determine the amount of prolactin secreted include amount of light an animal is exposed to, audition, olfaction, and stress (Freeman et al., 2000).

Animals who are suffering from fescue toxicosis and a decreased amount of circulating prolactin may display a shaggy hair coat that may be patchy and not look smooth, even in the summer months. The lack of hair shedding is due to the decreased prolactin levels and can add to the heat stress that the animal endures during the summer months when they are already suffering from other symptoms of fescue toxicosis (McClanahan et al., 2008). Studies have indicated that prolactin levels in cattle suffering from fescue toxicosis are often too low to initiate the shedding process, thus causing a delay in the growth of the summer hair coat. Observations of hair growth on cattle during the summer lead to the conclusion that there is excessive hair growth of the hair during the summer, which suggested that the rough hair coats that were observed during the summer could possibly be composed of some hair that is generated during the summer (Aiken et al., 2011). Studies have been conducted to determine if rough hair coats are comprised of mainly winter hair coats, or if there is also summer growth that emerges during the long-day lengths then exhibits excessive growth. It was found that more of the excessive hair growth that adds to the rough hair coat of animals grazing endophyte-infected tall fescue in the summer actually occurs in the spring and early summer and then adds to the retained winter coat (Aiken et al., 2011). Hair shedding scores are often used to determine the level of shedding that has occurred on cattle and can be used as an indicator of the toxicity levels of pastures. The scores are done on a 1 to 5 scale with 1 being completely shed off and slick, and a 5 being an animal that still has its full winter coat (Gray et al., 2011).

Prolactin plays a large role in the growth and development of the mammary gland, the synthesis of milk, and the maintenance of milk secretion. If a reduction in prolactin secretion occurs, the amount of milk that is available to offspring will be reduced and then subsequently effect the growth and well-being of that offspring. It is important to remember that prolactin is not solely responsible for all mammary gland functions, but it plays a role with many other hormones and growth factors that affect the mammary gland (Freeman et al., 2000). In a study by Schmidt et al. (1986), calf birth weights from beef cows that were constantly grazing endophyte-infected tall fescue were not affected by the treatment, however, milk production was affected. Milk production was determined via weigh-suckle-weigh and was reported to be reduced by 50% at 100 days post-partum. Another study by Bolt and Bond (1989) observed that pregnant heifers who grazed endophyte-infected tall fescue from the fifth month of gestation until calving gave birth to calves with reduced birth weights. However, it was also shown that the diet of post-partum cows can heavily influence the milk production and subsequent calf growth. Plasma protein was shown to be reduced in heifers grazing endophyte-infected tall fescue, but average daily gain in their calves was not negatively impacted because the heifers were put on a diet of corn silage after calving. The change to a high-energy feedstuff post-calving stimulated a higher milk output and illustrated that a cow's diet post-partum can possibly alleviate that symptoms of fescue toxicosis on their milk output and calf growth.

Progesterone. Progesterone is another hormone that has been shown to be negatively affected by the consumption of endophyte-infected tall fescue. In relations to prolactin, progesterone has been identified as a potent stimulator of decidual prolactin production (Maslar et al., 1986). Progesterone is a steroid hormone that is produced by the corpus luteum and placenta in order to maintain pregnancy, inhibit reproductive behavior, and inhibit GnRH secretion (Herring, 2014). Disruption in progesterone or insufficient levels will cause a pregnancy to be unviable. Puberty in young heifers is determined by the first increase in serum progesterone concentrations. Washburn et al. (1989) found that puberty was delayed in Angus heifers that grazed endophyte-infected tall fescue. The first service conception rates were also reduced by endophyte-infected tall fescue. Estienne et al. (1990) conducted a related study that used ultrasound to detect the first ovulation of heifers. The study found that 62% of the heifers grazing endophyte-infected tall fescue had reduced serum progesterone. Since the corpus luteum produces progesterone, reduced levels indicated that the corpus luteum function was suboptimal. When the ovaries of heifers grazing endophyte-infected tall fescue were examined, it was discovered that the corpus luteum had increased cellularity with a greater number of mitochondria, lipid droplets, and secretory granules (Ahmed et al., 1990). This could indicate that the peripubertal events that are relative to the corpus luteum may be altered by the presence of the endophyte in toxic fescue and a pregnancy may not be supported (Thompson and Stuedemann, 1993). Mares grazing toxic fescue experience a decrease in the levels of circulating prolactin and progesterone (Monroe et al., 1988; McCann et al., 1989). Mares were monitored before and after grazing endophyte-infected pastures to determine that there was a distinct decrease in circulating progesterone levels. Progesterone is a placental product in mares, so a decrease in circulating concentrations indicates that placental function is compromised by endophyte-infected tall fescue.

Burke et al. (2001) conducted a study where they looked at the impact of endophyte-infected tall fescue and environmental temperature on follicular and luteal development and function in beef heifers. Heifers were fed either endophyte-infected or endophyte-free tall fescue seed at either thermoneutral or heat stressed temperatures. The study found that the greatest decrease of serum progesterone concentrations occurred in heifers that were on a diet of endophyte-infected fescue seed under heat stress conditions. There was also a greater frequency of the heifers on endophyte-infected fescue seed and in heat stress conditions that were observed with dysfunctional corpus luteum. Dysfunctional corpus luteum were categorized as those that failed to produce progesterone, which is needed to maintain a pregnancy. One possible additional cause of the decrease in progesterone, along with the toxic seed and increased environmental temperatures, could be a decrease in total cholesterol in the blood since cholesterol is a precursor to progesterone produced by the corpus luteum.

Estradiol. Estradiol (E2) is a steroid hormone that is produced by the granulosa cells of follicles located on the ovaries, the placenta, and Sertoli cells in the testes. Estradiol promotes sexual behavior, GnRH, elevates the secretory activity of the entire reproductive tract, and increases uterine motility (Herring, 2014). Estradiol was found to decrease or not increase once heifers who were experiencing elevated temperatures consumed endophyte-infected tall fescue seed. This is abnormal because progesterone levels are decreased with elevated environmental temperature or heat stress in combination with endophyte-infected tall fescue seed, so estrogen should increase to compensate when there are undetectable levels of progesterone in cows with normal luteal function (Taft et al., 1999), however this did not occur in the study by Burke et al. (2001). This may suggest that there are altered hormonal feedback mechanisms between the ovary and the hypothalamus or pituitary

Testosterone. Testosterone is a steroid hormone that is produced by theca interna cells in females and is a substrate for estrogen synthesis. Testosterone is also responsible for abnormal masculinization of females, which includes hair growth, voice, and behavior (Herring, 2014). In a study by Hamernik et al. (1978), pregnant cows were injected with testosterone-propionate every other day during the time period of 40 to 60 days of pregnancy. Once the cows gave birth, the offspring (both heifers and bulls) were monitored. Four of the ten cows that were on the study aborted after the testosterone treatment. The four heifers that were born to cows injected with testosterone exhibited a more masculine phenotype, as well as internal reproductive organs more similar to those of males. The heifers were given estradiol to check luteinizing hormone (LH) reactions. The administering of estradiol first depressed serum luteinizing hormone concentrations in all animals, then induced a preovulatory-like LH surge in the heifers that had been exposed to testosterone *in utero* and the control heifers who had not been exposed. The study proves that if exogenous testosterone-propionate is provided during the 40-60-day time period of gestation that partial phenotypic heifer masculinization can occur. The treatment does not affect the sexual differentiation of the bovine hypothalamic centers that regulate LH release or the growth rates of the heifers who were exposed to exogenous testosterone-propionate *in utero*, however.

When stallions were exposed to ergot alkaloid infected seed, it was discovered that their testosterone levels were not changed, along with other breeding factors except for the gel-free volume of an ejaculate (Fayrer-Hosken et al., 2013). However, Alamer and Erickson (1990) found that 3-month-old beef bulls had reduced gonadotropic-releasing hormone-stimulated testosterone secretion along with reduced Sertoli cells after grazing endophyte-infected tall fescue forage. Reduced Sertoli cells in 9 and 12-month-old bulls was also observed, which may permanently impair testicular function in bulls. Other studies have shown that sperm motility is affected by ergot alkaloid consumption, however testosterone concentrations are not impaired compared to concentrations in bulls grazing novel endophyte-infected tall fescue (Looper et al., 2008). The interaction of ergot alkaloids with membrane receptors is complex and different alkaloids can have varying effects on receptors in various types of tissues (Wang et al., 2009).

Cortisol. Cortisol is a steroid hormone that regulates several bodily processes including metabolism and the immune response. Cortisol levels increase when the body is stressed. The release of cortisol in the adrenal cortex is a well-recognized response to numerous stressors in cattle, which includes heat stress (Abilay et al., 1975) that can be induced by fescue toxicosis and further affected by the environmental temperature. Another possible cause of an increased release of cortisol when animals graze ergot alkaloids is the fact that ergotamine has been shown to be a partial agonist of alpha 1-adrenoceptors (Badia et al., 1989). Corticotropic-releasing factor, corticotropin, and cortisol release are stimulated by alpha 1-adrenoceptors agonists (Plotsky et al., 1989), which includes ergotamine. These findings support the increased plasma concentrations of cortisol and thyroid hormones in cattle and supports that ergot alkaloids affect the secretory function of the thyroid and adrenal cortex (Browning et al., 1998).

anti-Müllerian Hormone. anti-Müllerian hormone (AMH) is a dimeric glycoprotein hormone that is only expressed in the gonads (Cate et al., 1986). Another name for the hormone can be Müllerian inhibiting substance (MIS) or Müllerian inhibiting factor (MIF). The hormone is responsible for the regression of Müllerian ducts in male fetuses (Hossam El-Sheikh Ali et al., 2017). The Müllerian ducts, or paramesonephric ducts, form on either side of the mesonephric duct and later form into the fallopian tubes, uterus, cervix and part of the vagina (Mullen and Behringer, 2015). At the early stages, the embryo is not committed to a sex since the morphologic discrimination cannot be made by a simple observation. The sex determination process is directed by a gene on the Y chromosome called the SRY gene. The SRY gene controls the SRY protein and can lead to testes development and a male reproductive tract. Females contain two X chromosomes; therefore, do not carry the SRY protein or gene needed to cause formation of male gonads. Presence of the SRY gene signals testes development. The Sertoli cells in the testes secrete anti-Müllerian hormone (AMH) and dihydrotestosterone, which will then result in the formation of a male reproductive tract (Senger, 2012).

anti-Müllerian hormone (AMH) can be used to predict fertility in heifers at an early age. AMH is expressed by granulosa cells of healthy, growing follicles (Monniaux et al., 2008). As mentioned previously, the age that heifers reach puberty is important at a production and financial standpoint. Reproductive tract scores (RTS) and antral follicle counts (AFC) can be used to assess pubertal status and ovarian cyclicity in heifers (McNeel and Cushman, 2015). If AMH concentrations are monitored in prepubertal heifers and cows and are determined to be relatively stable during this time period, along with a positive correlation with antral follicle counts, then single AMH measurements can be used as a biomarker for predicting antral follicle counts, ovarian reserve, superovulatory response to gonadotropins, and future fertility of cattle (Tilbrook et al., 1992; Batista et al., 2016; McKinley et al., 1992). Heifers that reach puberty earlier have significantly higher AMH concentrations than those heifers that reach puberty late. Also, plasma AMH at an early age around 16 weeks after birth positively correlates with post pubertal plasma AMH at 4 and 6 weeks of after puberty (Hossam El-Sheikh Ali et al., 2017).

Environmental factors that affect fetal growth

The amount of fetal growth of calves that has occurred *in utero* is determined by birth weight, which can be affected by many environmental factors that the dams experience. Factors that influence fetal growth include the number of fetuses *in utero*, sex of fetuses, the number of times the cow has calved, the age of the cow, breed of cow, sire of calf, heat or cold stress, and dam nutrition. Low calf birth weights can lead to low growth rates and average daily gain once the calf is born, decreased mature size of calf, reduced energy reserves, lowered ability of calves to thermoregulate their bodies, and increased risk of calf death at or near birth. Calves that are too large are associated with birthing difficulty, so producers strive for a middle ground that will produce healthy calves. During the early stages of embryo and fetal development when organs and body parts are forming, there is susceptibility to conditions that can cause teratological formations (Dziuk, 1992).

Heat stress is an environmental effect on calves *in utero* that can cause small calves because of decreased blood flow to the fetus, while cold weather can promote increased blood flow and increased fetal size due to a greater opportunity for blood flow to the uterus (Ferrell, 1993). Fescue toxicosis symptoms are the greatest when the toxin levels are higher in the forage and there are higher temperatures. Both the sire and dam can contribute to fetal growth and outcomes in terms of genetics, but the dam can exert influence on the offspring that is beyond her contribution to the fetal genotype. Several studies were conducted by Ferrell (1993) to examine the factors that influence fetal growth and birth weight in cattle. In one study, mature, bred Herefords were surgically implanted with catheters in their uterine artery so that the amount of blood flow could be monitored. The study found that uterine blood flow increased about 4.5-

fold during the time period at the end of the second trimester and the beginning of the third trimester, or days 137 to 250. This is important because if cattle are on a fall calving schedule, the blood flow to their uterus needs to increase during the time period when it would be the hottest temperatures and ergot alkaloid levels would be higher. The exact mechanism for why high temperatures has effects on the fetus has not been established with certainty, but strong circumstantial evidence exists that states that high temperatures cause a shunting of blood away from the uterus to the periphery when the animal is trying to maintain body temperature (Roman-Ponce et al., 1978; Reynolds et al., 1985). The vasoconstriction that occurs as a result of fescue toxicosis could be another source of the decrease in the normal influx of blood flow to the uterus during pregnancy. Reduction in blood flow to the uterus can reduce the supply of nutrients that are available to the fetus, thus affecting the size of the fetus at birth. In order to cool themselves off, many animals will pant. Panting in order to cool by evaporation from the lungs can change the concentration of blood gases, pH of the blood, and acid-based balance (Brown et al., 1988), which will then be transferred to the embryo or fetus. An increase in environmental temperature can cause a decrease in forage and feed consumption, so the issue of supplying nutrients to the fetus is compounded by the reduced amount of nutrient intake (Wetteman et al., 1984).

The dam's diet is a large contributor to the status of the fetus and any deficiencies can have a detrimental effect on the fetus (Hardy and Frape, 1982). The amount of exchange and the substances exchanged between the mother and the fetus through the placenta can determine that growth and relative size of the fetus (Dziuk, 1993). It has been found in several studies that male offspring are born heavier than female offspring, however, when maternal resources become strained, the female offspring tend to perform and do better than male offspring because males have greater demands and are accustomed to more input. When maternal resources become limited in humans during limited nutrients, vasoconstriction from smoking, or reduced uterine space, it has been proven that females will survive preferentially while males have apparent greater demands and will succumb to pressures (Wu et al., 1989). The size of the offspring can also be due to the genetics of the male. The genetics cannot always be determined phenotypically. If a young bull is smaller and is bred to a young heifer, the calves cannot be expected to also be smaller because the bull has not reached his full potential and could have more growing to do. If a sire or dam has been nutrient deficient and did not meet their full growing potential, the same cannot be said for their offspring. This is why environmental factors and nutrients can be important to take into consideration and need to be understood to help make the correct pairing of cows and bulls. The number of environmental factors, toxins, and teratogenic compounds can have a great effect on the fetus and the likelihood of correct formation and survival (Dziuk, 1992). Genetics play a large role in the makeup of offspring, but there are also some controllable and uncontrollable environmental aspects that need to be taken into consideration.

Plant-based solutions to fescue toxicosis

As previously discussed, fescue toxicosis is caused by Kentucky-31 tall fescue, otherwise known as endophyte-infected tall fescue. The forage is extremely prevalent in the Southeastern United States for its survivability and ease of establishment, yet it has numerous negative side effects on the animals that consume it. There are a few options that can help mitigate the toxic effects and possibly relieve the possibility of them occurring completely. These alternatives include planting in a mixture of other forages to dilute the toxic fescue, follow a forage management plan, and completely renovate the pastures and hay land to plant either endophyte-free or novel endophyte-infected tall fescue.

Completely renovating hay fields or pastures can be very costly and will take that piece of land out of the cutting and grazing rotation for possibly a year or more so that a new stand of grass can grow and develop a good root system, yet there will be benefits for years to come when the forage is safe for all animals and will not cause fescue toxicosis symptoms and effect production yield. As mentioned before, there are two other varieties of fescue that can be used which include endophyte-free (EF) fescue and novel endophyte (NE) fescue. Endophyte-free fescue does not contain an endophyte, as the name suggests. Without the endophyte there is no toxic ergot alkaloid production. This is both positive and negative. The animals consuming the forage are safe from the toxic compounds, yet the plant does not have protection from the pests or tolerance to drought or harsh conditions. This version can be harder to establish for this reason. The other alternative fescue option is novel endophyte-infected tall fescue. This version was founded in the late 1990's when scientists found strains of the tall fescue endophyte that did not produce toxic alkaloids. Novel endophyte-infected fescue does produce an endophyte that provides the plant with pest resistance, grazing tolerance, and drought and harsh weather resistance. Both endophyte-free and novel endophyte-infected fescues are non-toxic (Ball et al., 2015).

Another way to alleviate the effects of endophyte-infected tall fescue is to manage pastures more closely and plant other forage varieties in the pastures and hay fields. Good overall pasture management can help with the severity of fescue toxicosis. Some common forages that may be mixed into endophyte-infected fescue pastures in order to dilute the animal's diets are Kentucky bluegrass, orchardgrass, or bermudagrass. Applying nitrogen to pastures and fields during the summer will help boost the growth of warm season forages so that they are not outcompeted by endophyte-infected fescue. Planting legumes, which are high in protein and are nitrogen fixing plants, such as clovers, alfalfa, or annual lespedeza are a way to help combat the issue of little weight gain since they supply more nutrients. Hay fields that are primarily made up of endophyte-infected fescue can be an issue because this allows an opportunity for animals to be fed endophyte-infected fescue year-round. Producers need to be mindful of the type of hay that they cut and make sure that there are other types of forages in their hay other than endophyte-infected fescue. If the hay that is being fed contains endophyte-infected fescue, then it should be fed in a pasture that already contains endophyte-infected fescue so that the pastures are not contaminated and naturally reseeded. The most effective way to alleviate the effects of fescue toxicosis is to the eliminate endophyte-infected tall fescue from the diet of an animal, but heavily managing pastures is an alternative if eliminating the forage is deemed too costly or risky by a producer (Ball et al., 2015).

As mentioned, replacing toxic endophyte-infected fescue with non-toxic version of fescue is not the easiest or cheapest option to alleviate fescue toxicosis, so there are several things that need to be taken into consideration. The costliest portion of renovating fields is completely eliminating the current stand of grass. The grass must be sprayed with herbicide, then another crop is usually planted before the non-toxic fescue is planted later on. By the time there is a sufficient stand of novel or endophyte-free fescue, nearly a year can pass where production of that land is lost. Before a field is prepared for renovation, it is important to know if the seeds that were produced by the existing stand of endophyte-infected fescue are at least a year old to help prevent volunteer seeds from coming up. The endophyte typically dies in seed that has been unrefrigerated after about one year, so seed that has been out in the field for over a year will not have the ability to grow forage and produce toxic ergot alkaloids. Once the endophyte-infected fescue has been sprayed with herbicide, a cover crop that can be grazed or cut for hay should be planted. The cover crop should be cut or grazed very close before the field is sprayed with herbicide again and then the new non-toxic fescue version is drilled into the dead sod. The new fescue should not be grazed or cut until the root system has developed fully and it is at a healthy stand (Ball et al., 2015).

Novel Endophyte-Infected Tall Fescue. A novel endophyte-infected tall fescue variety was first released in 2000 and called MaxQ^{TM}. The variety was first developed by Dr. Joe Bouton at the University of Georgia and Dr. Gary Latch at Ag-Research Limited of New Zealand. Drs. Bouton and Latch used the novel endophytes that were discovered in the 1980's and 1990's to insert into "Jesup" and "GA 5" tall fescue cultivars that were developed in Georgia. The cultivars were tested to ensure their positive resistant properties remained and they were not toxic to the animals. The success of the trials that tested for forage yield, persistence, and animal performance led to the release of the novel varieties "Jesup MaxQ^{TM}" and "GA 5 MaxQ^{TM}". These varieties were sold by Pennington Seed, Inc. from Madison, Georgia at first, but then production was simplified so that only "Jesup MaxQ^{TM}" was sold. Ag-Research USA is now working to develop more varieties of novel fescue that will be able to be selected by producers for their climate and production goals.

The extra cost and labor that it takes to transition grasslands to novel endophyte-infected tall fescue has been put into question and tested over the years with several types of cattle. The majority of the cattle operations in the Southeast are cow-calf producers. Bouton et al. (2000) and Watson et al. (2001) conducted a study in northwest Georgia that found that cattle grazing novel endophyte-infected tall fescue tended to have higher body condition scores and weights than the cows that were grazing endophyte-infected tall fescue. The steer and heifer calves on the study that were grazing novel endophyte-infected tall fescue had approximately 50 and 60 pounds greater weaning weights than the steers and heifers that were grazing endophyte-infected tall fescue. Caldwell et al. (2013) conducted a larger experiment at the University of Arkansas that had 136 pregnant cows on the study that were split between grazing novel endophyte-infected tall fescue and endophyte-infected tall fescue. The performance of the cows and then later calves was tracked for two years. The results of the cow-calf performance showed that the cattle on novel endophyte-infected tall fescue had higher pregnancy rates and weaned heavier calves than those cows that were on toxic endophyte-infected fescue. The study also suggested that novel endophyte-infected fescue improves replacement heifer performance. Stocker cattle performance has also been proven to increase when they are grazed on novel endophyte-infected fescue rather than toxic endophyte-infected fescue. Studies have shown that the stocker cattle have smoother hair coats, lower body temperatures, and spend more time grazing rather than standing in the shade, mud, or pools of water. The stocker cattle that grazed novel endophyte-infected tall fescue were heavier and could meet weight and growth goals better other cattle (Hancock and Andrae, 2012). Novel endophyte-infected tall fescue has been proven to increase performance in each stage and type of production, so it has become a valuable option for grasslands renovation and sewing.

Fetal Programming

The term "fetal programming" has become of more interest in the recent decades in both humans and animals. It has emerged has a major health issue for humans, livestock, and other managed animals because of the long-term consequences for lifetime health and productivity (Zinn et al., 2017). The term refers to the concept of what a mother consumes or the conditions during pregnancy and even before pregnancy can have impact on her offspring. This is of interest when it comes to reproduction in animals because it has been proven that the reproductive performance of animals in their adult life can be determined, in part, by a variety of extraneous influences that act at various stages of development from before conception until birth. Studies have proven that the environment of the developing oocyte plays a role in the programming, which would extend into the preconception period (Rhind et al., 2001). Rhind et al. (1989) reported that there are effects of undernutrition on the fetal growth before placental development has even begun. Undernutrition resulted in restriction of the growth of the conceptus as early as day 11 of gestation, which is several days before implantation. Evidence of early fetal programming was exemplified by Putney et al. (1989) when the adverse effects of heat stress in cattle were studied. The study revealed that exposing heifers to high temperatures for a few hours during early Oestrus was associated with a reduction in embryo quality at day 7 after insemination. The normal pattern of embryonic development can be altered by just a brief adverse environmental event at a critical window in development (Rhind et al., 2001). Fetal programming can occur at any time before and during pregnancy and may be due to a single occurrence or event, or multiple events that interact to cause changes to the embryo or fetus. The fetus may be born with noticeable differences after an adverse occurrence during fetal programming, or the effects may not be noticeable until later on years after birth.

Placental growth. Fetal programming has a large impact on fetal growth, which is highly correlated with reduced uteroplacental growth and development (Reynolds and Redmer, 1995, 2001). Since adequate blood flow is essential to normal fetal growth, any conditions that restrict the fetal and placental growth can be traced back to reduced rates of placental blood flow and nutrient uptake by the fetus (Reynolds and Redmer, 1995). Maternal body composition and diet are thought to affect fetal development as a result of direct effects on nutrient availability to the fetus, and then indirectly through changes in the placental function and structure (Godfrey, 2002). The fetal programming effects that may occur due to placental effects include alterations in placental growth and vascular resistance, altered nutrient and hormone metabolism in the placenta, and changes in nutrient transfer and partitioning between mother, placenta, and fetus (Godfrey, Breier and Cooper, 1999). It has been hypothesized that any endocrine, nutrient, or cardiovascular restrictions that the fetus may endure while *in utero* may influence the expression of the fetal genome, which can lead to developmental adaptations that can help the fetus survive in the initial stages after birth. However, these developmental adaptations may only have an initial survival advantage and may predispose them to a degenerative disease later on in life (Godfrey, 2002). The size of the placenta has an important influence on fetal endocrinology and metabolism that can lead to a range of changes that includes lowering of fetal plasma concentrations of insulin-like growth factor-1 (IGF-1) (Owens, Owens and Robinson, 1989). Fescue toxicosis can cause vasoconstriction to the uterine arteries that can lead to a reduction of blood flow to the placenta, which can cause many issues with the amount of nutrients that are able to reach the placenta and the fetus (Duckett et al., 2014). All of the previously mentioned placental stressors and issues can be triggered by a number of things, but the stressors that come with fescue toxicosis can exasperate the conditions. Another placental issue associated with fescue toxicosis is the thickening of the placenta, which can be coupled with the issue of retained placentas at birth (Porter and Thompson, 2014).

Ruminants have a cotyledonary placenta which means there are many small discoid structures surrounding the fetus to provide nutrients. The cotyledonary placenta is made up of two portions, the cotyledons on the fetal side and caruncles on the maternal side. The entire structure is called a “placentome”. When parturition occurs, the two parts of the cotyledonary placenta separate so that the cotyledons are expelled from the uterus after birth and the caruncle portion stays with the uterus of the cow. Cattle usually have between 75 and 125 placentomes (Bowen, 2000). Vasoconstriction caused by fescue toxicosis can reduce the blood flow to the placentomes, which can then reduce the nutrients that reach the fetus.

Long et al. (2014) conducted a study that looked at several aspects of pregnant cattle that were divided into groups and either given a diet that met National Research Requirements (NRC) requirements, or one that was under the requirements and nutrient restricted. Cattle were selected from each group were then extinguished on either day 125 or day 245 of gestation to be necropsied. Multiple parameters of each placenta were looked at including the size of the placentomes, amount of amniotic fluid, uterine weights, uterine volumes, and other placental characteristics. Once the placentas of all of the cattle were examined, it was concluded that the cattle that were on a restrictive diet had reduced cotyledonary weight and cotyledonary weight divided by caruncular weight for cattle sacrificed at day 125 and day 245 of pregnancy. The total placental surface area tended to be reduced in the nutrient restricted cattle that were determined to have intrauterine growth restriction, but not in the control cows eating the recommended amount of nutrients or the nutrient restricted cattle that were deemed not to have any intrauterine growth restrictions at day 125 of gestation. At day 245 of gestation, the number of placentomes tended to be decreased, whereas the average surface area per placentome tended to be increased in all nutrient restricted cows compared to the control cows. This resulted in a similar placentome surface area for both nutrient restricted and control groups at day 245 of gestation. This information is of importance when considering fescue toxicosis and the placenta because fescue toxicosis has the ability to cause nutrient restriction to the uterus and placenta by vasoconstriction, so there is similarity in the opportunity for the restrictive property.

Calf performance. The performance of a calf can be influenced by many aspects once the calf is born, but the fetal programming that occurs has the opportunity to provide the calf with a strong start *in utero* and start life at a healthy weight and overall physical state. Fetal programming, in terms of maternal nutrition during pregnancy, has especially been recognized in the past few years as a large factor in offspring growth. Several studies have been conducted that look at human programming based on nutritional status. Naturally occurring situations that lead to a lack of food and starvation have been used to study the effects that the lack of balanced nutrition has on those people later on in life. During these studies, it was found that individuals that were exposed to a famine while *in utero* were often times obese, which is defined in this case as someone who has a weight to height ratio of more than 120% when compared to the reference population (Lumey et al., 2011). This means that the people did not grow tall, but then still gained weight later on.

As mentioned earlier, vasoconstriction occurs when animals consume ergot alkaloids. Ergovaline has the ability to induce contraction of the bovine uterine and umbilical cord arteries by interacting with $5HT_{2A}$ serotonergic receptors, which has the ability to restrict blood flow to the fetus. These restrictions can induce fetal growth restriction that is similar to maternal hyperthermia or nutrient deprivation (Dyer, 1993). Duckett et al. (2014) studied the effects of endophyte-infected tall fescue versus endophyte-free tall fescue on pregnant ewes. The study found that the birth weight of lambs was reduced by 37% for the endophyte-infected fescue group versus the endophyte-free group. In another study by Watson et al. (2004), calf birth weights for cows grazing endophyte-infected versus endophyte-free fescue during gestation was found to be reduced by 15%. These growth restrictions for the endophyte-infected fescue diets are similar to the results of studies looking at high ambient temperature exposure throughout pregnancy, which has been found to produce the most severe intrauterine growth restriction (Bell et al., 1987, 1989; Thureen et al., 1992; Anthony et al., 2003; Arroyo et al., 2006). Duckett et al. (2014) also observed that the organ and muscle weights were lighter for the t endophyte-infected group versus the endophyte-free group, so the exposure to ergot alkaloids *in utero* reduced fetal growth and muscle development. Prolactin is important for mammary development and milk secretion, so it is a vital component of parturition and lactation. The study found that there were drastically lowered levels of prolactin at day 130 of pregnancy for the group of ewes that were on a toxic endophyte diet. The lowered levels of prolactin could indicate post-partum issues with the ewe's metabolism and mammary growth, which would negatively impact the growth of the lambs later on. When the gestation lengths of the ewes were looked at, it was found that the ewes on endophyte-infected fescue had gestation lengths approximately 4 days shorter ($P < 0.05$) than the ewes on endophyte-free fescue. Long et al., (2010) found that cows that had been nutrient restricted from day 32-83 of gestation had shorter gestation lengths. Horses that have been exposed to endophyte-infected fescue during gestation, however, have increased gestation lengths (Putnam et al., 1991).

When considering the calf performance measurements, it is important to think about performance at birth and weaning, but it is also important to remember that fetal programming impacts the entire life of the animal and that there may not be a way for that animal to recover and catch up to their peers that were not exposed to endophyte-infected fescue *in utero*. In the study by Duckett et al. (2014), it was found that the ingestion of endophyte-infected toxic fescue during critical time periods of gestation in ewes, such as the second trimester when the majority of muscle development occurs, will alter the offspring's muscle growth and development. The altered physiology can have a lasting impact on postnatal muscle growth, carcass composition, and the palatability of the offspring. These factors are important to think about for animals that will be going to slaughter, but it is also important to remember that replacement offspring that will be kept in the herd to reproduce can pass on these qualities or express negative physiological traits themselves that may affect their reproduction and mothering ability.

Calf performance can also be measured in reproductive efficiency and production, which are important to the income and sustainability of a cattle operation. As previously mentioned, embryo development can be manipulated by various occurrences at different times of gestation. Undernutrition has been proven to have an effect on gonadal development, tissue differentiation, and the establishment of associated enzyme systems, which can have a fundamental effect on the subsequent function of these organs (Rhind et al., 2001). For females, a reproductively critical window is the period up to the end of folliculogenesis because the number of ovarian follicles and potential for the number of offspring cannot be modified past this point. The critical reproductive development periods are not as defined in males since there are many stages to the development of the testes. In both sexes, the development of the hypothalamic-pituitary axis and the associated synthesis of gonadotropins is a critical time period that is potentially sensitive to nutritional and other influences. The effects of fetal programming do not always end with the reproductive performance of the current generation. The gene activity can be altered by environmental factors, which can then be passed on to the next generation (Rhind et al., 2001). This aspect of fetal programming was proven by Cavalli and Paro (1998) when laboratory fruit flies were exposed to a brief heat shock, which resulted in the activation of a gene that caused the flies to have red eyes. The gene activation was then passed on to the next generation and caused them to have red eyes also. Keeping these examples in mind, the performance of the subsequent generation needs to be considered when determining the environment and nutrition of the dam.

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CHAPTER 2

IMPACTS OF FESCUE TOXICOSIS ON CATTLE PERFORMANCE

INTRODUCTION

Endophyte-infected tall fescue (Lolium arundinaceum [Schreb.] Darbysh) is a cool season, perennial forage that is the most utilized forage for cattle producers in the Southeast United States. The forage, otherwise known as 'Kentucky-31', gained its popularity from its ease of establishment and hardiness in the area. The prominent forage is great for lower maintenance pastures and hay fields, yet it has a downside because of its toxic characteristics. The forage contains an endophytic fungus that has a symbiotic relationship with the plant that provides protection from elements including drought, insects, and close grazing stress (Ball et al., 1993). The symbiotic relationship benefits the forage, however, the cattle that are grazing the tall fescue suffer from many side effects of the toxic compounds produced. The endophytic fungus is located within the plant and has the ability to produce ergot alkaloids, which causes animals to experience a condition called fescue toxicosis when consumed.

Fescue toxicosis is known for causing conditions in cattle which include vasoconstriction, reduced average daily gain, reduced circulating steroid hormones, reduced reproductive performance, reduced hair shedding, and overall reduced performance of the animal. Heifers that have been exposed to endophyte-infected fescue have shown a delay in the age of puberty, which is denoted by an increase in progesterone levels (Washburn and Green, 1991). The second trimester is a pivotal period in gestation with significant muscle and reproductive tract development, specifically ovaries, in heifer fetuses. The topic in question is if toxins from endophyte-infected tall fescue can enter the blood stream of cattle and then go to the uterus and placenta where the calf resides and sources nutrients from. If this can occur, there may be possible consequences on calf development.

Fescue toxicosis is detrimental to the cattle industry in the Southeastern United States, especially the cow-calf industry, with an annual loss of $1 billion to the livestock industry in the United States (Strickland et al., 2011). With the detrimental loss to the cattle industry as a result of endophyte-infected fescue, several other fescue cultivars have been created and utilized to help relieve the situation. One of those options is novel endophyte-infected tall fescue, which has the positive characteristics of the symbiotic relationship of the endophyte yet does not produce the ergot alkaloid toxins to harm the animals that consume the forage. Novel endophyte-infected tall fescue can be used to replace toxic endophyte-infected tall fescue, but many producers are hesitant because of the cost and time investment that it would require.

MATERIALS AND METHODS

This study was conducted over a course of two years (2017-2018) at Butner Beef Cattle Field Laboratory (BBCFL) in Bahama, NC. All animal procedures were approved by the North Carolina State University Institutional Animal Care and Use Committee (NCSU IACUC #17-043-A).

Animals and Treatment

Cattle performance and forage data were collected over a treatment period of April to late July of the years 2017 and 2018 to monitor the effects of novel endophyte-infected tall fescue versus endophyte-infected tall fescue on mid-gestational cattle and their heifer calves after birth (see experimental timelines in Figure 2.1 and Figure 2.2). Angus and Angus x Simmental cows were bred in late January 2017 and 2018 via artificial insemination (AI) at BBCFL. The cattle were ultrasounded each year at day 30 after artificial insemination to confirm pregnancy, then again at day 60 of gestation to determine the sex of the fetus. Any cattle that were deemed to be carrying heifer calves were chosen for the study (n=54 Year 1; n=33 Year 2). Cattle were further divided into treatment groups blocked by age (2-3 y, 4-7 y, >7 y), body weight, and breed each year. The groups were randomly assigned to one of two treatments, endophyte-infected tall fescue (E+) pastures, or novel endophyte-infected tall fescue (EN) pastures (n=27 E+ Year 1; n=27 EN Year 1; n=17 E+ Year 2; n=16 EN Year 2). The cattle grazed their assigned forage for the entirety of the treatment period, which lasted for 14 weeks each year. Cattle were provided ad libitum water and trace minerals throughout the treatment period, as well as provided natural shade structures in the pastures.

In order to monitor cattle physiological response to the treatments and overall performance, several weekly measurements were taken. Measurements included body weight

(BW), body condition scores (BCS) on a 1-9 scale with 1 being emaciated and 9 being obese (as adapted from Richards et al., 1986), hair shedding scores (HSS) on a scale of 1-5 with 1 being completely shed off and 5 having a full winter coat (as adapted from Gray et al., 2011), hair coat scores (HCS) on a 1-5 scale with 1 being a more slick, thinner coat and 5 being a thicker, more course coat (as adapted from Olsen et al., 2003), rectal temperatures, and jugular blood samples were taken from each animal each week during the treatment periods. Body weight measurements were taken each week by using a Tru-Test Livestock Scale as the animals were being worked through a cattle squeeze chute. Body condition scores (BCS), hair shedding scores (HSS), and hair coat scores (HCS) were taken by two highly trained technicians on a subjective basis, then scores were composited to get an average score for each measurement for each individual animal each week. Rectal temperatures were collected by using a digital thermometer each week. Blood samples were collected each week via jugular venipuncture using 20-gauge 1-inch VACUETTE® multiple use drawing needles and sterile 10.0 mL vacutainer tubes that did not contain additive (Becton Dickerson, Franklin Lakes, NJ). At the time of blood collection, blood samples were placed on ice until transport to the laboratory for processing. Once in the laboratory, whole blood samples were immediately centrifuged for 25 minutes at 1,500 X g at 4°C. Serum was then drawn from the vacutainer tubes using once-use pipettes and then aliquoted into glass dram vials and plastic micro-centrifuge tubes that were labeled for each specific animal. Weekly serum samples were stored at -20°C until analysis was conducted.

Once the 14-week treatment periods were complete, cattle were managed together on either endophyte-infected tall fescue (E+) or novel endophyte-infected tall fescue (EN), depending on forage availability. The cows calved from mid-October until the beginning of November in one pasture while being fed hay. Once cows calved, the calves were weighed using a Tru-Test Livestock digital sling scale. Any bull calves that may have been born were castrated immediately, identified with an ear tag, and then removed from the study. Out of the 2017 calves, 21 were heifer calves from the E+ group and 21 were heifer calves from the EN group, giving a heifer birth rate of 78% of the 54 cows total on the study that year. Gestation lengths of 2017 calves were calculated using an artificial insemination date of January 26, 2017 and the date of birth of each calf. Once heifer calves were born, the cows were monitored until placentas were delivered. Once placentas were delivered, trained technicians would immediately collect the cotyledonary portion of the placenta that had been delivered and place it in a heavy-duty grade trash bag with two different forms of identification. Each bag had a laminated tag of the cow number attached to the outside of the bag, as well as a notecard with the cow number, date, time collected, and sex of calf recorded that was placed in a Ziploc bag. Placentas were immediately weighed, not accounting for the weight of the bag and labels. Placentas were stored at -20°C until transport to the laboratory at NC State University for further examination. Once all placentas were collected and calving season had concluded, placentas were cleaned in the lab to remove any hay, manure, and grass that may have been accrued during delivery, and examined for several measurements including weight for a second time, cotyledon count, and collective cotyledon weight. From these measurements, the percentage of each placenta that was made up of cotyledons was found. Weaned 2017 heifers were managed as a group on either endophyte-infected tall fescue or novel endophyte-infected tall fescue, depending on forage availability at the field laboratory.

Year 2 of the study consisted of cows that were deemed to be pregnant with heifer calves at 60 days of gestation. Some cows had been on the study the previous year, but those cows were not necessarily on the same treatment again since cattle were randomly assigned to treatment groups.

Temperature Humidity Index (THI) Measurements

Ambient temperature and humidity were collected weekly during data collection. Additionally, records were obtained from the National Weather Service Henderson Oxford Airport station, approximately 40 km from BBCFL. Temperature-humidity index (THI, Buffington et al., 1977) was calculated using the formula:

$$THI = T_{db} – [0.55-(0.55 \text{ x } RH / 100) \text{ x } (T_{db} – 58)$$

where T_{db} represents dry bulb temperature (°F) and RH represents relative humidity.

Forage Measurements

Cattle grazed either endophyte-infected tall fescue (E+) pastures or novel endophyte-infected tall fescue (EN) pastures depending on the random assignment of treatment. The two different groups were located at different locations of the farm that have well-established stands of their respective forages. The endophyte-infected tall fescue pastures are planted in Kentucky-31, while the novel endophyte-infected tall fescue pastures are planted in MaxQ II that was established in 2013. Pastures were rotationally grazed with approximately 4 acres in each section. Cattle were rotated every 2 weeks during the 14-week treatment periods of Year 1 and Year 2 to ensure adequate forage availability. Forage samples were collected prior to each pasture rotation (bi-weekly) in an established collection method so that analysis would reflect the forage that was available to cattle at the time they were introduced to the pasture. Composite samples were then taken from each pasture sample to be evaluated for nutrient quality, percentage of available forage that was fescue (separations), and alkaloid levels (toxicity of pastures). In addition to the bi-weekly forage samples taken during the treatment period, fescue tiller samples were collected in mid-November 2017 to evaluate the percentage of endophyte present and also the percentage of tiller that contained ergot alkaloids in each pasture utilized during the treatment period. This measurement supplied the infection rate of the toxic endophyte in each pasture (Table 2.4).

Composite forage samples were collected then placed in their respective labeled Ziploc bags and then stored on ice until transported for analysis or stored at -20°C. One portion of the composite samples were submitted on a bi-weekly basis on the day of collection to the North Carolina Department of Agriculture Forage Laboratory in Raleigh, NC to test for nutrient quality (Table 2.1 and Table 2.2). Another portion of the same composite samples were taken back to the in-house laboratory at NC State University to be evaluated by trained technicians for the different species of forage in the sample. Samples were separated into two groups, fescue and other. Separation samples were then placed in individual paper bags by type of forage and data taken and weighed to gather a wet weight. The separations were then placed in a drying oven for 48 hours at 60°C and then taken out and weighed again for a dry matter weight. These measurements were further calculated to find the percentage of each pasture that was fescue at the time of sampling on a dry matter (DM) basis (Table 2.3). Another portion of the bi-weekly composite forage samples were freeze dried by established methods in house by a trained technician, then ground through a 1 mm screen in a Wiley Mill. Tiller samples that were collected in mid-November 2017 were rinsed, trimmed to remove any extra roots and non-tiller portion collected, then shipped on ice the morning following collection to determine the infection rate of the pastures (Agrinostics Ltd. Co., P.O. Box 882, Watkinsville, GA 30677; Table 2.3). The final portion of the bi-weekly composited forages were retained in case of an issue with the other portions of the sample.

Serum Assays and Analysis

Serum progesterone concentrations (P4) were analyzed for Year 1 and Year 2 for weeks 0, 2, 4, 6, 8, 10, 12, and 14 of the treatment periods for each year. These weeks represent bi-weekly sampling during the treatment periods and align with the forage sampling and subsequent rotation of cattle to a new pasture section so that serum analysis represents the serum P4 concentration of the cattle from the prior 2 weeks on a pasture. Progesterone concentrations were determined by a commercially available radioimmunoassay, Immuchem Coated Tube Progesterone I^{125} RIA assay (ICN Pharmaceuticals, Inc., Costa Mesa, CA; Lyons et al., 2016). Concentrations were reported in ng per mL. The intra-assay coefficient of variation was 9.41% while the inter-assay coefficient of variation was 7.0%.

Serum prolactin concentrations (PRL) were analyzed for a subset of cattle from Year 1 for weeks 0, 4, 10, and 14. These weeks represent evenly distributed times that forage was sampled to determine the toxicity level from the beginning of the treatment period until the end. Concentrations were determined by a commercially available Bovine Prolactin ELISA assay (MyBioSource, San Diego, CA). Concentrations were reported in ng per mL. The inter-assay coefficient of variation based on the single plate ran was 3.75%.

Statistical Analysis

Statistical analysis was completed by using the MIXED procedure of SAS 9.3 (SAS Inst. Inc., Cary, NC, 1996) with repeated measures. Results are reported as least square means $\pm$ SEM with statistical significance reported at $P<0.05$ and statistical tendency reported at $0.05 \leq P \leq 0.10$. Model statement is the following: $Y_{ijkl} = FS_i + A_j + T_k + \varepsilon_{ijkl}$ where FS= fescue treatment (KY-31 or MaxQ), A= cow age block (2-3 yo, 4-7 yo, or >7 yo), and T= time (week 0-14).

RESULTS AND DISCUSSION

Cow Performance

Average Daily Gain. The results show that the average daily gain (ADG) for cattle grazing novel endophyte-infected tall fescue (EN) was greater than those cattle grazing toxic endophyte-infected tall fescue (E+) for Year 1 and Year 2. Statistical significance ($P<0.05$) was shown for ADG for Year 2 with TRT: $P<0.0001$ in Figure 2.15. There was a statistical tendency ($0.05 \leq P \leq 0.10$) for ADG in Year 1 of the study with TRT: $P=0.09$, which is shown in Figure 2.3.

Cattle experiencing fescue toxicosis display several signs including reduced average daily gain. Studies have shown that cattle that are grazing endophyte-free tall fescue, or a non-toxic version, and then are switched to toxic endophyte-infected tall fescue display decreased forage intake within days. Animals that are grazing toxic endophyte-infected tall fescue and then are switched to grazing endophyte-free tall fescue still display signs of fescue toxicosis for several weeks (Schmidt and Osborn, 1993). These studies prove that the ergot alkaloids in toxic endophyte-infected tall fescue can reduce productivity in cattle extremely quickly and then cause side effects that will last for weeks until their system can then rid itself of the ergot alkaloids.

The average daily gains for the two treatments differ in statistical significance. There was not a large difference between the forage quality between Year 1 and Year (Table 2.1 and Table 2.2). During Year 1, the dry matter (DM) of the forage sampled for wk 12 was 29.8% and 27.4% for E+ and EN pastures, respectively. Whereas the DM at wk 12 for Year 2 of the study was 47.9% and 44.2% for E+ and EN, respectively. Other nutrients, such as crude protein (CP) and total digestible nutrients (TDN), remained similar and did not show a large numerical change between the forage type and Year 1 and Year 2. One possible contributing factor to the differences of statistical significance between Year 1 and Year 2 of the study was the temperature humidity index (THI) (Figure 2.25). Overall, the temperature humidity index was greater for Year 2 versus Year 1, along with the average THI.

Body Condition Scores. During Year 1, body condition scores were statistically significant ($P<0.05$) for treatment and age effects (TRT: $P=0.0004$, AGE: $P=0.0003$). In Year 2, however, the model was not significant by treatment (TRT: $P=0.3397$) but was for treatment and age interaction (TRTxAGE: $P=0.0013$). Both Year 1 and Year 2 displayed higher body condition scores for cattle grazing novel endophyte-infected tall fescue rather than the cattle grazing toxic endophyte-infected tall fescue (Figure 2.4 and Figure 2.16, respectively). Year 1 cattle that were 2-3 years old had the lowest body condition scores compared to cattle that were in the 4-7-year-old and >7-year-old groups (Figure 2.5). This can be explained by the younger cattle not being as mature and not having the time to build up body condition such as the older cows. Also, the younger cattle do not have the number of parities that they older cows have; therefore their bodies may experience more stress during lactation and they may not have the body condition that the older cows do to account for the added stress during parturition and lactation. As previously discussed, consumption of toxic endophyte-infected tall fescue can have effects on feed intake and digestibility, so 2-3-year-old cattle that were grazing the toxic forage may have had lower body condition scores as a result.

Body condition scores (BCS) were taken each of the 14 weeks of Year 1 and Year 2 of the study. At the beginning of the treatment period, the cows had recently weaned their calves from the previous year and were entering the second trimester of gestation. With this in mind, the cattle were all expected to gain weight and body condition score to prepare for calving again in the fall. In a study conducted in northwest Georgia, cows that were grazing novel endophyte-infected tall fescue tended to have better body condition scores and weights than those cattle who grazed toxic endophyte-infected tall fescue (Hancock and Andrae, 2012).

In a study conducted by Renquist et al. (2006), cattle that were in a range of 3 to 10 years old were monitored for several measurements and differences in production based on age. The study proved that cattle in the 3-year-old group had the lowest body condition scores out of the cattle. The cattle that were 8 years old had the greatest body condition scores. In this study, Year 2 cattle were significant for body condition scores for the treatment by age interaction (Figure 2.17) where the cattle that were in the 2-3-year-old group for EN and E+ had the lowest body condition scores (TRTxAGE: P=0.0013). The cattle grazing E+ that were >7 years old had the highest body condition scores when the expectation is that the cattle grazing EN would have the highest body condition scores in each age group. This unexpected result may be due to natural genetic selection of cattle who perform well on toxic endophyte-infected tall fescue. The animals in beef cattle herds in the Southeastern United States are often indirectly selected for those who perform best in toxic endophyte-infected fescue environments since it is the most popular forage.

Hair Shedding Scores. During Year 1 and Year 2, the model was significant ($P<0.05$) for the treatment by week interaction (TRTxWEEK: $P<0.0001$, $P<0.0001$, respectively). Figure 2.8 and Figure 2.21 both display that as the number of weeks of exposure progress, the amount of hair shedding increases with lower hair shedding scores. The cattle that are grazing novel endophyte-infected tall fescue pastures had lower hair shedding scores, overall, compared to those cattle grazing toxic endophyte-infected tall fescue meaning that they shed their hair more quickly. Year 2 hair shedding scores were significant for age (AGE: $P<0.0001$). Figure 2.20 displays that the cattle in the 2-3-year-old group had the lowest hair shedding score meaning that they were shed the most out of the three age groups.

Hair shedding has been proven to be affected by toxic endophyte-infected tall fescue in several studies. The cattle who graze toxic endophyte-infected fescue usually have decreased levels of prolactin, which then effects the amount of hair shedding that will occur and the hair coat roughness. Gray et al. (2011) found the correlation that cattle who shed their winter hair coats earlier in the summer will suffer less from the negative effects of fescue toxicosis during the spike in ergot alkaloids during the summer months. In this study, hair shedding scores were taken weekly during the treatment period to monitor the amount of shedding that occurred during that time period. The expectation was that cattle grazing novel endophyte-infected tall fescue (EN) would shed their winter coats more quickly than those animals are toxic endophyte-infected tall fescue (E+).

Hormone Profiles

Progesterone Concentrations. Circulating progesterone concentrations were measured biweekly during Year 1 and Year 2 of the study. Year 1 and Year 2 progesterone concentrations were higher in those cattle grazing novel endophyte-infected tall fescue (EN) compared to cattle grazing toxic endophyte-infected tall fescue (E+) as shown in Figure 2.10 and Figure 2.24. The model for Year 1 was significant ($P<0.05$) for the treatment by week interaction (TRTxWEEK: $P=0.0036$). The model for Year 2, however, only showed numerical differences between the two treatment groups and the weeks of exposure (TRTxWEEK: $P=0.1287$). Like Year 1, the data for Year 2 displays that the cattle who grazed novel endophyte-infected tall fescue (EN) had higher levels of circulating progesterone than those grazing toxic endophyte-infected tall fescue (E+).

Previous research supports that grazing toxic endophyte-infected tall fescue causes cattle to have reduced concentrations of circulating hormones including progesterone, cortisol, and prolactin (Mahmood et al., 1994; Jones et al., 2003; Porter, 1995). Progesterone is an important reproductive hormone that helps to establish and maintain pregnancy, so it has been studied from conception to birth in animals, including cattle grazing toxic endophyte-infected tall fescue, to find the effects that different levels of progesterone have on the mother and offspring. Research looking into the mechanisms that reduce the concentration of circulating progesterone in cattle grazing E+ has been limited, however several theories have been developed from the research. Strickland et al. (2011) speculates the reduction in progesterone, which is a cholesterol-based hormone, may be due to lowered serum cholesterol. Lowered serum cholesterol was observed in steers that were consuming toxic endophyte-infected tall fescue. As previously discussed, a symptom of fescue toxicosis is vasoconstriction, so another theory is that vasoconstriction reduces the amount of blood flow in the reproductive organs, thus reducing the amount progesterone that is able to circulate properly (Klotz et al., 2015). (Poole et al., 2018) found that there was a significant decrease in the diameter of arteries and veins that service the ovaries and uterus during a period of the estrous cycle for heifers grazing toxic endophyte-infected tall fescue versus endophyte-free tall fescue. This could contribute to reduced ovarian function and pregnancy rates in cattle experiencing symptoms of fescue toxicosis.

Prolactin Concentrations. The subset of prolactin values (EN: n=5, E+: n=5) from Year 1 shown in Figures 2.26 and 2.27 show no significant differences ($P<0.05$) or tendencies ($0.05 \leq P \leq 0.10$) when comparing treatments (TRT: $P=0.96$) or interactions between treatment and week (TRTxWEEK: $P=0.30$). There was, however, significance by week (WEEK: $P=0.03$). Figure 2.26 displays the treatment and week interaction. Cattle grazing novel endophyte-infected tall fescue have more steady prolactin concentration values, whereas cattle grazing endophyte-infected tall fescue vary more throughout the different weeks. Figure 2.27 displays the prolactin levels between the subset of treatments (EN: 81.01 ng/mL, E+: 81.41 ng/mL).

Prolactin serum concentrations have been determined to be an indicator of animals who are suffering from fescue toxicosis, so the measurement can help estimate the severity of ergot alkaloid concentration in endophyte-infected tall fescue and the amount consumed by cattle (Klotz, 2015). Prolactin concentrations are usually decreased in animals that graze endophyte-infected tall fescue (Schmidt and Osborn, 1993). Decreased prolactin prevents cattle from shedding their winter coats and causes their coats to have a shaggy and patchy look where the hair is not smooth, even in the summer months. The added heat stress can exasperate the effects of fescue toxicosis in cattle (McClanahan et al., 2008). The subset of cattle for Year 1 that were measured for prolactin levels throughout the trial did not show any differences between treatments like expected. This lack of difference could be due to the size of the subset since there were only five cattle from the novel endophyte-infected group and five cattle from the endophyte-infected tall fescue group. If serum concentrations were determined for all cattle, more differences may have been seen. Another aspect that could have led to the lack of differences could be the temperature during the treatment period. The temperature humidity index averaged 80.72 for Year 1, which was lower than Year 2. Some additional factors that determine the amount of prolactin secreted by an animal include the amount of light exposure, audition, olfaction, and stress (Freeman et al., 2000). Circulating prolactin concentrations vary according to the photoperiod and are greater during times of the year when there is the most light daily and are lower during the time of the year when there is less light daily (Tucker and Ringer, 1982; Tucker et al., 1984; Critser et al., 1988). The treatment period was during the summer months when there are the longest days and maximum amount of light of the year, so this may have caused the prolactin levels to stay higher than if serum concentrations were determined for parts of the year that had shorter days.

Calf Performance

Gestation Length. Calves born to the cattle in Year 1 of the study in the Fall of 2017 were documented and the gestation lengths were calculated based on the AI date of January 26, 2017. The gestation lengths of cattle that grazed novel endophyte-infected tall fescue (EN) and toxic endophyte-infected tall fescue (E+) during their second trimester are displayed in Figure 2.11. Cattle who were in the EN treatment group had longer gestation lengths on average than cattle who were in the E+ treatment group, numerically, however the values were not significantly ($P<0.05$) different (TRT: $P=0.51$). The average gestation lengths of the treatment groups were only different by approximately 1 day with EN being 277.2 days and E+ being 276.1 days.

The normal gestation length of Angus and SimAngus cattle is considered to be around 283 days. The calves in this study were born within a few days of their expected due date, however other studies have seen more drastic differences in gestation length. This could be due to the short treatment period that was only during the second trimester of pregnancy for this study. Duckett et al. (2014) used sheep that were either fed toxic endophyte-infected tall fescue seed (E+) or non-toxic endophyte-free tall fescue seed in a controlled environment during gestation to look at the differences between the dams during pregnancy and the differences in offspring at birth. Ewes that were on the E+ diet had gestation lengths that were approximately 4 days shorter than the ewes on the non-toxic endophyte-free diet. Shorter gestation lengths have also been reported in ewes that are determined to have placental insufficiency (Chen et al., 2010) and cows that were nutrient restricted d 32-83 of gestation (Long et al., 2010). Horses, however, are different because there are longer gestation lengths observed in those who consume toxic endophyte-infected tall fescue during gestation (Putnam et al., 1991).

Birth Weight. Figure 2.12 displays that birth weights of the calves born to cows in each treatment group were not statistically ($P<0.05$) different, however were numerically different. Calves born to dams that were in the EN treatment group were numerically greater in weight (32.21 kg) than those calves born to cows that were in the E+ treatment group (30.11 kg) (TRT: $P= 0.13$).

Watson et al. (2004) conducted a study that compared pregnant cows grazing novel endophyte-infected tall fescue (AR542) with cattle grazing toxic endophyte-infected tall fescue (E+). The cattle that were grazing the novel fescue gave birth to calves that were heavier when compared to the calves that had dams that grazed E+ pastures ($P<0.05$). The differences in the Watson et al. (2004) study and this study is that all of the cattle were on treatment early on in pregnancy as well as half way through, so the cattle had more exposure to their treatment. This study, however, did not use treatments until the second trimester and then the type of fescue was not monitored for the third trimester, which may have led to some differences, or lack thereof, for calf birth weights. Also, the cattle that Watson et al. (2004) used had never been exposed to toxic endophyte-infected fescue prior to the study, which has been known to change the outcome of performance. Bolt and Bond (1989) conducted a similar study and found that heifers who were on either a novel endophyte-infected tall fescue or toxic endophyte-infected tall fescue treatment showed differences in calf birth weights where the cows grazing EN fescue had increased birth weights compared to those cattle who grazed E+ fescue. The clear difference in this study was that heifers were used so their bodies did not have a tolerance built up to consuming toxic endophyte-infected fescue, so the effects may have been greater for them. The difference in calf birth weight is hypothesized to be as a result of compromised blood flow to the uterus and fetus as a result of vasoconstriction because of the animal consuming toxic endophyte-infected tall fescue (Porter and Thompson, 1992). The possible reason that greater differences were not seen in calf birth weights from this study is that the treatment period was only during the second trimester, so there may have been more variance in the birth weights between treatment groups if the treatment period was longer. Godfrey and Barker (2001) suggested that the fetal size and proportions at birth are proxy measures for mechanisms that program the long-term effects for the offspring.

Placental Weight. When comparing the average placenta weights between the group that grazed novel endophyte-infected tall fescue (EN) and the group that grazed toxic endophyte-infected tall fescue (E+) as shown in Figure 2.13, the data displays that the cattle grazing EN fescue had numerically greater average placenta weights (3.10 kg) than those cattle grazing E+ fescue (3.02 kg). However, there was no statistical significance ($P<0.05$) when looking at differences between treatment groups (TRT: $P=0.83$).

Placental biology has been proven to be affected by the mother's environment in several species, including humans. Fetal programming plays a vital role in the development of the placenta and then the offspring development as a result of placental physiology. As discussed previously, cattle grazing E+ fescue experienced decreased concentrations of circulating progesterone compared to the cattle grazing EN fescue. The same patterns in progesterone concentrations have been found in pregnant mares. Progesterone is a placental product; therefore, a decrease would indicate a compromise in placental function (Thompson and Stuedemann, 1993). However, in cattle, the corpus luteum produces progesterone until a switch occurs later in gestation when the placenta takes over. In human placenta research, there have been several correlations with what the mother consumes or her environment while pregnant and the health of the child. Keeping fetal programming in mind, it has been acknowledged that placental weight and the placental weight/birthweight ratio, otherwise known as the placental ratio, give some insight into the role that the placenta has in fetal programming and predicting the future health and performance of the offspring.

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TABLES

Table 2.1: Nutritive Value of forages on a DM basis for Year 1

Year 1	Wk 0		Wk 2		Wk 4		Wk 6		Wk 8		Wk 10		Wk 12	
Toxic (E+) or Novel (EN)	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**
DM (%)	20.8	22.6	22.7	27.3	29.6	30.8	22.8	42.4	30.6	42.0	38.6	37.5	29.8	27.4
CP (%DM)	15.6	15.1	13.3	10.5	9.9	10	10.8	10.8	10.6	7.6	9.1	12.0	12.3	13.2
NDF (%DM)	52.1	51.7	57.9	58.6	59.8	59.6	61.6	58.8	58.4	65.2	72.	63.8	56.7	58.7
ADF (%DM)	29.4	29.0	33.1	34.	37.3	37.7	27.5	38.3	36.7	43.6	43.5	38.4	35.5	34.7
TDN (%DM)	69.1	69.4	66.2	65.5	62.8	62.5	70.6	62	63.3	57.8	57.9	62.0	64.2	64.9
Fat (%DM)	3.1	3.2	2.2	2.3	2.2	2.18	2.4	2.3	2.4	2.1	2.14	2.8	2.9	2.9
Ca (%DM)	0.3	0.3	0.3	0.3	0.2	0.2	0.3	0.5	0.3	0.3	0.3	0.3	0.3	0.4
P (%DM)	0.4	0.3	0.3	0.3	0.1	0.3	0.3	0.3	0.3	0.2	0.1	0.2	0.3	0.4
S (%DM)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.3
Mg (%DM)	0.2	0.3	0.2	0.3	0.2	0.2	0.2	0.3	0.2	0.3	0.2	0.2	0.3	0.3
Na (%DM)	0.01	0.02	0.02	0.02	0.01	0.03	0.01	0.03	0.02	0.03	0.01	0.1	0.01	0.02
K (%DM)	2.9	2.0	2.2	1.5	1.8	1.3	2.4	1.9	2.3	1.2	1.5	1.6	2.2	2.1
Cu (ppm)	5	5	5	4	4	4	5	5	5	3	4	4	5	8
Fe (ppm)	66	71	54	55	46	47	103	126	100	73	180	222	120	76
Mn (ppm)	54	76	57	82	47	102	63	69	86	106	90	106	69	58
Zn (ppm)	20	17	40	17	17	14	19	21	22	10	17	13	17	22

E+ indicates cattle on toxic endophyte-infected tall fescue pastures; EN indicates cattle on novel endophyte-infected tall fescue pastures.

Table 2.2: Nutritive Value of forages on a DM basis for Year 2

Year 2	Wk 0		Wk 2		Wk 4		Wk 6		Wk 8		Wk 10		Wk 12	
Toxic (E+) or Novel (EN)	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**	**E+**	**EN**
DM (%)	23.7	26.4	24.9	26.5	28.6	31.0	31	35.6	28.1	30.2	37.0	39.3	47.9	44.2
CP (%DM)	13.6	14.1	12.6	10.7	9.2	7.9	11	7.6	11.1	9.5	10.0	9.6	9.3	10.7
NDF (%DM)	48.1	45.1	56.6	53.1	63.1	63.9	59.9	64.1	59.4	58.6	66.4	62.6	64.2	59.2
ADF (%DM)	26.7	24.1	33.8	31.5	39	38.3	36.3	39.1	36.2	34.5	40.8	39.1	40.1	37.5
TDN (%DM)	71.3	73.4	65.6	67.5	61.5	62.0	63.6	61.4	63.2	65.0	60.1	61.4	60.6	62.7
Fat (%DM)	2.9	3.0	2.4	2.1	1.8	1.8	2.2	2.0	2.9	2.7	2.6	2.9	2.4	2.7
Ca (%DM)	0.3	0.3	0.2	0.3	0.2	0.2	0.3	0.2	0.3	0.3	0.3	0.4	0.2	0.4
P (%DM)	0.3	0.3	0.2	0.2	0.3	0.2	0.2	0.2	0.3	0.3	0.2	0.3	0.2	0.3
S (%DM)	0.2	0.2	0.2	0.1	0.2	0.1	0.2	0.1	0.2	0.2	0.2	0.2	0.1	0.2
Mg (%DM)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.2	0.3	0.2	0.4
Na (%DM)	0.0	0.01	0.0	0.03	0.01	0.04	0.01	0.03	0.01	0.01	0.0	0.01	0.01	0.02
K (%DM)	2.5	1.8	1.8	1.2	2.1	1.0	2.1	1.1	2.0	1.6	1.8	1.4	1.3	1.0
Cu (ppm)	4	4	5	3	4	3	4	4	4	4	4	4	3	5
Fe (ppm)	45	50	34	34	48	50	59	111	91	88	101	81	100	79
Mn (ppm)	58	69	46	55	44	54	67	72	60	79	75	78	51	66
Zn (ppm)	18	16	19	16	16	12	18	14	14	15	17	13	14	16

E+ indicates cattle on toxic endophyte-infected tall fescue pastures; EN indicates cattle on novel endophyte-infected tall fescue pastures.

Table 2.3: E+ and EN Endophyte-infected tall fescue percentage

	Wk 0		Wk 2		Wk 4		Wk 6		Wk 8		Wk 10		Wk 12	
Year	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
Percent fescue (%) EN	80.9	98.2	74.6	99.3	81.1	98.7	53.7	91.1	66.9	76.3	76.5	74.2	40.7	94.5
Percent fescue (%) E+	78.0	92.7	68.5	84.7	81.2	92.6	76.6	80.1	60.0	79.4	52.3	89.9	62.7	88.7

Table 2.4: Tiller Results for Year 1

	EN (MaxQ II)	E+ (KY-31)
% Forage with Endophyte Present	97.5	100
% Tillers with Ergot Alkaloids	0	98.75

FIGURES

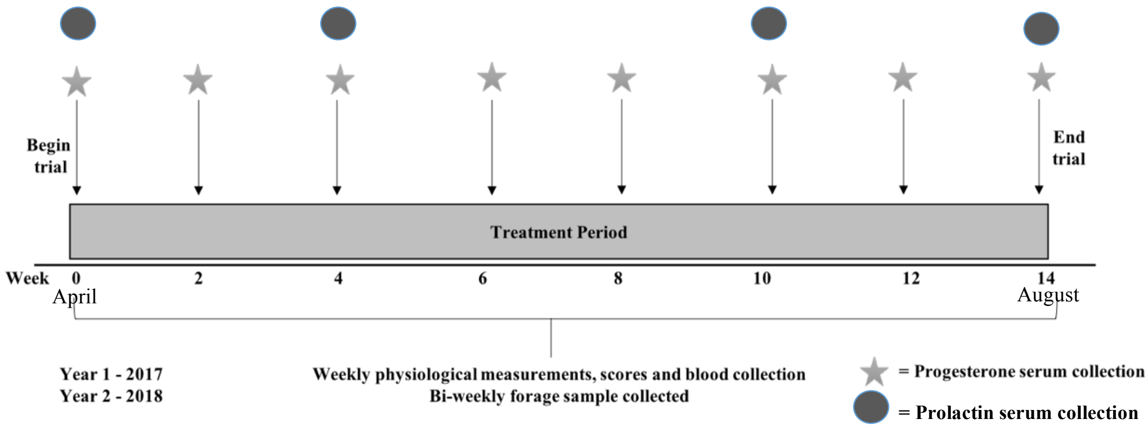

Figure 2.1: Experimental timeline used during cow performance phase of data collection from late-April to late-July 2017 and 2018.

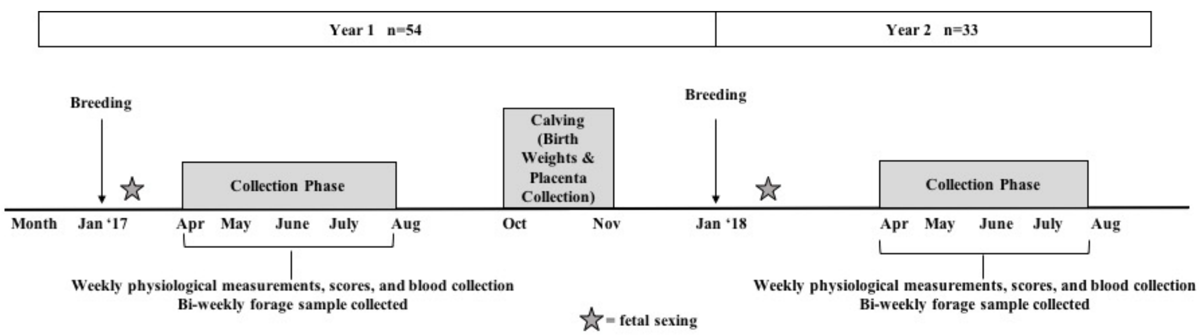

Figure 2.2: Experimental timeline used during cow performance and calf performance phase of data collection from January 2017 to late-July 2018.

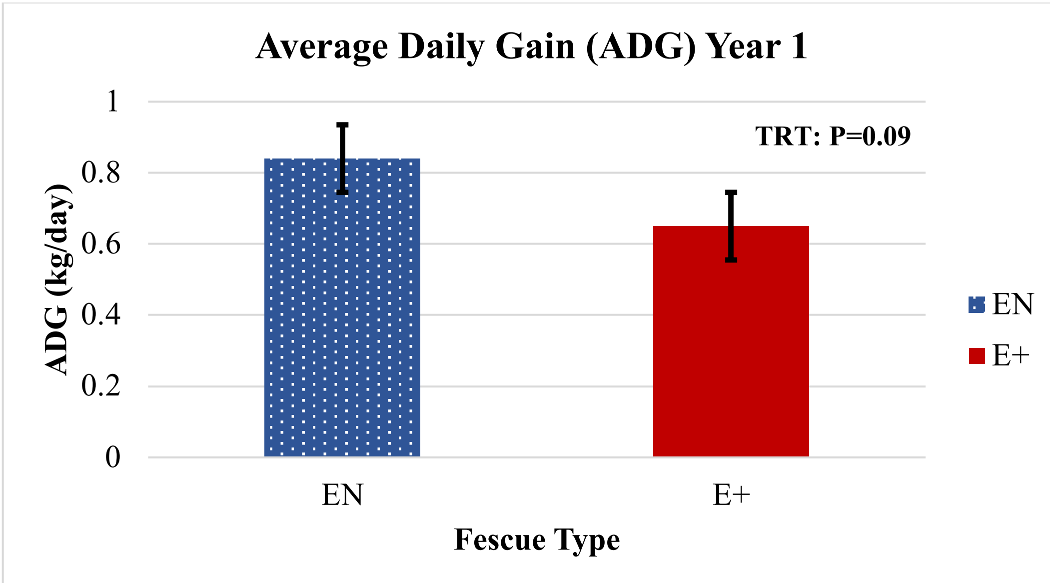

Figure 2.3. Average Daily Gain (ADG) for Year 1: Year 1 Cows grazing EN pastures (n=27) tended to have a higher ADG vs. those grazing E+ pastures (n=27). (EN: 0.84 kg/day; E+: 0.65 kg/day). Model had a trend by treatment (trt P=0.09). Data represented as LS Means ± Standard error of the mean (SEM).

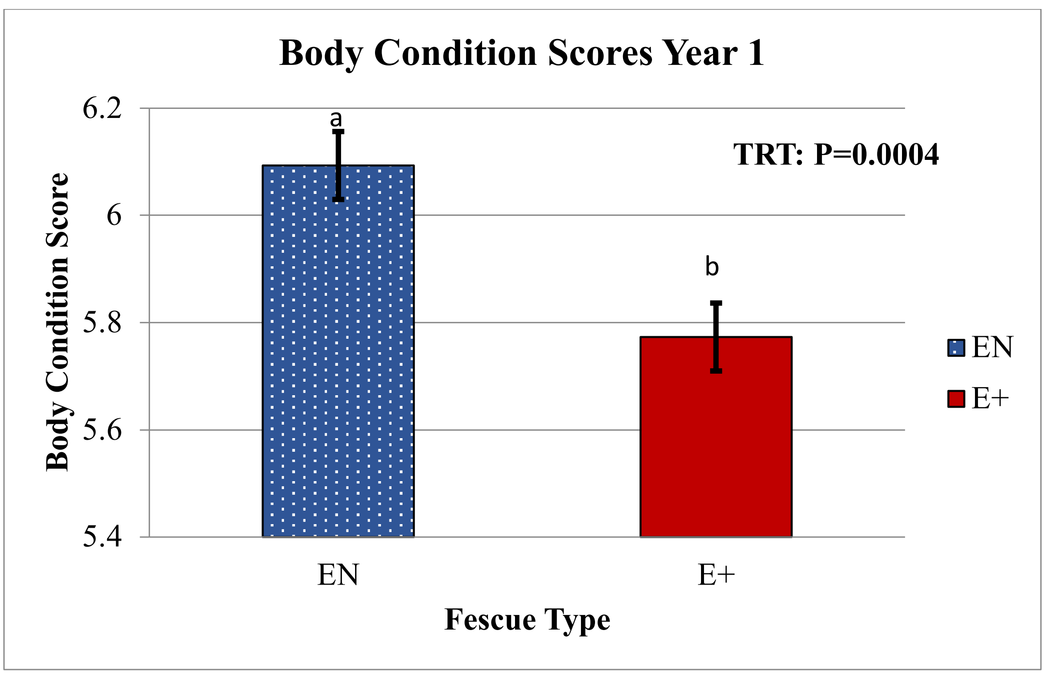

Figure 2.4: Body Condition Scores for Year 1: Year 1 Cows grazing novel EN pastures (n=27) had a greater BCS on a 1-9 scale (1 being emaciated to 9 being obese) than those grazing toxic E+ pastures (n=27). (EN: 6.09, E+: 5.77, respectively). Model was significant for treatment (trt P=0.0004). Data represented as LS Means ± Standard error of the mean (SEM).

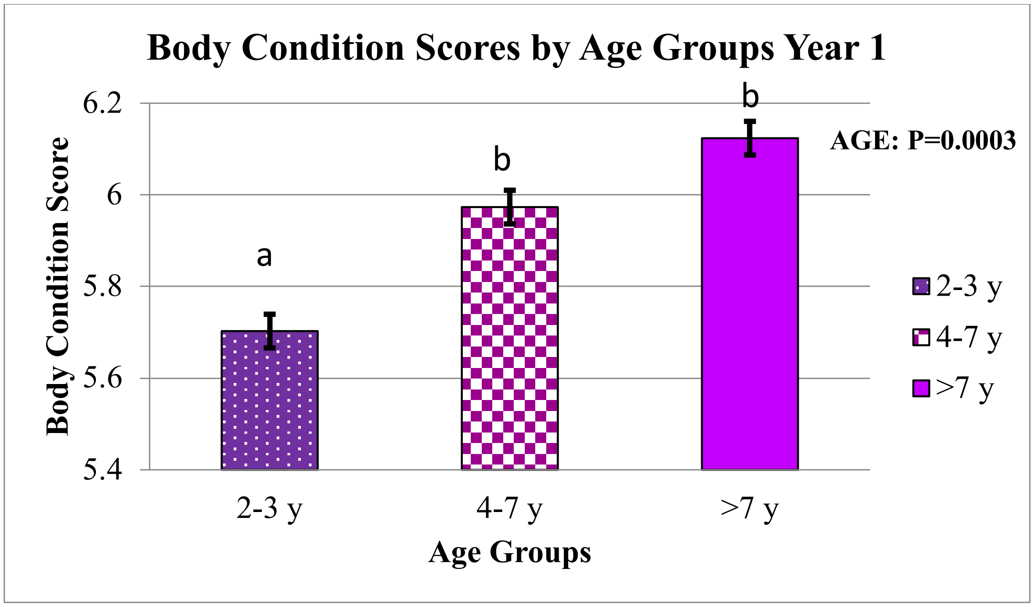

Figure 2.5: Body Condition Scores by Age Groups for Year 1: 2-3 y cows had a lower BCS on a 1-9 scale (1 being emaciated to 9 being obese) compared to older cows (4-7y & >7 y). (2-3 y: 5.70, 4-7 y: 5.97, >7 y: 6.12, respectively.) Model was significant by age of cattle (AGE: P=0.0003). Data represented as LS Means ± Standard error of the mean (SEM).

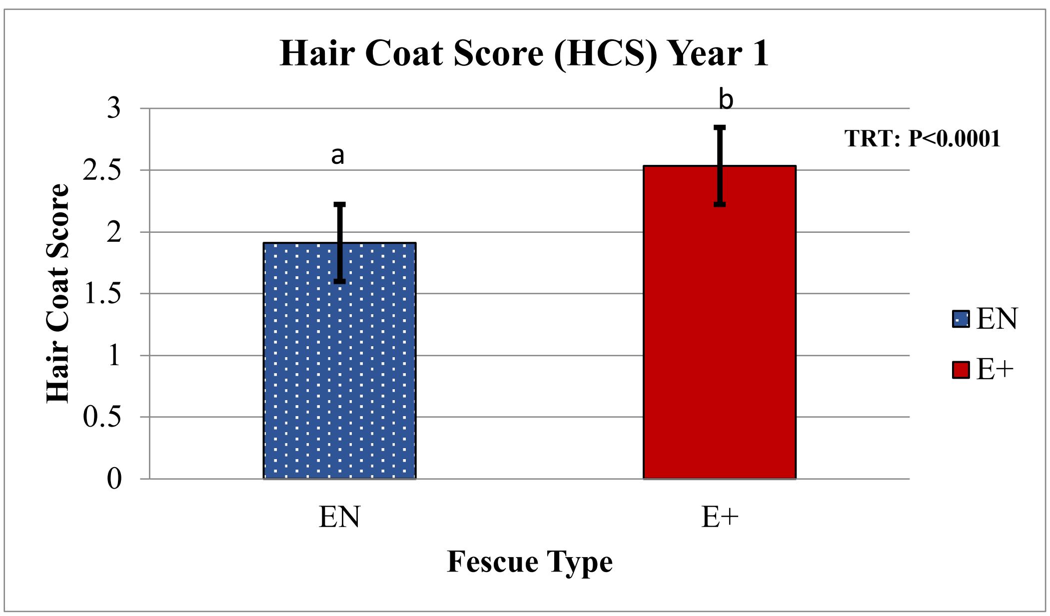

Figure 2.6: Hair Coat Scores of Year 1: Year 1 cattle grazing toxic E+ (n=27) had a greater HCS than those grazing novel EN pastures (n=27). Hair coat scores are on a 1-5 scale with 1 being fine, small diameter hair, and 5 being thick, rough, large diameter hair. (EN: 1.91, E+: 2.53, respectively.) Model is significant for treatment (TRT: P<0.0001). Data represented as LS Means ± Standard error of the mean (SEM).

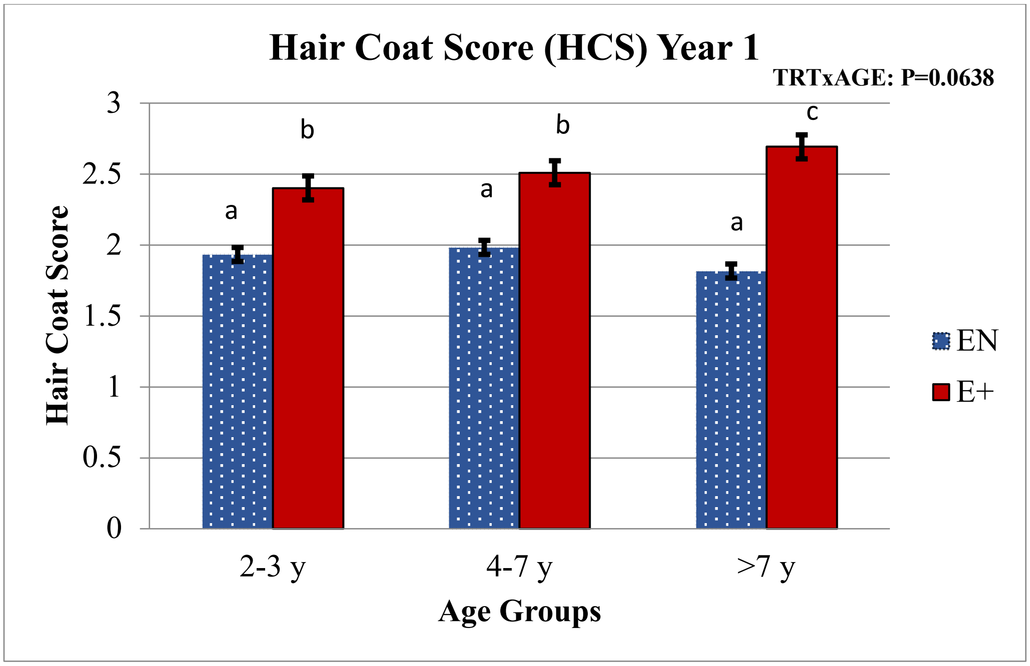

Figure 2.7: Hair Coat Score (HCS) from Year 1: Year 1 >7 year old cows grazing toxic E+ pastures (n=24) tended to have a greater HCS than younger cows (2-3y and 4-7 yo) grazing toxic E+ pastures. (2-3 y EN:1.93, E+: 2.40; 4-7 y EN: 1.98, E+: 2.51; >7 y EN: 1.82, E+: 2.69, respectively). Tendency was shown for treatment x age interaction (TRT x AGE: P=0.0638). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

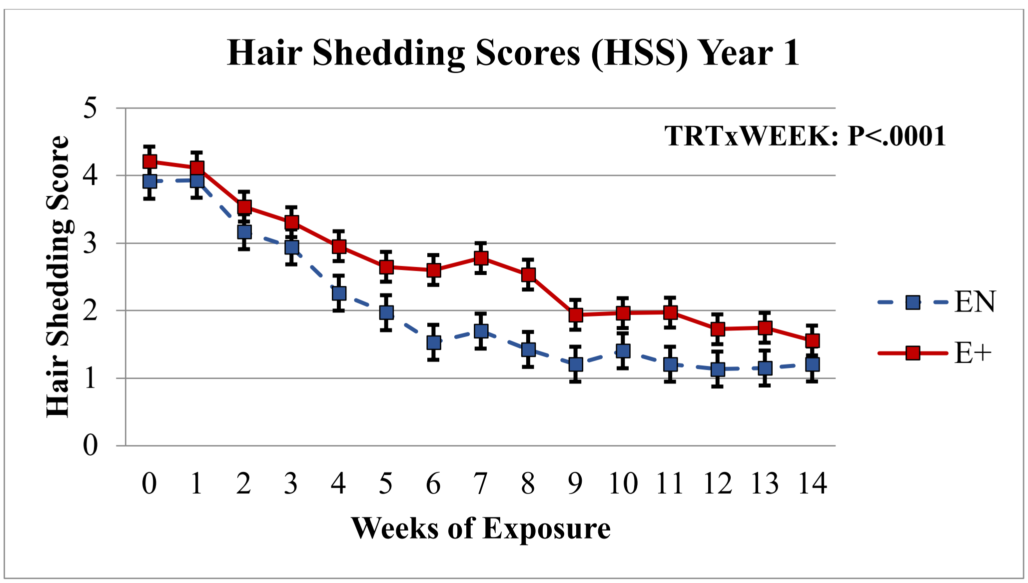

Figure 2.8: Hair Shedding Scores (HSS) for Year 1: Cattle grazing toxic E+ pastures (n=27) shed their hair coats at a slower rate than those cattle grazing novel EN pastures (n=27). Hair shedding scores are on a 1-5 scale with 1 being completely shed with no winter coat and a 5 being a full winter coat and no shedding. Model is significant for treatment x week interactions (TRT x WEEK: P<0.0001). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

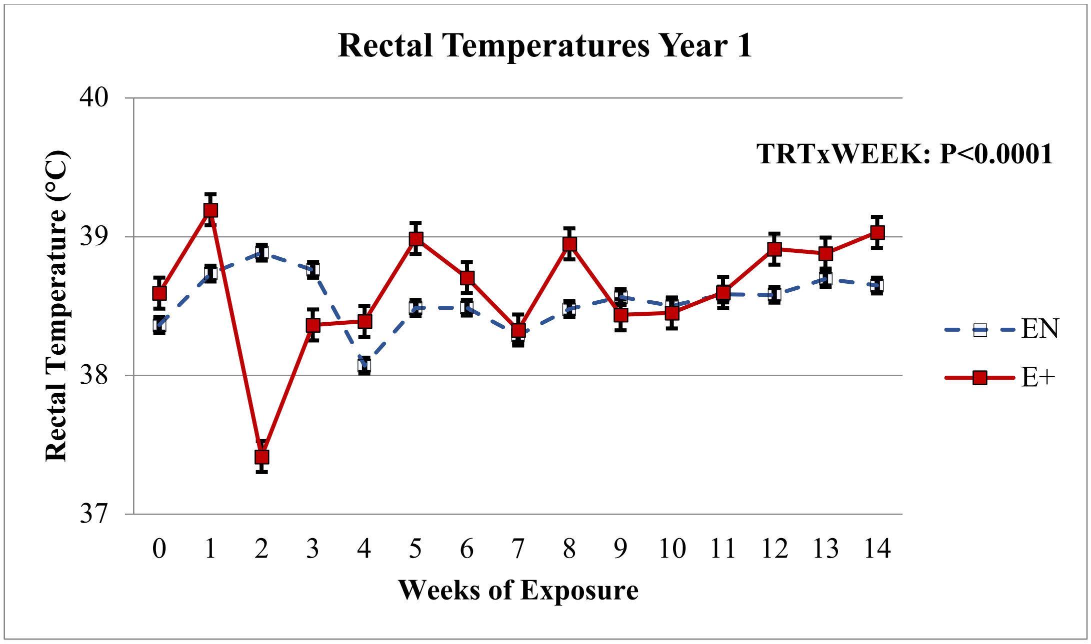

Figure 2.9: Rectal Temperatures for Year 1: Overall, cattle grazing toxic E+ pastures (n=27) had greater rectal temperatures than those grazing novel EN pastures (n=27). Model was significant for treatment x week interaction (TRTxWEEK: P<0.0001). Data represented as LS Means ± Standard error of the mean (SEM).

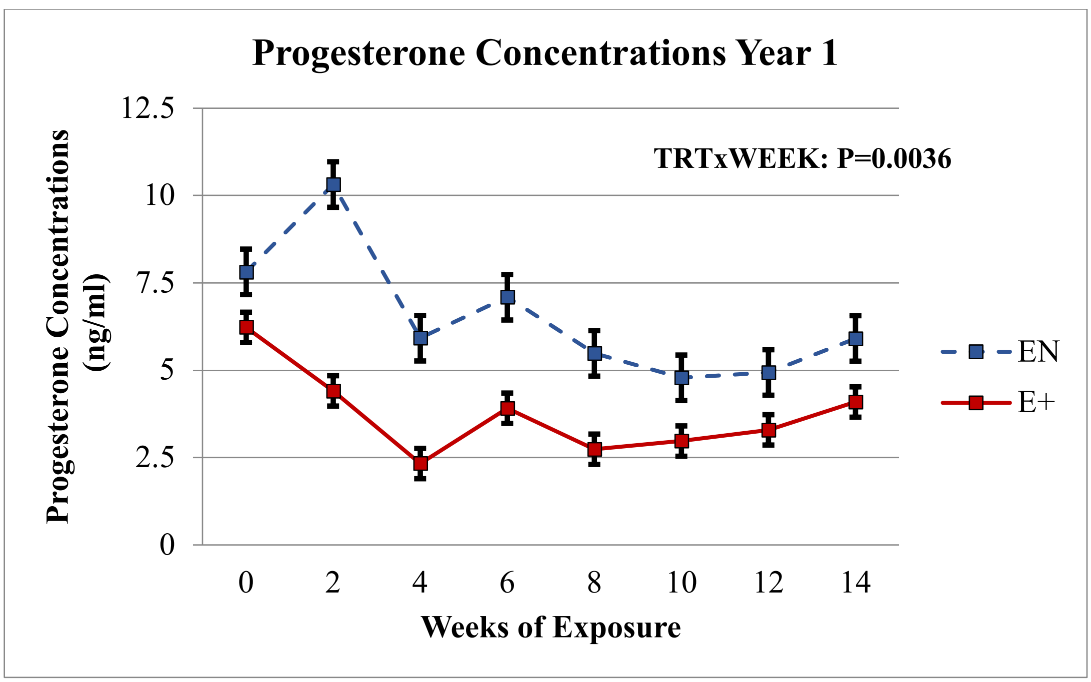

Figure 2.10: Progesterone Concentrations for Year 1: Year 1 cattle grazing novel EN pastures (n=27) had greater circulating progesterone concentrations than those grazing toxic E+ pastures (n=27). Model was significant for treatment x week interactions (TRTxWEEK: P=0.0036). Data represented as LS Means ± Standard error of the mean (SEM).

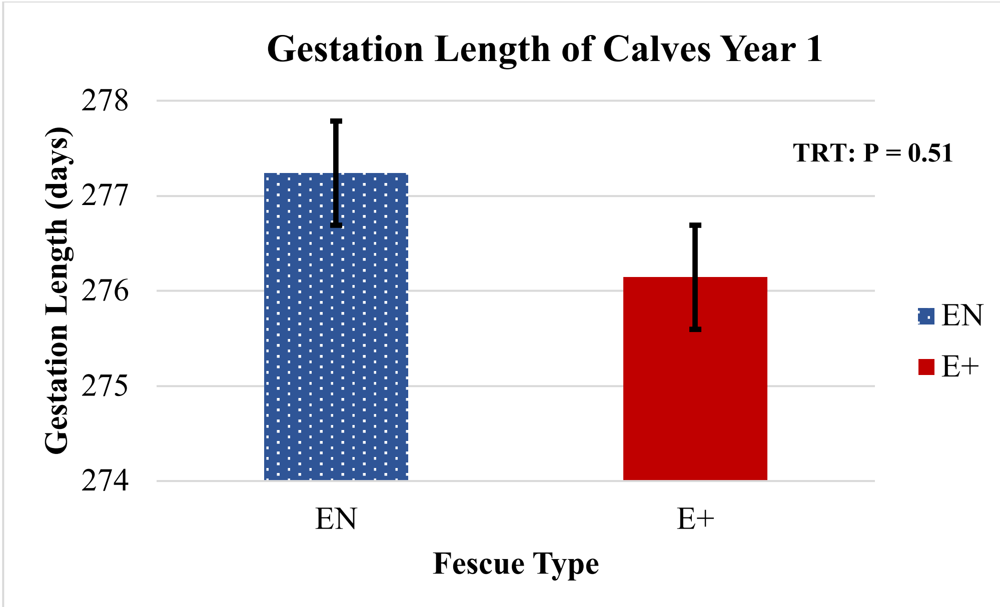

Figure 2.11: Gestation Length of Calves for Year 1: Cattle grazing novel EN pastures (n=10) had gestation lengths that were numerically greater than those of cattle grazing toxic E+ pastures (n=11). (EN: 277.2 days; E+: 276.1 days, respectively). There were no significant differences or tendencies between treatment groups (TRT: P=0.51). Data represented as LS Means ± Standard error of the mean (SEM).

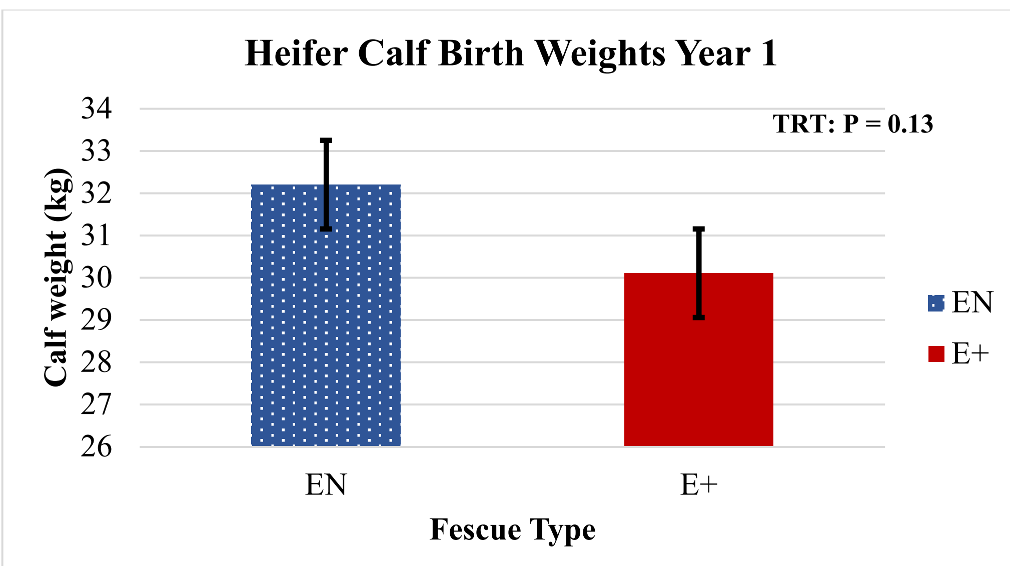

Figure 2.12: Heifer Calf Birth Weights for Year 1: Cattle grazing novel EN pastures (n=10) had numerically higher heifer calf birth weights than those grazing toxic E+ pastures (n=11). (EN: 32.21 kg; E+: 30.11 kg, respectively). No significant differences or tendencies were found between the treatment groups (TRT: P=0.13). Data represented as LS Means ± Standard error of the mean (SEM).

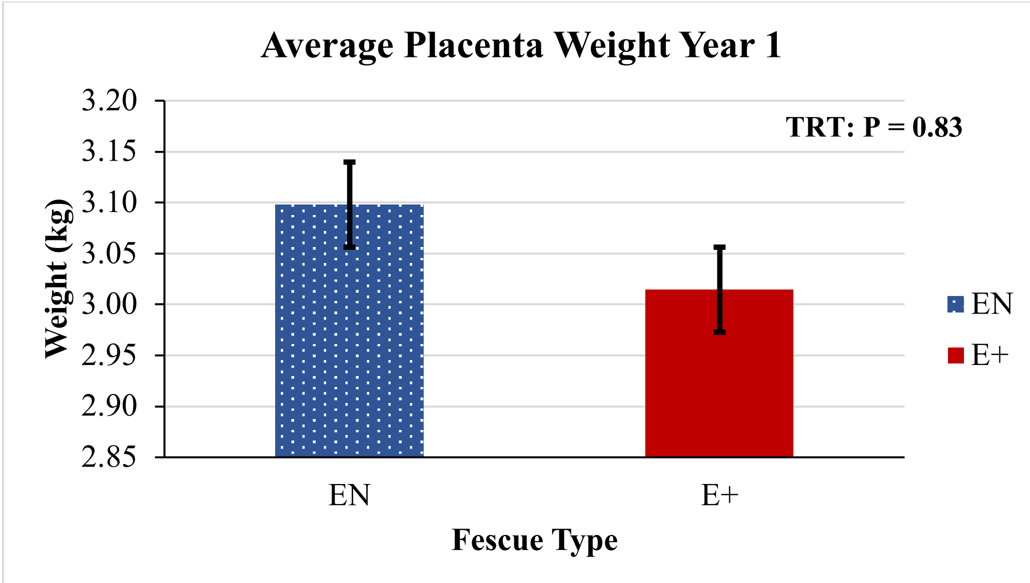

Figure 2.13: Average Placenta Weight for Year 1: Cattle grazing novel EN pastures (n=10) delivered numerically heavier placentas than those cattle grazing toxic E+ pastures (n=11). (EN:3.10 kg; E+: 3.02 kg, respectively.) There were no significant differences or tendencies between the treatment groups out of the cattle that actually delivered heifer calves (TRT: P=0.83). Data represented as LS Means ± Standard error of the mean (SEM).

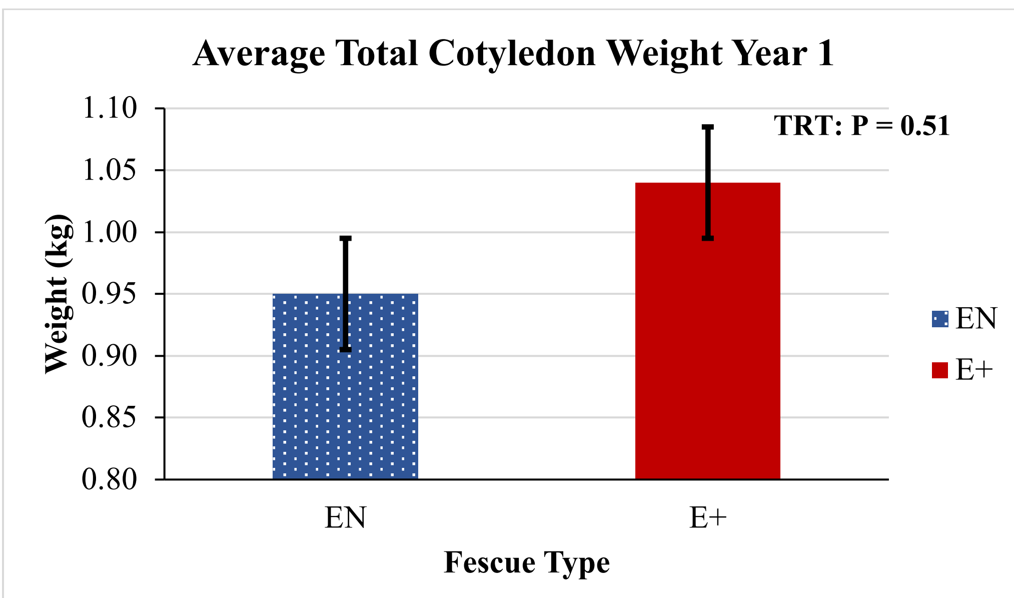

Figure 2.14: Average Total Cotyledon Weight for Year 1: Cattle grazing toxic E+ pastures (n=11) had greater total cotyledon weights, numerically, than those grazing novel EN pastures (n=10). (EN: 0.95 kg, E+: 1.04 kg, respectively.) There were no significant differences or tendencies between the treatment groups out of the cattle that actually delivered heifer calves and their placentas (TRT: P=0.51). Data represented as LS Means ± Standard error of the mean (SEM).

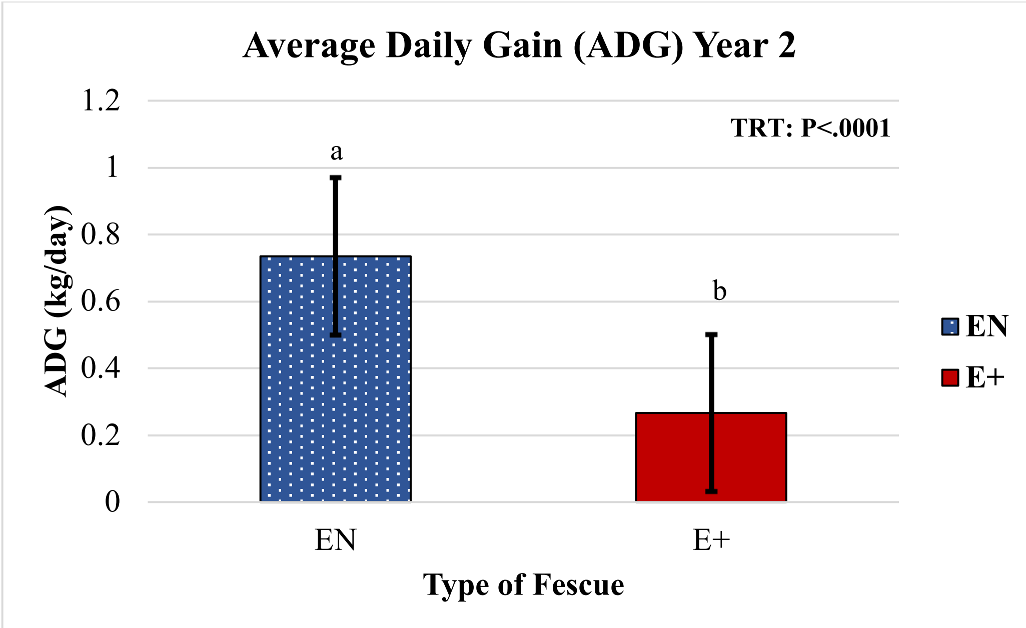

Figure 2.15: Average Daily Gain (ADG) for Year 2: Cattle grazing novel EN pastures (n=16) had greater average daily gain than those grazing toxic E+ pastures (n=17). (EN: 0.73 kg/day, E+: 0.27 kg/day, respectively). The model was significant for treatment (TRT: P<.0001). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

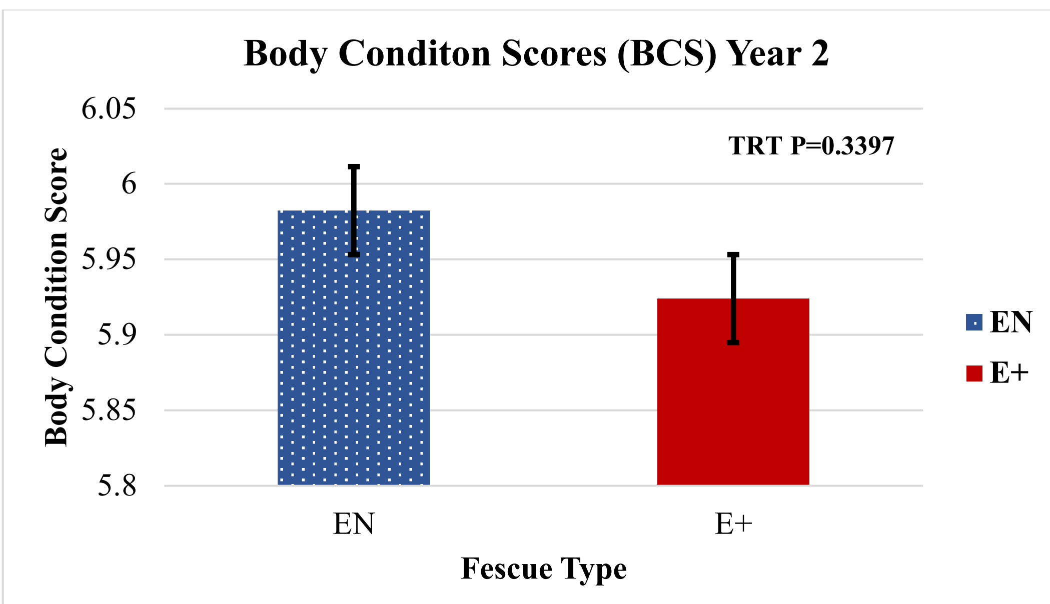

Figure 2.16: Body Condition Scores (BCS) for Year 2: Cattle grazing novel EN pastures (n=16) had greater body condition scores, numerically, than those cattle grazing toxic E+ pastures (n=17). (EN: 5.98, E+ :5.92, respectively.) There were no significant differences or tendencies for treatments for body condition scores (TRT: P=0.2297). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

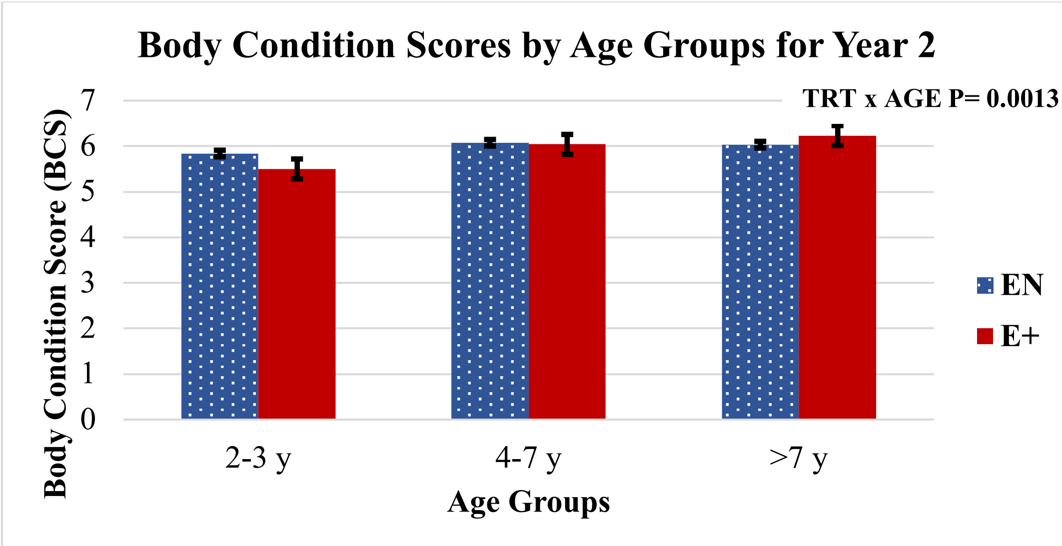

Figure 2.17: Body Condition Scores by Age Groups for Year 2: Cattle that were in the 4-7 y and >7 y age groups had greater body condition scores than those cattle in the 2-3 y age group. Cattle grazing toxic E+ pastures that were >7 y had the greatest body condition scores. (2-3 y EN: 5.84, 2-3 y E+ :5.5, 4-7 y EN: 6.08, 4-7 y E+ :6.04, >7 y EN: 6.03, >7 y E+ : 6.23, respectively.) The model was significant for treatment by age interactions (TRT x AGE: P=0.0013). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

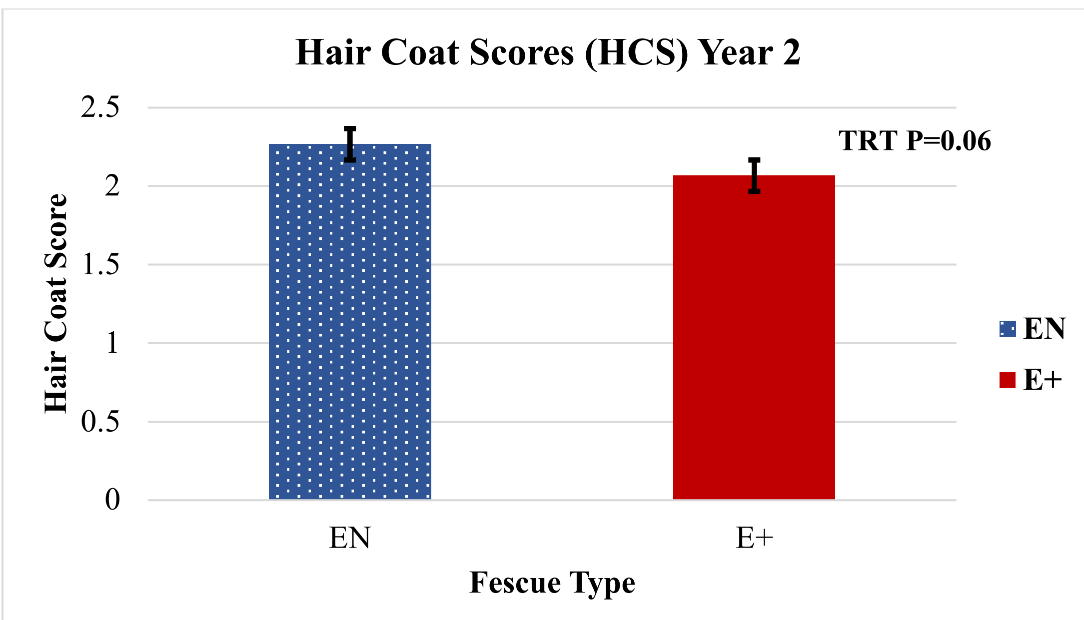

Figure 2.18: Hair Coat Scores (HCS) for Year 2: Cattle grazing novel EN pastures (n=16) had greater hair coat scores than those cattle grazing toxic E+ pastures (n=17). (EN:2.27, E+ : 2.07, respectively.) The model was significant for treatment (TRT: P=0.06). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

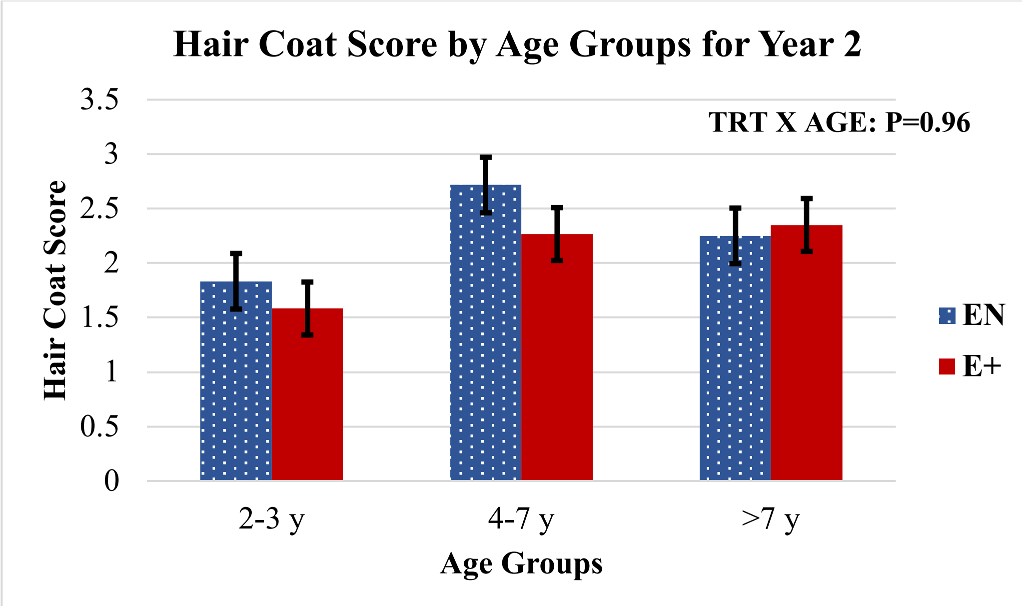

Figure 2.19: Hair Coat Score by Age Groups for Year 2: Cattle grazing novel EN in the 4-7 y age group had the highest hair coat score, while both treatments for those cattle in the 2-3 y age group had to lowest hair coat scores. (2-3 y EN: 1.83, 2-3 y E+ : 1.58, 4-7 y EN: 2.72, 4-7 y E+ : 2.67, >7 y EN: 2.25, >7 y E+ : 2.35, respectively.) The model was not significant for treatment by age interactions (TRT x AGE: P=0.96). Data represented as LS Means ± Standard error of the mean (SEM).

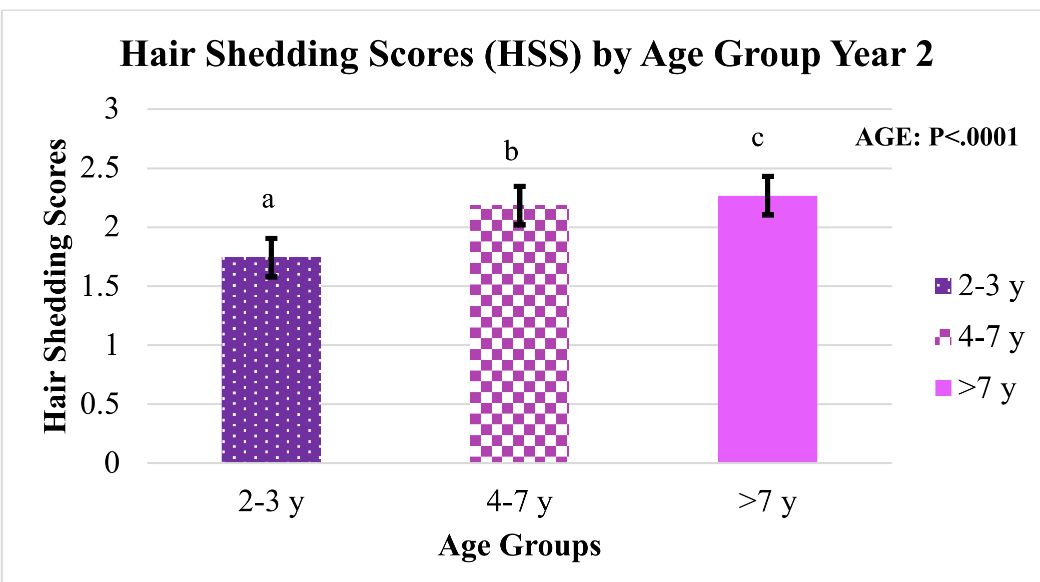

Figure 2.20: Hair Shedding Scores (HSS) by Age Group for Year 2: Cattle in the 2-3 y age group have lower hair shedding scores compare to the cattle in the 4-7 y and >7 y age groups. (2-3 yo: 1.74, 4-7 yo: 2.81, >7 yo: 2.67, respectively.) The model was significant for age (AGE: P<.0001). Data represented as LS Means ± Standard error of the mean (SEM).

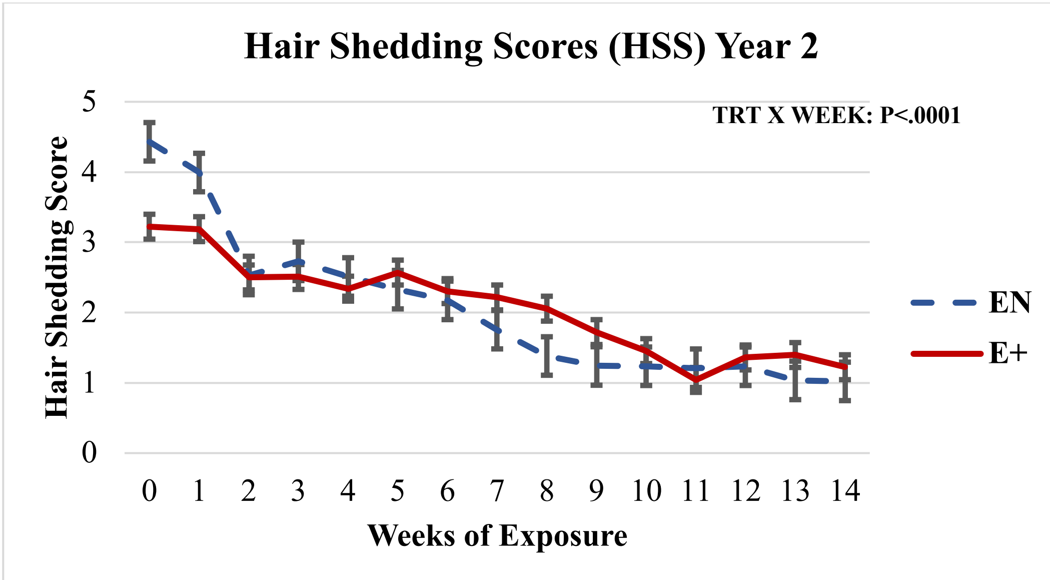

Figure 2.21: Hair Shedding Scores (HSS) for Year 2: Cattle who were grazing novel EN pastures (n=16) shed their hair at a faster rate than those cattle grazing toxic E+ pastures (n= 17). Hair shedding scores are on a 1-5 scale with 1 being completely shed with no winter coat and a 5 being a full winter coat and no shedding. The model was significant for treatment by week interactions (TRT x WEEK: P<.0001). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

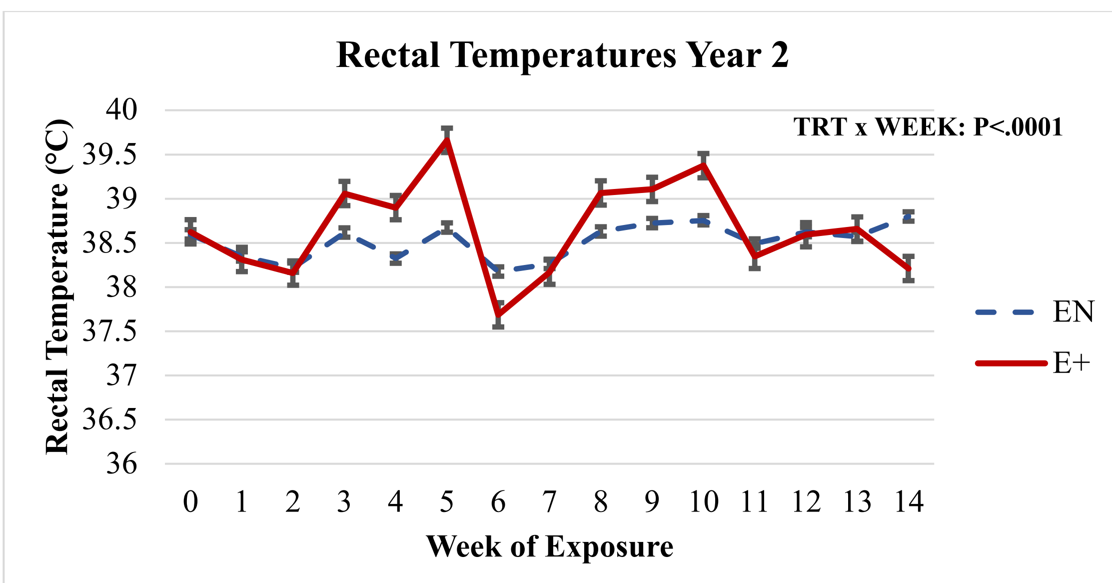

Figure 2.22: Rectal Temperatures for Year 2: Cattle grazing novel EN pastures (n= 16) had overall lower rectal temperatures than those grazing toxic E+ pastures (n= 17). The model was significant for treatment by week interactions (TRT x WEEK: P<.0001). Data represented as LS Means $\pm$ Standard error of the mean (SEM).

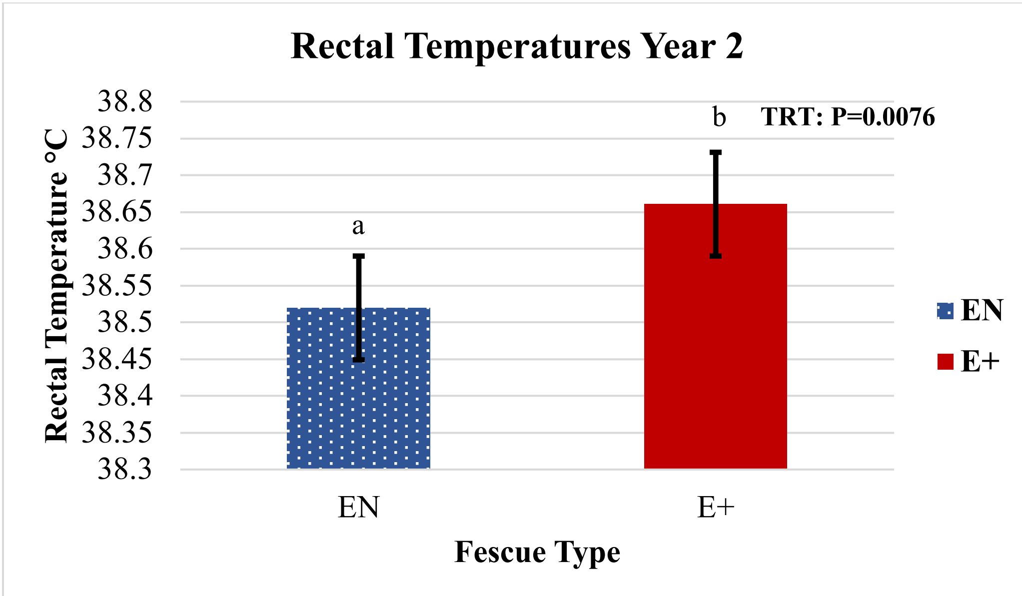

Figure 2.23: Rectal Temperatures for Year 2: Cattle grazing novel EN pastures (n=16) had significantly lower rectal temperatures than those grazing toxic E+ pastures (n=17). (EN: 38.52°C, E+ : 38.66°C, respectively.) The model was significant for treatment (TRT: P=0.0076). Data represented as LS Means ± Standard error of the mean (SEM).

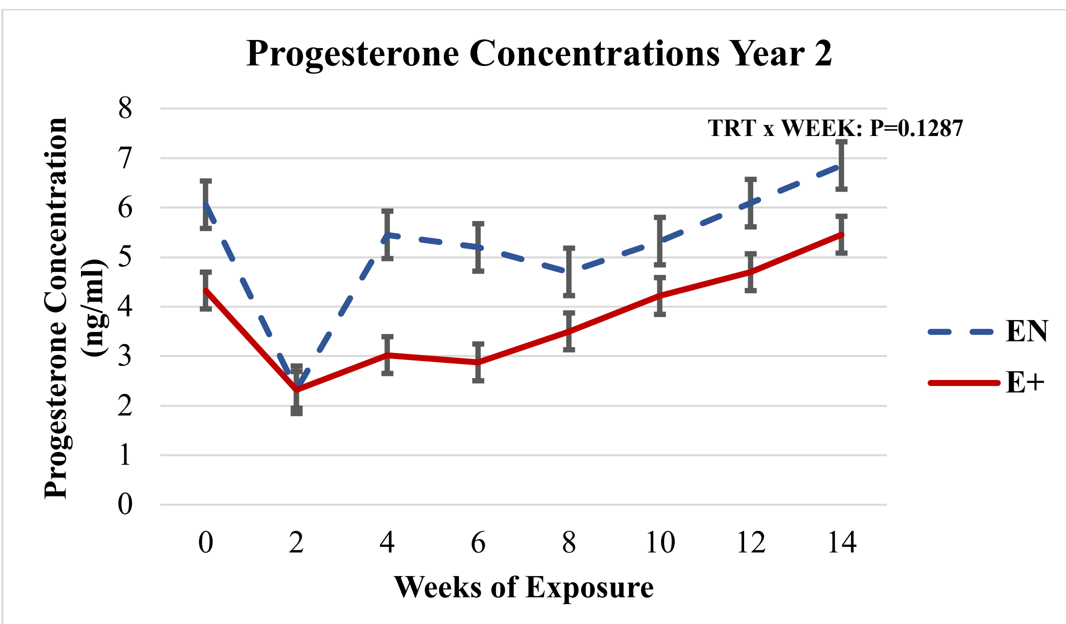

Figure 2.24: Progesterone Concentrations for Year 2: Cattle grazing novel EN pastures (n=16) had overall higher progesterone concentrations, numerically, than those grazing toxic E+ pastures (n=17). The model is not significant or show a tendency for the treatment by week interaction (TRT x WEEK: P= 0.1287). Data represented as LS Means ± Standard error of the mean (SEM).

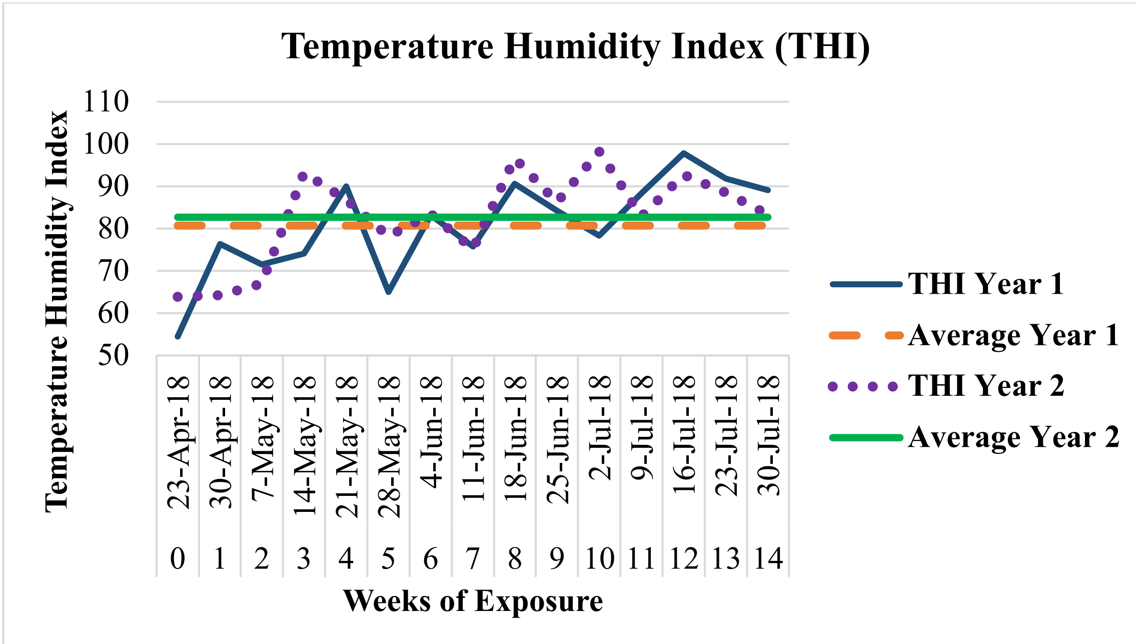

Figure 2.25: Temperature Humidity Index: Overall, the temperature humidity index was greater for Year 2 of the study, along with the average THI for Year 2 (Average THI Year 1: 80.72, Average THI Year 2: 82.70).

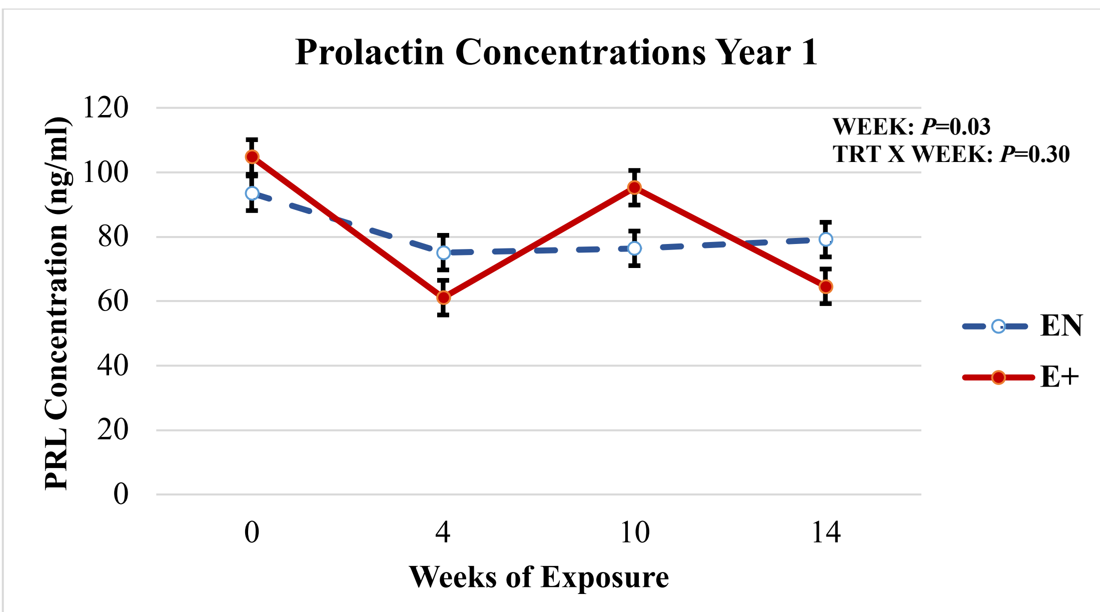

Figure 2.26: Prolactin Concentrations for Year 1: The model was significant (P<0.05) for week (WEEK: P= 0.03), however there was no significance or tendency (0.05≤P≤0.10) found for treatment by week interaction (TRT X WEEK: P= 0.30). Concentrations were taken from a subset of cattle from each treatment (EN n=5; E+ n= 5).

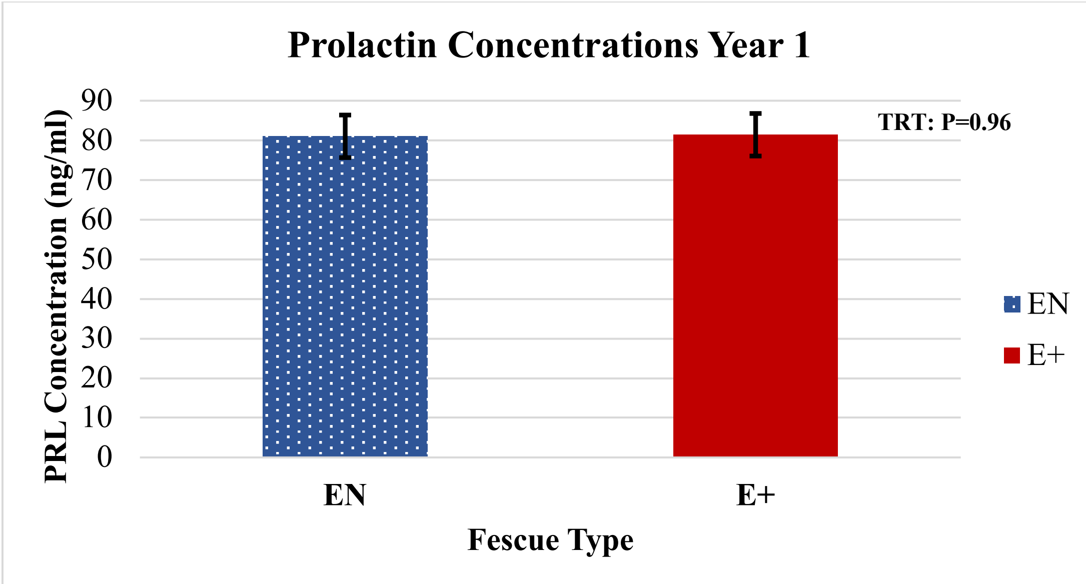

Figure 2.27: Prolactin Concentrations for Year 1: There was no significance (P<0.05) found when looking at the difference prolactin levels between treatments (TRT: P=0.96; EN : 82.01 ng/mL, E+ : 81.41 ng/mL). Concentrations were taken from a subset of cattle from each treatment (EN n=5; E+ n= 5).

CHAPTER 3

OVERALL CONCLUSIONS AND IMPLICATIONS

Cow Performance Conclusions. Numerous studies have compared the performance of cattle grazing either toxic endophyte-infected tall fescue versus a non-toxic version such as novel endophyte-infected tall fescue, however not many have included a fetal programming aspect with heifers. This study sought out to use data from multiple years in order to gain more concrete evidence on the effects that toxic endophyte-infected tall fescue has on Angus and SimAngus cattle during their second trimester of carrying heifer calves. With the information that has been gathered for the cow treatment period of the study, the conclusion can be made that cattle perform better during their second trimester of pregnancy if they graze novel endophyte-infected tall fescue versus toxic endophyte-infected tall fescue.

This conclusion can be reinforced with the fact that the performance measurements taken during the treatment period show greater production levels in those cattle who were grazing novel endophyte-infected tall fescue. Measurements of production consist of average daily gain, body condition scores, hair shedding scores, rectal temperatures, and circulating progesterone concentrations. Year 1 and Year 2 data has shown that cattle grazing novel endophyte-infected tall fescue have greater average daily gain and better body condition scores so they can recover from calving and lactation more rapidly to prepare their bodies for calving again in the fall of the year. The cattle grazing novel endophyte-infected fescue during each year also shed their winter coats faster, therefore were better able to release body heat and were not under as much heat stress as cattle that grazed toxic endophyte-infected tall fescue. Rectal temperatures for each year prove that cattle grazing toxic endophyte-infected tall fescue had higher body temperatures, overall. There were some weeks where cattle grazing novel endophyte-infected tall fescue would have higher rectal temperatures, however this may be due to the time of day that collections were taken. Collections always began with the group of cattle grazing toxic endophyte-infected tall fescue at 8:00 am, therefore the group grazing novel endophyte-infected fescue had more time to stand in the sun on pasture or in an enclosed area and possibly have more stress until they could begin to have measurements taken around 9:00 am or 9:30 am. The cattle grazing toxic endophyte-infected tall fescue had measurements taken at a time that had lower temperatures, yet the cattle still had higher rectal temperatures, overall. Blood samples from cattle for Year 1 and Year 2 also displayed that cattle grazing novel endophyte-infected tall fescue had higher progesterone concentrations, which is positive since progesterone is needed to sustain pregnancy. Cattle who grazed toxic endophyte-infected tall fescue did not have as high of progesterone concentrations, which shows that vasoconstriction of the blood pathways could possibly affect reproductive organs and hinder reproduction or fetal development as a result.

Calf Performance Conclusions. The calves from Year 1 were born in the Fall of 2017 during October and the beginning of November. Several measurements were taken at the time of birth and placental tissues were analyzed later on to see if there were differences between the calves of dams who had been grazing novel endophyte-infected tall fescue versus calves of dams who grazed toxic endophyte-infected tall fescue during the second trimester of gestation. The initial measurements were taken at birth, but the second portion of the project will gather additional measurements and data while following the heifer calves through puberty and reproduction to see how their intrauterine environment affected their performance, specifically reproductively.

Unfortunately, there were no significant differences in the measurements taken between calves who were in an intrauterine environment during the second trimester of a dam who was grazing novel endophyte-infected tall fescue versus toxic endophyte-infected tall fescue, however there were numerical differences. The calves born to dams grazing novel endophyte-infected tall fescue during the second trimester of gestation had longer gestation lengths on average, higher average birth weights, higher placental weights on average, and lower average total cotyledon weight on average, numerically. The longer gestation length, increased birth weight, and greater placenta weights of the novel endophyte-infected tall fescue exposed calves may be due to an increased level of blood flow during the second trimester and a greater opportunity for fetal growth. These dams were concluded to be performing better than those that were on toxic endophyte-infected tall fescue and showing signs of fescue toxicosis, therefore they should not have been suffering from vasoconstriction. The reason for the increased total cotyledon weight on average of the placentas from the cows that were on toxic endophyte-infected tall fescue during the second trimester of gestation could have been because of the lack of blood flow that was reaching the uterus and placenta. In order for the body to cope with this decreased level of blood flow and nutrient supply to the fetus, the cotyledons increased in size to help provide the proper amount of nutrients to the fetus. Overall, the calf and placenta data from the time of birth shows that calves born to cows that grazed novel endophyte-infected tall fescue during their second trimester had a greater advantage at birth which could subsequently lead to greater production and reproductive performance later on in life.

IMPLICATIONS

The conclusions from both Year 1 and Year 2 of this study exemplify how cattle who graze novel endophyte-infected tall fescue perform better and have calves who have a greater advantage at birth than the cows that grazed toxic endophyte-infected tall fescue during their second trimester and exposed their calves *in utero* to the toxins. Using this knowledge, cattle producers in the Southeastern United States will have a greater understanding and reason for transitioning their pastures to novel endophyte-infected tall fescue, at least enough that can sustain cattle during gestation. Cattle will not suffer from fescue toxicosis and the calves will not experience the potential negative fetal programming aspects that come along with dams grazing toxic endophyte-infected tall fescue once they are born. If the hypothesis holds true, the heifer calves that were exposed to toxic endophyte-infected tall fescue while *in utero* will not perform as well later on in life, both physically and reproductively, as those heifers that were exposed to novel endophyte-infected tall fescue. This increase in productivity and efficiency should lead to economic benefits for producers. Cattle will have the ability to remain productively efficient with the same or less nutritional input while grazing novel endophyte-infected tall fescue compared to endophyte-infected tall fescue.