ABSTRACT

MACKEY, JOSEPH CHRISTOPHER. Impact of Progesterone Supplementation on Pregnancy Rates Following Timed Artificial Insemination or Embryo Transfer in Beef Cattle Consuming Endophyte-Infected Tall Fescue. (Under the direction of Dr. Daniel H. Poole).

Most tall fescue (*Lolium arundinaceum* [Schreb.]) is infected with a fungal endophyte (*Epichloë typhina)* that produces ergot alkaloids; hindering reproductive success by decreasing pregnancy rates and suppressing progesterone (P4) concentrations. The objective of this study was to determine if P4 supplementation following timed artificial insemination (TAI) or embryo transfer (ET) increases pregnancy rates (PR) of cattle consuming endophyte-infected tall fescue. Nulliparous and multiparous beef cattle were maintained on stockpiled endophyte-infected tall fescue. All cattle were synchronized using the Select Synch + CIDR® program. Cattle were inseminated followed by estrus detection 12 h after visual observation of estrous. Cattle that did not display estrous were inseminated 72 h after CIDR removal. In the ET group, cattle received either a fresh or frozen embryo on d 10 post-CIDR removal. Cattle were randomly assigned to receive either a CIDR blank (C) or active CIDR (Trt) on d 7 post insemination or at the time of embryo transfer and remained in the vagina through d 18. Pregnancy and embryo area were determined by ultrasonography at d 30 of gestation. Data were analyzed using a PROC MIXED procedure of SAS and examined for effects of treatment, year, location, and age. Statistical significance was determined at $P < 0.05$ and a tendency at $0.05 < P < 0.10$. There was no difference in pregnancy rate with supplemental P4 7d following TAI in multiparous cattle (Trt- 45.91% vs. C- 53.98%; $P > 0.05$) or nulliparous cattle (Trt- 57.76% vs. C- 57.53%; $P > 0.05$). However, PR in heifers receiving P4 supplementation tended to differ by location (BBCFL- 43.75% vs. UPRS- 71.78%). There was a significant effect of year ($P < 0.05$) for ET groups, thus yr 1 and 2

were analyzed independently. In yr 1, P4 supplementation increased PR in ET cattle compared to controls (84.6% vs. 60.1%, respectfully; $P < 0.05$). Additionally, supplemental P4 improved PR in cattle >7 yrs old (Trt- 98.7% vs. C- 57.2%; $P < 0.05$) and increased embryo retention in cattle receiving a frozen embryo (Trt- 96.7% vs. C- 59.7%; $P < 0.05$); this was not observed with fresh embryos. In yr 2, there was no difference in PR with supplemental P4 (Trt- 36.8% vs C- 34.5%; $P > 0.05$). Additional P4 did not affect embryo area in either the TAI or ET groups. While P4 supplementation throughout maternal recognition of pregnancy significantly increased PR in cattle receiving embryos in yr 1, it did not show significant impact in yr 2 or following TAI in cattle consuming endophyte-infected tall fescue for both years. Progesterone supplementation is well documented using dairy cattle, fewer data is available for beef cattle.

Impact of Progesterone Supplementation on Pregnancy Rates Following Timed Artificial Insemination or Embryo Transfer in Beef Cattle Consuming Endophyte-Infected Tall Fescue

by
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DEDICATION

This thesis is first and foremost dedicated to my wonderful family! I am so thankful and blessed to have a home support system that has always been there for me through the worst and best of times. Our family journey has climbed many high mountains and struggled through some of what seemed to be the lowest valleys. But no matter the circumstance, we have faced this adversity head on and as a team! Mom and dad, thank you for all of the sacrifices that you have made to provide for our family so that we can continue to live our “normal” life in the barn, or where ever we seem to find ourselves. I have learned so much from you all and it amazes me how much I continue to learn as we grow together.

BIOGRAPHY

Joseph Christopher Mackey was born in the belt buckle of the Appalachian Mountains, more specifically Mars Hill, NC. He, along with his younger sister Bethany and brother Burgin, were raised by their parents, Dewain and Kathy, on a small, diverse livestock and Burley Tobacco operation. Chris and his younger siblings continue to raise and exhibit their own cattle, sheep, and hogs at the local, state, and national levels. Their involvement on their family's farm led them to be actively involved in their local 4-H and high school FFA chapters. Chris was a member of very competitive livestock, dairy, and horse judging teams in both 4-H and FFA. Following high school, Chris attended Walters State Community College in Morristown, TN then transferred to the University of Tennessee at Knoxville. While attending UT, Chris was a member of the 2012 Collegiate Livestock Judging Team, was a member and student coach for the beef and sheep show teams, and was involved in Block and Bridle while working at the East Tennessee Research and Education Center. In the fall of 2013, Chris graduated with a Bachelors in Agriculture with a major in Education. His passion for the livestock industry and teaching led him to pursue a Masters at North Carolina State University in Animal Science where he was involved in the revitalization of the Collegiate Livestock Judging Team. After completion of his Masters work, Chris will be moving back to East Tennessee to work as the cow herd and show barn manager for Woodlawn Farms in Greeneville, TN.

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INTRODUCTION

Tall fescue *(Lolium arundinaceum* [Schreb.]) is the most abundant, cool-season, perennial forage that accounts for nearly 16 million ha in the Mid-Atlantic and Southeastern portion of the United States (Hoveland, 1993). The most common variety of fescue is Kentucky-31, which was made publically available in the U.S. in the early 1940's. The wide spread use of this forage was mainly due to its unique ability to be used as a winter stockpiled forage, its relative tolerance to drought, and high adaptability. Fescue was found to have a symbiotic relationship with a fungal endophyte (*Epichloë typhina*) in the late 1970's. This fungus aids in the plant's ability to withstand severe environmental stresses by producing ergot alkaloids (Aiken, 2013a). Unfortunately, these ergot alkaloids are toxic and when consumed have adverse effects on cattle, small ruminant, and horses; commonly referred to as fescue toxicosis. Cattle that suffer from fescue toxicosis may show many symptoms such as: increased body temperatures, elevated respiration rates, decreased ability to shed their thick winter hair coat, decreased ability to maintain homeostasis, and decreases in feed intake, milk production and overall performance; these symptoms are intensified during periods of heat stress. Even during the winter months, cattle that graze toxic fescue have negative reproductive effects such as a reduction in circulating concentrations of luteinizing hormone, progesterone, and prolactin; ultimately leading to a disruption of the normal estrous cycle, declining pregnancy, and calving rates. The United States annually produces an estimated 25 billion lbs of beef where 25% originates in the areas where toxic fescue is prominent. Recent studies have estimated that the annual loss in beef production is over $1 billion (Strickland et al., 2011). The negative impacts that fescue has on beef production has led to countless hours of research to uncover the mystery of the relationship that these alkaloids have on normal animal physiology; not to mention the development of methods to prevent and aid in the alleviation of fescue toxicosis.

Tall Fescue

Tall fescue (*Festuca arundinacea* [Schreb.]) is a hardy, cool season, perennial forage that was introduced to the United States from Europe in the late 1800's (Siegel et al., 1985). Since its introduction to the U.S., over 100 varieties have been developed and utilized in several different sectors of the agriculture industry. Fescue is commonly used as a forage source for livestock through production of pastureland and hay, various turf purposes including housing developments and golf courses, and has been used to aid in erosion control (Ball, 1991). The most common variety of fescue is Kentucky-31 (KY-31), which was made commercially available in 1943 and had wide spread use in the Mid-Atlantic and Southeastern portions of the U.S. It is estimated that over 16 million ha are currently planted in fescue (Ball, 1984; Hoveland, 1993).

Tall fescue gained wide spread use in the 1940's and 50's for it relative drought tolerance, ease of establishment, high yields, and ability to withstand harsh grazing conditions. Fescue grows in a wide variety of soil types and conditions; however, fescue does not perform well in moderately flooded and sandy soils (Arachevaleta et al., 1989; Jennings et al., 2008). Fescue is a cool season perennial, bunch grass that is deep-rooted, upright, and course-leaved with mature height ranging from 0.6-1.22 m in height (Jennings et al., 2008). While the optimum growth rate for fescue occurs between 20ºC and 25ºC, growth rate drastically declines when temperatures exceed 30ºC and cease below 5ºC (Jennings et al., 2008). As a cool season forage, fescue has two periods of growth; the majority occurring in the spring followed by a short second period of growth during the fall. Consequently, fescue has the unique characteristic of being utilized as a stockpiled forage. Stockpiling is the act of accumulating forage in situ for grazing at a later time. This allows livestock producers to better utilize pasture management and maximize grazing options further into the winter months when pasture-based forages are limited. Subsequently, this minimizes a producer's need for relying heavily on stored forages and concentrates for winter feeding, ultimately decreasing production costs.

Nutritional values for fescue vary during each stage of growth, season, and method of storage. In general, tall fescue ranges from 2-6 % lignin, 12-20% crude protein (CP) 23-38% acid detergent fiber (ADF), 45-55% neutral detergent fiber (NDF), and 60-80% in vitro dry matter digestibility (IVDMD) (Burns and Chamblee, 1979; Poore et al., 2006). During the stockpiling periods of fescue, there is generally a decrease in CP, ADF, and IVDMD and reduced NDF and lignin during the fall and spring through the emergence of new growth (Burns and Chamblee, 1979; Poore et al., 2006). However, some research including Fribourg and Bell's study (1984) showed no variations in ADF or NDF during the winter stockpiling period. Also, a more recent study conducted by Burns and Chamblee (2000) showed that crude protein had minimal change from November through March. A recent study by Lyons and coworkers (2016) determined protein supplementation was needed for developing beef heifers on stockpiled winter fescue from November through January. The study found that those heifers on a conservative forage allotment had significant decreases in average daily gains, final body weight, and final body condition scores compared to heifers that received extra forage allocation or protein supplementation. Consequently, supplementation may need to be provided during winter months for developing replacement females or growing stockers; however, winter stockpiled fescue has the capabilities of providing an adequate source of nutrition for gestating, and lactating cattle (Fribourg and Bell, 1984; Burns and Chamblee, 2000; Poore et al., 2006; Lyons et al., 2016).

Endophytic Fungus: *Epichloë typhina*

Unlike dicotyledons, grasses lack the ability to produce secondary metabolites that aid in the plants fitness and survival from biotic and abiotic stressors (Kuldau and Bacon, 2008). However, there are several mutualistic relationships between plants and microorganisms, such as fungal endophytes, that produce these secondary metabolites. Endophytic fungus, such as *Epichloë typhina*, is an example of a microorganism that aids in the plants persistence and hardiness (Clay, 1988). The infection of *Epichloë typhina* in fescue was first reported by Bacon et al. (1977). *Epichloë typhina* is one of the genera that belongs to the Clavicipitaceae family of endophyte fungi. This fungus enhances the plants survival by increasing its tolerance to pests, drought, extreme temperatures, and diseases (Arechavaleta et al., 1989; Arechavaleta et al. 1992; Clay, 1988; Siegel et al., 1990). It has also shown to improve the plants ability to withstand harsh grazing conditions (Hill et al., 1991) and increase plant material and seed production of fescue (Clay, 1988; 1990).

The mutualistic relationship between fungi and plants are common worldwide (Latch et al., 1987; White, 1987; Kuldau and Bacon, 2008). Endophytes such as *E. typhina* are harmless to their plant host and colonize intracellularly, only in the above ground tissues of the plant including the leaf sheath, stem, inflorescences, and seed (Kuldau and Bacon, 2008). More specifically, the hyphae of endophytic fungus lies in the apoplasm, or between the nutrient-rich, empty portions of the plant cells (Kuldau and Bacon, 2008). Consequently, the hyphae of the fungus are found and are more abundant in the regions of the plant with the most richness of energy. This allows for minimal competition with other microorganisms and serves as a protective environment for the fungus to survive. Many members of the Clavicipitaceae family are spread from plant to plant by producing fruit bodies and ascospores on the exterior portion of the host (Clay, 1988). However, *E. typhina* is maternally transmitted by the growth of hyphae into developing ovules and seeds (Clay, 1988). Unlike many of the Claviceps, the asexual genera, including *E. typhina*, are not contagious to non-infected plants; therefore, these fungi can only be spread through infected plants by enhancing survival, growth, and/or reproduction of the host.

There are two general classes of mechanisms that aid in the enhancement of host fitness, intrinsic and extrinsic mechanisms. Intrinsic mechanisms are specific to the infected host that alter the physiology, biochemistry, and/or morphology of the plant. Endophytes have shown to improve plants ability to withstand drought, flooding, heat, and survive in a wide variety of soil types (Arachevaleta et al., 1989; Bacon, 1993; Malinowski and Belesky, 2000; Kuldau and Bacon, 2008). Specifically, endophyte-infected (E+) tall fescue plants that have endured drought stress have shown to have increased regrowth and tiller production as well as overall survivability when compared to non-infected endophyte (E-) contemporaries (Arachevaleta et al., 1989). Fungal hyphae have shown to alter the pH of the plants apoplasm, reducing the concentrations of soluble carbohydrates (Tetlow and Farrar, 1993).

Fluctuating the pH changes the enzymatic activity and host cell sugar acquisition of the plant. It is unclear the mechanisms of hyphae nutrient uptake, but there is evidence that shows fungal endophytes possess hydrolytic enzymes which are used in the plants nutrient uptake and photosynthesis (Lindstrom et al. 1993; Reddy et al., 1996; Moy et al., 2002). Rather than altering a plants biochemistry or physiology, extrinsic mechanisms are those that look at the interaction between the host plant with other competitors, herbivores, and pathogens. A study conducted by Clay (1990) compared the difference in the presence of E+ and E- fescue in central Louisiana pasture communities. After 3 years, E+ plants had a 50% higher survival rate when compared to E- plants. In addition, E+ plants produced 70% more biomass, 50% more tillers, 40% more inflorescence. Other studies have shown that E+ plants are more resistant to wilting through improved water useage and greater efficiency of resource utilization (Arachevaleta et al., 1989; Hill et al., 1990). One of the most highly researched extrinsic mechanism is the protection of host plants against animal and microbial pests. Secondary metabolites are produced by endophytic fungi and aid in deterring herbivory of livestock and other pests by producing toxic compounds as well as decreasing the palatability of the infected plant (Bacon et al., 1977; Panaccione et al., 2006).

Ergot Alkaloids

Ergot alkaloids are naturally produced compounds that aid in plant survival and resistance to many different environmental stressors (Bush and Fannin, 2009). These alkaloids are categorized into several classes with the main three being: clavinet alkaloids, lysergic acid and derivatives, and ergopeptine alkaloids. The most prominent class is the ergopeptines accounting for 10-50% of the compound found in blades (up to 1.5 mg/kg) and sheaths (up to 14 mg/kg) of E+ tall fescue (Yates et al., 1985; Lyons et al., 1986; Bush and Fannin, 2009). Ergovaline is the most prominent member of the ergopeptine class comprising 84 to 97% of the total fraction (Yates et al., 1985; Lyons et al., 1986). Other members of the ergopeptine class include: ergocornine, ergocryptine, ergocrystine, ergonine, ergoptine, ergosine, lysergic acid, and lysergol (Boling et al., 1975; Bond et al., 1984a; Strickland et al., 2011). Each ergopeptine consists of a lysergic acid ring and 3 amino acids: L-alanin, L-valine, and L-proline (Panaccione et al., 2001). Ergot alkaloids are similar in structure to mammalian neurotransmitters such as dopamine, epinephrine, norepinephrine, serotonin, and lysergic acid diethylamide (LSD) (Burt et al., 1976; Berde, 1980; Larson, 1995). These compounds have been shown to bind to the D2 dopamine receptors with the same affinity as dopamine (Berde and Sturmer, 1978; Larson et al., 1995) as well as serotonin receptors (Schoning et al., 2001). The ability for these compounds to mimic the natural biological compounds found in animals and the binding to their specific receptors via antagonistic activity are still unclear; making it more challenging for researchers to pinpoint exact methods of preventing these secondary metabolites from altering normal biological functions.

Ergot alkaloids play a critical role in plant survival by decreasing the incidence of herbivory by mammals and pests. The study conducted by Panaccione et al. (2006) reported that rabbits consuming endophyte-infected perennial ryegrass had suppressed appetite from clavine alkaloids produced by the fungus. The cause is thought to be associated with the agonistic activity of ergovaline at serotonin receptors suggesting that there is potentially a neuroendocrine response to decrease the rabbit's appetite from the consumption of the ergot alkaloids. Other research as shown that cattle and horses are more selective when consuming fescue seed heads (Aiken et al., 1993). Steers have also been found to prefer clover in E+ pastures, but consumed more fescue than clover in E- stands (Fribourg et al., 1991). This selectivity may also be attributed to the typical bitter taste of infected grasses, in turn overgrazing or completely eliminating the noninfected grasses and other forages within the respective community. While it is still unknown how insects have the ability to distinguish between E+ and E- plants, research has shown that Aphids, crickets, and various other insects consume less and grow slower when consuming E+ plants (Latch et al., 1985; Siegel et al., 1985; 1990).

Endophyte-infected tall fescue does not contain every type of ergot alkaloid; in fact, class and concentration of alkaloids are specific to host genotype and endophytic strain. Depending upon the maturity, season, and environmental conditions, alkaloid concentrations fluctuate throughout the year and lifespan of the host plant (Bond et al., 1984a; Arechavalia et al., 1992; Hill et al., 2002). Ergot alkaloid concentrations reportedly are the lowest and are reduced by approximately 80% from December to late winter (Kallenbach et al., 2003; Curtis and Kallenbach, 2007). Following the first month of winter dormancy, ergovaline concentrations will increase throughout the spring months and reach their highest concentrations in late spring followed by a decrease in concentration during the summer months (Belesky et al., 1988; Peters et al., 1992). The increase in ergot alkaloid concentration seen in late spring correlates with tall fescues reproductive maturity, as the seed heads of this grass have been reported to contain up to three times the concentration of ergot alkaloids than the leaf blades (Rottinghaus et al., 1991). Peak concentrations of ergovaline occur in the spring and is 10-fold higher than in the summer months due to the increase in average ambient temperature and the presence of the seed head (Rottinghaus et al., 1991). Rogers et al. (2011) reported that the absence of a spring peak in ergovaline concentration can be contributed to the method of suppressing reproductive development; all plots were mowed every month to a 10-cm stubble height, preventing plants from developing past early stem elongation. In the same study, ergovaline concentrations in the month of April coincided with ambient temperature. The ergovaline concentrations at 3 locations, Missouri, South Carolina, and Georgia, were 75, 277, and 283 μg kg^{-1}, respectfully. During the month of April, the highest temperatures at the MO location averaged 11.5ºC compared to SC and GA locations which averaged 18.2ºC. Additionally, average low temperatures for MO, SC, and GA were -0.5ºC, 3.4 ºC, and 4.1ºC, respectfully. According to Ju et al. (2006), the minimum temperature for most endophytic fungus is 5ºC warmer than for tall fescue growth. Consequently, areas such as South Carolina and Georgia with warmer average temperatures allow for greater endophyte fungal growth and therefore increase ergovaline concentrations. Studies including that of Roberts et al. (2009) showed fluctuations in ergot alkaloid concentrations with storage length. This study evaluated tall fescue hay for ergovaline and ergot alkaloid concentrations that were harvested in June. Twenty hay core samples following baling were taken over a 540 day period. At harvesting, ergovaline concentrations ranged from 578-586 µg kg^{-1} and total ergot alkaloid concentrations ranged from 537-688 µg kg^{-1}. After the first day of samples, both ergovaline and ergot alkaloid concentrations significantly decrease, particularly within the first three days of harvest. By the end of the 18 month study, ergovaline concentrations remained above 250 µg kg^{-1}, which is well above the 150 μg kg^{-1} threshold proposed to initiate symptoms of fescue toxicity in animals (Stamm et al., 1994). The toxicity of fungus has been extensively researched for several decades, but much remains unclear of the exact mechanisms and contributing agents that lead to decreased animal performance and associated negative effects. In addition, the most prominent ergot alkaloid is ergovaline and it is thought to be the leading cause of toxicity in tall fescue; however, more recent research has reported that other alkaloid compounds may be more highly transportable than ergovaline.

A review by Strickland et al. (2011) suggested ruminants are more efficient and better able to metabolize and excrete toxins than non-ruminants. The review proposes that it is potentially due to rumen microbial metabolism which occurs before gastrointestinal absorption. Gastrointestinal absorption of ergot alkaloids involves the passive or facilitated/active mechanism transports across the gastrointestinal epithelia. Eckert et al. (1978) showed that many ingested toxins and drugs are absorbed via passive transport. The extent and rate of alkaloid absorption is based upon the solubility within the digestive tract and the extent of ionization, which determines the splitting of alkaloids between water and lipid phases (Strickland et al., 2011). Most ergot alkaloids possess both polar and nonpolar components, making them extremely sensitive to subsequent absorption based on the pH of their surrounding environments. In environments with low pH, such as the abomasum, these compounds are not thought to be highly absorbed because these compounds are weak bases (Eckert et al., 1978). Consequently, it is thought that the absorption of these compounds occur in the forestomach and intestine of ruminants (Westendorf et al., 1992; Hill et al., 2001). Hill et al. (2001) reports that ergot alkaloids were actively transported across ruminal, reticular, and omasal tissues of sheep. However, 50% more lysergic acid appeared on the serosal side after 4 hours than lysergol, ergonovine, ergotomine, and ergocryptine. Ayers et al. (2009) more recently demonstrated that lysergic acid crossed gastric barriers and were present in rumen fluid and urine. In addition, they find no evidence of ergovaline being transported across the rumen or omasum nor in ruminal fluid or urine. These findings are contradictory to many other studies that have found evidence of ergot alkaloids in urine as well as milk, bile, and adipose tissue (Westendorf et al., 1993; Stuedemann et al., 1998; Durix et al., 1999; Schultz et al., 2006). As a result, it is believed that these ergot alkaloids reach the circulatory system by means of the lymphatic system, portal system and liver following absorption. While evidence has been shown that lysergic acid has greater transport potential than other ergopeptine alkaloids, research continues to focus on ergopeptine compounds as the contributory factor(s) of toxicity symptoms in livestock.

Fescue Toxicosis

While there are numerous benefits of using fescue as a primary forage for livestock production, the endophyte-fescue relationship and subsequent production of ergot alkaloids can be detrimental to livestock production. What was once the term “summer slump”, is now referred to as fescue toxicosis (Schmidt and Osborn, 1993). Characteristics of fescue toxicosis include and are not limited to increased body temperature, decreases respiration rate, vasoconstriction, decrease in body condition and average daily gains, as well as decreased reproductive performance (Peters, 1992; Schmidt and Osborne, 1993; Mahmood, 1994; Paterson, 1995; Foote, 2003; Watson et al., 2004; Aiken et al., 2013).

Effects on Animal Temperature Regulation and Vasoconstriction

Alone, ergot alkaloids suppress many physiological and biological processes in livestock, but in combination with extreme environmental conditions the effects of toxic fescue are intensified. Vasoconstriction has shown to reduce blood flow by constriction of blood vessels and arteries to the skin, extremities, brain, and other vital internal organs such as the digestive and reproductive tracts (Rhodes et al., 1991; Paterson et al., 1995; Aiken et al., 2007; Foote et al., 2013, Johnson et al., 2015). Reports have shown that the reduction in blood flow through the circulatory system in animals consuming E+ forages have thickened blood vessel walls and a reduction in lumen area (Williams et al., 1975; Garner and Cornell, 1978). While it is not fully understood the exact mechanisms that alkaloid compounds have on compressing the circulatory system, a study conducted by Klotz et al. (2008) took biopsied bovine lateral saphenous veins from fescue naïve, crossbred heifers to determine their contractile response to different ergot alkaloids. Ergovaline showed to have a greater response compared to that of lysergic acid and N-acetylloline. There was also an additive effect when ergovaline and lysergic acid were combined, suggesting that multiple ergot compounds contribute to vasoconstriction. Other research including a study by Aiken et al. (2007) demonstrated that within 4 hr, cattle fed E+ grass seed containing 0.85 µg of ergovaline had smaller caudal artery area than cattle fed E- grass seed and remained suppressed throughout the duration of the study. Similar results were seen in a reduction of the auricular artery luminal area in goats (Aiken et al., 2014). Due to inadequate blood flow to extremities, skin, and vital organs in combination with retaining winter hair coats and decreased ability to shed, cattle and livestock have a reduced ability to appropriately regulate their body temperature, decreasing their ability to tolerate periods of heat stress (Walls and

Jacobson, 1970; Hoveland, 1983; Rhodes et al., 1991). McClanahan et al. (2008) and Aiken et al. (2011) report that as ambient temperature rises, rectal temperatures in animals with rough hair coats are higher than those with slick or clipped hair coats. During periods of heat stress, livestock that consume E+ forages have shown to have increased respiration rate, body temperatures, and salivation compared to those consuming E- forages (Walls and Jacobson, 1970; Bond et al., 1984a; Rhodes et al., 1991; Browning et al., 1998a; Burke et al., 2001a). Few of the studies have also reported increases in heart rates in association with fescue toxicosis and vasoconstriction, which would be expected if animals have altered respiration rates and body temperatures (Walls and Jacobson, 1970; Bond et al., 1984a). Other studies have reported that in addition to an increase in body temperature, a decrease in skin vaporization was observed in steers (Aldrich et al., 1993a) and sheep (Aldrich et al., 1993b) that consumed an E+ diet.

It has also been reported that during periods of lower ambient temperatures, livestock consuming E+ forages are still likely to suffer from vasoconstriction and one of the most visibly dramatic disorders from fescue toxicosis; fescue foot (Jensen et al., 1956; Williams et al., 1975; Garner and Cornell, 1978; Yates et al., 1979). Yates (1963) stated in his review that Goodman was the first to report the incidence of fescue foot in 1952. Yates (1963) defines fescue foot as a noninfectious disease in cattle that is characterized by thrombosis and lameness in the hind quarters, weight loss, rough hair coat, and predisposing to dry gangrene of infected areas with the potential of the peripheral portion of the limb to slough off. It is generally thought that toxic ergot concentration is closely related to environmental temperatures and development of gangrenous ergotism. Tor-Agbidye et al. (2001) suggested that ergovaline concentrations of 400 to 750 ppb to cattle and 500 to 800 ppb to sheep and temperatures less than 16 ºC are estimated threshold values for inducing fescue foot. Cattle grazing tall fescue pastures have shown to suffer from lameness and lesions on one or both of the rear feet due to dry gangrene within 50 days of grazing (Jensen et al., 1956). Further investigation reported that post-mortem dissection of the vasculature of the infected feet showed thrombosis of the arteries (Jensen et al., 1956). Williams et al. (1975) reported that calves receiving an ergot alkaloid containing crude extract made from tall fescue hay showed symptoms of lameness, swelling, and reddening of the coronary bands of the hoof and discoloration of the tail.

Effects on Animal Gain and Behavior

Steer/Heifer Performance. Regardless of endophyte status, heat stress alone has shown to alter the feed/forage intake and water consumption of livestock, but is amplified when livestock are put on an E+ diet (Fuquay, 1981; Jackson et al., 1984, Aldrich et al., 1993a; Burke et al., 2001a). Studies from across the Southeast of the U.S. have reported that steers grazing E+ pastures have a decrease in average daily gain (ADG) from 30 to 100% when compared to steers grazing E- pastures (Stuedemann & Hoveland, 1988; Ball et al., 1991; Paterson et al., 1995) and it is suggested that for every 10% increase in endophyte fescue stand infection, there is a 45 g/d decrease in steer ADG (Thompson et al., 1993). In the study conducted by Aldrich et al. (1993), found that Holstein steers housed at 32ºC had a reduction in feed intake by 22% and water consumption increased by 62% when compared to steers housed at 22ºC. In the same study, steers on an E+ diet had a 10% reduced feed intake than those on an E- diet; water consumption was similar between E+ and E- diets (Aldrich et al., 1993). Similar results reported a reduction in feed intake under heat stress (HS) conditions in beef heifers, but when animals were put on E+ grass seed and HS conditions, feed intake drastically declined (Burke et al., 2001a). However, Burke et al. (2001) did not find a difference in feed intake when comparing heifers fed E+ to E- seed under thermoneutral (TN) conditions. Johnson et al. (2015) looked at the response of heat stress and E+ fescue on Angus steers from two locations, those that were fescue naïve (Oklahoma) and those that had been raised on E+ fescue pastures (Missouri). During the periods of TN (19-22ºC), steers on an E+ diet had reduced feed intake of nearly 2.0 kg/day regardless of location (Johnson et al., 2015). Feed intake significantly decreased in E+ treated cattle compared to E- treated animals (6.9±0.2 vs. 8.4±0.2 kg, respectively) over the entire period of HS (26-36ºC). In addition, this study observed that during the HS period there was an overall reduction in feed intake of -4.5 kg below the TN period (Johnson et al., 2015). This reduction was significantly exacerbated when animals consumed an E+ diet, which occurred during the TN (-3.9 kg) and HS (-5.1 kg) periods (Johnson et al., 2015). It is also well documented that E+ fescue diets reduce average daily gain (ADG) in steers and can range from 0.14-0.76 kg/day when compared to steers grazing E- diets (Schmidt et al., 1982; Stuedemann et al., 1986). A five year winter study conducted by Drewnoski et al. (2009a) looked at the impact of growing cattle performance during the winter months when grazing stockpiled Jesup tall fescue with varying endophyte concentrations. Regardless of endophyte status, ADG did not differ between years. In a different study, Drewnoski et al. (2009b) showed similar results in beef heifers grazing winter stockpiled Jesup tall fescue with an endophyte status of E+, E-, or novel endophyte (EN). Regardless of endophyte status, during winter months there were no differences in feed intake, ADG, BW, or body condition scores (BCS). However, during the spring months, as ambient temperature and endophyte concentrations began to rise, the weight gain of heifers differed between treatments (0.24, 0.75, and 0.71 kg/d for E+, E− and EN, respectively) (Drewnoski et al., 2009b). The evidence of heat-stressed environment studies of Aldrich et al. (1993) and Burke et al. (2001) and the thermoneutral/cool environments in the studies of Drewnoski et al. (2009a; 2009b) show that as the average ambient temperature rises, feed intake is reduced and more significantly when cattle consume E+ diets compared to E-.

Cow-calf Performance. The majority of the 16 million ha of tall fescue in the U.S. is grazed by cow-calf pairs; while much research on grazing tall fescue has been conducted using steers and heifers, much fewer data is available on the comparison of cow-calf pairs grazing E+ fescue to pairs grazing E- fescue pastures. Similarly to steers, it has been shown that cows grazing E+ pastures compared to those grazing E- pastures have reduced feed intake, weight gain, and milk production, consequently reducing overall calf performance. (Schmidt et al., 1983; Peters et al., 1992; Watson et al., 2004). Peters et al. (1992) reported that during a two year grazing trial (May-September 1988 & 1989), lactating beef cows grazing E+ pastures had an 18% reduction in feed intake, lost three times more body weight (BW), and produced 25% less milk than cows grazing E- pastures. Similarly, slower calf gains were noted for E+ than for E- (0.72 vs. 0.89 kg/d, respectively; Peters et al., 1992). It is estimated that milk production decreases 0.15 kg/d for each 10% increase in pasture endophyte infection (Danilson et al., 1986). This reduction in milk production results in calf weight gains and ultimately lower weaning weights. Watson et al. (2004) reported that the average weaning weight for steer and heifer calves (28.2 & 19.8 kg, respectively) were higher if they were raised on E- pastures than those raised on E+.

Feed Intake/Digestibility. The suppression of feed intake on E+ diets resulting in a reduction in weight gain and ADG is thought to be due to several different factors such as a decrease in dry matter intake (DMI) and digestibility, and a lower plane of nutrition (Jackson et al., 1984; Aldrich et al., 1993a; Matthews et al, 2005). In ruminants, it is generally thought that when feed intake is reduced then apparent digestibility should increase (Ferrell et al., 1993). However, studies that have compared the digestibility of E+ and E- diets have shown to have mixed results in that digestibility increased in some (Goetsch et al., 1987; Koontz et al., 2015) and decreased in others (Aldrich et al., 1993a; Matthews et al., 2005). Other studies that fixed dry matter intake in diets with varying degrees of endophyte concentrations report lower dry matter (Aldrich et al., 1993a; Matthews et al., 2005) and crude protein (Westendorf et al., 1993; Matthews et al., 2005) digestibility. It has also been shown that steers on a diet with high ergovaline concentrations have elevated volatile fatty acid (VFA) concentrations, a reduction in liquid passage and a tendency for reduced particulate passage rate and outflow; suggesting that animals gain less on E+ diets because they eat less (Goestch et al., 1987; Stamm et al., 1994; Foote et al., 2013; Koontz et al., 2015). It is likely that the increase in VFA concentrations is due to a decrease in blood flow to the rumen epithelium and ergovalines interruption with the acetate flux across the tissue (Foote et al., 2013). Additionally, ergot alkaloids are known to interact with serotonin receptors in vascular smooth muscle (Schoning et al., 2001), it is thought that these ergot alkaloid compounds interrupt the serotonergic receptors of the gut, thereby negatively disturbing motility and passage rate (Pan & Galligan, 1994; Briejer et al., 1997).

Grazing Behavior. It is also thought that the decline in performance is due to the altered grazing behaviors of cattle cosuming E+ tall fescue. Bond et al. (1984b) found that steers grazing different varieties of E+ fescue tended to graze more at night than those on E- during the summer months. However, Seman et al. (1999) reported no significant differences in grazing time, but did note that cattle grazing pastures with mixed varieties of legumes and fescue spent on average 1.4 h/d more grazing than those grazing monoculture pastures of fescue. Other studies have found that cattle grazing E+ fescue pastures spend more time standing, idling, and consume more water; whereas cattle grazing E- fescue pastures spent more time grazing, lying down, and took more prehensile bites; thus having a higher ADG (Howard et al., 1992, Parish et al., 2003b). Many livestock producers that utilize pasture based systems in the Southeastern portion of the U.S. rely heavily on their animal's ability to put on weight quickly and efficiently in order to maintain operational financial stability. However, it is apparent that E+ fescue can have negative effects on weight gain, ADG, and grazing behaviors; in addition to the endless other biological and physiological processes that livestock suffer from consuming high concentration of E+ tall fescue.

Effects on Animal Reproduction

There are many different factors that can affect the success or failure of an operation; reproductive efficiency may arguably be one of the most critical contributing factors. It is well documented that livestock on toxic fescue have decreased reproductive success (Porter & Thompson, 1992, Mahmood et al., 1994; Burke et al., 2001a; Looper et al., 2010). As seen previously with other animal processes, it is thought that there are many different interactions between failed reproductive performance and consumption of toxic fescue such as ambient temperature and length of exposure to E+ fescue, genetics, age, BCS, and nutritional management (Strickland et al., 2011). While the effects of ergot alkaloids on reproduction has been extensively researched with varying observations looking at the direct effects (ovary, follicle development, and corpus luteum) and indirect effects (reduced nutritional intake and BCS) on reproduction, much still remains unclear which is why scientists strive to uncover the facts about fescues toxicosis. It is thought that one of the largest contributors to reproductive failure is the influence that ergot alkaloids have on altering the function of the hypothalamus, pineal and pituitary glands of the brain by decreasing the concentration of circulating reproductive hormones that are critical for sustaining normal cyclicity and maintenance of pregnancy (Sibley and Creese, 1983; Schillo et al., 1988; Porter et al., 1990; Burke et al., 2001a).

Prolactin. A decrease in serum prolactin is one of the many reproductive hormones that have been used as an indicator for ergot alkaloid exposure in sheep (Gooneratne et al., 2011), cattle (Burke et al., 2001a; Watson et al., 2004) and horses (Monroe et al., 1988). Prolactin is a protein hormone synthesized within the anterior pituitary gland, uterus, and mammary gland (Freeman et al., 2000). Along with many diverse functions of prolactin, this hormone has been linked to lactation and mammogenesis (Houdebine et al., 1985). While decreased serum prolactin concentrations in lactating animals has not been shown to directly influence a reduction in milk production (Porter et al., 1992), suppressed milk production has been seen to be associated with cattle (Peters et al., 1992; Watson et al., 2004), sheep

(Stidham et al., 1982) and agalactia in horses (Monroe et al., 1988) consuming E+ tall fescue. Additionally, increased prolactin concentrations in association with day length have been related to shedding of winter coats in several species (Thompson et al., 1997; McClanahan et al., 2008; Littlejohn et al., 2014). A common indicator that cattle are on a toxic fescue diet is an unthrifty appearance and retained winter hair coat, and it has been reported that prolactin concentrations were too low to initiate shedding of the winter coat delaying the start of summer hair coat growth (Aiken et al., 2011). Burke et al. (2001) looked at the impact of heat stress on prolactin concentrations in beef heifers fed E+ tall fescue seed. During TN conditions, prolactin concentrations were suppressed in heifers on E+ diets and were further exasperated during the HS period of the study (Burke et al., 2001a). It has also been reported in grazing studies conducted in the fall and winter months when ambient temperatures and ergot alkaloid concentrations begin to decline that serum prolactin concentrations are suppressed in cattle consuming E+ tall fescue (Watson et al., 2004; Drewnoski et al., 2009a). Normally, dopamine is responsible for the secretion of prolactin (Lamberts and MacLeod, 1990). However, due to the structural similarities that ergot alkaloids share with dopamine, it is generally thought that this suppression of prolactin in the anteriory pituitary (Schillo et al., 1988) is due to the antagonistic abilities of these alkaloid classes to interact and bind to dopamine receptors (Sibley and Creese, 1983; Larson et al., 1995). Prolactin receptors have been found in bovine corpa lutea (Poindexter et al., 1979) and granulosa cells (Lebedeva et al., 2004) and has been suggested to influence the release of gonadotropins in sheep (Tortonese et al., 1998) and horses (Gregory et al., 2000).

Progesterone. Unlike prolactin, progesterone is a steroid hormone necessary for establishment and maintenance of pregnancy, in most ungulates, and is produced by the corpus luteum (CL) and placenta. Reduced serum progesterone concentrations have been reported in mares (Monroe et al., 1988), ewes (Burke et al., 2006), and heifers (Burke et al., 2001a; Jones et al., 2003) fed E+ diets. Mahmood et al. (1994) reported that weaned heifers grazing E+ tall fescue had a greater suppression of serum progesterone concentrations compared to yearling heifers. Heat stress alone has been shown to reduce CL size and suppress progesterone concentrations in beef heifers (Burke et al., 2001a) regardless of endophyte status. However, Burke and Rorie (2002) found no differences CL diameter or serum progesterone concentrations of mature beef cows grazing either E+ or E- tall fescue. While this study used mature cows and average ambient temperatures were not as high as the previously mentioned studies that reported suppressed serum progesterone concentrations and CL diameter, it may be suggested that cows are more well adapted to handling HS conditions than heifers and that the reduction in CL diameter of heifers may be associated more with extreme environmental conditions than solely on toxic fescue. Decreased luteal function from consumption of ergot alkaloids may also be attributed to these ergot compounds ability to stimulate uterine smooth muscle movement (Saameli, 1978). These alkaloids could potentially serve as a mechanism responsible for the release of prostaglandin-F2α, compromising luteal function (Browning et al., 1998b) and ultimately decreasing progesterone. Cholesterol is a precursor molecule for progesterone synthesis and it has been reported that heifers consuming E+ tall fescue seed had both a reduction in serum progesterone and cholesterol concentrations regardless of HS or TN conditions (Bond et al., 1984a; Burke et al., 2001a). It has been shown that mature beef cows grazing E+ tall fescue had reduced serum cholesterol concentrations compared to cows grazing E-, but did not see an associated difference in serum progesterone concentrations (Burke et al., 2001b). In contrast, mature cows given an intravenous administration of ergotamine tartrate immediately had increased cholesterol concentrations (Browning, 2003). Ergot alkaloids interact with several different receptors throughout the body. Research has reported localized vasoconstriction of blood vessels; it is possible that impaired luteal and ovarian function could be due to a decrease in blood flow to these tissues, consequently inhibiting the release of progesterone (Jones et al., 2003; Aiken et al., 2007). Bond et al. (1988) reported that ewes grazing E+ tall fescue showed early embryonic loss due to decreased luteal function. It was also observed that in beef heifers grazing E+ tall fescue showed less estrus activity at 96 hours after synchronization (Mahmood et al., 1994). Additional research has reported erratic estrous cycles in heifers and ewes consuming toxic fescue (Jones et al., 2003; Seals et al., 2005; Burke et al., 2006) which could be contributed to a reduction in luteal function.

Gonadotropins. Fewer data report the effect that ergot alkaloids have on other hormone synthesis and release, for instance the gonadotropins, and results available are highly variable. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are released from the anterior pituitary where ergot alkaloids are known to effect prolactin secretion (Schillo et al., 1988), so it possible for these compounds to interfere with normal secretions of LH and FSH. Similarly to prolactin and progesterone, luteinizing hormone (LH) concentrations have been found to be suppressed in cattle consuming E+ tall fescue in comparison to E- and when given intravenous injections of ergonovine maleate and ergotamine tartrate (Browning et al., 1998a; 1998b), which could decrease luteal function. However, changes in LH were not observed in heifers fed E+ fescue seed (Mizinga et al., 1992) or in ewes that were subcutaneously administered with ergocornin hydrogen melate (Louw et al., 1974). It has been speculated that ergot alkaloids interact with the dopamine receptors and/or norepinephrine neurons that stimulate FSH receptors on the follicle in cattle (Jones et al., 2003) as seen in rodents (Mayerhofer et al., 1997). Hodson et al. (2012) used ovine pituitary cell cultures to see effect of bromocriptine, a dopaminergic receptor agonist derived from ergocryptine, on the LH and FSH secretory responses to gonadotropin-releasing hormone (GnRH). Bromocriptine was reported to have inhibited secretory responses of the cells to GnRH for both hormones (Hodson et al., 2012). Regardless of the mechanism, the effects that ergot alkaloids have on impeding normal cyclicity in animals has also altered normal follicular function and has been shown to reduce conception rates.

Follicular Development. Normal follicular development and function are vital for successful conception. It is thought that decreased follicle size may cause a decrease in conception rates (Bridges et al., 2000). Exposure to E+ diets has been shown to decrease the number of large follicle in beef heifers and mature cows and small follicles are at risk to damage from HS conditions (Wolfenson et al., 1995; Burke et al., 2001a; Burke and Rorie, 2002). Burke et al. (2001a) reported that heifers under HS conditions and consuming E+ tall fescue had smaller pre-ovulatory follicles and fewer large follicles (≥ 10mm) during estrous as compared to heifers under HS conditions alone, or those on E+ or E- diets under TN conditions. Despite this, the previous reports only found differences in the diameter of the dominant follicle in beef cattle only when ambient temperatures were high (Burke et al., 2001a; Burke and Rorie, 2002). Also, Seals et al. (2005) found no differences in total numbers of follicles (> 5mm), the diameter of follicles during specific waves, or size of the ovulatory follicle in heifers fed E+ or E- diets.

Conception/Pregnancy Rate. The negative associated effects of ergot alkaloids on irregular estrous cycles and inhibited follicular development in animals can result in decreased conception and pregnancy rates. Heat stress alone has shown to reduce conception rates in dairy and beef cattle (Wolfenson et al., 1995; Burke et al., 2001a). Gay et al. (1988) reported a significant decrease in pregnancy rates in lactating beef cows grazing toxic fescue compared to pairs grazing nontoxic pastures (55.0% vs. 95.0%, respectfully). However, other studies have found no differences in pregnancy rate in mature beef cows grazing E+ or E- fescue at 30 d (93.5% vs. 93.8%, respectfully) or 90 d (83.3% vs. 88.1%, respectfully) post breeding (Burke et al., 2001b; Burke and Rorie, 2002). However, age, nutritional management and genetics of the animals, in addition to alkaloid concentration and ambient temperature can contribute to the variations in these conception rates in cattle consuming toxic fescue.

Effects of Gestational Consumption of Ergot Alkaloids

Fetal Growth/Birth Weight. While the effects of ergot alkaloids on conception and pregnancy rates are variable, other research has looked at how these compounds affect both the cow and fetus on further through the gestation period. Studies have reported decreased birth weights for lambs (Duckett et al., 2015) and calves (Watson et al., 2004) from maternal consumption of ergot alkaloids. It is possible that this reduction in birth weight is caused from a decrease in blood flow, consequently vital nutrients, to the fetus knowing ergot alkaloids vasoconstrictive abilities particularly on bovine uterine and umbilical arteries (Dyer, 1993). However, Caldwell et al. (2013) saw no differences in birth weight between spring or fall born calves, regardless of endophyte status. Interestingly, this study did report that cows grazing pastures with 75% E+ load compared to 100% had greater calving rates for both spring and fall (Caldwell et al., 2013). Additionally, fall calving cows had a 31% greater calving rate and averaged 11 d shorter calving interval compared to spring calving cows no matter the endophyte load on pastures (Caldwell et al., 2013). This might be due to the fact that at the start and end of the breeding season, fall calving cows BW was greater and fall calving cows lost less weight compared to spring calving cows. Other research has looked at the effects of ergot alkaloid consumption in pregnant mares. Research reports that mares exposed to E+ tall fescue pastures have increased mare loss due to dystocia, thickened placentas, and prolonged gestation period of up to 3 to 4 weeks (Monroe et al., 1988; Cross, 2009).

Energy Reserves. Consumption of E+ fescue diets has been show to decrease dry matter intake (DMI) in ruminants (Parish et al., 2003b; Looper et al., 2007) which results in loss of body energy reserves (Brown et al., 1992), thus limiting reproductive fitness by inhibiting follicular growth, conception, and calving rates. It has been found that subsequent body energy losses resulted in smaller dominate follicles in beef heifers (Rhodes et al., 1995a), and both mature beef (Ciccioli et al., 2003) and dairy (Lucy et al., 1991) cows. Britt (1992) estimated that it takes 60 to 80 d for bovine preantral staged follicles to reach a mature stage for ovulation, and that follicles exposed to adverse conditions, such as a reduction in DMI from consumption of ergot alkaloids, may result in inadequate development. It has been shown that cows with greater nutrient intake also had greater plasma prolactin concentrations than cows with less nutrient intake (Wright et al., 1987). Looper et al. (2010) reported that thin conditioned cows grazing E+ tall fescue has reduced calving rates than cows in good condition and grazing E+ tall fescue. Caldwell et al. (2013) reported that fall calving cows had higher BW at the beginning of the breeding season and had no change in body condition during the breeding season compared to spring calving cows which started the breeding season at a lower BW and lost weight during the breeding season. In addition, fall calving cows had higher calving rates and shorter calving intervals than spring calving cows. While the interaction of ergot alkaloids on animals and livestock production has been extensively researched, much still remains unclear to the exact mechanisms that suppress the normal biological and physiological processes of the affected individual and populations. The results of this research has led to the continued support for discovering more and updated solutions and methods of reducing the effects of these harmful compounds to improve overall animal wellbeing.

Methods of Alleviating Fescue Toxicosis

Despite the known beneficial characteristics that E+ tall fescue has been shown to have, such as ease of establishment, adaptability, and stockpiling capabilities, the toxic properties of tall fescue have many negative effects on livestock production. It has been reported that losses in cattle production in the United States have been estimated to almost $600 million dollars (Hoveland et al., 1993); however, Strickland et al. (2011) suggested that combined small and large ruminant production loss exceeds $1 billion annually. The uncovered findings from many hours of research have led to both plant and animal based solutions of alleviating the harmful effects of these toxic compounds on production livestock.

Plant Based Solutions. There are alternatives to grazing endophyte-infected tall fescue; such as a novel endophyte variety (NE+, non-toxic). Research has reported sheep and stocker cattle grazing NE+ have similar ADG when compared to E- (Parish et al., 2003a; 2003b). While these varieties cannot contract toxic alkaloids, NE+ are not as persistent or as adaptable as their infected cousin, making them more susceptible of being choked out by more competitive forages and pests. Additionally, it is extremely costly to transition infected fescue pastures to non-toxic varieties. Increased cost of seed, fuel, labor, loss of pasture productivity, and increased pasture management are all factors that should be considered before re-establishing E+ pastures into NE+. However, it may prove be beneficial to livestock production through a more intensive pasture management program. Kentucky-31 can be used as a winter stockpiled forage which allows livestock producers to better utilize pasture management and maximize grazing options further into the winter months when pasture-based forages are limited, and alkaloid concentrations and ambient temperatures are at their lowest (Kallenbach et al., 2003; Curtis and Kallenbach, 2007). Subsequently, this minimizes producer's needs for relying heavily on stored forages and concentrates for winter feeding, and reduces the incidence of fescue toxicosis through suppressed alkaloid concentrations and no risk of heat stress. However, the stockpiling of tall fescue has been shown to decrease in nutritive value through late winter (Ocumpaugh and Matches, 1977). While this reduction may be suitable for maintenance in mature livestock, supplementation may be needing for growing animals (Lyons et al., 2016). Poore et al. (2006) reported that heifers grazing winter stockpiled tall fescue and were supplemented with whole cottonseed (24.4% CP) had greater ADG and increased BCS compared to heifers not supplemented with whole cottonseed. Other studies have reported improved conception and pregnancy rates in mature cows grazing toxic fescue and supplemented with fishmeal, a rich source of fatty acids and protein, compared to control cows (Bruckental et al., 1989; Armstrong et al., 1990).

Research has reported an absence of a spring peak in ergovaline concentrations which may be contributed to the prevention of plants developing past the early stem elongation stage (Rogers et al., 2011). Therefore, the plant was not allowed to produce a seed head which has been found to contain three times the amount of ergot alkaloids when compared to the blade (Rottinghaus et al., 1991). It is possible that livestock producers could reduce the intensity of fescue toxicosis through introduction of non-toxic varieties of fescue or other cool-season forages into already established E+ fescue pastures, in addition to preventing toxic fescue plants from maturing to the sexually mature stage. Thompson et al. (1993) combined grazing studies to show that ADG was not affected when comparing clover added to high endophyte-infected pastures to stands with low endophyte-infection and no clover. Additionally, livestock producers may want to utilize more warm season forages for pasture during summer months. This would either eliminate or reduce the consumption of E+ tall fescue when heat becomes an additional stress factor, consequently minimizing the risk of livestock being affected by fescue toxicosis.

Animal Based Solutions. Knowing that ergot alkaloid concentrations begin to rise and are highest in the spring months with additional heat stress during the summer months, producers may want to operate their herds in a fall calving program rather than spring. The breeding season for fall calving herds usually ranges from late November to February when ambient temperatures and ergot alkaloid concentrations are at their lowest. Breeding cattle during this time period would eliminate heat stress conditions and the consumption of high E+ concentrations, thus improving reproductive performance in cattle consuming endophyte infected tall fescue. Caldwell et al. (2013) reported that calving rates averaged 31% greater and calving intervals were on average 11 d shorter for fall calving cows compared to spring calving cows that were consuming E+ tall fescue. In addition, calves born in the fall had higher preweaning BW gain, actual and adjusted weaning weights, and ADG compared to spring born calves. The report also calculated that at weaning fall born calves averaged an $82 increase in value compared to calves born in the spring.

Bos indicus cattle are known for their tolerance to heat. Grazing studies comparing the growth performance of *Bos indicus* cross steers and British cross on toxic fescue pastures reported that ADG for cattle with Brahman influence on average had a 21% higher ADG compared to British cross cattle (Goetsch et al., 1988; McMurphy et al., 1990). The Senepol breed of *Bos indicus* cattle that have been found to have a slick gene; which is identified as a short, slick hair coat. It is thought that this trait aids in the ability to regulate body temperature. While it is the only study of its kind to date, Devine et al. (2016) compared the reproductive performance of Senepol x Angus heifers that either expressed the slick gene (Hh) or normal hair coat (HH) while consuming either E- or E+ fescue seed. The study reported that E+HH heifers had reduced ADG, lower BCS, increased skin surface temperatures, and had greater fluctuations in body temperatures than those animals that were E-HH, E+Hh, and E-Hh (Devine et al., 2016). Based on data presented from these studies, it may be advantageous to incorporate *Bos indicus* cattle and/or the slick gene in to cattle to offset some of the negative effects that are associated with fescue toxicosis. There are several methods that producers can utilize to offset the negative effects associated with fescue toxicosis. Having a better understanding of how these toxins affect the physiology and performance during all stages of an animals life will allow us to increase profits for all sectors of the livestock market by improving animal health and well-being.

The Estrous Cycle in Cattle

There are several hormones that regulate normal estrous cycle function, such as gonadotrophin-releasing hormone (GnRH) of the hypothalamus, follicle-stimulating hormone and luteinizing hormone (FSH and LH) from the anterior pituitary, progesterone, estradiol (E2) and inhibins, by the ovaries and prostaglandin $F2_{\alpha}$ (PGF) from the uterus (Roche, 1996).

The Hypothalamo-Hypophyseal Portal System

Gonadotropin releasing hormone, a decapeptide, is synthesized in the medial basal hypothalamus and secreted in a pulsatile manner (Sealfon et al., 1997) which acts on the anterior pituitary. The hypothalamo-hypophyseal portal system is responsible for the transporting of GnRH from the hypothalamus to the anterior pituitary. Once GnRH arrives to the anterior pituitary, it binds to its G-protein-coupled, 7-transmembrane domain receptor (Sealfon et al., 1997) and then induces the synthesis and secretion of FSH and LH (Brinkley, 1981). Research has shown that the pulse frequency of GnRH determines the ratio of FSH and LH (Vizcarra et al., 1999; Ferris and Shupnik, 2006). Low pulse frequencies of GnRH induces the secretion of FSH compared to high pulse frequencies of GnRH induce LH release

(Molter-Gerard et al., 1999; Ferris and Shupnik, 2006). Follicle stimulating hormone stimulates the recruitment of follicular waves (Adams et al., 1992; Ginther, 2000), whereas LH is needed for the final growth and development stages of the dominant follicle and production of estradiol (Savio et al., 1993; Gong et al., 1995). Additionally, LH determines synthesis and secretion of estradiol by the DF (Schallenberger et al., 1984; Rhodes et al., 1995b) and is critical for the proper development of the CL following ovulation (Peters et al., 1994). Progesterone and estradiol are ovarian steroids that regulate the release of LH and FSH from the pituitary (Walters et al., 1984; Cupp et al., 1995). Through a negative feedback system, LH pulse frequency is inhibited when progesterone concentrations are elevated which are inadequate for ovulation of the DF (Ireland et al. 1980; Stumpf et al., 1993; Bergfeld et al., 1996). During luteolysis, progesterone concentrations begin to decline allowing for the increased secretion of LH and estradiol (Wettemann et al., 1972; Shallenberger et al., 1984). This increase in estradiol concentrations is required to induce a surge in GnRH and LH which initiates ovulation (Evans et al., 1997).

Cattle Estrous Cycle

The onset of estrous cycles in heifers occurs at the time of puberty (6-12 months of age). Duration of the estrous cycle is on average 20 days in heifers and 21 days in cows within a normal range of 18–26 days (Olds and Seath, 1951; Beal et al. 1980). During the estrous cycle, female cattle progress through several physiological and hormonal changes which lead to the culmination in ovulation of the dominant follicle, development of the corpus luteum (CL), and preparation of the reproductive tract for gestational pregnancy. There are two major phases of the estrous cycle: the luteal phase which is the period following ovulation when the CL is formed that is approximately 14-18 days in length and the follicular phase characterized by the regression of the CL until ovulation and is approximately 4-6 days in length. The estrous cycle is further broken down into 4 subcategories: proestrus, estrus, metestrus, and diestrus. Proestrus and estrus fall under the follicular phase and represents the period from luteolysis to ovulation. During the luteal phase, metestrus is the period from ovulation to the formation of the CL and secretion progesterone; whereas diestrus is the period from the peak concentration of progesterone through luteolysis.

The CL is developed from the collapsed ovulated follicle (corpus haemorragicum) in which the granulosa and theca cells of the ovulated follicle lutenise and produce progesterone (Ireland et al. 1980). The small and large steroidogenic cells from the CL are derived from the theca interna and granulosa cells of the ovulatory follicle (Smith et al., 1994). It is reported that the large luteal cells, derived from the granulosa cells, produce approximately 80% of the progesterone (Niswender et al., 1985). The preovulatory rise in estradiol during the proestrus period increases the number of granulosa cells in the follicle (Gaytan et al., 1997; Murdoch and Van Kirk, 1998); however, it has been shown in ewes that prematurely induced the ovulation of the DF can reduce the number of granulosa cells (Murdock and Van Kirk, 1998). Additionally, it has been reported that during the proestrous period when elevated estradiol concentrations are elevated, prevents granulosa cell apoptosis by blocking FasL-induced apoptosis and increasing cell progression through the cell cycle (Quirk et al., 2004, 2006). This data may indicate that sufficient estradiol concentrations during the preovulatory period may be needed for proper luteal functions. Luteinizing hormone is also important in the development and maintenance of the CL (Peters et al., 1994; Milvae et al., 1996). During the first half of the estrous cycle in cattle, the size of the CL increases in weight over 6-fold and reaches maximum size at approximately d 12 of the estrous cycle (Zheng et al., 1994). In Latin, the term corpus luteum means yellow body, which in the cow, the yellow coloration is due to the high levels of ß carotene (Graves-Hoagland et al., 1989; Milvae et al., 1996). In brief, progesterone is produced by large luteal cells of the CL from the binding of LH to its receptors in the small luteal cells of the CL; this initiates a secondary messenger system where adenyl cyclase synthesizes cyclic-AMP (Milvae et al., 1998). In turn, this activates enzymes that are required for steroidogenesis of progesterone from cholesterol precursors (Milvae et al., 1998). However, large luteal cells have been shown to be able to synthesis progesterone without the stimulation of LH (Fitz et al., 1982). Chegini et al. (1984) reported that there was minimal difference between bovine small and large luteal cell progesterone synthesis. Regardless, the elevated production of progesterone by the CL during the diestrous period of the estrous cycle inhibits LH secretion by reducing the LH pulse frequency and amplitude (Stumpf et al., 1993). While follicular development continues and is initiated throughout di-estrous by the release of FSH from the anterior pituitary, dominant follicles that grow during the luteal phase do not ovulate. Consequently, inhibiting follicles from producing elevated estradiol concentrations prevents estrus, the surge in LH, and ovulation (Rahe et al., 1980).

In order for ovulation to occur, luteolysis or regression of the CL must occur. Between d 16 and 19 of the estrous cycle, PGF is secreted in a pulsatile fashion from the uterine endometrium and reaches the ipsilateral CL via local veno-arterial countercurrent exchange system; initiating the regression of the CL and a reduction in progesterone concentrations (Hixon and Hansel, 1974; Ginther and Del Campo, 1974). In order for the CL to undergo luteolysis, there are several physiological events that must take place to induce the release of PGF (Milvae et al., 1993; McCracken et al., 1999). It has been reported that estradiol and oxytocin secretion from the pituitary and luteal cell oxytocin may or may not play a role in luteolysis (Beard and Lamming, 1994; McCracken et al., 1999). Armstrong and Hansel (1959) reported that daily oxytocin administration to mature cows between days 2 to 6 of the estrous cycle resulted in shortened cycles of 8 to 12 days. During proestrus, estradiol stimulates the release of oxytocin from the pituitary gland and induces increased expression of oxytocin receptors in the uterine endometrium (Beard and Lamming, 1994; McCracken et al., 1999). It is hypothesized that the pulsatile nature of PGF is the result of a positive feedback loop in which luteal oxytocin binds to endometrial receptors to enhance the release of PGF at intervals of 6 hours to complete luteal regression (Flint et al., 1991; Silvia et al., 1991, McCracken et al., 1999).

Following the regression of the CL and the binding of LH to its receptors results in the synthesis of androgens that diffuse into the granulosa cells of the DF. Follicle stimulating hormone binds to the large luteal cells and increases aromatase activity that converts androgens from the small luteal cells to estradiol (Fortune and Quirk, 1988). Reports have shown that the increased frequency of LH pulses, during the follicular phase, enhance dominate follicle growth, leading to the production of enough estradiol to induce behavioral estrus and a preovulatory surge of LH and FSH (Savio et al., 1988; Bergfeld et al., 1994). Behavioral estrus, or the period of the estrous cycle where the female is the most sexually receptive to the male or homosexual mounting of another female, is brought on by the peak concentration of estradiol which will stimulate the preovulatory surge of LH followed by ovulation of the dominant follicle (Wettemann et al., 1972; Chenault et al., 1975). The preovulatory surge in LH occurs 2-6 hours after the onset of estrus (Chenault et al., 1975; Christenson et al., 1975) followed by ovulation; which occurs 26-31 hours after the period of behavioral estrus (Christenson et al., 1975).

Follicular Development, Selection, and Atresia. Throughout the estrous cycle, follicles transition through several morphological changes. An ovarian follicle consists of an oocyte surrounded by both granulosal and thecal cells. Follicles progress from their initial primordial stage with a single layer of flattened granulosa cells to a primary follicle with multiple layers of cuboidal granulosa cells (Fair et al., 1997a; 1997b). Primary follicle cell proliferation is supported by transcribing mRNA for various proteins such as follistatin, activin A, and growth differentiation factor 9 (Braw-Tal, 2002). Primary follicles further develop into a secondary follicle where the zona pellucida forms on the oocyte (Fair et al., 1997b). Secondary follicles mature into a tertiary follicle, or antral follicle, due to the increase in size from the accumulation of follicular fluid into the development of an antral cavity. Antral follicles have the capabilities to ovulate if they are exposed to the surge in LH (Fair et al., 1997b). Large, fluid filled preovulatory follicles are refered to as Graafian follicles after Regnier d Graaf who was the first to describe these follicles in rabbits.

Throughout the estrous cycle, follicle growth in cattle occurs in a wave-like fashion with 2–3 waves per estrous cycle, but as little as one or as many as five (Savio et al., 1988; Ginther et al., 1989). It has been observed that the number of follicular waves influences the length of the estrous cycle. Cows with three follicular waves have a longer estrous cycle and ovulate a smaller dominant follicle compared to cows that have two follicular waves (Ginther et al., 1989). Townson et al. (2002) reported that mature dairy cows with three follicular waves had increased fertility compared to cows with only two. There are several different factors that contribute to the number of follicular waves and development such as nutritional status (Lucy et al., 1992), breed (Simpson et al., 1994), and heat stress (Wolfenson et al., 1995). Cattle follicular waves involve the synchronous development of a group of follicles followed by the selection and growth of a dominant follicle, suppression of subordinate follicles, and either atresia or ovulation of the dominant follicle (Ginther et al., 1989). Follicles that are selected from the follicle pool are dependent upon FSH for continued growth and development (Driancourt, 2001). The FSH surge begins 2-4 d before the emergence of a follicular wave, peaks 1 or 2 d before emergence of follicles, and begins to decrease when a DF is selected (Adams et al., 1992). A single follicle is selected to deviate from the group and become the DF when it is approximately 8.5 mm (Ginther et al., 1997, 2001). Following the selection of the DF, FSH dependent subordinate follicles cease to thrive due to the reduced concentration of FSH (Ginther et al., 1996). The reduction in FSH is thought to be from the production of inhibin and estradiol (E2) by the granulosa cells of the dominant follicle by inhibiting the transcription of activin in the pituitary gland which are necessary for FSH synthesis (Good et al., 1995; Ginther et al., 2000; Nett et al., 2002). As the DF matures, it shifts its dependence from FSH to LH. In the presents of a CL and elevated concentrations of progesterone, LH secretion is suppressed and the DF cannot ovulate thus undergoes atresia. However, if luteolysis has occurred and progesterone concentrations are low, increased LH secretion results in increased E2 production by the DF that stimulates a surge in GnRH/LH and ovulation (Sunderland et al., 1994).

Maternal Recognition of Pregnancy

The difference between cyclic and pregnant animals is the presences of a conceptus, membrane bound embryo, in utero and the presence of the CL with the subsequent production of progesterone. Ovarian cyclicity must be blocked for early conceptus survival and the CL must be maintained to produce progesterone for the duration of gestation. The process by which the periattachment conceptus signals its presence to the maternal unit, as reflected by luteal maintenance, has been referred to as maternal recognition of pregnancy (MRP; Short, 1969).

Maternal recognition of pregnancy occurs between d 15 to 17 of the normal 21 d estrous cycle (Thatcher et al., 1986) and it is during this time period that most critical for establishment of pregnancy. It has been reported that up to 40% of total embryonic losses occur between d 8 to 17 encompassing the period of maternal recognition of pregnancy (Thatcher et al., 2001). The establishment of pregnancy involves the interaction and communication between both the conceptus and the maternal unit (Thatcher et al., 1984). By the 1980's, Type I interferon (IFN), had been identified as the main signal for MRP in ruminants and is now referred to as interferon tau (INFT; Bazer, 1992; Roberts et al., 1992). Interferon tau is an antiluteolytic protein that is produced by the trophectoderm of the conceptus (Bazer et al., 1991; Bazer, 1992). Research has shown that uterine factor secretion of granulocyte macrophage-colony stimulating factor, interleuken 3, and insulin-like growth factors –I and –II enhance IFNT secretion by the conceptus by activating the Ets-2 enhancer region (Ko et al., 1991; Imakawa et al., 1995; Ezashi and Roberts, 2004). Interferon tau production from the bovine conceptus begins at the blastocyst stage, where expression on a per cell basis is low then rises during conceptus elongation (Farin et al., 1990; Ealy et al., 2001). At approximately d 12 of gestation, trophoblast cells begin to transcribe mRNA for IFNT with maximal transcription occurring on d 15 to 17 and continuing through 25 when the initial adhesion of the conceptus to the luminal epithelium of the uterus halts IFNT expression (Bartol et al., 1985; Farin et al., 1990).

A primary function of IFNT is to prevent luteolysis and the subsequent decline in progesterone production by inhibiting endometrial release of PGF (Farin et al., 1990). While the main target tissue of IFNT is considered to be the uterine endometrium and not the CL, the release of luteolytic pulses of PGF must be blocked if a pregnancy is to be maintained (Bazer et al., 1991). Studies have reported that the presence of an embryo or administration of rbIFNT, recombinant bovine interferon α, *in vivo* inhibits endometrial oxytocin receptor expression and secretion of oxytocin-induced PGF (Plante et al., 1991; Meyer et al., 1996; Robinson et al., 1999). Additionally, IFNT has been reported as a stimulator of an endometrial prostaglandin synthesis inhibitor to prevent the conversion of arachidonic acid into PGF (Thatcher et al., 1994). Others have reported that IFNT prevents the up-regulation of estrogen receptor-alpha resulting in an increase in oxytocin receptor numbers blocking the secretion of PGF from the endometrium (Spencer et al., 2006). Interferon tau is also responsible for enhancing the expression of IFNT-stimulated genes which contribute to the regulation of uterine receptivity and development of the conceptus during early gestation (Charleston & Stewart, 1993; Hansen et al., 1998; Spencer et al., 2004). Mann and Lamming

(1999) concluded that insufficient production of IFNT is the main reason for early embryonic failure in cattle. It has been well documented that larger bovine conceptuses produce greater concentrations of IFNT (Mann & Lamming, 2001; Mann et al., 2006). Mann et al. (2006) reported that early progesterone supplementation post breeding (d 5-9) and not late (d 12-16) increased trophoblast length fourfold and a sixfold increase in uterine concentration of IFNT. In the same study, progesterone concentrations during both early and late supplementation increased progesterone concentrations compared to controls. While conceptus elongation and maximal IFNT production varies between individuals within the same species, it has been reported to be correlated with the rise in maternal serum progesterone concentrations (Ashworth & Bazer, 1989). These reports of increased progesterone concentrations and subsequent conceptus development during early gestation may increase pregnancy success by improving the ability of the conceptus to signal MRP.

Estrous Behavior and Detection in Cattle

Regardless of operation or species, estrus detection is an important factor affecting overall reproductive performance. The improvements in advanced reproductive technologies such as artificial insemination, embryo transfer, and *in vitro* fertilization has increased the demand for trained personnel to effectively observe and detect those animals that are displaying behavioral estrous characteristics. Failure to detect cows in estrus or misdiagnosing estrus may result in a drastic economic loss to the producer (Xu et al., 1998). There are several distinct estrus behaviors and visual signs that need to be understood for successful estrous detection.

The primary and most reliable sign of behavioral estrus is the immobilization response or the act of a female allowing homosexual mounting of a herdmate or the mounting of the bull (Baker & Seidel, 1985; Diskin & Sreenan, 2000). Observed mountings, standing heat, are normally caudal but can be cranial as well. The duration of standing heat from the first to the last mounting varies among individual cows and heifers and ranges from 3 to 28 hours with the average range being 12 to 16 hours (Esslemont & Bryant, 1976; Coe & Allrich, 1989; Hein & Allrich, 1992; Rorie et al., 2002). The large range in standing heat makes estrus detection more challenging for untrained personnel to detect; extra precautions should be used to develop effective estrus detection schemes. Behavioral estrus is used for cow herd managers to estimate when a heifer or cow will ovulate. It has been reported that the highest conception rates occurred between 4-12 h after the onset of estrus (Dransfeild et al. 1998). Studies have shown that during continuous observations, lactating multiparous cattle are mounted from 3 to 140 times during the period of displaying estrus (Esslemont & Bryant, 1979) compared to nulliparous heifers ranging in 3 to 225 standing mounts (Coe & Allrich, 1989).

Standing heat may not always be observed, secondary signs of estrus may indicate that a cow is coming into heat but are less reliable than the immobilization response and, therefore, should be given closer attention over the following 48 hours especially when making breeding decisions. These secondary signs include: swelling of the vulva, restlessness, vocalization, walking fence lines, discharge of a clear mucus from the vulva, decreased feed consumption, and displaying the Flehmen posture (French et al., 1989; Diskin and Sreenan, 2000). These secondary signs that are associated with estrus do not have and abrupt onset of termination (Esslemont et al., 1980; Hurley et al., 1982; Amyot & Hurnik, 1987). During the prereceptive phase, when a female approaches estrus, these behaviors gradually intensify approximately 12 hours before estrus. Likewise, during the postreceptive phase, these signs begin to decrease in frequency and stop about 12 hours after the end of estrus (Allrich, 1993). These signs associated with behavioral estrous are not repeatable from one estrous cycle to the next or highly passed on to the next generation. Hurley et al. (1982) noted that repeatabilites were low for the duration of estrus, the time of day of onset of estrus, and the number of standing mounts displayed during estrus. The variation in the number of standing mounts, duration of standing estrus, and less reliable secondary signs are all factors that complicate estrus detection.

There are several different methods that producers can utilize to help alleviate the challenges associated with heat detection. One of the more overlooked aids in estrus detection is a legible means of identifying animals. Large ear tags with legible hand writing, freeze or hot iron brands, and spray-painted numbers are a must for recording which females are in heat (Allrich, 1993). While hand written charts are useful for calculating the anticipated period a female should come into standing estrus, there are other technologies that can be utilized that more precisely predict when animals should be or are in standing estrus. Mounting detectors are usually a patch that contains a red-fluid-filled capsule that is glued to the tail head of the female. When the female is mounted the capsule breaks and the inner portion of the patch turns red. Marking chalk or paint can also be applied to the tail head and top of hip so that when mounted it will rub off the female. While these are one of the cheapest options, these methods may not accurately determine which animals are in estrus unlike other electronic technologies. Due to the increase in mobilization leading up to estrus, pedometers may be used on females to aid in estrous detection. Pedometers are attached to the neck or leg bands as stand-alone devices or are incorporated into electronic animal identification systems (Rorie et al., 2002). However, this method is more readily seen in dairy operations and can be costly. Rump mounted electronic monitoring devices, such as HeatWatch, monitor the time and duration of each mount via radio signal to the receiver. Studies have looked that the effectiveness of using electronic mounting detectors such as that of the HeatWatch system (DDx Inc., Denver, CO) compared to twice daily visual obersvations for estrus detection. The HeatWatch system increased the efficiency of estrus detection by 37% in beef heifers over visual observations (Stevenson et al., 1996). Similarly, Borger et al. (1996) found that the use of the HeatWatch system improved the efficiency of estrus detection over visual observations (91.1% vs. 65.8%, respectfully), however, accuracy was slightly greater in visual observation over HeatWatch (91.5% vs. 87.5%, respectfully). Regardless of the efficiency and increase in cost of the system, there is an advantage to electronic estrus detection particularly in determining exact synchrony between embryo donors and recipients. Electronic mount-monitoring devices such as HeatWatch provide precise enough information on the onset of estrus to control the timing of insemination or embryo transfer to ± 12 h synchrony (Rorie et al., 2002). The HeatWatch system aids in estrus detection and makes calculating the length of estrus easier in order to determine the optimum time to breed or implant embryos into the recipient. While there are advantages and disadvantages to these methods of estrous detection, all of these devises aid in determining those animals that are in estrus consequently improving reproductive efficiency.

Estrous Manipulation and Synchronization

Estrus detection is a critical component for successful outcomes when utilizing artificial insemination and embryo transfer. While detection of estrus can be a tedious task, success or failure of an operation depends upon reliable personnel to determine those animals that are coming into standing heat. Estrous manipulation and synchronization can be utilized to aid in calculating the approximate time of estrus and improving overall herd reproductive performance. Current research has focused on the development of methods to more effectively synchronize estrus in postpartum beef cows and nulliparous heifers by minimizing the number and frequency of handling cattle and minimizing the detection of estrus by utilizing timed artificial insemination (TAI) so that producers can implement these technologies to improve the genetic diversity and quality of their herd (Greary et al., 2001; Lamb et al., 2006; Larson et al., 2006).

Strategies for manipulating the estrous cycle have been based on controlling the life span of the CL with prostaglandins, induction of ovulation with GnRH/agonists, or preventing estrus with treatments of progesterone (Driancourt, 2000; Diskin et al., 2002). Early estrus synchronization protocols focused on regressing the CL with a single injection of PGF followed by estrus detection (Lamb et al., 2010). This method can be used to synchronize an ovulatory estrus in cycling cows; however, this is not effective in females that are in anestrous. The variations in stage of follicular waves at the time of PGF injection directly contributes to the variation in onset of estrus during the synchronized period (Macmillan & Henderson, 1984; Sirois & Fortune, 1988). A single injection of GnRH given to mature cows at different stages of the estrous cycle has been shown to release LH, leading to synchronized ovulation or luteinization of the larges follicle or DF greater than 10 mm and a new follicular wave is initiated in all cows within 2 to 3 d of GnRH administration (Garverick et al., 1980; Bao & Garverick, 1998; Sartori et al., 2001). Additionally, luteal tissue that forms after GnRH administration is capable of undergoing PGF-induced luteolysis 6 or 7 d later (Twagiramungu et al., 1995). Using these methods resulted in only 70 to 83% of cows being synchronized over a 4 d period (Twagiramungu et al., 1995). It is for these reasons that the improvements in estrus synchronization by researchers focused on developing a reliable protocol that required minimal handling periods without compromising fertility in mature beef cows and replacement heifers.

An Ovsynch protocol in dairy cattle was the foundation for TAI protocols used for beef cattle estrous synchronization (Pursley et al., 1995). In the Ovsynch protocol, an injection of GnRH is given to control the follicular wave followed by administration of PGF 7 d later to initiate the regression of the CL. Forty-eight hours following the administration of PGF, a second injection of GnRH is given to initiate ovulation of the DF followed by TAI 16 h later. The Co-Synch protocol is similar to Ovsynch with the exception that TAI occurs at the time of the second GnRH injection. Unfortunately, using the Ovsynch protocol has shown that approximately 5 to 15% of cows can be detected in estrus on or before the injection of PGF, thus reducing the number of females that were detected in estrus and inseminated during the timed synchronized period (Kojima et al., 2000). It is likely that these cows were in the late stages of the estrous cycle when synchronization was initiated and without estrous detection, these females will fail to become pregnant after TAI as part of the Co-Synch protocol (Geary et al., 2000). The development of the controlled internal drug releasing device (CIDR) had a significant impact of estrous synchronization protocols for beef cattle production. The CIDR is a vaginal insert device that contains 1.38 g of progesterone (Macmillan & Peterson, 1993). It was hypothesized that the addition of the CIDR to the Co-Synch protocol would prevent premature occurrence of estrus before the administration of PGF; as a result, fertility should be enhanced (Lamb et al., 2010). The new Co-Synch + CIDR protocol had increased overall pregnancy rates compared to the Co-Synch treatment (59.0 vs. 48%, respectfully; Lamb et al., 2001). Not only did the CIDR delay the onset of ovulation in cows with spontaneous early luteolysis before the administration of PGF, the new protocol was more effective at initiating a fertile ovulation in anestrous cows or those that lacked a CL when PGF was administered (Lamb et al., 2001). Larson et al. (2006) reported that the Co-Synch + CIDR protocol yielded similar pregnancy rates in mature beef cows to a Select Synch + CIDR protocol with a clean-up TAI at 84 h which requires estrous detection (54 vs. 58%, respectfully).

Development of an effective TAI protocol for beef heifers has not been as easy or as successful as in mature cows due to poor synchronization of follicular waves in heifers (Kojima et al., 2000; Atkins et al., 2008). After an injection of GnRH at random stages of the estrous cycle, 75 to 90% of postpartum beef and dairy cows ovulated a follicle (Pursley et al., 1995; Thompson et al., 1999; El-Zarkouny et al., 2004) compared to 48 to 60% of beef and dairy heifers ovulating follicles in response to GnRH (Macmillan & Thatcher, 1991; Pursley et al., 1995; Moreira et al., 2000). Lamb et al. (2006) reported that beef heifers at 12 different locations had similar pregnancy rates when comparing the TAI protocol, Co-Synch + CIDR, to protocols requiring estrus detection, Select Synch + CIDR, or CIDR-PGF. Average pregnancy rates for these protocols in beef heifers range from 53 to 58% compared to data from others that have reported pregnancy rates using a 14 d CIDR or melengestrol acetate (MGA), which range between 60 to 75% (Kojima et al., 2000; Lamb et al., 2000, 2004; Patterson et al., 2003; Busch et al., 2007). Melengestrol acetate is a progestogen that is fed to cattle at a rate of 0.5 mg/(animal/d). While the use of MGA has shown to have increased pregnancy rates compared to TAI in beef heifers, it is imparitive that females have the appropriate amount of bunk space for proper consumption of MGA. The disadvantage of using MGA is that producers are required to feed their cattle during the synchronization period, which increases costs and requires more labor compared to other protocols. There are several advantages and disadvantages to using these protocols and are dependent to practical application and successful administration by producers. The technology of estrus detection that is available to producers has made significant improvements in the last two decades and it is possible to achieve acceptable fertility in mature cows and young heifers when utilizing protocols for both TAI and estrous detection. While these protocols may not fit every operation, there are a variety of options for producers to adopt into their herd management, allowing for greater genetic improvements using superior genetic traits from elite donors and herd sires at costs that are far below those of purchasing a herd sire of similar quality.

Conclusion

Kentucky-31 tall fescue is a cool season, perennial, bunch grass that is extremely persistent, has increased ability to withstand harsh grazing management, and can survive in a variety of extreme environmental conditions compared to many other forages (Arachevaleta et al., 1989; 1992; Bacon, 1993). Additionally, tall fescue makes an attractive option for livestock producers to utilize in their pasture based grazing systems because of fescue's unique characteristic of winter stockpiling. However, tall fescue has a mutualistic relationship with a fungal endophyte that produces compounds known as ergot alkaloids. The production of these alkaloids from the fungus are what aid in the plants ability to out compete other forages and deter insects and livestock from consuming the plant (Aiken, 2013). When endophyte-infected tall fescue is consumed, the toxic ergot alkaloids have been shown to have many negative impacts on livestock production and causes a condition referred to as fescue toxicosis. Symptoms of fescue toxicosis including increased body temperatures, elevated respiration rates, decreased ability to shed their thick winter coat, decreased ability to maintain homeostasis, and a decrease in feed intake, milk production and overall performance (Schmidt, 1993; Paterson, 1995; Foote, 2003; Aiken, 2013b). These effects are intensified during periods of heat stress. It has been well documented that cattle grazing toxic fescue, regardless of ambient temperature, have negative reproductive effects such as a reduction in circulating concentrations of luteinizing hormone, progesterone, and prolactin; ultimately leading to a decline in breeding performance as well as pregnancy and calving rates (Mahmood, 1994; Browning, 1998; Burke, 2001; Watson et al., 2004; Caldwell et al., 2013; Pratt, 2015). In order for pregnancy to occur, the conceptus must be able to signal to the maternal unit and the CL must be maintained to carry out gestation. The period of maternal recognition of pregnancy in beef cattle occurs between days 15 to 17 (Thatcher et al., 1986) of the normal 21 d estrous cycle. There are several different hormones that play a critical role in normal cyclicity and maintenance of pregnancy in cattle. However, reproductive failure is one of the leading factors that contributes economic loss in livestock production. It is imperative that producers and personal are trained to be able to recognize the signs of standing estrus in order to appropriately calculate the optimum time for artificial insemination or embryo transfer. Estrous synchronization has made drastic improvements over the last two decades and is easier and reliable for producers to incorporate these reproductive technologies into their herd management without sacrificing overall herd fertility and economic stability.

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CHAPTER 2

Impact of Progesterone Supplementation on Pregnancy Rates Following Timed Artificial Insemination or Embryo Transfer in Beef Cattle Consuming Endophyte-Infected Fescue

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INTRODUCTION

Tall Fescue (*Lolium arundinaceum* [Schreb.]) is estimated to cover approximately 16 million ha across the Mid-Atlantic and Southeast portions of the United States (Hoveland, 1993). Tall fescue is a cool-season, perennial grass that is relatively tolerant to drought, has value as a stockpiled winter forage, and ability to withstand harsh grazing conditions. Fescue has become one of the primary forages for cow/calf and stocker programs in the Southeast U.S. and has reasonably low maintenance costs to producers. In 1943, “Kentucky 31” was the first variety of fescue that was commercially available in the United States and gained wide interest among livestock producers throughout the Midwest and a large portion of the South (Ball, 1991). In the mid-1970’s, fescue was discovered to contain a fungal endophyte (*Epichloë typhina*). Fescue and fungal endophyte have a mutualistic relationship, producing ergot alkaloids that aid in pest resistance and decrease forage palatability to livestock (Aiken, 2013). These ergot alkaloids are toxic and, when consumed, have negative adverse effects on cattle production; commonly referred to as fescue toxicosis. In 1993, Hoveland estimated that approximately $600 million are lost annually in beef production due to fescue toxicosis. More recent studies have projected that the annual loss is over $1 billion (Strickland, 2011). It has been well documented that consumption of infected fescue decreases cattle performance and the animal’s ability to maintain homeostasis (Schmidt, 1993; Paterson, 1995; Foote, 2003; Aiken, 2013). These effects are intensified during periods of heat stress. Reports have indicated that cattle grazing toxic fescue, regardless of ambient temperature, have negative reproductive effects such as a reduction in circulating concentrations of luteinizing hormone, progesterone, and prolactin; ultimately leading to a decline in breeding performance as well as pregnancy and calving rates (Mahmood, 1994; Browning, 1998; Burke, 2001; Caldwell et al., 2013). Therefore, the objective of this study was to determine the impact of progesterone supplementation on pregnancy rates in timed artificial insemination or embryo transfer in cattle consuming endophyte-infected fescue.

MATERIALS AND METHODS

This study was conducted over three years at the Butner Beef Field Laboratory (BBCFL) in Bahama, NC and the Upper Piedmont Research Station (UPRS) in Reidsville, NC. All animal procedures were approved by the North Carolina State University Institutional Animal Care and Use Committee.

Animals

Multiparous Angus and Sim-Angus influenced multiparous and nulliparous heifers were maintained on stockpiled endophyte-infected (E+) tall fescue from December through March and were supplemented with E+ tall fescue hay when needed. Cattle were offered ad libitum water via plastic tubs. Mature cows that were artificially inseminated were housed at two locations, BBCFL (n = 130) and UPRS (n = 320). An additional group of cows housed at BBCFL (n=198) received embryo transfer (ET). All heifers were bred via artificial insemination and were housed at BBCFL (n = 45) and UPRS (n = 88).

Animal Measurements

A Tru-Test Livestock Scale was used to individually weigh the cattle at the time of AI or ET. At this time, all cattle were given a body condition score (BCS) and were recorded by two trained individuals based on a 1 to 9 scale, with a score of 1 being extremely thin and 9 being very obese (Richards et al., 1986). While in the squeeze chute, blood samples were collected via jugular venipuncture using 20 gauge needles and sterile vacutainer serum tubes without additive (Becton Dickinson, Franklin Lakes, NJ). Blood samples were taken on d 7, 12, and 18 post-breeding to represent the beginning, middle, and end of the treatment period. During collection, blood samples were placed in ice then transported to the on-campus lab to collect serum samples. Whole blood was centrifuged (25 min at 1,000 x g and 4°C) and serum was aliquoted into individual storage glass vials and stored at -80°C until analysis. Blood serum samples were analyzed for progesterone concentration using ImmuchemTM Coated Tube Progesterone ^{125}I RIA Kit (MP Biomedicals, Costa Mesa, CA) and the Cobra II Auto Gamma counter (Packard Instrument Company, Meriden, CT).

Breeding Protocol/Pregnancy Diagnosis

The experimental timeline including estrous synchronization, treatment period of progesterone supplementation, and pregnancy diagnosis is shown for the AI group in Figure 2.1 and the ET group in Figure 2.2.

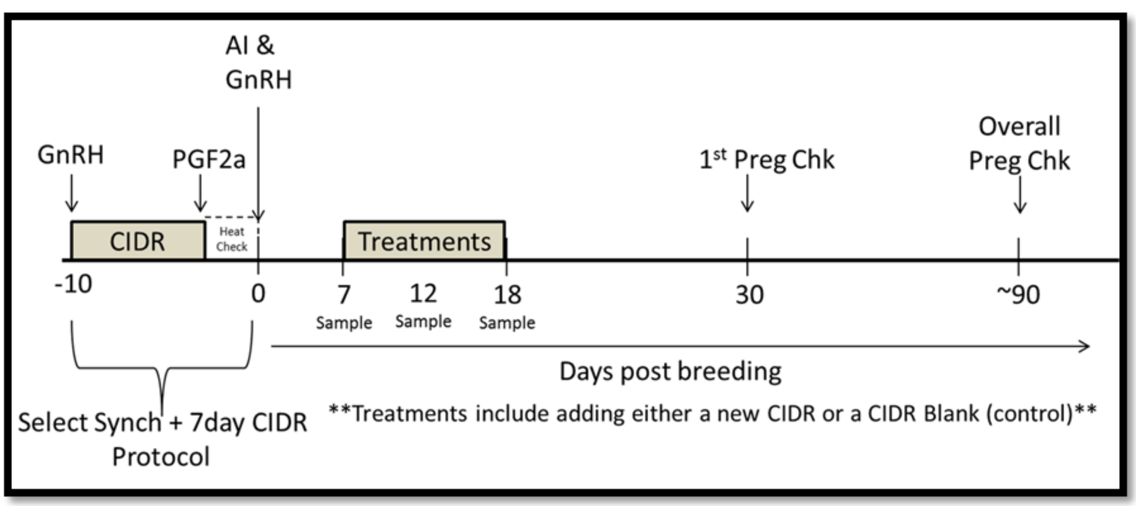

Figure 2.1: Experimental timeline for AI

Initial synchronization for all three years occurred during the month of January. All cattle were synchronized using the standard Select Sync. + 7 d CIDR® protocol. An Eazi-Breed™ controlled internal drug release insert (CIDR®) containing 1.38 mg of progesterone was placed in the vagina on d -10. A 2mL injection of gonadotropin releasing hormone (GnRH; Factrel®) was administered intramuscularly (IM) at the time of CIDR® insertion to increase the response to synchronization. A 5mL injection of prostaglandin F2α (25 mg per animal; Lutalyse®, dinoprost tromethamine, Zoetis, Madison, NJ) was administered IM at the time of CIDR® removal on d -3. Following CIDR® removal, animals were observed for standing estrus and artificially inseminated with a bull of known fertility. Cattle that failed to display estrus in the first 72 h were artificially inseminated by a trained technician 72 h post CIDR® removal with an additional 2mL IM injection of GnRH.

Rather than breeding on d 0, cows that were in the embryo transfer group were implanted with either a fresh or frozen embryo on d 7. Pregnancy status was determined by a veterinarian or faculty member of North Carolina State University using ultrasonographic diagnosis at approximately 30 and 60 d post TAI and 23 and 53 d post ET. At the time of the first pregnancy check, embryo area of pregnant cattle were calculated and recorded.

Embryo Transfer

Angus donor females were selected based upon their phenotypic quality and superior expected progeny differences from the Upper Piedmont Research Centers Registered Angus herd. At the scheduled time of embryo transfer, a trained technician performed transrectal palpation and ultrasonic examinations of the ovaries of recipient females for the presences or absence of the corpus luteum and tone of the reproductive tract. Those recipients with a corpus luteum deemed unsuitable for maintenance of pregnancy did not receive an embryo. Only recipients that were at least 60 days post-partum were initially synchronized for this study. Those recipients considered to be fit for embryo transfer based on the ultrasonographic evaluation randomly received a single fresh or frozen-thawed embryo using a standard embryo transfer technique in accordance with the International Embryo Transfer Society (Savoy, IL). In year 1, 83 out of 144 recipients were used and in year 2 115 out of 147. In brief, embryos frozen in 10% glycerol were individually thawed for 20 seconds in a 30ºC water bath. Fresh embryos were loaded individually into straws and were transferred within 2 h of flushing. Recipients of embryos were housed at the Butner Beef Field Laboratory in Bahama, NC.

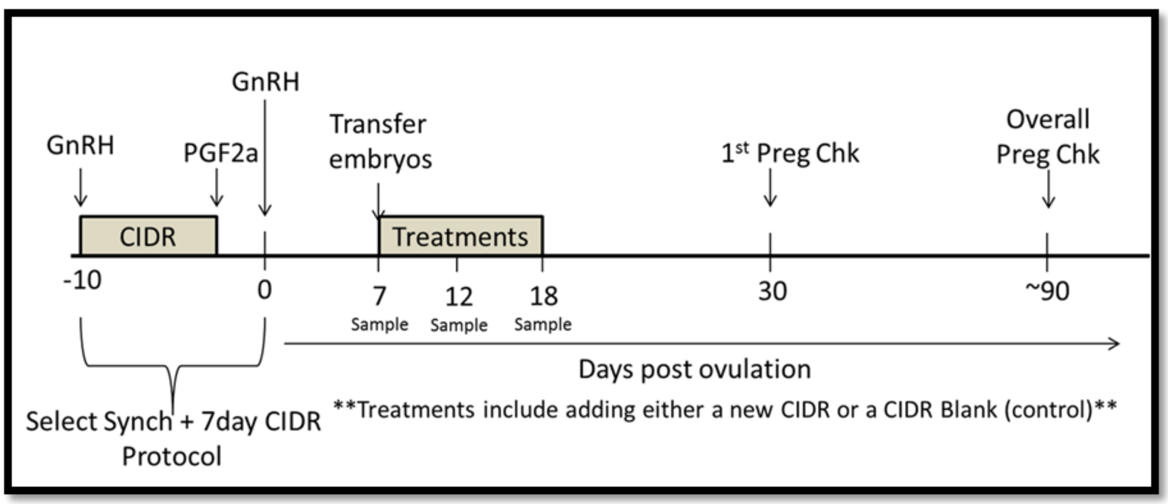

Figure 2.2: Experimental timeline for ET

Treatment Group

Regardless of breeding method (standing estrus, timed AI, or ET), cattle were randomly assigned to a control group which received a CIDR blank containing no progesterone (No P4 Supp) or a treatment group which animals received an active CIDR containing 1.38g of progesterone (P4 Supp). Blank CIDRs were used to eliminate the effect of devise. All CIDRs were inserted on d 7 post timed AI or at the time of ET. CIDRs remained in the vagina for 11 d and were pulled on d 18. Both treatment and control CIDRs were implanted using separate Eazi-Breed™ applicator, rinsed, and dipped in a diluted Nolvasan® Solution (Zoetis Inc., Kalamazoo, MI) to minimize the risk of vaginitis. Only first time used active and blank CIDRs were used for treatment groups and for the CIDRs used in the initial estrous synchronization. Timelines for treatment can been seen for AI in Figure 2.1 and Figure 2.2 for ET.

Statistical Analysis

Data were analyzed using the PROC MIXED procedure of SAS with lsmeans (SAS Inst. Inc., Cary, NC). The model for TAI included year, age, treatment, breed, method, embryo area, location, and random error ($Y=Y_i + A_j + T_K + Br_L + M_m + EA_n + L_o + E_{ijkLmno}$) with the parameter of interest being AI pregnancy rate. The model for ET included year, age, treatment, breed, embryo area, embryo status, and random error ($Y=Y_i + A_j + T_K + Br_L + Ea_m + Es_n + E_{ijkLmno}$) with the parameter of interest being ET pregnancy rate. For progesterone data, the model included time, treatment, and random error ($Y=T_i + Tr_j + Ps_k + E_{ijk}$) with the parameter of interest being progesterone concentration over time. Significant differences were defined as P values of ≤ 0.05 and values of $0.1 > P > 0.05$ were defined as tendencies.

RESULTS AND DISCUSSION

Multiparous and Nulliparous Cattle Artificial Insemination

Progesterone (P4) supplementation 7d following timed artificial insemination did not have a significant difference in AI pregnancy rates (AIPR) in multiparous cattle (Figure 2.3); however, cattle that were 2-3 years old and treated with supplemental progesterone tended to have higher AIPR than treated cows >7 years old (Figure 2.4). Additionally, cows receiving P4 Supp in year 3 had a higher pregnancy rate compared to treated cows in years 1 and 2 (Figure 2.5; 60.0%, 38.9%, 29.4%, respectfully; $P < 0.05$). Heifers receiving P4 supplementation by tended to differ by location (Figure 2.6; UPRS- 43.75% vs. BBCFL- 71.78%; $P < 0.06$) but has no impact on pregnancy rate compared to controls. Additionally, when comparing standing heat (SH; $n = 74$) vs. TAI ($n = 59$), TAI pregnancy rates tended to increase for the standing heat compared to TAI bred heifers (Figure 2.7; 65.03% vs. 50.27%, respectfully; $P = 0.08$) but no effect of treatment. Interestingly, cows that were bred during the TAI period tended to have increased pregnancy rate than those bred in SH in year 2 (50.0% vs. 30.0%, respectfully; $P < 0.10$), but was not observed in year 1 or 3 (Figure 2.8). However, animals bred during TAI in year 3 tended to have a higher pregnancy rate than cows bred during TAI in year 1 (Figure 2.8). Interactions of breed of animal were analyzed in purebred Angus and the Simmental/Angus (Sim-Angus) commercial based multiparous cattle (Figure 2.9). However, there were no differences in pregnancy rates between Angus of Sim-Angus multiparous cattle (49.8% vs. 51.7%, respectfully; $P > 0.10$). Nulliparous cattle were all

Supplemental progesterone following artificial insemination has been well researched over the past few decades with the majority of research being conducted using dairy cows (MacMillan & Peterson, 1993; Mann and Lamming, 1999; Yan et al., 2016). In general, these studies show that progesterone treated dairy cows following artificial insemination have increased pregnancy rates compared to controls. Much fewer data is available for dairy heifers, beef cattle, and embryos transfer. To our knowledge, this is the first study comparing the effects of progesterone supplementation on pregnancy rates following TAI and ET for cattle that are consuming solely toxic tall fescue. Research has shown that cattle consuming tall fescue have decreased conception and calving rates when compared to cattle grazing pastures without the presence of endophyte infected fescue (Gay et al., 1988; Brown et al., 1992; Looper et al., 2010; Caldwell et al., 2013). This reduction in breeding performance is thought to be due to a reduce in dry matter and forage intake (Parish et al., 2003; Looper et al., 2007) which results in loss of body energy reserves (Brown et al., 1992).

Research has shown that cows consuming toxic fescue during the breeding season had a reduction in body condition and body weight compared to cows on lower E+ fescue pasture (Looper et al., 2010; Caldwell et al., 2013) resulting in decreased calving rates. Regardless of endophyte status, it has been reported that both thinner conditioned dairy and beef cattle or poor body condition scores (BCS) have decreased pregnancy rates compared to cattle with greater amount of energy reserves (Rae et al., 1993; Moreira et al., 2000). These reports are similar to these findings in that those cows with BCS of 4.5, and 5 did have reduced conception rates when compared to cows with a BCS of 6 (Figure 2.10; 39.69%, 43.33%, 74.60%, respectfully; $P < 0.05$) which was observed only in control cows. Body condition scores did not show to have major differences in pregnancy rates within treatment groups; however, treated cows with BCS of 6 had a significantly higher pregnancy rate than treated cows with a BCS of 5 (70.0% vs. 28.5%, respectfully; $P < 0.05$; Figure 2.10). The majority of cattle in this herd were in poorer body condition and had subsequently lower BCS. If BCS were higher during the breeding season, there could also potentially be an increase in pregnancy rates as well. Numerically, cows with BCS of 6.5 and treated had higher pregnancy rate compared to cows with BCS of 6.5 on control, but with a small population of animals in 6-6.5 BCS, it cannot be definitively suggested that progesterone supplementation would have a positive impact of progesterone supplementation. While embryo area was not affected by treatment in multiparous or nulliparous (Figure 2.11, Figure 2.12; respectfully), embryos from heifers in yr 1 were significantly larger than in yr 2 for both control and treated groups (Figure 2.12).

Embryo Transfer

In this study, there was a significant effect of year ($P < 0.05$) for ET groups, therefore yr 1 and 2 were analyzed independently (Figure 2.13). In yr 1, 144 mature beef cows were initially synchronized; however, only 83 were deemed suitable to receive a fresh or frozen-thawed embryo. In yr 2, 115 of 147 initially synchronized received an embryo. Progesterone supplementation during the period of maternal recognition of pregnancy increased pregnancy rates (PR) in ET cattle compared to controls in yr 1 (Figure 2.14; Trt- 84.6% vs. C- 60.1%, respectfully; $P < 0.05$); however in yr 2, pregnancy rates were not impacted from supplemental P4 compared to controls (Figure 2.15). When broken down into three different age groups cows in year one that received supplemental progesterone and were >7 years old

(YO) had significantly increased ET pregnancy rate compared to controls (Figure 2.16; Trt- 98.7% vs. 57.1%, respectfully; $P < 0.05$) but was not observed in 2-3 and 4-7 YO in yr 1 and no interactions of any age group in yr 2 (Figure 2.17).

Embryo retention was increased in cattle receiving a frozen embryo (Trt- 96.7% vs. Control-59.7%; $P < 0.05$) but was not observed with fresh embryos (Figure 2.18) in yr 1. Due to the benefit of progesterone supplementation on embryo retention in frozen-thawed embryos in yr 1, no fresh embryos were transferred in yr 2. These results differ from the findings of other studies where embryos transferred fresh had higher conception rates compared to frozen-thawed (Sernan & Dinskin, 1987; Marshall & Minyard, 2002). However, pregnancy rates in yr 2 of this study are similar to those reported in Niemann et al. (1985) which found that only 45.1% of frozen-thawed transferred embryo maintained through 30 d pregnancy check. Spell et al. (2001) looked at the pregnancy rates in Angus cow recipients receiving either a fresh or frozen-thawed embryo at two different locations, Kansas and Virginia. Spell and coworkers (2001) reported that fresh transferred embryos had significantly higher pregnancy rates compared to frozen-thawed (83% vs. 69%, respectfully; ($P < 0.05$). Environmental conditions are not similar between the east coast and the Midwest, while there was no report of observations of location effect on pregnancy rates or embryo retention, the results from Spell and coworkers (2001) do not mimic the results from our study between pregnancy rates of fresh vs frozen-thawed embryos. Interestingly, recent research has found that progestin supplementation following ET in goats increases pregnancy rates and embryo retention compared to controls (D'Alessandro & Martemucci; 2016).

Supplemental progesterone tended to increase pregnancy rates in Angus cows compared to controls (n = 41; 92.85% vs. 65.68%, respectfully; $P < 0.06$) in yr 1 (Figure 2.19). While not significant, Sim-Angus cows receiving progesterone supplementation had numerically higher pregnancy rates compared to controls (Figure 2.19). However, these observations were not seen in yr 2 (Figure 2.20). Hasler et al. (1987) reported no effects of age or breed of the recipient female; however, their research did find that embryos flushed from cows older than 15 years of age had significantly reduced pregnancy rates compared to younger cows.

At the time of pregnancy detection, embryo area of pregnant animals were calculated and it was found that in both years 1 and 2, supplemental progesterone did not have a significant impact on embryo size (Figure 2.21, Figure 2.22, respectfully). Beltman et al. 2009 showed no difference in progesterone supplementation on conceptus size and survival at d 25, but Carter et al. (2008) found that embryo size at d 16 was greater when progesterone was supplemented from d 3 onwards. Mann et al. (2006) and Carter et al. (2008) looked at the effect of time of progesterone supplementation in dairy and beef cattle on embryo development. Both studies found that circulating progesterone concentrations were elevated in treated animals compare to controls. In addition, supplemental progesterone devices inserted in animals from d 3-9 post insemination had significantly increased embryo development at d 16 compared to controls or those that received progesterone supplementation from d 12 to 16 (Mann et al., 2006; Carter et al., 2008). Mann et al. (2006) also reported that uterine interferon tau (INFT) secretions were increased sixfold in treated animals compared to controls. The increase in embryo development and subsequent increase in IFNT should aid in increasing embryo survival and ability to signal to the maternal unit during the period of maternal recognition of pregnancy. While CIDRs were implanted during the similar time period of Mann et al. (2006) and Carter et al. (2008), results from this study did not see a significant difference in embryo area when comparing treated animals to controls.

Progesterone

Multiparous cattle progesterone concentrations during the treatment period are seen in Figure 2.23 and Figure 2.24 for heifers. For both multiparous cattle (Figure 2.23), P4 concentrations were similar among treatment groups and pregnancy status. However, on day 18 post breeding pregnant animals had significantly higher P4 concentrations compared to cattle that were not pregnant. Additionally, multiparous cattle that were treated and not pregnant had higher concnetrations compared to control multiparous cattle that were not pregnant (4.1 ng/mL vs. 3.0 ng/mL, respectfully; $P < 0.05$). Heifers that received no progesterone supplementation and were not pregnant had significantly lower P4 concentrations on days 7 and 12 compared to all other cattle, but was similar to heifers that received progesterone supplementation and were not pregnant on day 18. Pregnant heifers regardless of treatment or control had similar P4 concentrations on days 7, 12, and 18 post breeding (Figure 2.24). This data is similar to other reports for both dairy and beef cattle. It is reported that the optimum range of circulating P4 concentrations to establish pregnancy is 2.0-5.0 ng/mL in cattle (Remsen et al., 1982; Niemann et al., 1985). However, Spell et al. (2001) reported that low progesterone concentrations as low as 0.58 ng/mL or exceeding 16 ng/mL did not report any differences in pregnancy rate.

Summary

The negative physiological effects that toxic fescue has on livestock production continues to be a major concern for producers in the Southeast despite the ongoing research to improve performance and fertility in livestock that consume toxic tall fescue. The aim of this study was to determine if progesterone supplementation during the critical period of maternal recognition of pregnancy could improve pregnancy rates following artificial insemination and ET in beef cattle consuming endophyte-infected tall fescue. In summary, progesterone supplementation during the period of maternal recognition of pregnancy did not improve TAI pregnancy rates or embryo area in multiparous or nulliparous cattle; however, treated heifers did tend to differ by location. Results from the ET group differed between years 1 and 2 in that animal treated with progesterone supplementation in yr 1 had significantly increased pregnancy rate compared to controls (84.5% vs. 60%, respectfully; $P < 0.05$). Additionally, supplemental progesterone had a greater impact on pregnancy rate in frozen-thawed embryos compared to controls or fresh embryos. These results are not similar to what other studies have reported when comparing fresh vs. frozen-thawed embryo pregnancy rates. The difference between years may be attributed to the selection of the recipient female between years 1 and 2. A larger portion of the initially synchronized cows in yr 1 were not utilized due to a lack of CL or an abnormally sized CL in comparison to yr 2 (83/144 vs. 115/147 respectfully).

While breed results varied in both the TAI and ET groups, other research has not reported differences of breed in dam or recipient. There were variations in observations of age and pregnancy rate between TAI and ET in that progesterone supplementation did not have a major impact on TAI pregnancy rate between the three age groups; however, treated animal that were >7 years old tended to have reduced pregnancy rates compared to treated cows that were 2-3 years old. In contrast, treated cows >7 years old had significantly higher ET pregnancy rate compared to controls or of the other two age groups. In addition, embryo area was not increased as hypothesized in either TAI or ET. There were no main effects of breed and pregnancy rates in yr 2 for ET or in TAI; however, treated Angus cows in yr 1 for ET tended to have a greater impact on pregnancy rates compared to controls, but not for SimAngus cattle. Results from this study were varied greatly for both TAI and ET in addition to yearly effects. There is limited research that looks at the relationship between progesterone supplementation and lactating beef cattle, therefore, further research needs to be conducted looking at the interaction of progesterone in lactating beef cattle and embryo survival particularly in the Southeastern portion of the United States.

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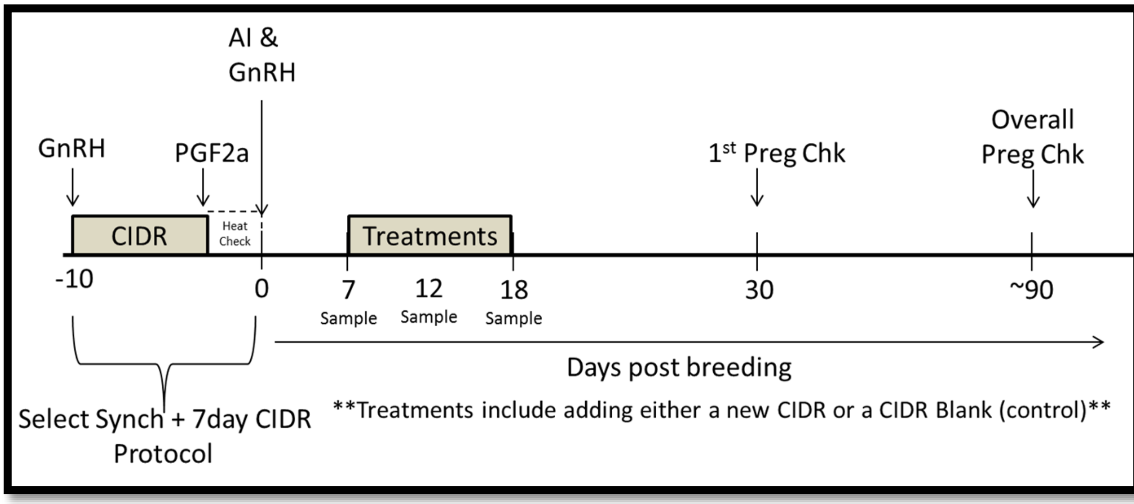

Figure 2.1: Experimental timeline for TAI.

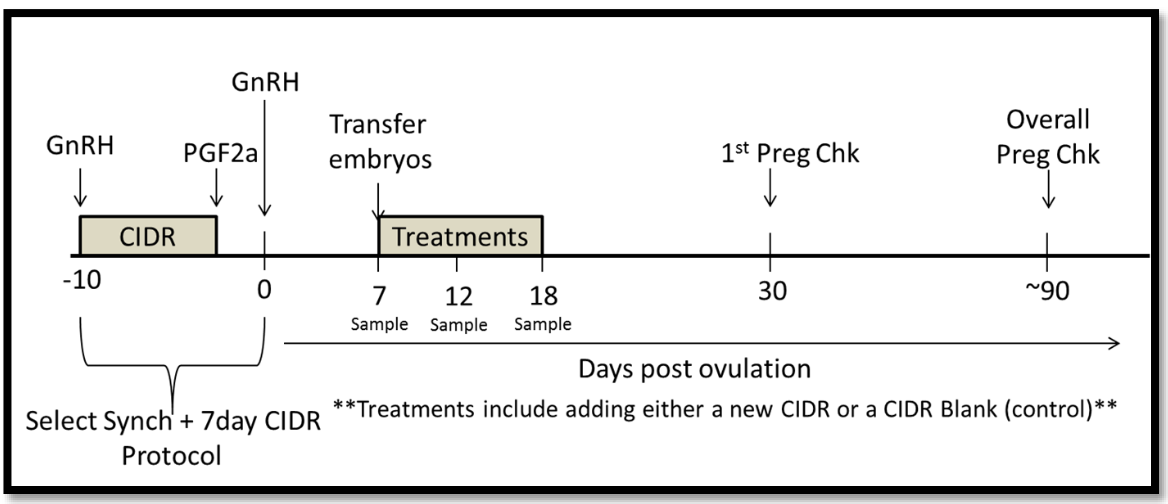

Figure 2.2: Experimental timeline for ET.

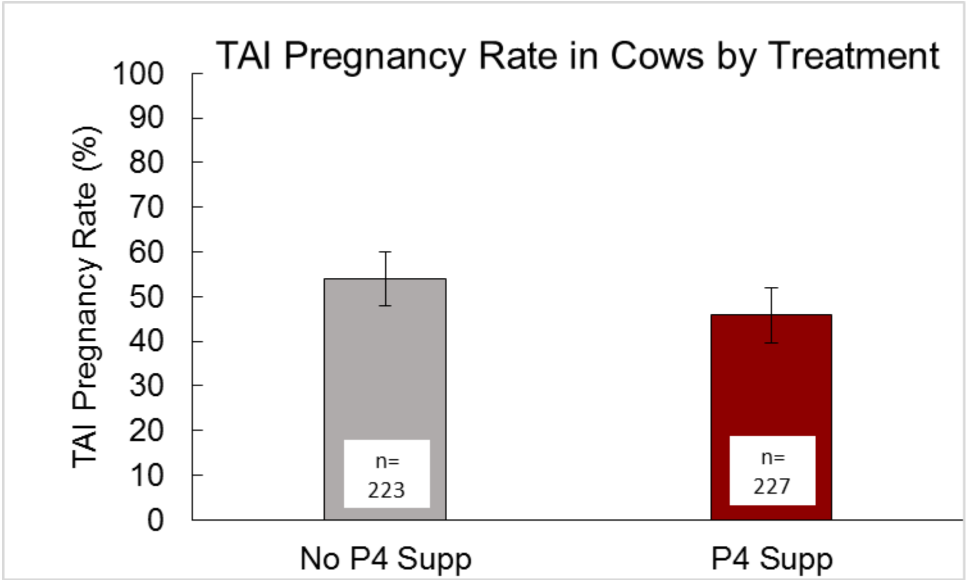

Figure 2.3: Timed artificial insemination pregnancy rates in cows by treatment.

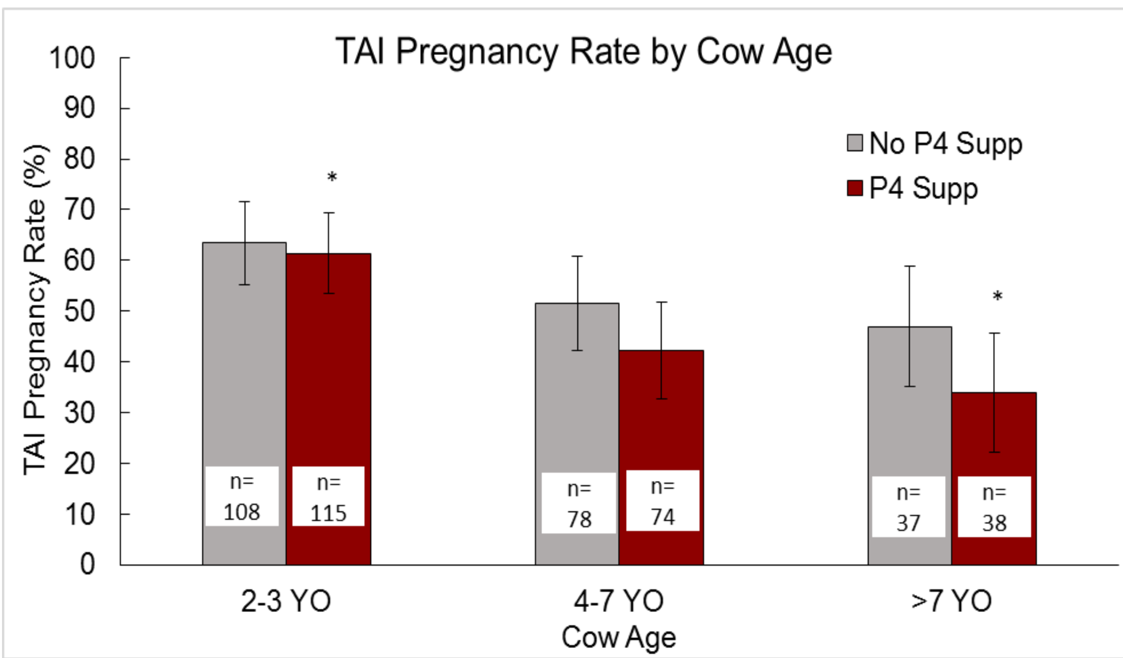

Figure 2.4: Timed artificial insemination pregnancy rates by cow age and treatment.

2-3 YO multiparous cattle that received treatment tended to have higher TAI pregnancy rates compared to cattle >7 YO that were treated (0.10 > P > 0.05) denoted by *.

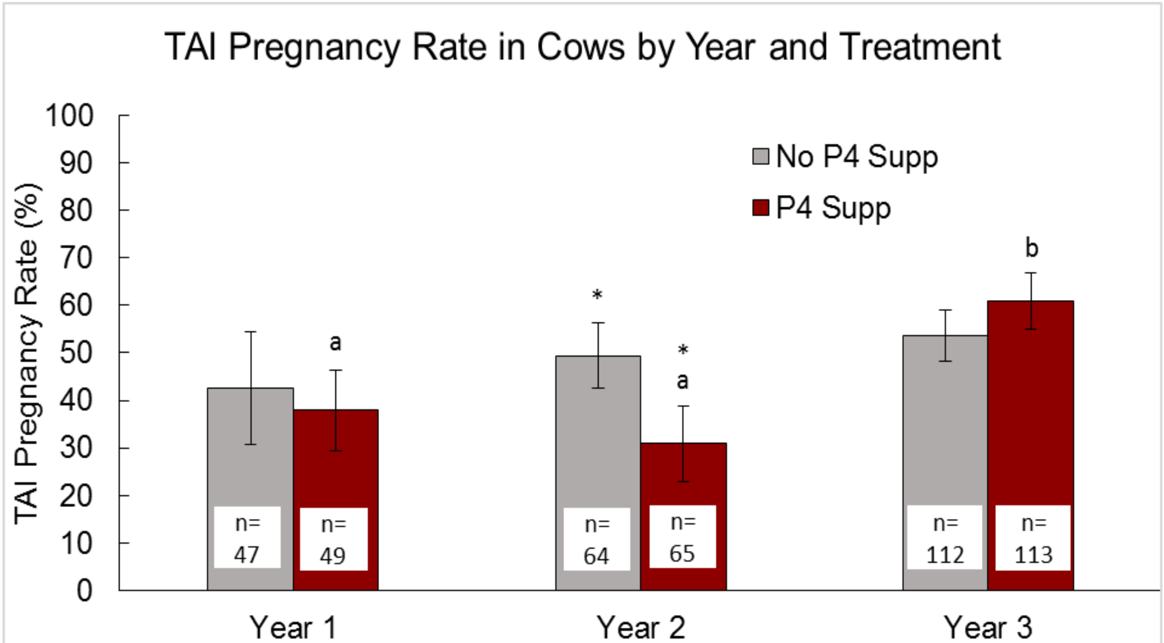

Figure 2.5: Pregnancy rates in TAI cows by year and treatment.

In Year 2, control cattle tended to have higher pregnancy rates compared to treated cattle ($0.10 > P > 0.05$) denoted by *. Pregnancy rates in cattle receiving treatment in years 1 and 2 were lower compared to cattle receiving treatment in year 3 (a vs. b; $P < 0.05$).

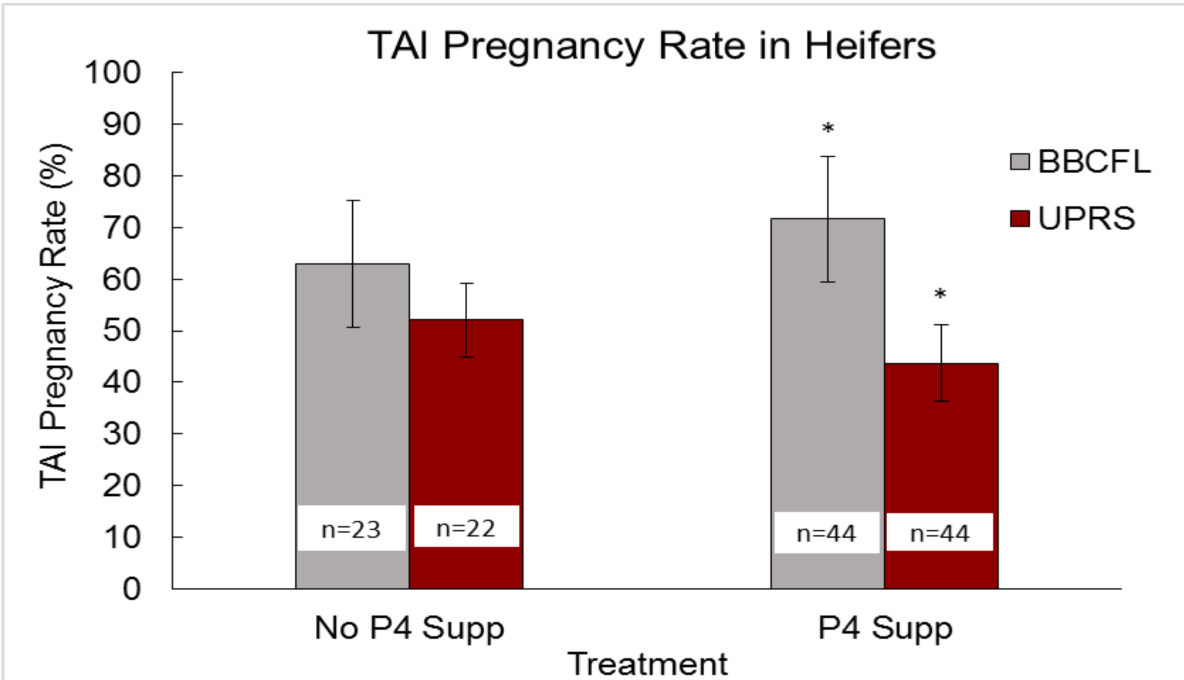

Figure 2.6: Heifer TAI pregnancy rates by location and treatment.

Heifers receiving progesterone supplementation tended to differ by location (0.10 > P > 0.05) denoted by *.

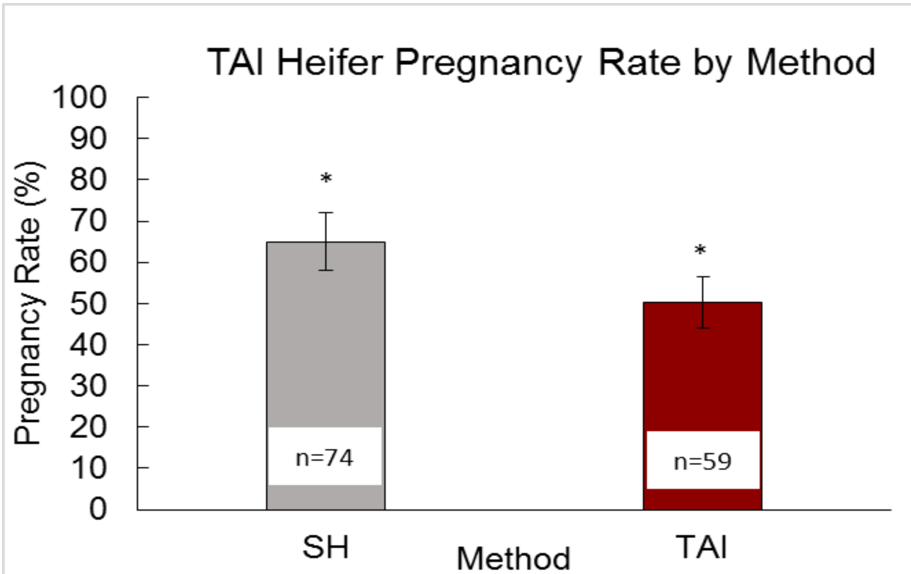

Figure 2.7: Heifers TAI pregnancy rate by breeding method.

Heifers that were bred upon standing heat tended to have higher pregnancy rates compared to heifers that were bred at the period of TAI ($P < 0.10$) denoted by *.

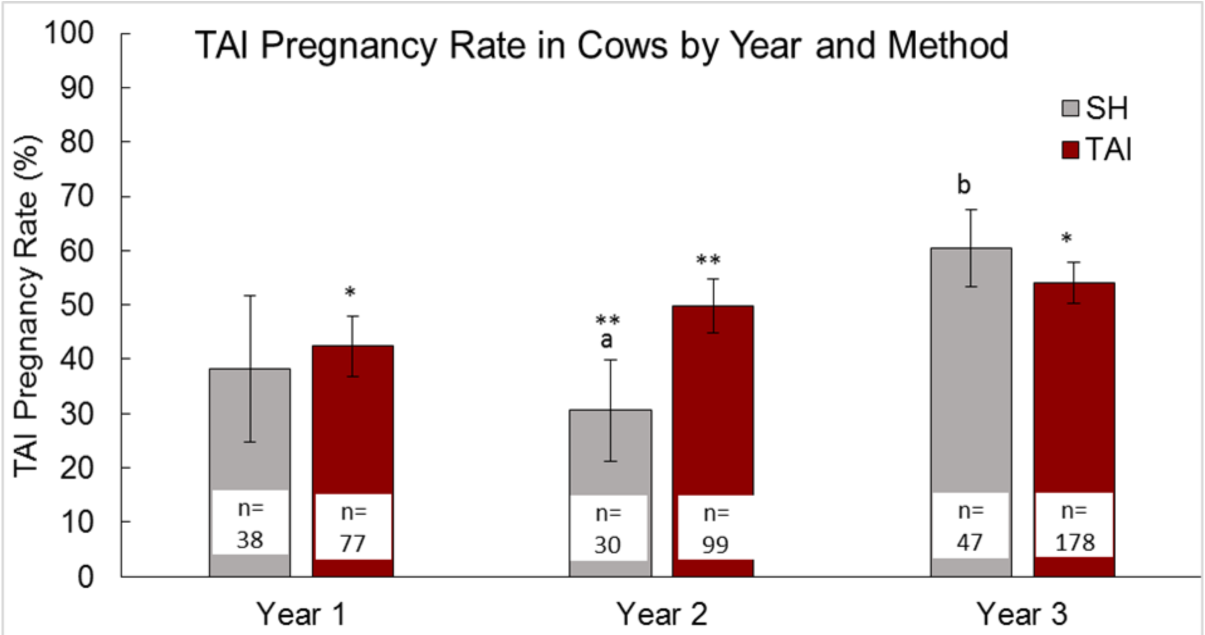

Figure 2.8: Timed artificial insemination pregnancy rates in cows by year and method.

Cattle that were bred during standing heat in year 3 was significantly higher compared to year 2 (a vs. b; P < 0.05). Cattle that were bred at the period of TAI in year 1 tended to have lower conceptions rates compared to year 3 and those cattle bred upon standing heat tended to have a lower pregnancy rate compared to cattle bred during the period of TAI in year 2; similarities in subscripts denoted by *,** represent tendencies (0.10 > P > 0.05).

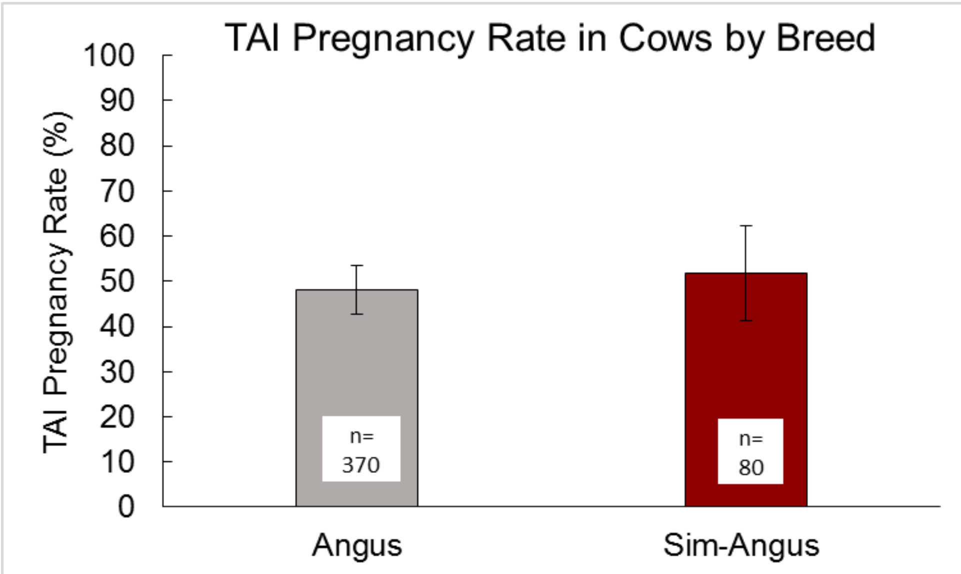

Figure 2.9: Timed artificial insemination pregnancy rates by cow breed.

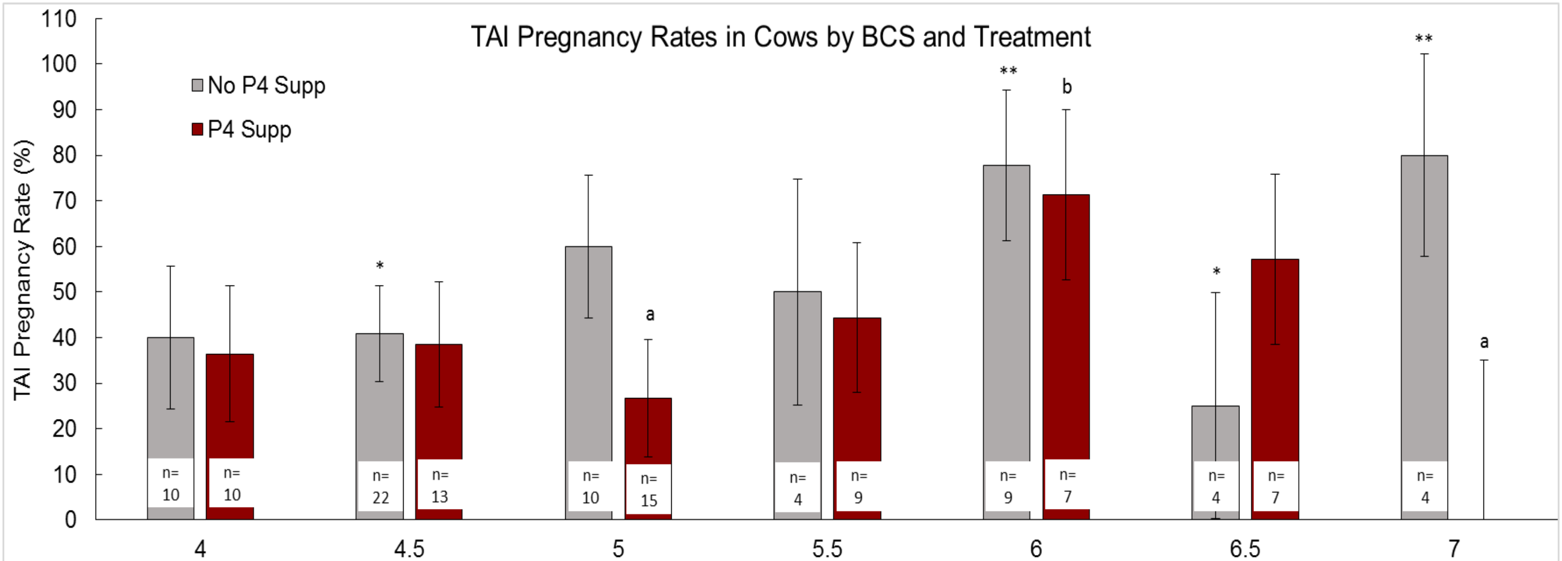

Figure 2.10: Timed artificial insemination pregnancy rates in cows by body condition scores and treatment.

Treated multiparous cattle with a BCS of 5 and 7 had significantly lower pregnancy rates compared to treated cattle with a BCS of 6 (a vs. b; $P < 0.05$). There were only 2 cows with a BCS of 7 that received treatment and were not pregnant. Control cattle with a BCS of 4.5 and 6.5 tended to have lower pregnancy rates compared to control cattle with a BCS of 6 and 7 ($0.10 > P > 0.05$) denoted by *,**.

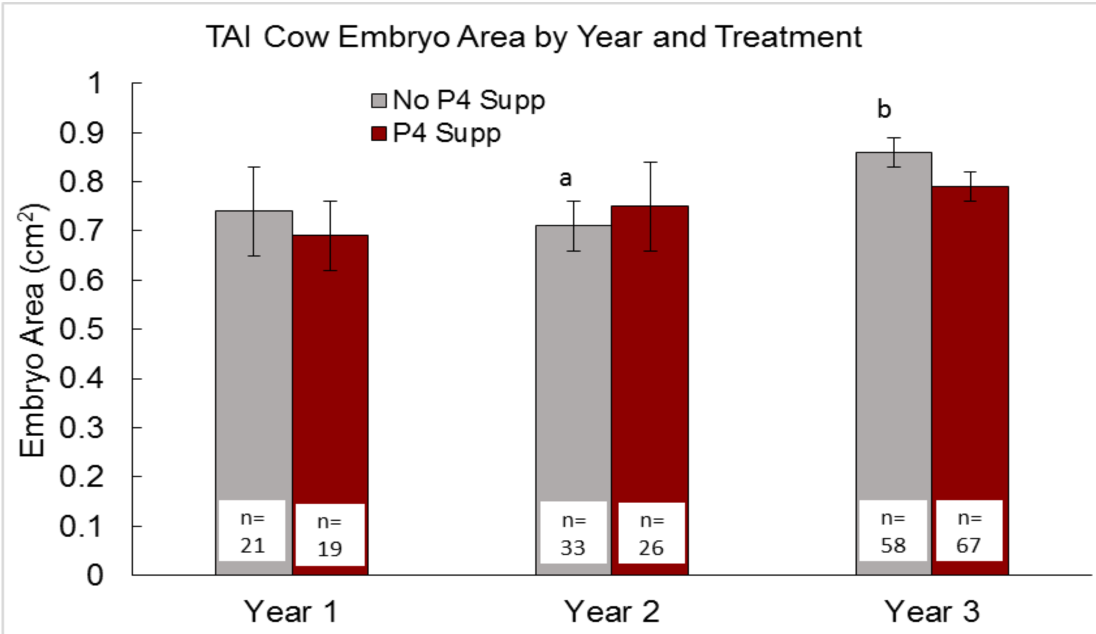

Figure 2.11: Embryo area for TAI cows by year and treatment.

Embryo area of control cattle were smaller in year 2 compared to year 3 (a vs. b; $P < 0.05$).

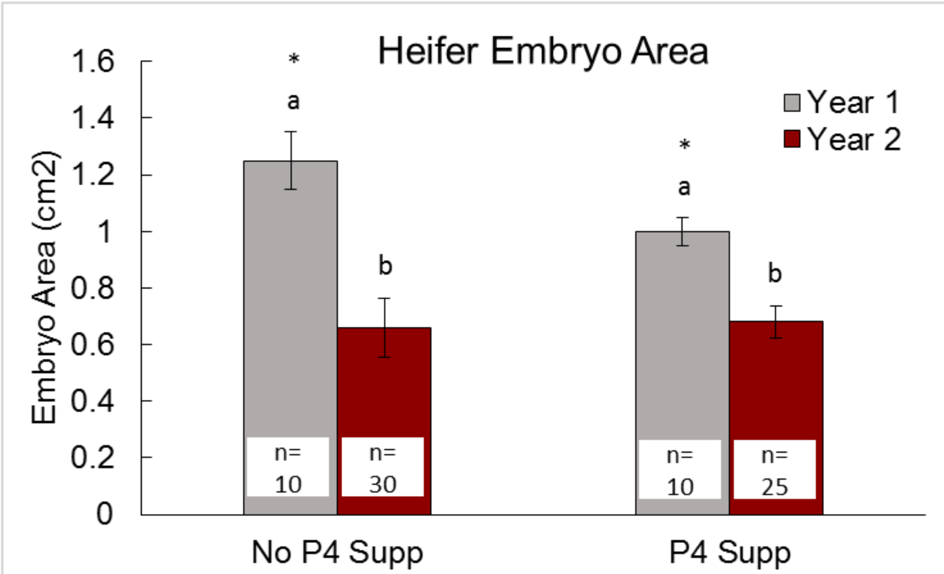

Figure 2.12: Heifer embryo area by treatment and year.

Heifer embryo area regardless of treatment or control was greater in year 1 compared to year 2 (a vs. b; $P < 0.05$). Control heifers tended to have a larger embryo area compared to treated heifers in year 1 ($0.10 > P > 0.05$) denoted by *.

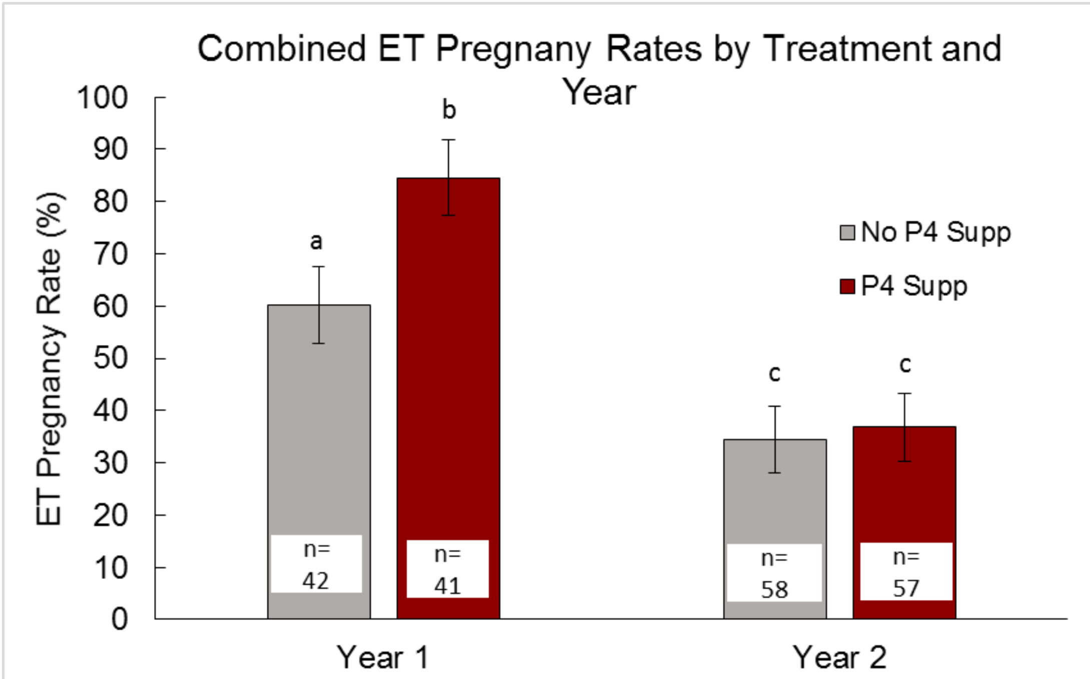

Figure 2.13: Year 1 ET pregnancy rates by treatment.

There was a significant effect of year with ET pregnancy rates regardless of treatment or control were greater in year 1 compared to year 2 (a vs. b; P < 0.05).

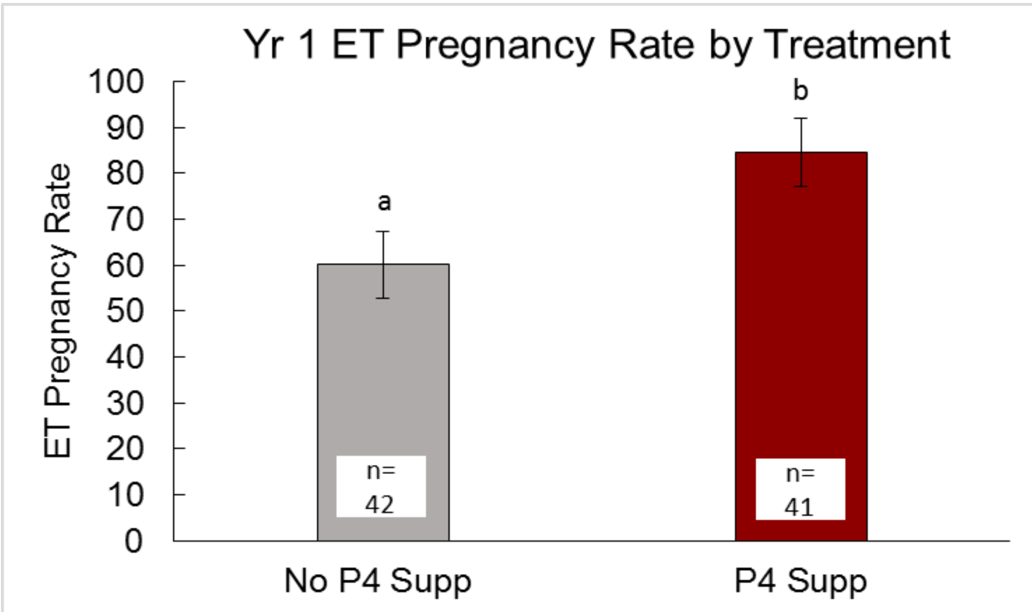

Figure 2.14: Year 1 ET pregnancy rates by treatment.

Year 1 pregnancy rates in treated multiparous cattle were significantly higher compared to controls (a vs. b; $P < 0.05$).

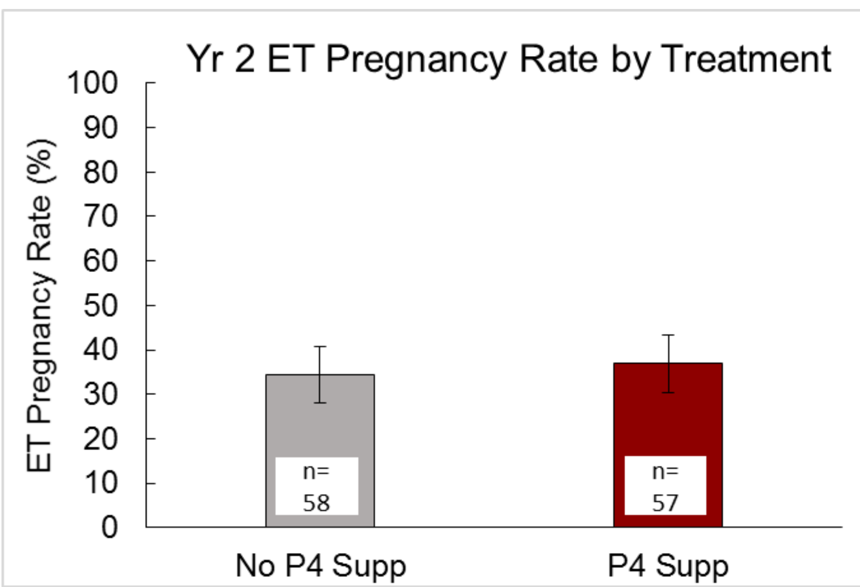

Figure 2.15: Year 2 ET pregnancy rates by treatment

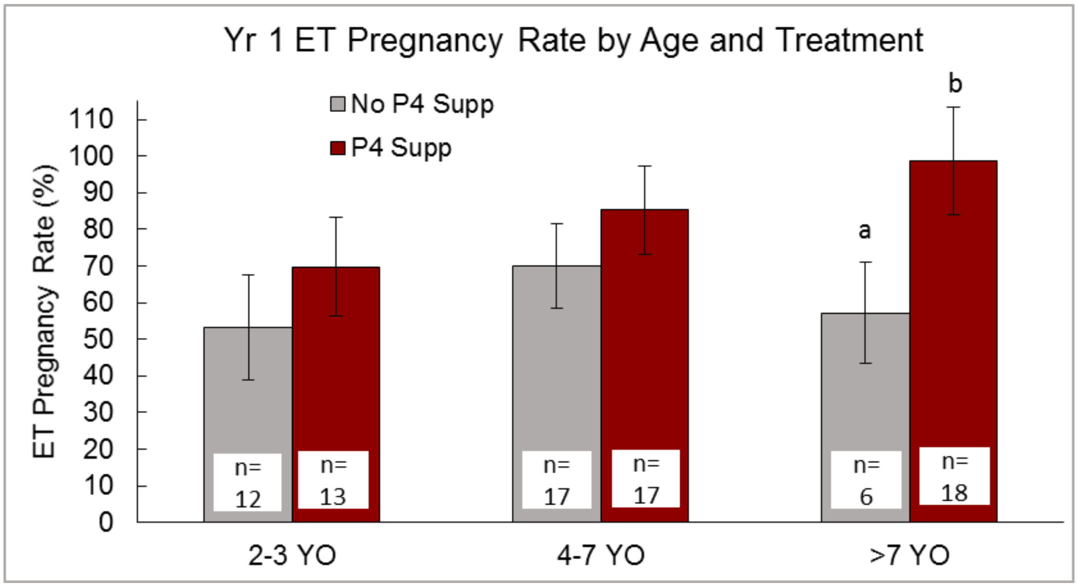

Figure 2.16: Year 1 ET pregnancy rates by age and treatment of recipient.

Treated cattle that were >7 YO has significantly higher ET pregnancy rates compared to controls (a vs. b; P < 0.05).

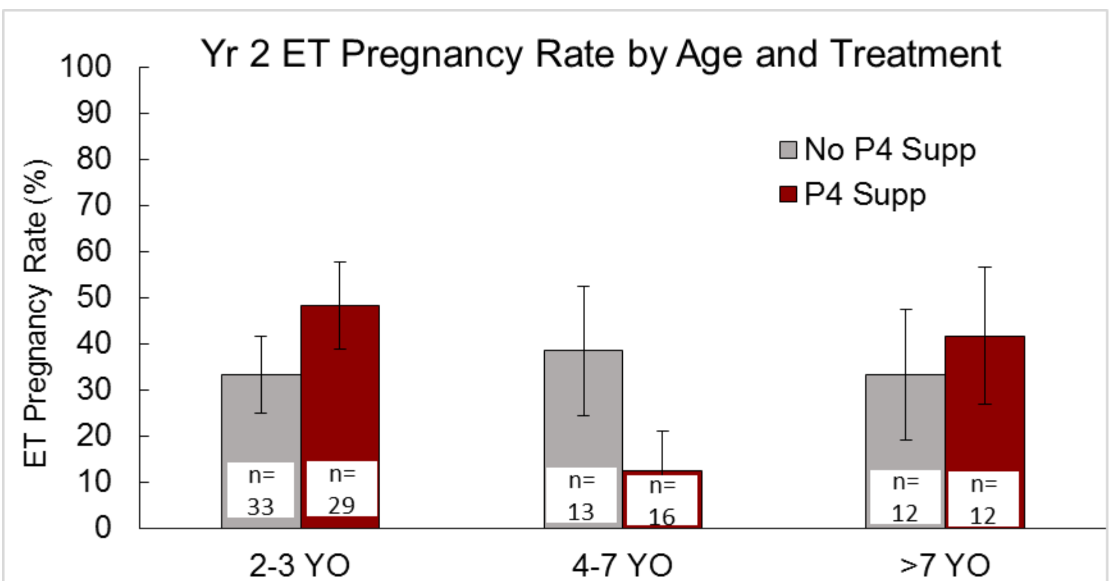

Figure 2.17: Year 2 ET pregnancy rates by age and treatment of recipient.

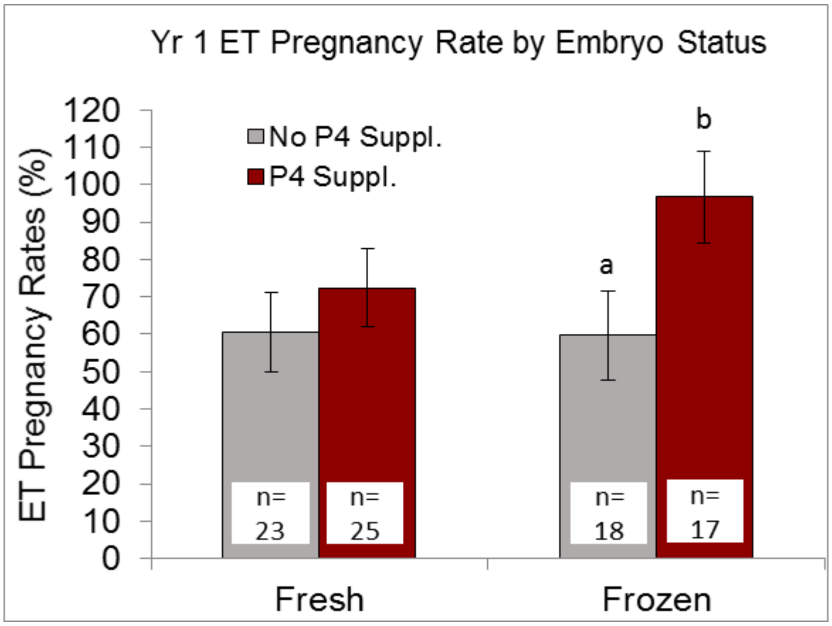

Figure 2.18: Year 1 ET pregnancy rates by embryo status and treatment.

Treated cattle receiving a frozen embryo had higher pregnancy rates compared to controls in year 1 (a vs. b; $P < 0.05$).

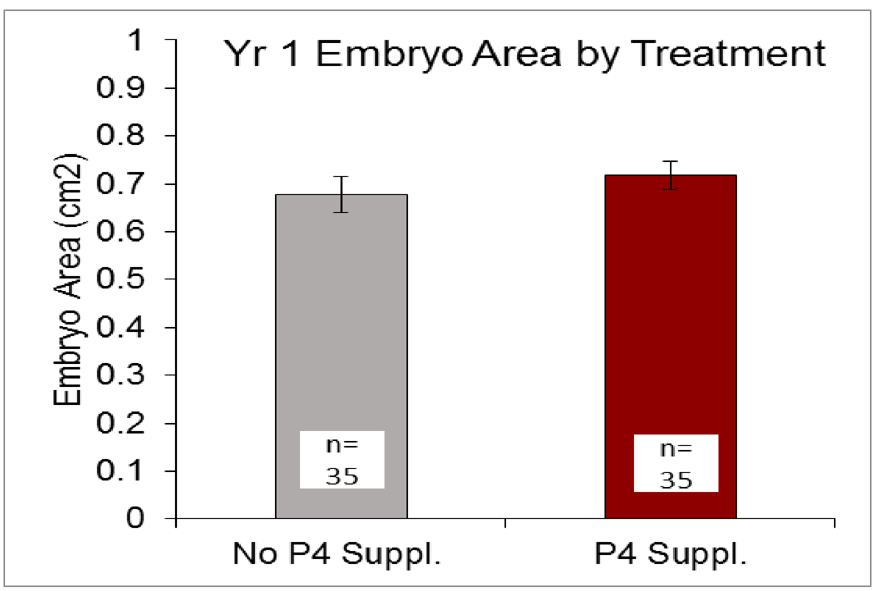

Figure 2.19: Year 1 ET embryo area by treatment.

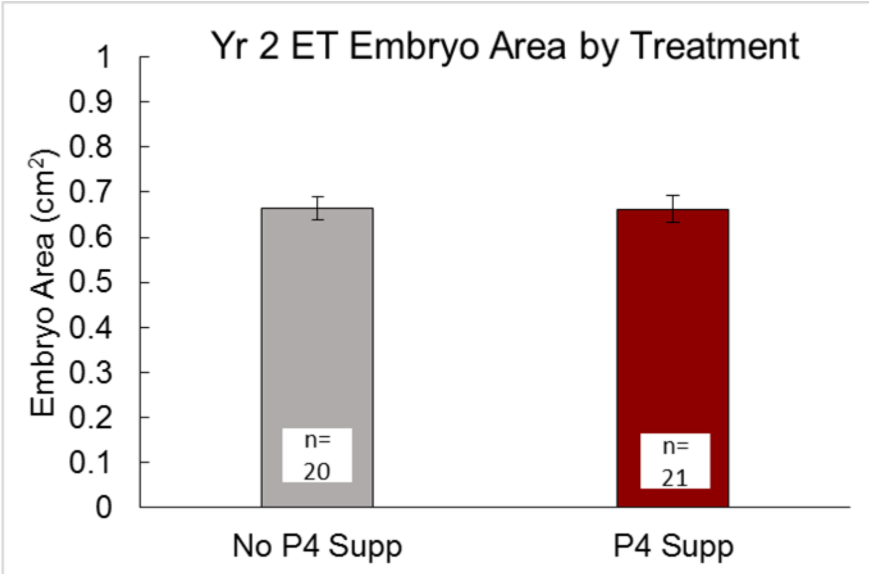

Figure 2.20: Year 2 ET embryo area by treatment.

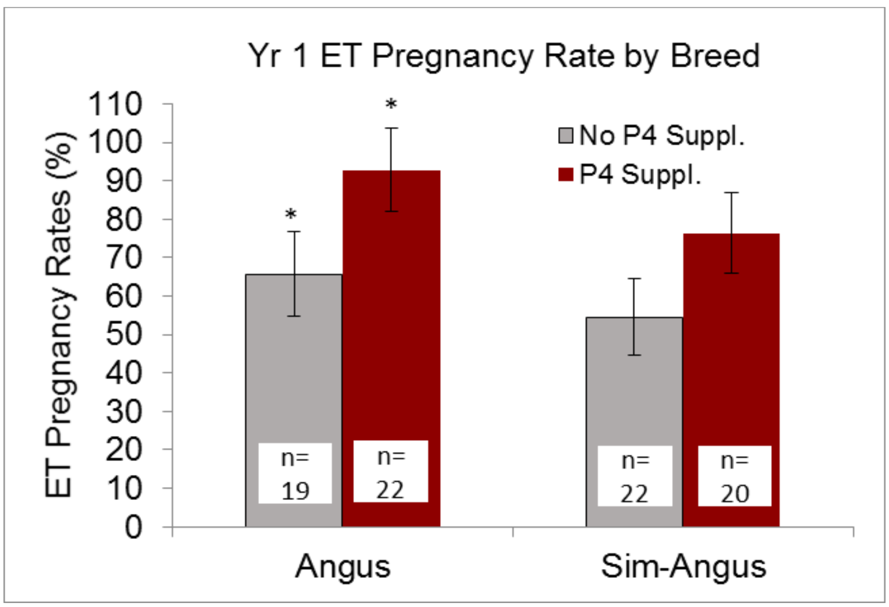

Figure 2.21: Year 1 ET pregnancy rates by breed.

Angus cattle that were treated tended to have higher pregnancy rates compared to controls in year 1 (0.10 > P > 0.05) denoted by *.

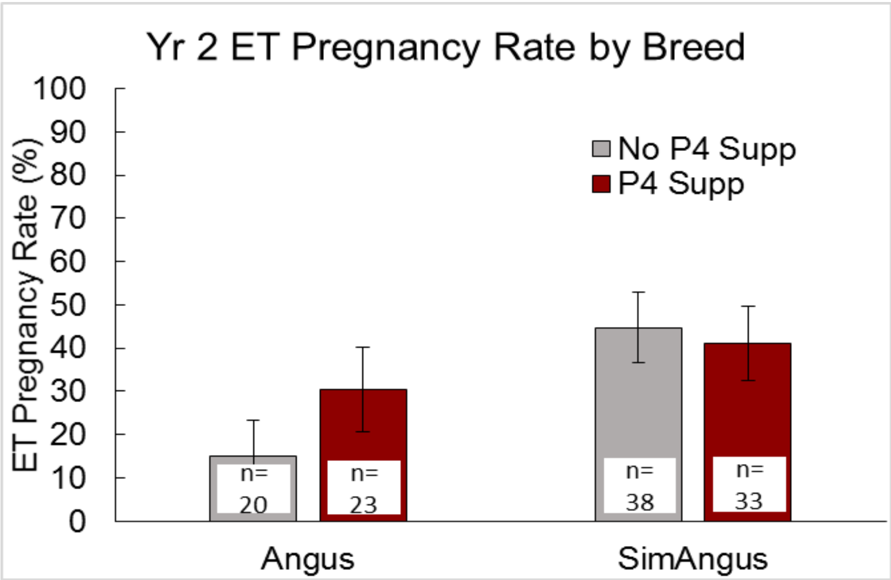

Figure 2.22: Year 2 ET pregnancy rates by breed.

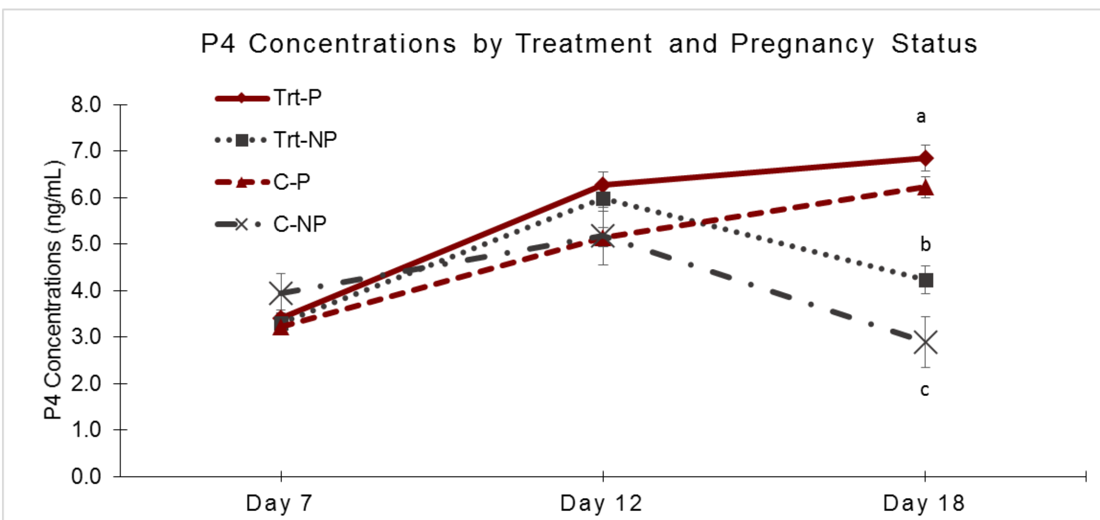

Figure 2.23: Multiparous cow P4 concentrations during the treatment period.

Abbreviations are as follows (Trt-Treatment, C-Control, P-Pregnancy, NP-Not pregnant). Cow progesterone concentrations remained similar up to day 12 post breeding. Pregnant cattle regardless of treatment or control were similar at day 18, but different to Trt-NP and C-NP (a vs. b, $P < 0.05$).

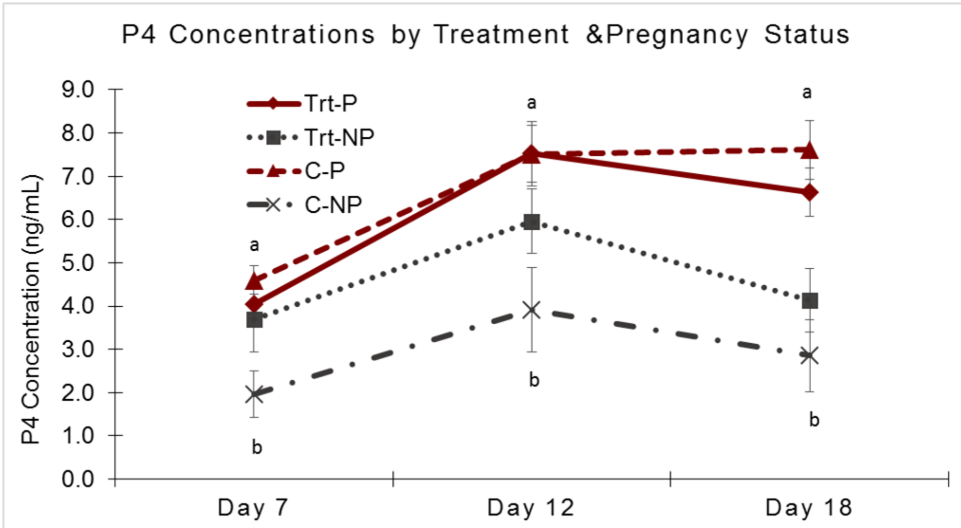

Figure 2.24: Differences in nulliparous heifer P4 concentrations during the treatment period.

Abbreviations are as follows (Trt-Treatment, C-Control, P-Pregnancy, NP-Not pregnant). Heifers that received no progesterone supplementation and were not pregnant had significantly reduced P4 concentrations on days 7 and 12 from all other groups. On day 18 post breeding, all heifers that were NP had lowered concentrations compared to pregnant heifers (a vs. b, $P < 0.05$).