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CURRENT APPLICATIONS TO ALLEVIATE ANIMAL STRESS ASSOCIATED WITH FESCUE TOXICOSIS

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Endophyte-infected tall fescue (**EI-TF**; *Festuca arundinacea* (Schreb), syn, *Lolium arundinaceum* (Schreb.) Darbysh) is a common pasture forage throughout the transition zone and one of the most persistent and productive forages in the world. The agronomically beneficial characteristics of EI-TF are a result, at least in part, of the presence of endophytic fungi (*Neotyphodium coenophialum*), which produces numerous ergot alkaloids (Bacon et al., 1977). It is estimated that approximately 70% of the more than 40 million acres of tall fescue grown in the southeastern U.S. is infected with these fungi (Shelby and Dalrymple, 1987). Ruminants grazing EI-TF generally exhibit a stressful multifaceted disease syndrome called fescue toxicosis (Hoveland et al., 1983; Paterson et al., 1995). Further, we have recently found that ruminants consuming EI-TF seed diets shed more *E. coli* O157:H7 in their feces (Looper et al., 2007). It is estimated that economic losses from animal consumption of EI-TF in the U.S. exceed $600 million annually (Allen and Segarra, 2001); consequently, U.S. beef producers need solutions for reducing animal stress resulting from the consumption EI-TF.

Management strategies to minimize or alleviate fescue toxicosis

The following considerations are by no means intended to be an exhaustive listing of all possible management considerations that minimize stress associated with fescue toxicosis. An excellent review of current research findings regarding fescue toxicosis can be found in the annual proceedings of the Southern Extension and Research Activities Information Exchange Group at http://animalscience.ag.utk.edu/SERA-IEG8/, as well as the book titled *Neotyphodium in Cool-Season Grasses* (2005; Roberts, West, and Spiers, Eds.; Blackwell Publishing).

Forage management. Several traditional options exist to minimize the physiological stress associated with EI-TF consumption including reseeding of EI-TF pastures with endophyte-free tall fescue, dilution of EI-TF pastures with legumes or other grasses, and(or) clipping EI-TF pastures to remove the more toxic seedheads.

Within the last 10 years, novel endophyte-infected ("animal friendly") tall fescue (**NE-TF**) varieties have been developed (West et al., 1998; Bouton et al., 2002) with endophytes that do not produce ergot-alkaloids and do not reduce animal performance. Researchers from Georgia (Parish et al., 2003; Watson et al., 2004) and Arkansas (Nihsen et al., 2004) found average daily gain and gain/acre were greater in cattle grazing NE-TF pastures than cattle grazing EI-TF. We (USDA-ARS, Booneville, AR) are completing a 3-year study investigating the influence of EI-TF and NE-TF on performance of pregnant heifers. Our preliminary data suggest cattle grazing NE-TF gain 0.6 lb/day more than EI-TF cattle. Further, cattle grazing EI-TF spend more time in the shade and around water tanks than heifers grazing NE-TF pastures.

The major issues with renovation of existing EI-TF pastures with improved forage varieties are the costs, both the input, as well as the opportunity costs of reseeding. Opportunity costs are those losses in profit due to not grazing newly renovated NE-TF pastures during the establishment time. Beck et al. (2006) recently estimated that it cost $232/acre to establish NE-TF pastures with almost $80 of that being opportunity costs. In comparison, cool-season annuals (ryegrass and winter wheat) cost an average of almost $115/acre. To minimize input costs to farmers, University of Arkansas researchers (K. Coffey), with assistance from USDA-ARS, Booneville, AR have initiated a study to determine the impact (both animal performance and economics) of renovating a portion (approximately 20%) of EI-TF pastures with NE-TF. Cattle will graze NE-TF during warmer months of the year instead of EI-TF pastures to minimize the stress associated with fescue toxicosis. A second major concern of incorporating NE-TF varieties is persistence of the stand. Several studies are ongoing to determine the persistence of NE-TF in comparison to EI-TF pastures.

There has been a renewed interest in stockpiling of EI-TF mainly due to a reduction in winter feed costs by approximately 60 to 75% when compared to conventional winter supplementation practices (Bishop-Hurley and Kallenbach, 2001; Jennings et al., 2004). Tall fescue provides sufficient forage growth and quality during winter months, and concentrations of ergovaline that induce fescue toxicosis are lower during the colder months (Kallenbach et al., 2003; Looper et al., 2005). In a 2-year supplementation study using market cows, research from USDA-ARS in Booneville, AR (Looper et al., 2005) showed nutritive content of stockpiled and spring-growth EI-TF exceeded the nutrient requirements of pregnant market cows, and as long as EI-TF forage was not limited, supplementation was not necessary to maintain body weight of cows. Further, concentrations of ergovaline did not exceed values that are associated with fescue toxicosis suggesting stress of EI-TF consumption may be reduced during the winter.

Animal management. Supplementation of either protein or energy to cattle grazing EI-TF causes a 'substitution effect' that may help in alleviating fescue toxicosis (Aiken et al., 1998). Adjusting stocking rate of cattle grazing EI-TF pastures also may help in minimizing fescue toxicosis. The decrease of EI-TF canopy height by either close grazing or clipping may decrease the toxicity of standing EI-TF pastures since a greater amount of ergot alkaloids are found in the seed. However, Aiken et al. (2006) reported serum prolactin (a physiological indicator of fescue toxicosis) decreased as stocking rate increased suggesting greater consumption of rapidly growing EI-TF in overstocked pastures may actually exacerbate fescue toxicosis. The limited availability of forages with heavy stocking rates also would affect animal performance.

Obviously one approach to reduce animal stress associated with EI-TF is to remove cattle from pastures with EI-TF. Extensive research has been conducted on removal of cattle for a certain amount of time (often referred to as recovery) to alleviate the effects of EI-TF during the warm summer months or before transport to the auction barn or feedyard. Aiken et al. (2001, 2006) reported that physiological indicators of fescue toxicosis (i.e., rectal temperatures and concentrations of prolactin) in steers consuming EI-TF returned to normal values after 3 to 4 days of a EI-TF-free diet for Brahman-influenced steers and 8-10 days of a EI-TF-free diet in British-influenced steers. For a more detailed report of research investigating recovery of cattle from the toxic effects of EI-TF, see Dr. Glen Aiken's manuscript in these proceedings.

Numerous animal studies during the past 25 years have investigated the use of pharmacological compounds, such as anthelmintics and steroid implants that minimize stress related to consumption of EI-TF. The use of anthelmintics to reduce stress associated with

fescue toxicosis has not been consistent. Bransby (1997) reported that steers grazing EI-TF had greater weight gain when administered ivermectin; however, others (Goetsch et al., 1988; Rosenkrans et al., 2001) reported no effect of ivermectin on weight gains of steers. Similarly, studies with steroid implants administered to cattle grazing EI-TF have had mixed results. Steroid implants increased average daily gain by 14% in steers grazing EI-TF (Coffey et al., 2001) but steroid implants did not impact recovery of steers after grazing EI-TF (Aiken et al., 2006). Type of implant, as well as forage quality and availability would affect animal performance and may explain differences in results among studies.

Novel approaches to an old problem

It is evident from the aforementioned research findings, development of plant and animal management strategies have made substantial progress in minimizing some of the stress associated with EI-TF consumption. However, there is still much we do not fully understand of the plant-animal interaction concerning EI-TF consumption. Novel approaches to this 'old' problem are needed and are currently being investigated, especially those that may be widely implemented by producers. Although not a comprehensive list, a few of the novel approaches that have interesting preliminary data are discussed here.

A majority of the research of how EI-TF consumption affects reproductive performance of cattle has focused on the female. Recognizing that the fertility of 1 bull may impact 20 to 25 cows, research efforts are now investigating the impact of EI-TF on the fertility of the bull. Bulls fed a pelleted EI-TF seed diet had smaller scrotal circumferences and tended to have decreased semen motility after 6 weeks exposure to EI-TF than non-EI-TF diets (Jones et al., 2004). Although semen motility and morphology did not differ between bulls fed control or ergotamine tartrate (alkaloid found in EI-TF) supplemented diets, development of embryos fertilized with semen from bulls fed ergotamine tartrate were decreased (Schuenemann et al., 2005). To confirm and expand these results, a study has been initiated at the USDA-ARS laboratory in Booneville, AR in collaboration with University of Arkansas researchers to assess how EI-TF and NE-TF impact bull performance and semen quality.

A considerable amount of research with horses has been conducted with the dopamine receptor blocker, domperidone (Cross et al., 1999). Domperidone was effective in alleviating a majority of the signs/symptoms of fescue toxicosis in pregnant mares. Work in cattle indicates that heifers consuming EI-TF seed diets and administered domperidone had similar daily weight gains as heifers consuming non-EI-TF seed diets (Jones et al., 2003). Further, domperidone may help in minimizing the toxic effects of EI-TF on reproduction in cattle. The USDA-ARS laboratory in Lexington, KY has ongoing studies to investigate the influence of domperidone on mammary development of heifers consuming EI-TF in their diets.

The implementation of doppler ultrasonography to determine blood flow in cattle consuming EI-TF shows extreme promise to further our understanding of the physiological mechanisms of fescue toxicosis. Research recently completed at the USDA-ARS laboratory in Lexington, KY (Aiken et al., 2007) reveals that short-term exposure to EI-TF will result in vasoconstriction of blood vessels in heifers consuming EI-TF.

For years, livestock producers have unintentionally or in some cases intentionally selected cattle that were more productive when grazing EI-TF. Cattle that did not maintain an annual calving cycle or that consistently produced a lighter calf at weaning were eventually culled from the cowherd. However, use of traditional selection techniques is slow, usually occurring over several years for individual animals. This process may be accelerated by the use of non-

traditional methods such as physiological and(or) genetic markers. Understanding the animal response to the EI-TF stressors, particularly at the genetic and physiologic levels, is an area needing further exploration to develop new approaches to confront this problem. The liver is a detoxification organ involved in metabolism of toxins. Using DNA microarray techniques, University of Missouri researchers have shown that even short-term exposure to EI-TF diets down-regulated genes involved in cholesterol and lipid metabolism found in the liver of rodents (Bhusari et al., 2006; Settivari et al., 2006). Researchers at the University of Arkansas in collaboration with USDA-ARS, Booneville, AR have demonstrated that linking physiological changes to their genetic origins can be related to cow profitability traits. Current efforts focus on genetic and(or) physiological markers that can be useful in selecting cattle that are more productive on EI-TF. Specifically, how polymorphisms (specific genetic variations between individual animals) in the prolactin gene enhancer region and heat shock protein gene in cattle are related to productivity while grazing EI-TF is being investigated. Dr. Charles Rosenkrans' manuscript in these proceedings thoroughly discusses the genetic variations in cattle consuming EI-TF.

Endophyte-infected tall fescue is one of the most persistent and productive forages grown throughout the Southeast U.S. with one major disadvantage, a reduction in animal performance due to fescue toxicosis. Much progress has been made to help livestock producers minimize animal stress associated with consumption of EI-TF; however, additional work is still needed to alleviate this very economically costly problem. Currently, several innovative techniques and technologies seek alternative solutions to the endophyte problem. An increased understanding of animal responses to EI-TF forages will be the basis of new and(or) improved best management practices for cost-effective beef production in the U.S.

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