Immunologic and Other Strategies to Overcome Fescue Toxicosis

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Tall fescue (*Festuca arundinacea*) is a perennial grass grown on approximately 35 million acres primarily in the southeast portion of the U.S. This grass is the predominant cool-season forage grown in the transition zone between the latitudes of Indianapolis, IN and Macon, GA, and the meridians of Eastern Kansas and the eastern edge of the Appalachian piedmont area. It is estimated that somewhere between 20-30% of the nation's beef cows graze this forage.

Tall fescue has desirable compositional characteristics, withstands heavy grazing and environmental stresses. However, animal performance (body weight gains and reproductive efficiency) is depressed in animals grazing this forage. The signs exhibited by affected animals are exacerbated by elevated environmental temperatures and humidity. Affected animals have long, rough hair coats, excessive salivation and avoid sunlight. Increased respiratory rates and body temperatures are also observed. Relative to reproduction, milk yields and pregnancy rates are depressed. No microscopic or gross lesions are associated with the general syndrome of fescue toxicosis.

Two other conditions in cattle are associated with tall fescue: fescue foot and fat necrosis (Stuedemann and Hoveland, 1988). Fescue foot is a gangrenous condition of the hooves, tail and occasionally ears occurring primarily during winter months. Early signs of fescue foot include a rough hair coat, scouring, lameness, arched back, loss of body weight, increased body temperature and respiratory rate. Fat necrosis occurs in mature cows and is associated with masses of hard fat in the abdomen leading to poor digestion and calving problems. Signs of fat necrosis include weight loss, scant feces and bloat.

Fescue toxicosis is associated with a fungal endophyte (*Acremonium coenophialum*) that, in conjunction with the grass, results in the presence of toxic alkaloids in the grass. It is generally regarded that the ergopeptine alkaloids or ergot alkaloids are the causative agents. Of the ergopeptine alkaloids, ergovaline is present in the greatest concentration (Bacon *et al.*, 1986). The ergot alkaloids are located throughout the above ground parts of the plant but are in the greatest concentration in the stems and seeds. The relationship between the endophyte and the grass is symptomless requiring that the endophyte be detected microscopically following excision and staining stem tissue. The endophyte is passed to succeeding generations through the seed allowing endophyte-infected and endophyte-free stands of tall fescue to coexist in close proximity without appreciable contamination. The endophyte confers resistance to the plant to environmental stresses and results in greater forage production. Similarly, the endophyte prevents overgrazing and insect depredation.

Endophyte free tall fescue is available, however, stands of this grass lack persistence in response to biotic and abiotic stresses. Because of the beneficial aspects of the endophyte to the plant and the large land mass in endophyte-infected fescue, an animal solution to fescue toxicosis is desirable. Much of the land now in endophyte-infected fescue is highly erodible and with renovation there is the risk of top soil loss. Additionally, land renovation results in a temporary loss of production with its costs.

The reduction in average daily gains can be explained partially, at least, by a decreased intake (Stuedemann and Thompson, 1993). The reduced intake would appear to be the result of decreased time spent grazing as a result of avoiding sunlight. Perhaps the alkaloids additionally have a direct neural effect that reduces appetite. The increased body temperature appears to be the result of increased vasoconstriction with the resultant decreased ability to dissipate body energy. The relative inability to dissipate heat would appear to explain the increased respiratory rates.

Since ergot alkaloids act as adrenergic agonists, dopaminergic agonists and serotinergic antagonists (Berde and Schild, 1978), a variety of effects are expected. A reduction in serum prolactin commonly observed in cattle grazing endophyte-infected fescue is a dopaminergic effect as a dopaminergic antagonist increased serum prolactin in cattle on endophyte-infected fescue (Lipham *et al.*, 1989). Vasoconstriction is due to

adrenergic activity (Solomons *et al.*, 1989). Conception rates in cattle do not appear to be reduced by the endophyte, however, pregnancy maintenance is reduced (Nasti *et al.*, 1994). The reproductive effects of the endophyte in general have been reviewed (Porter and Thompson, 1992).

Many management options for overcoming fescue toxicosis have been explored (Stuedemann and Thompson, 1993). Dilution of endophyte-infected fescue with clovers is practiced, however, in a controlled study this had little value in overcoming the toxicosis. The potential for utilizing clovers varies greatly with regions. Clovers are sensitive to diseases and are comparatively shallow rooted and are consequently susceptible to drought. While the effects of dilution of the alkaloids from endophyte-infected fescue with clovers or other grasses is not well defined scientifically, it is a major technique used by producers to minimize the effects. In this regard, grain supplementation of wintering cows pastured on endophyte-infected and non-infected fescue resulted in similar pregnancy rates (Tucker *et al.*, 1989). The benefits of ivermectin treatment if any, in overcoming the toxicosis remains to be scientifically proven via using parasite free animals and pastures. While Goetsch *et al.* (1988) found that neither ivermectin nor fenbendazole was effective in this regard, Crawford and Garner (1991) reported that ivermectin given at 14d intervals improved animal gains. Further research using ivermectin given at a 56d interval (Bransby *et al.*, 1993) revealed a greater improvement in performance in animals grazing endophyte-infected compared to endophyte-free fescue. The effects of anabolic ear implants to overcome the toxicosis has revealed both beneficial and no effects. The combination of Synovex ear implants and ivermectin treatment has been reported to be beneficial (Bransby, 1994).

Vaccination may be an appropriate strategy to reduce losses to fescue toxicosis. The use of an immunologic approach to a mycotoxicosis is not unique to this toxicity as vaccines have been protective against lupinosis (Ralph, 1990 and trichothecene T-2 toxin (Chanh *et al.*, 1991). Conversely, vaccination against zearalenone intensified the condition (MacDonald *et al.*, 1990 and Smith *et al.*, 1992). Similarly, immunization of ewes against sporidesmin, another mycotoxin and the etiologic agent for facial eczema failed to protect the animals (Fairclough *et al.*, 1984).

The ergot alkaloids are of insufficient molecular size to be antigenic, however, following conjugation to a protein they are immunogenic (Thompson and Garner, 1994). The ergot alkaloids so used are haptens. Variables that affect immunologic success include number of haptens per protein molecule, choice of ergot alkaloid and adjuvant used. Antibodies produced should bind ergovaline with a high affinity. Also, the immunogen must be constantly presented to the animal since absorbed ergot alkaloids are not immunogenic.

A mouse monoclonal antibody directed against ergot alkaloids was produced that binds a variety of ergot alkaloids with a high affinity for ergovaline. Infusion of this antibody to steers grazing endophyte-infected fescue resulted in increased serum prolactin (Hill *et al.*, 1994). While prolactin is not thought to be an important determinant of growth, a decrease in serum prolactin is indicative of the effects of the endophyte. Consequently, the increase in serum prolactin following antibody infusion indicated that the toxic effects of the alkaloids had been attenuated and was the first definitive evidence that ergot alkaloids are causative.

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Select Immune Response in Beef Calves Grazing Endophyte-infected Tall Fescue

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Copper status and immune response of weaned beef steers that grazed endophye-infected (*Acremonium coenophinlum, Morgan Jones and Gams*) tall fescue (*Festuca arundinacea* Schreb.) was evaluated in a 6 month, bi-location study (Ridge-Valley [R-V] and Southern Piedmont [SP] regions of Virginia). Forty-two steers were blocked by weight and breed to: 1) endophyte-infected (EI) fescue and 2) endophyte-free (EF) fescue pastures at the two locations. Plasma Cu concentrations were higher in steers grazing EF fescue at both study sites (R-V, $P < 0.01$ and SP, $P < 0.05$) compared to those grazing EI tall fescue. Ceruloplasmin oxidase activity was increased ($P < 0.01$) in steers that grazed EF versus EI fescue at the R-V site. Immune status was measured as total leukocyte count and monocyte cell activity. Steers grazing infected fescue had lower ($P < 0.01$) leukocyte counts compared to steers on non-infected fescue. Phagocytic activity and MHC class II antigen expression of monocytes from steers grazing EI fescue at the R-V site was lower ($P < 0.05$) compared to EF steers. Monocytes from EF steers at the SP study site were more responsive (MHC antigen expression, $P < 0.001$ and hydrogen peroxide release, $P < 0.05$) compared to monocyte activity of EI steers. Steers grazing EI fescue had lower body weights ($P < 0.05$) and body condition ($P < 0.001$), rougher hair coats ($P< 0.001$), and greater incidence of facial warts, nasal and occular discharge ($P < 0.05$) compared to the EF groups at the end of the grazing period. These data suggest a relationship may exist between endophyte infection and Cu status in regard to immune function in growing steers.