Influence of Trace Nutrients on the Health of Dairy Cows

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INTRODUCTION

Historically, the link between trace nutrients and animal health has been clinical deficiency diseases. With the feeding practices used today, classical deficiency diseases are rarely encountered. Nutrition scientists are now examining the effects of marginal deficiencies of trace nutrients on less specific areas of animal health. Trace nutrients are involved in several aspects of immunity. Some minerals and vitamins are part of the antioxidant system that protects phagocytes and other cells from oxidative damage. The role of antioxidants in maintaining health is an area of active research (Bendich, 1993; Miller et al., 1993). Some nutrients stimulate lymphocyte proliferation and antibody production. The effects of marginal deficiencies are subtle, which makes measuring responses to supplementation difficult. Three types of experiments are used commonly to assess the relationship between trace nutrients and animal health. Clinical experiments determine the effect of feeding a nutrient on the incidence, severity, and duration of a disease. Survey studies compare the nutrient status of different herds to incidence of disease. Immune function experiments are designed to study the effects of supplementation on immune system parameters, usually in vitro. Clinical data should be given more weight than in vitro or survey data.

Reviews have been published on the relationship between trace nutrients and animal health (Suttle and Jones, 1989; Nockles, 1991). This paper will concentrate on recently published data.

TRACE MINERALS

Chromium. Chromium (Cr) is an essential nutrient for humans and laboratory animals, but until very recently, essentially no information was available on Cr requirements of ruminants. Indeed, the NRC (1989) has not established a Cr requirement for cattle. Recent research conducted by Mowat and co-workers, however, shows that dietary Cr may be important to cattle under certain conditions. In their first experiment (Chang and Mowat, 1992), steers (250 kg) were fed diets containing 0 or .4 ppm of supplemental organic Cr (provided by high Cr yeast) upon arrival at the feedlot. During the first 28 d on feed, calves fed .4 ppm Cr had higher average daily gains (ADG) and feed efficiencies than did calves not supplemented with Cr. Supplemental Cr had no effect on ADG or feed efficiency during the growing phase (d 42 to 112). Morbidity was not influenced by supplemental Cr during the experiment. In a subsequent experiment (Mowat et al., 1993), steers (230 kg) were fed 0 or 4 mg of Cr/d (provided by high Cr yeast or amino acid-chelated Cr) upon arrival to the feedlot. Chromium supplementation reduced morbidity during the first 21 d. The response was greater to chelated Cr than to Cr provided by yeast. After 21 d, Cr had little effect on morbidity. The reduction in morbidity and increase in ADG in recently shipped feedlot calves by Cr supplementation was confirmed by Moonsie-Shageer and Mowat (1993).

Supplemental Cr has been shown to influence both humoral and cellular immunity in beef and dairy cattle. Feedlot calves (Moonsie-Shagerr and Mowat, 1993) fed supplemental Cr (.2 to 1.0 ppm) had higher serum antibody titers to human erythrocytes than did cattle fed 0 ppm of

Cr. Titers were similar for all Cr treatments (no dose response). Concentrations of IgG_1 in serum were elevated in cattle fed .5 ppm of Cr on d 14 but not on d 28. In another experiment, dairy cows were fed 0 or .5 ppm Cr (from a chelate) starting 6 wk prepartum and ending 16 wk postpartum (Burton et al., 1993). Cows fed supplemental Cr consistently had increased antibody titers to ovalbumin. Antibody titers to human erythrocytes were not affected by Cr. Chromium supplementation increased blastogenic activity of mononuclear cells (a measure of cellular immunity) in dairy cattle. The response was especially pronounced at 2 wk prior to parturition and at parturition.

The mode of action for the immunostimulatory effects of Cr is not understood fully. Chromium is involved in glucose metabolism. Some studies have shown that Cr supplementation reduces cortisol concentrations in plasma. Cortisol is thought to cause immunosuppression.

Data on Cr supplementation to cattle is limited, but available research suggests that cattle under stress (feedlot cattle during transport and periparturient dairy cows) respond favorably to supplemental Cr. Cattle are at increased risk to infectious diseases during periods of stress. Current research suggests that supplementing diets for stressed cattle with approximately .5 ppm of Cr from *organic* sources increases immune response, reduces morbidity, and may increase animal productivity. Supplemental Cr has not shown positive responses when fed to non-stressed cattle.

Copper. Copper (Cu) is involved in hemoglobin synthesis, and anemia is a common sign of a clinical Cu deficiency. Currently NRC recommends that diets fed to all classes of dairy animals contain 10 ppm of Cu. Unless diets contain molybdenum (Mo) or excess sulfur (which interfere with Cu absorption), 10 ppm of Cu is adequate to prevent anemia in ruminants. Copper also is part of an enzyme called copper-zinc superoxide dismutase (Cu,Zn-SOD) and also is found in ceruloplasmin, a plasma protein. These two proteins are important components of the antioxidant system in animals.

A study showing a link between disease resistance in ruminants and Cu status was conducted by Wooliams et al. (1986). They found that sheep genetically selected for low concentrations of Cu in plasma had significantly higher mortality (mostly caused by infectious diseases) than did sheep selected for high plasma Cu. Other data support the importance of Cu for disease resistance, especially immunocompetence.

The antioxidant role of Cu appears to be extremely important in phagocytic cell function. Activity of Cu,Zn-SOD in neutrophils is depressed even with marginal Cu deficiencies (Babu and Failla, 1990a; Xin et al., 1991). In those studies, killing ability of neutrophils from animals fed diets that were marginally deficient in Cu was reduced relative to controls. Macrophage killing ability also is depressed during Cu deficiency (Babu and Failla, 1990b). Copper could be affecting phagocytic cell function via at least three mechanisms. Since Cu,Zn-SOD activity in both neutrophils and macrophages is reduced during Cu deficiency, superoxide concentration could increase within the cell and cause oxidative damage to the phagocyte. Research conducted with rats suggests that Cu deficiency interferes with the respiratory burst of phagocytic cells (Babu and Failla, 1990a). A third possible mechanism for improved neutrophil function with Cu supplementation is via ceruloplasmin. Increased concentrations of that protein has been shown to reduce extracellular concentrations of superoxide and to reduce adhesion of neutrophils to endothelial cells (Broadley and Hoover, 1989) which can result in reduced oxidative damage to cells.

The effect of Cu status on humoral and cellular immunity is much less certain than is the relationship between phagocytic cell function and Cu. Copper has been shown to influence humoral and cellular defense systems of laboratory animals (Sherman, 1992). Mixed results have been reported for ruminants. Ward et al. (1993) reported that Cu status had essentially no effect on lymphocyte response; whereas, Wooliams et al. (1986) reported that lymphocyte proliferation was enhanced by Cu supplementation.

Current information suggests a strong connection between Cu status and phagocytic cell

function. Copper via Cu,Zn-SOD and ceruloplasmin is an important component of the antioxidant system of animals. Quantitative data on Cu requirement relative to maintaining phagocytic cell function and reducing oxidative stress are not available. Current research suggests that when Mo and S interferences are not a concern, 10 to 20 ppm of Cu is probably adequate for optimal immune function in cattle. Feeding excess Cu can result in increased oxidative stress because free Cu acts as a pro-oxidant.

Selenium. Selenium (Se) is a constituent of glutathione peroxidase (GSH-px), an enzyme that converts hydrogen peroxide to water. The positive effects Se supplementation has on many aspects of animal health and immune function can be linked to its antioxidant role. The amount of supplemental Se allowed in diets is regulated by the US Food and Drug Administration (FDA). For the past several years (1987 until September, 1993) FDA allowed diets fed to beef and dairy animals to contain up to .3 ppm of supplemental Se. Effective September, 1993, FDA revised the regulation and presently diets for beef and dairy animals can be supplemented with a maximum of .1 ppm of Se.

A large body of data is accumulating that shows a relationship between Se deficiency and disease in cattle (Hogan et al., 1993). A clinical deficiency of Se produces white muscle disease in cattle and sheep. Deficiencies of Se also have been linked to increased incidence of retained placenta, metritis, and clinical mastitis. Harrison et al. (1984) reported that dairy cows fed a Se-deficient basal diet (.05 ppm of Se) had a high incidence of retained placenta. Injecting approximately .1 mg Se/kg of body weight 3 wk prior to parturition and feeding 1000 IU of supplemental vitamin E/d essentially eliminated retained placenta and greatly reduced incidence of metritis. Incidence of retained placenta was not reduced when only Se was supplemented.

Selenium supplementation without supplemental vitamin E reduces the duration of clinical mastitis (Smith et al., 1984). Maddox et al. (1991) reported that cows supplemented with .3 ppm of supplemental Se (basal diet contained .05 ppm of Se) recovered better from acute *Escherichia coli* mastitis than did cows fed no supplemental Se. Three of the four Se-deficient cows had to be euthanized after infection, but all Se supplemented cows recovered without intervention. The response to Se supplementation appears to depend on type of mastitis. Duration of *E. coli* mastitis was reduced when cows were fed 2 mg of supplemental Se/d (basal diet contained .04 ppm of Se; Erskine et al., 1989), but Se did not affect duration of *Staphylococcus aureus* mastitis (Erskine et al., 1990). *E. coli* infection caused an acute inflammatory response resulting in a massive influx of neutrophils into the mammary gland; whereas, *S. aureus* infection did not cause an acute inflammatory response. Neutrophil influx was much less with *S. aureus* infection than with *E. coli* infection. Selenium supplementation increases the killing ability of bovine neutrophils (Grasso et al., 1990; Hogan et al., 1990). Survey data have shown that herds with high Se concentrations in blood have reduced incidence of mastitis and (or) lower SCC (Weiss et al., 1990; Braun et al., 1991; Ndiweni et al., 1991).

Supplementation of Se to ruminants fed Se-deficient diets often increases lymphocyte proliferation (Finch and Turner, 1989; Stabel et al., 1990; Cao et al., 1992). Most data on the influence of Se supplementation on antibody production has been negative. Antibody titers to several antigens have shown no response to supplemental dietary or parenteral Se (Droke and Loerch, 1989; Nemec et al., 1990; Nicholson et al., 1993). Stabel et al. (1989) reported that Se supplementation (.1 ppm) reduced antibody titers to *P. haemolytica* as compared to calves fed no supplemental Se. In that study, Se supplementation increased production of IgM. In a subsequent study, Stabel et al. (1991) reported that adding Se to culture media (organic and inorganic forms) stimulated IgM production by bovine lymphocytes. The response was greater for organic than inorganic Se.

Data from clinical, survey, and in vitro studies strongly support a link between Se status and disease resistance (especially mastitis) in cattle. Basal diets that are deficient in Se (<.1 ppm of Se) should be supplemented with .1 ppm of Se (current maximum legal amount). Blood

tests can be used to determine if additional Se is required. We recommend that whole blood contain approximately .2 mg Se/ml and plasma contain approximately .08 mg/ml for dairy cows. Injecting Se or providing feedstuffs that contain high amounts of Se (e.g. linseed meal) can be used to provide additional Se if necessary.

Zinc. In humans and laboratory animals, zinc (Zn) deficiency clearly reduces immune function (Keen and Gershwin, 1990). Protein synthesis is reduced when Zn status is low and much of the effect Zn has on immune function could be caused by altered protein synthesis. In ruminants fed practical diets, supplemental Zn has not been shown to influence immune function or disease resistance greatly. Kellogg et al. (1989) increased Zn concentration in the diet of dairy cows from approximately 60 ppm to 80 ppm (from Zn methionine) and reported no effects on production or mammary gland health. Heinrichs et al. (1984) supplemented diets for dairy cows with Zn methionine (control diet had 40 ppm and supplemented diet had 56 ppm of Zn) and found no effect on performance or immune function. Chirase et al. (1991), however, reported that feedlot cattle recovered more quickly (body temperatures and feed intake) after challenge with IBR virus when they were fed supplemental Zn (90 ppm of supplemental Zn from Zn-methionine). The basal diets contained approximately 30 ppm of Zn.

Several studies have found that plasma Zn concentrations and (or) Zn balance decrease during periods of stress or infection (Goff and Stabel, 1990; Erskine and Bartlett, 1993; Nockles et al., 1993). The decrease in plasma Zn or Zn balance could indicate an increased need for Zn during periods of stress. Conversely, animals could sequester Zn during infections so that less is available to the pathogen.

The NRC recommends that dairy cattle be fed 40 ppm of Zn (30 ppm for beef cattle). At the current time, insufficient data exist to recommend increasing that amount to improve immune function and reduce disease. During periods of stress, additional Zn may be needed, but more research is needed.

VITAMINS

Vitamin A and β-carotene. Vitamin A is needed to maintain the integrity and proliferation of epithelial cells. Vitamin A is not a strong antioxidant, but has been shown to improve cellular and humoral immunity (Chew, 1987; Bendich, 1993). However, little, if any, improvement in immunity has been reported by feeding more vitamin A than currently recommended by NRC (approximately 70,000 to 100,000 IU/d).

The NRC has not established a requirement for β-carotene (BC), however, recent research has suggested a metabolic role for BC that is independent of its pro-vitamin A activity (Chew, 1993). Cattle, unlike many other species, can absorb significant quantities of BC from their diets and BC is a strong antioxidant. Chew (1993) reviews several experiments conducted at Washington State University that show improved cellular immunity and neutrophil function when periparturient dairy cows were fed 300 to 600 mg/d of BC. Feeding 400 mg/d of supplemental BC to dry cows prevented the normal suppression in phagocytic activity observed during the periparturient period (Tjoelker et al., 1990). Data from clinical experiments have been conflicting. One study found that feeding BC reduced incidence of mastitis; another study reported no response (reviewed by Chew, 1993).

β-carotene is an important lipid soluble antioxidant; therefore, many of the observed effects of supplemental BC could be caused by reduced oxidative damage. Although BC affects neutrophil activity, bovine neutrophils contain little, if any, BC (Chew et al., 1993; Weiss et al., 1994). Lymphocytes, however, contain substantial amounts of BC (Chew et al., 1993). Chew (1993) discusses many of the potential mechanism by which BC could influence phagocytic cell function, and cellular and humoral immunity.

Fresh forages contain large amounts of BC and a response to supplemental BC by cattle fed fresh forage is unlikely. Stored forages contain much lower concentrations of BC. Concentrations of BC in plasma decrease during the periparturient period (Johnston and Chew, 1984; Weiss et al.,

1994). Improvements in immune function have been observed when periparturient cows were fed supplemental BC. Current data does not support the routine supplementation of BC, but supplementing 300 to 600 mg/d of BC during the periparturient period may be beneficial to cows fed stored forages.

Vitamin E. The primary role of vitamin E is as an antioxidant in cellular membranes. Current NRC recommendations for vitamin E are 15 IU/kg of DMI which corresponds to a daily intake of approximately 150 IU and 300 IU for dry and lactating dairy cows. Those recommendations are usually adequate to prevent muscular dystrophy and other acute signs of deficiency. Data are accumulating that show vitamin E supplementation above NRC is required to maintain immune function and reduce disease in cattle.

Smith et al. (1984) reported that supplemental vitamin E (1000 IU/d) fed and Se injected at .1 mg/kg bodyweight) during the dry period reduced incidence and duration of clinical mastitis in dairy cows. Some survey studies have shown a beneficial effect of vitamin E supplementation (Atroshi et al., 1986; Weiss et al., 1990), but others have shown no relationship between vitamin E supplementation and mastitis (Ndiweni et al., 1991; Braun et al., 1991). In the two studies that showed no response, plasma concentrations of α-tocopherol in all herds were much higher than those reported in the two positive studies.

Although vitamin E has been reported to enhance cellular and humoral immunity in some species (reviewed by Hogan et al., 1993), the most significant effect of vitamin E appears to be on phagocytic cell function. Neutrophils from cows supplemented orally (Hogan et al.,1990) or parenterally (Hogan et al., 1992) with vitamin E had improved killing ability as compared to unsupplemented cows. Injecting approximately 6000 IU of vitamin E 1 to 2 wk prepartum prevented the normally observed depression in neutrophil killing ability during the peripartum period. Bovine neutrophils can contain appreciable quantities of α-tocopherol. Administration of ACTH and epinephrine to simulate stress caused marked reductions in α-tocopherol concentrations in neutrophils (Sconberg et al., 1993). Reduced neutrophil function at parturition may be caused by high levels of cortisol; additional vitamin E during this time may be beneficial. Many of the positive responses in neutrophil function to vitamin E supplementation can be ascribed to the antioxidant role of α-tocopherol.

Clinical, survey, and in vitro data show that current NRC recommendations for vitamin E are too low for optimal immune function and disease prevention. Titration studies with regard to immune function or animal health have not been conducted. Feeding dry cows approximately 1000 IU and lactating cows approximately 500 IU of supplemental vitamin E per day reduces incidence and duration of mastitis and increases killing ability of neutrophils. Peripartum cows have low concentrations of α-tocopherol in plasma and this may be related to depressed neutrophil function at calving. Injecting 6000 IU of vitamin E (equivalent to approximately 18,000 IU of d,l-α-tocopheryl acetate given orally) increased α-tocopherol concentrations in plasma and in neutrophils from peripartum cows. Feed intake is depressed during this period, and parenteral administration of vitamin E may be beneficial at this time.

CONCLUSIONS

- Feeding approximately .5 ppm of supplemental Cr from an organic source may be helpful to stressed cattle.

- Copper is essential in maintaining phagocytic cell function. Diets should contain 10 to 20 ppm of Cu (more if dietary Mo or S are a concern).

- In areas of the country with low soil Se, diet should be supplemented with the maximum legal amount of Se. Blood tests can be used to determine if additional Se (injections, high Se feedstuffs) is needed.

- Feeding approximately 40 ppm of Zn appears adequate to maintain immune function in cattle.

- Supplemental β-carotene improves phagocytic cell function, but probably is only necessary during the periparturient period.

- The NRC recommendation for vitamin E is too low to promote optimal phagocytic cell function and disease resistance. Current data support supplementing dry cows with 1000 IU of vitamin E/d and lactating cows with 500 IU/d.

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