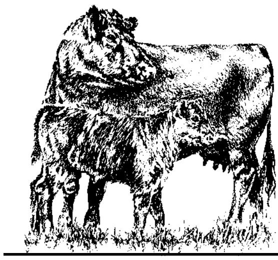

Trace Minerals and the Immune System in Cattle

Jason K. Ahola, University of Idaho
Terry E. Engle and Jack C. Whittier
Colorado State University

The Immune System in Beef Cattle

Beef cow/calf and feedlot operations often experience substantial economic losses due to morbidity and mortality of calves. One cause of loss is the inability of the animal to respond immunologically to an antigen.

Respiratory disease is prevalent in calves arriving at the feedyard, based on evidence that 14.4 percent of calves placed into U.S. feedyards develop respiratory disease (USDA-APHIS 2000). Similar data indicate that the majority (nearly 70%) of death losses in small U.S. feedlots can be attributed to respiratory disease (USDA-APHIS 1994). Respiratory disease also can lead to substantial economic losses due to treatment costs and depressed cattle performance, including lower average daily gains.

To avoid death loss or reduced performance due to disease, a calf's immune system needs to be viable when it encounters a stressful situation, such as occurs at weaning time. Cattle are able to overcome infectious pathogens through use of an elaborate immune system.

The immune system's primary goal is to recognize and defend itself against foreign materials (including bacteria, viruses, and other substances) that may be harmful to the body. The immune system includes several components that work together to initiate an immune response in order to maintain the health and well-being of an animal.

Materials and compounds foreign to the body are known as antigens. The body's immune system recognizes these antigens as foreign, and ultimately tries to destroy them by initiating an immune response.

Cattle producers in the U.S. commonly take advantage of a calf's ability to recognize and respond to antigens when they vaccinate cattle at branding and/or weaning in order to "trigger" an immune response. Administration of a small dose of antigenic material to a calf via a vaccine (which may include a killed or modified live virus) can improve the speed and efficiency of the calf's next immune response to that same antigen, which involves the "memory" component of its immune system.

A proper immunological response to an antigen is necessary to help a calf's immune system overcome future immune challenges. Therefore, to ensure a proper immunological response to an antigen, a calf's immune system must be working properly. This requires sufficient nutrition including adequate concentrations of several trace minerals shown to be vital for proper immune system function.

Components of an Immune Response

A healthy calf's immune system basically reacts to foreign material using two types of responses that work in harmony to overcome pathogens. These responses include a specific immune response and a non-specific immune response:

Specific Immune Response—A specific immune response to an antigen involves either a humoral or a cell-mediated immune response. A **humoral immune response** involves the systemic production and secretion of antibodies into the extracellular space. Antibodies are proteins produced in direct response to an antigen, and act on specific antigens by binding and inactivating them.

Furthermore, a humoral immune response can be either primary or secondary. A *primary immune response* is an immune response to an antigen for the first time, which takes several days to occur and provides limited protection against the antigen. A *secondary immune response* is a response to an antigen that had been responded to previously (e.g., when the calf was vaccinated), and involves a much faster, larger, and more effective response to an antigen.

In addition to the systemic humoral response, the body also has a **cell-mediated immune response**, which involves finding and eliminating abnormal body cells that contain foreign material (such as bacteria or viruses). A cell-mediated immune response involves the production of lymphocyte cells, ultimately leading to the destruction of specific antigens.

Non-Specific Immune Response—In addition to the specific humoral and cell-mediated immune responses, the body also has a more primitive and nonspecific immune response to an antigen. Part of this response involves phagocytes that migrate to the site of an infection. Phagocytes surround, engulf, and lead to the destruction of foreign materials; however, they are much less specific than either the humoral or cellmediated immune responses.

Some phagocytic cell types destroy foreign material through the use of free radicals that must then be detoxified by the body via specific enzymes. These enzymes require specific trace minerals to be active.

Nutrition and Immunity

Producing antibodies and lymphocytes in order to initiate an immune response requires a proper plane of nutrition for various functions (Table 1). This need for nutrients often occurs when stress is increased, such as at weaning time when calves are physically stressed and need to immunologically respond to infectious agents. However, it has been suggested that actual mineral requirements do not increase when calves are stressed (Orr et al. 1990).

Nockels and others (1993) did observe that retention of zinc (Zn) by steers was reduced during stress (caused by feed and water deprivation and injection of a hormone that increased the release of cortisol, a stress hormone), indicating that stress can affect trace mineral metabolism.

Trace Minerals and the Immune System

Recommended concentrations of trace minerals in beef cattle diets, as reported by the NRC (1996), are primarily based on animal growth and reproduction responses, and not on immune response measures. However, several trace minerals have been identified as necessary for proper immune function. Most trace minerals are essential for enzyme activity, including enzymes for energy production, protein synthesis, and cell replication.

Table 1. Nutrient requirements of the immune system—a partial list of functions.[a]

Item	Needed for:
Energy	Rapid proliferation of immune cells
Protein	Cell replication Synthesis of antibodies and cytokines
Minerals (Cu, Zn, Mn, Se, Fe, S)[b]	Antioxidant systems Energy production Protein synthesis Membrane integrity (physical barrier to pathogens)
Vitamins (A, D, E, C, B complex)[c]	Antioxidant systems Cellular differentiation Energy production Protein synthesis Membrane integrity

[a]Adapted from Nockels and Whittier (1995).

[b]Cu = copper, Zn = zinc, Mn = manganese, Se = selenium, Fe = iron, S = sulfur.

[c]Vitamins D, C, and the B complex are needed in the immune system; however, no specific cattle data are available.

In addition, several trace mineral-dependent enzymes act specifically within the immune system, such as those removing free radicals from the body. The predominant trace minerals involved in the immune function of cattle include copper (Cu), Zn, manganese (Mn), and selenium (Se).

Copper—Copper has been shown to be important for immune system function, based on evidence that Cu metabolism affects the function of several classes of immune system cells, particularly those involved in producing antibodies. Copper is also vital for the activity of an enzyme responsible for removing toxic free radicals from the body (Cu-Zn superoxide dismutase) as well as for the activity of phagocytes.

Copper deficiencies are not uncommon in cattle. This can be due to inadequate Cu concentrations in feedstuffs and/or elevated concentrations of Cu antagonists, such as molybdenum (Mo), sulfur (S), and/or iron (Fe), which can substantially hinder Cu absorption and metabolism.

Zinc—In the body, Zn plays an important role in numerous enzymes. Zinc has a structural role in some enzymes, while with others Zn functions as an enzyme activator. In the immune system, Zn is important for antibody production and is vital for the proper functioning of lymphoid tissue for cell production.

Many forages in the U.S. are deficient in Zn (Corah et al. 1996), however, there is a large amount of variation among locations. Therefore, it is important for producers to evaluate feed and water samples over several seasons to determine the proper amount of nutrients that should be supplemented to grazing cattle.

Manganese—Manganese is also necessary for the normal activity of many enzymes, including a Mn-dependent form of superoxide dismutase, the free radical-quenching enzyme within the immune system. Manganese has also been shown to be important for the activity of cells produced in response to an immune challenge.

In the U.S., most forages contain adequate concentrations of Mn; however, situations of Mn deficiency are possible.

Selenium—A major function of Se is to protect biological membranes from oxidative degeneration due to the presence of free radicals, which can lead to tissue breakdown. The Se-dependent enzyme responsible for protecting cellular membranes from this oxidative damage—glutathione peroxidase—requires Se as a constituent.

Selenium is also closely linked to vitamin E, another antioxidant, and serves as an additional line of defense against free radicals. Selenium deficiencies in beef cattle can occur in many areas of the U.S., although locations should be evaluated on an individual basis to determine if supplementation is justified.

Copper and Zinc Supplementation and Immunity

Extensive research has been conducted to evaluate the effects of trace minerals on immune function and health status in beef cattle. The effects of trace minerals on immune response have been evaluated via determination of:

1. Morbidity and mortality rates,
2. Concentrations of antibodies produced in response to a virus (e.g., infectious bovine rhinotracheitis virus) or other foreign proteins (via injection of pig red blood cells or ovalbumin) during both primary and secondary humoral immune responses,
3. Skin swelling via a cell-mediated response to a foreign protein (via injection of phytohemagglutinin into the skin), and
4. Activity of specific immune-related enzymes.

Copper—Four studies used ovalbumin as an antigen to stimulate an immune response in beef cattle—two of the studies observed a greater immune response with Cu-supplementation vs. non-supplemented controls (Dorton et al. 2003; Ward and Spears 1999), while two studies reported that Cu supplementation had no effect on antibody concentrations during a primary immune response (Ward et al. 1997; Ward et al. 1993).

When a secondary immune response was evaluated using pig red blood cells as the antigen, a reduced secondary immune response occurred in Cu-supplemented cattle vs. non-supplemented controls (Ward et al. 1997).

When the effect of stress on immune response was evaluated in calves, Cu supplementation led to increased antibody concentrations to pig red blood cells in stressed steers, while lower antibody concentrations occurred in the non-stressed steers supplemented with Cu vs. nonsupplemented controls (Ward and Spears 1999).

Relative to cell-mediated immune response, researchers reported that a greater immune response occurred in calves receiving supplemental Cu compared to non-supplemented controls (Ward et al. 1997). However, other researchers observed no effect of Cu supplementation on immune response in calves (Ward and Spears 1999; Dorton et al. 2003) and a lower response in young calves receiving supplemental Cu compared to non-supplemented controls (Ward et al. 1997).

Experiments using feedlot cattle to evaluate the activity of the superoxide dismutase enzyme have reported inconsistent results. Greater enzyme activity in Cusupplemented cattle vs. non-supplemented controls was reported (Ward and Spears 1997), in addition to no effect of Cu supplementation on enzyme activity (Dorton et al. 2003; Ward et al. 1993).

Zinc—Spears and others (1991) reported that antibody concentrations to the Infectious Bovine Rhinotracheitis Virus (IBRV) tended to be greater in Zn-supplemented steers (from Zn-methionine or Zn-oxide) vs. non-supplemented control steers. Cell-mediated immune response has also been evaluated, but results have been variable.

In calves depleted of Zn for 21 days, those receiving no supplemental Zn had a decreased cell-mediated immune response compared to Zn-supplemented calves (Engle et al. 1997), while in another study heifers supplemented with Zn had a greater response compared to non-supplemented controls (Kegley et al. 2001). In contrast, however, Zn supplementation had no effect on cell-mediated immune response in steers (Spears and Kegley 2002).

Since feed intake is important to maintain the health status of newly weaned calves, the effects of Zn on feed intake have been evaluated. In two experiments Chirase and others (1991) observed that after an IBRV challenge, intake decreased in non-supplemented control steers vs. steers receiving supplemental Zn. In addition, steers receiving supplemental Zn returned to pre-challenge feed intakes three to five days sooner than non-supplemented controls.

Based on this research, it is apparent that the effects of trace minerals on immune response can be variable. The interactions among trace minerals, animal production, and disease resistance are extremely complex. Many factors can affect an animal's response to trace mineral supplementation, such as the duration and concentration of trace mineral supplementation, physiological status of an animal (e.g., pregnant vs. open), the absence or presence of dietary antagonists, environmental factors, and the influence of stress on trace mineral metabolism. Breed differences in trace mineral metabolism have also been documented (Gooneratne et al. 1994; Ward et al. 1995).

When Are Trace Minerals Most Important?

In beef cattle, the weaning process exposes calves to infectious agents (through commingling with other cattle, transportation on trucks, and visits to multiple facilities including sorting corrals, sale barns, and feedyards). Weaning also causes significant stress due in part to reduced access to feed and water, modified environment and climate, transportation, removal of milk from the diet, vaccination, and procedures such as castration and dehorning.

Stress caused by weaning and transportation can have a negative effect on the immune system (Blecha et al. 1984). Stress can affect mineral metabolism in cattle, particularly in young cattle arriving into a feedlot. Effects of stress can be exaggerated due to decreased feed intake, which can hinder a calf's ability to overcome pre-weaning nutritional deficiencies and can lead to an increased susceptibility to infection.

Based on the effects of stress, the NRC (1996) suggests that several nutrients be increased in the receiving diets of stressed calves, including increased concentrations of Cu, Fe, Mn, Zn, Co, Se, and iodine. These increases should be included in the 14-day receiving diet, since they are based primarily on decreased feed intake common in stressed calves.

Managing Trace Minerals to Maximize Immunity

To avoid a compromised immune system and immune response in cattle, efforts should be made to support a calf's immune system through proper nutrition. Feed and water samples should be collected properly and evaluated for trace mineral concentration in order to determine the amount of trace minerals being consumed by cattle.

In addition, blood and liver biopsy samples can be collected by a licensed veterinarian and analyzed for trace mineral concentration in order to determine the incidence of trace mineral deficiencies. To avoid or overcome deficiency situations, trace mineral mixtures should be formulated with the help of a nutritionist and/ or a university extension faculty member and provided as a supplement to both cows and calves.

It is important to use mineral concentration data from forage, water, and tissue samples collected over several seasons when formulating a mineral mix, in addition to monitoring consumption patterns by cows and calves in order to avoid a toxicity situation.

A calf's immune system includes several key components that must be supported via proper nutrition in order to function properly. In addition to adequate energy and protein, a calf's diet and body tissues should contain adequate trace minerals including Cu, Zn, Mn, and Se, which are important for immune system function.

Based on reported research, trace minerals are involved in immunity. If deficiency situations (energy, protein, minerals, etc.) can be avoided, calves should be able to develop and maintain an effective immune system. A properly functioning immune system will fight off immune challenges from the environment, enable vaccines to be more effective at preventing future health problems, and will help to avoid economic losses due to morbidity, mortality, and decreased performance.

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