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Role of trace minerals in cow-calf cycle examined

Although trace minerals are needed for a variety of physiological processes related to growth, reproduction and health, priority of use for the trace minerals in these physiological processes varies. Trace mineral requirements are often based upon the ability of the animal to maintain production performance parameters, therefore, when feeding trace minerals to maintain growth efficiency, other physiological processes might be encumbered.

By L. WAYNE GREENE, A. BRUCE JOHNSON, JOHN PATERSON and RAY ANSOTEGUI

Trace minerals function in various biological processes in cattle. They are needed for vitamin synthesis, optimum hormone production, enzyme activity, collagen formation, tissue synthesis, oxygen transport, chemical energy production and many other physiological processes related to growth, reproduction and health. Priority of use for the trace minerals in these physiological processes varies. For example, growth, feed intake and feed efficiency may not be altered during sub-clinical deficient states of certain trace minerals although impairment of reproduction or immunocompetence may be observed. The dietary requirement (National Research Council [NRC], 1996) of trace minerals is often based upon the ability of the animal to maintain production performance parameters. Therefore, when feeding trace minerals to maintain growth efficiency, other physiological processes might be encumbered.

Table 1 shows the trace mineral requirements for growing and finishing cattle, and cows (NRC, 1996). These requirements are based upon average cattle consuming average diets. Cobalt is required for the synthesis of vitamin B_{12} by the microbial population in the rumen. A vitamin B_{12} deficiency will primarily reduce rumen function and subsequent growth and efficiency. Dietary concentrations of cobalt at 0.1 mg/kg usually provide adequate vitamin B_{12} synthesis. Cobalt is not often reported to be deficient in the U.S. Copper requirements are set at 10 mg/kg and vary greatly depending upon other dietary components. Dietary molybdenum and sulfur form thiomolybdates in the rumen when fed in excess. Thiomolybdate complexes copper at both the gastrointestinal and tissue level rendering it unavailable to the animal (Suttle, 1991; Gooneratne et al., 1989). To correct for this negative interaction, it is recommended to supplement copper in most production environments. Iodine requirements are set at 0.5 mg/kg but this is based on limited data. Iodine is a component of thyroxine (T_4) and triiodothyronine (T_3), which regulates metabolism. A reduction in T_3 or T_4 can have dramatic effects on feed intake, growth and feed efficiency. Iodine is often supplemented in the organic form (ethylenediamine dihydroiodide, EDDI) in therapeutic doses to maintain hoof health. The Food & Drug Administration regulates EDDI use in cattle diets. Excess iodine will be excreted readily through urinary excretion. Iodine was often deficient before the use of iodized salt, but today, does not pose a significant problem due to the widespread use sodium iodide.

Manganese requirement for growing and finishing beef cattle is defined to be 20 mg/kg. Manganese is often supplemented to cattle to prevent any deficiencies that may exist. However, little information is available on the specific needs of manganese supplementation to cattle. Manganese content of feedstuffs is variable and usually higher than the animals' requirement. Identification of a manganese deficiency is difficult to determine due to the inconspicuousness of the deficiency symptoms. It is thought that in most environments, manganese is not severely deficient. Excess manganese supplementation does not create a problem because it is relatively non-toxic with a wide margin of safety. Iron requirements are recommended at 50 mg/kg. From a practical standpoint, iron is not deficient in beef cattle diets and is often found in excessive quantities. It is not uncommon to find dietary iron concentrations well more than 100 mg/kg in the dietary ingredients. Excess dietary iron (>100 mg/kg) will have detrimental effects on the bioavailability of other minerals. In many cases, significant amounts of iron are consumed directly from the environment by consumption of soil and other feed contaminants. The soil matrix holds iron tightly and soil iron is poorly absorbed through the gastrointestinal tract, but soil iron can be exchanged for other dietary elements to a limited degree and perhaps reduce the availability of other divalent cations. Selenium requirements are set at 0.1 mg/kg. Although deficiencies severe enough to cause clinical signs of white muscle disease are scarce, subclinical deficiencies do occur and often impacts production efficiency and health. Due to the rather small window of safety, excess selenium supplementation should be avoided. Recent concerns on the toxicity of selenium to wildlife have resulted in the FDA more closely scrutinizing the use of supplemental selenium in animal feeds. Zinc requirements of 30 parts per million in feedlot diets to maintain optimum growth is fairly easy to maintain. Formulation of diets with routine feed ingredients will provide a minimum of 25-30 ppm of zinc. Zinc is intimately involved with animal health due to its

■ *L. Wayne Greene is with the department of animal science, Texas Agricultural Experiment Station, Texas A&M University, Amarillo and Division of Agriculture, West Texas A&M University, Canyon; A. Bruce Johnson is with Zinpro Corp., Eden Prairie, Minn., and John Paterson[c] and Ray Ansotegui are with Animal & Range Sciences, Montana State University, Bozeman. Versions of this article were presented at the National Cattlemen's Beef Assn. mid-year meeting in July and a Zinpro Corp. beef nutrition symposium held earlier this month.*

role in various enzyme systems. As a consequence, supplementation of zinc for its therapeutic properties is often practiced in feeding livestock. It is not uncommon to find diets containing 60-100 mg/kg zinc. The extra zinc is not detrimental to animal production and may be extremely beneficial if animals are subjected to environmental stressors or are immuno-deficient. However, zinc is often deficient in forage-based diets. Other divalent cations (calcium, copper, manganese, iron) when found in the diet in excessive amounts can increase the requirement for zinc due to a reduced bioavailability.

Several factors will affect mineral requirements of beef cattle. Breed of cattle, level and stage of production, dietary interactions and form of supplemental minerals are a few factors that must be evaluated when developing mineral supplementation programs. Of these, mineral interactions and bioavailability are of practical importance when developing supplementation programs for grazing cattle.

Figure 1 shows some of the key interactions between trace minerals and other minerals found in the diet (Tillman, 1969). Depending on the interaction, these will act to either increase or decrease the level of supplementation required in the diet. For example, diets containing excessive amounts of iron, molybdenum and sulfur will result in significant increases in the requirement of copper and diets containing excessive amounts of copper will result in an increased requirement of zinc.

The supply of minerals in forages to grazing cattle does not meet the dietary requirement of most trace minerals (Table 1) because of a low forage mineral content or the presence of antagonists. Table 2 shows the average mineral composition of selected forages throughout the U.S. Copper is below the dietary requirement (10 mg/kg) in all forages evaluated except for legumes. Zinc is borderline deficient to deficient, whereas iron is above cattle requirements (50 mg/kg) in all cases. As shown in Figure 1, higher dietary intakes of iron interact negatively with copper and zinc to increase their requirement.

Oftentimes molybdenum and sulfur are high in forages, which also exacerbates a copper deficiency. Forage manganese concentrations appear to be adequate in most cases to meet the animals' requirement. Forage selenium concentrations are highly correlated with soil selenium concentrations. Forages grown in the Plains often have high concentrations of selenium and forages grown in the northeastern and northwestern U.S. are low in selenium, with forages grown in other areas of the U.S. being highly variable in selenium content.

When dietary trace minerals are not adequate to meet the animals' requirement either due to a deficiency or an antagonistic interaction, they must be supplemented. In fed cattle, incorporation of the mineral into the diet is the most efficient way of ensuring adequate intake. However, in grazing environments, supplementation of the mineral in free-choice mineral supplements is a necessity. Development of palatable mineral supplements is essential. Many sources of trace minerals are not available for absorption when fed, so the selection of mineral sources becomes critical. Table 3 shows the bioavailability of several minerals supplied from different sources. For inorganic sources of minerals, the oxide form is usually the least available and the sulfate form is usually the most available. Most data suggest that the organic sources of minerals are more available than their inorganic counterpart. Herd (1994) indicated that there are areas and times when forage mineral supply will provide all the minerals beef cattle need, especially if the production is low. He suggested that for higher levels of production, using a well-formulated inorganic mineral supplement employing the more available sulfate, chloride or carbonate forms will work very well. Herd (1994) further suggests that when dealing with nutritional stress, the organic sources of minerals will be advantageous. This may be especially true when supplementing to ameliorate the adverse effects of negative mineral interactions in the digestive tract.

The immune system

Overview of the immune system. In order to respond immunologically, whether it be to a foreign antigen that has been given as in a vaccine or one from the production environment, an animal needs to have an immune system that is responsive and capable of meeting any challenge. This defense system must attempt to eliminate these harmful challenges or antigens. Specific cells and proteins are produced to neutralize or destroy these specific antigens. This is the "acquired immune response" in action.

The immune system can be divided into two categories: (1) specific immunity — cell-mediated and humoral, and (2) nonspecific immunity — phagocytes, macrophages and polymorphonuclear neutrophils.

Primary lymphoid organs regulate the production and differentiation of these lymphocytes. The cell-mediated immune response involves the T-lymphocytes maturing within the thymus accumulating in lymph nodes and other lymphoid areas and then responding to a particular antigen in the form of T-cells. The function of T-cells are to help B-cells make antibodies, kill virus-infected cells, regulate the level of immune response and stimulate the microbial killing and cytotoxic activity of other immune effector cells, including macrophages. T-cells have a long life, months to years, which is beneficially responsible for delayed cell-mediated sensitivity.

B-lymphocytes develop in lymphoid tissue before migrating to thymus independent areas to become B-cells. From these B-cells is derived the humoral immune response which involves the production of antibodies or immunoglobulins. The time of antibody production following the exposure from a particular antigen that is new to the animal is relatively short and will maximize at about 10 days. In order to produce an antibody response, most B-cells require the presence of an antigen (T-dependent antigen) together with help from antigen specific T-cells. However, some antigens (T-independent) can directly stimulate B-cells without T-cells. The antibody response is measured as a titer, which will not become very high and persist for a short period of time (2-3 weeks). This first antigen response is termed the primary immune response. If this antigen is again administered, a secondary immune response will be more rapid and result in a higher titer level. This secondary response will usually persist for months.

Since the T-cell and B-cell response may require days to respond, the immediate immune defense are the phagocytes, PMN (polymorphonuclear neutrophils) and macrophages. The main function of PMN is phagocytosis and subsequent destruction of foreign materials. Macrophages belong to the mononuclear phagocytic system. Macrophages are capable of sustained phagocytic activity and they repair tissue by removing dead, dying or damaged tissue.

Role of trace minerals in the immune system. Several trace minerals play a major role in preparing the immune system to respond to such challenges. Zinc, copper, iron, manganese and selenium are usually considered the predominate players in such a role. Each trace mineral plays a unique, individual role. However, several may be involved in the same enzyme mechanism or response mode.

Zinc. Of the essential trace minerals, zinc has been studied most extensively. Zinc functions as a cofactor for more than 200 enzymes. The importance of zinc as a component of these enzymes could explain how zinc modulates immune function. Zinc is essential to the integrity of the immune system. Although the predominant influence of zinc deficiency is on various T-cell functions, the diversity of its effects is illustrated by a list of functions influenced by zinc deprivation. This includes thymus activity, lymphocyte function, natural killer function, antibody dependent cell-mediated cytotoxicity, neutrophil function and lymphokine production.

Zinc deficiency has been shown to produce gross atrophy of both the thymus and the T-dependent regions of the spleen. Helper T-cell function is also impaired. Zinc is also important in B-cell activity. In addition to level of deficiency, the timing of the deprivation in relation to the life cycle of the animal is an important determinant in the effect of zinc on immunity. For example, deprivation during fetal or early postnatal life suppresses the growth of the lymphoid organs to greater extent than the growth of other organs. Immunodeficiency induced by zinc deficiency during pregnancy may persist for up to three generations.

Another major consideration when considering trace mineral metabolism is the interaction between trace minerals. Zinc, copper and manganese are all known to interact with each other and with other trace minerals such as cadmium, molybdenum, iron, silver, mercury, selenium, arsenic and chromium. One of the more widely studied interactions is that between zinc and copper. This is due to the fact that competition between these metals is for binding sites on enzymes and on a class of metalloproteins called metallothioneins. Plasma metallothionein is one available measure for zinc and copper status.

Copper. Two copper containing enzymes, ceruloplasmin and superoxide dismutase, have been shown to exhibit anti-inflammatory activity. Thus like zinc, copper can be considered to have strong effects on the immune system. Copper deficiency has been shown to cause a basic T-lymphocyte defect reflected by increased susceptibility to T-cell mediated infections. The mechanism by which copper acts in altering immune responses may involve an interaction at the level of the plasma membrane. Copper has been shown to ameliorate the toxic effects on both T-cells and PMN leukocytes. It also has been shown that copper is involved in the structure of immunoglobulins. Although many aspects of the role of copper in host defense remain to be investigated, preliminary results indicate the potential for a significant interaction.

Iron. It has been shown that both cell-mediated and humoral immunity are compromised in iron deficient animals. Studies indicate that iron deficiency may have both augmenting and inhibitory effects on host defense mechanisms, with the ultimate result being dictated by the relative influence of the many pathways in which iron plays a role. While studies indicate an iron deficiency is associated with immune dysfunction, conditions associated with excess iron have been demonstrated to be immunomodulatory. Excessive serum iron may contribute to the virulence of certain iron-dependent bacterial pathogens by promoting their growth.

Manganese. There is little evidence that manganese plays a major role in immunological function. It has been reported to increase antibody titers and other nonspecific resistance factors in certain animals. Rats marginally deficient in manganese showed lower IgG agglutinins and a fraction of gammaglobulins. Interaction of manganese with neutrophils and macrophages has also been demonstrated. Increasing manganese has been shown to enhance the killing ability of macrophages via increased enzymatic activity within non-specific immunity.

Selenium. The interaction of selenium and the immune function focuses around the selenoprotein, glutathione peroxidase. Studies have shown a depression of humoral immune response. Selenium appears to be very important as an antioxidant and as a factor in the energy metabolism of phagocytic cells but the mechanism of its modulation of humoral immunity remains speculative yet centered around free-radical activity.

Research: Improving the immune status. Stressful conditions at any time during the lifecycle emphasize the need for adequate dietary levels of trace minerals (Table 4). The changes in status indicate the animal's need to respond as well as the ability to provide an adequate level of response. Stress from any source can cause this need to respond.

North Carolina researchers showed the one major cause in reducing early mortality of turkey poults was increasing the zinc and manganese levels and varying these sources in their diet. Increasing level of zinc and manganese increased the humoral antibody response (Figure 2), while sources were more important in increasing macrophage killing (Figure 3).

Graham et al. (1992) studied the effect of zinc source (zinc methionine) on health status in dairy cows. This study, which covered one year, showed a significant decrease in spontaneous abortion in cows supplemented with zinc methionine (Table 5).

There was a reduction in milk somatic cell count with the addition of zinc methionine from 320,000 to 200,000. In addition, the zinc-supplemented group demonstrated lowered levels of mastitis, lameness, calves born dead and removal from the herd because of poor performance (Table 6).

Galton (1989) evaluated the efficacy of zinc supplementation on dairy cow udder health when challenged with Strep. agalactia *(Table 7). The cows selected for this trial were infection free. The trial was conducted over a 120-day period. The cows were challenged daily. The zinc methionine group had a significantly lower somatic cell count. However, there was no difference in new mammary infections.*

Researchers at Montana State University (Ansotegui et al., 1994) measured skin fold swelling response over time in heifers fed no trace minerals, or equal levels of either inorganic or organic trace minerals. Significant increased responses were measured with supplementation with the complex treatment yield the higher, more rapid and complete swelling. These data suggest that the level of mineral intake effects skin fold swelling but source may influence the initiation of this response (Figure 4).

Lee (1991) demonstrated that both performance and health can be improved by complexed zinc or copper (Tables 8 and 9). Both improved average daily gain (ADG) 20%, while copper reduced number of sick cattle and treatment costs. Unknown in this study was the initial zinc and copper status of the calves.

Ward et al. (1992) demonstrated that source is a major concern by showing both improved performance and swelling response in incoming feedlot calves (Table 10). While all trace mineral treatments received the same amount, only the complex form increased performance above sulfate.

Skinfold swelling can be used as a very broad indication of the ability of an animal to respond immunologically. Rate of response, maximum level of response and prolonged activity of response are all critical measurements. This study revealed that source will alter all three of these response criteria (Figure 5).

Colorado researchers (George et al., 1994) investigated the possibility of increased trace mineral status rapidly by feeding increased levels. Performance was improved by varying source from inorganic to complexed (Table 11). Feeding three times these levels as complexes for 14 days then reducing this back to the more standard treatment levels showed significant improvements in period gains and overall feed efficiency.

A simultaneous companion trial using cattle from the same origin measured more closely the immunological parameters of these increased levels (Figure 6). Primary IBR antibody titers were increased by varying source of trace minerals. Increasing trace mineral levels for a short time (14 days) then returning to “normal” did not improve titer response.

This short-term increase did however exhibit a significant response in skin fold swelling (Figure 7). This 14 day 3X increase then return to normal levels with the complexes increased swelling response indicating the level is important in speeding up this general indication of immunity.

A responsive immune system is absolutely necessary to ensure proper performance under today’s diets and production standards. Trace minerals are an integral part of this response system. Selenium, although not discussed, is essential and regarded as primary in establishing this immunological response. As shown, zinc, copper, manganese exhibit integral roles as well. There is a wealth of additional data on IBR challenge models, PHA swelling responses, performance studies and now liver status levels.

Future work is needed on establishing status models, economic immunological models and measurements. Keep in mind that response time is a key function. Nutrients that are being used to help reduce a problem must be fed an adequate time before the stress or problems occur and continue to be fed during the problem or stress period.

Where do we stand?

Liver biopsy survey data from Texas to Montana. Copper deficiency has been identified as a serious problem for grazing ruminants (Ammerman et al., 1995). A deficiency may be due to low concentrations of copper in forage and can be further exaggerated when molybdenum and sulfur levels are increased. Molybdenum and sulfur interfere with copper absorption by forming thiomolybdates that bind copper resulting in compounds that cannot be absorbed by the animal (Gooneratne and Christensen, 1989; Spears, 1991). Decreased liver copper levels can be caused by excessive iron in the diet (Bremer et al., 1987).

Mineral status of beef cattle is not easily assessed. Evaluating serum copper concentrations has been a common practice to determine herd mineral status. Identifying trace mineral deficiencies from low levels in blood serum may be misleading. Serum copper levels do not correspond to liver copper, and are not considered a reliable indicator of copper status in cattle (Clark et al., 1993). All copper circulating in the blood is not available to the animal, and serum copper values can be affected by a number of factors, which include dietary molybdenum and sulfate, infection, trauma and stage of gestation (Puls, 1990).

Trace mineral supplementation can influence liver storage of copper and zinc (Swenson et al., 1996). Table 12 summarizes the status of several trace minerals in the liver. For copper and zinc, approximately 100 ppm (dry matter basis) is assumed to be adequate for the bovine.

Researchers from several states (Ansotegui and Swenson, Montana State University; Brink, University of Nebraska; Wikse, Texas A&M University; Corah, Kansas State University; Whittier, Colorado State University, and Johnson, Zinpro Corp.) provided liver biopsy data for approximately 1,100 cows. Figure 8 shows the average copper liver values (dry matter basis) for states surveyed and the variation within and among cows.

Table 13 summarizes average copper, zinc and molybdenum values from liver biopsies. If an average value of 80 ppm is considered adequate for liver copper, then all states had cows that would be considered marginally to severely deficient. These data would indicate that North and South Dakota had the lowest averages for liver copper. Zinc concentrations in the liver did not appear to be as negatively affected as were copper levels.

To determine how liver and serum concentrations of copper and zinc varied throughout the year, Swenson et al. (1996) collected liver samples five times from 60 first-calf heifers allotted to one of three mineral treatments: (1) complexed forms of copper, zinc, manganese and cobalt; (2) sulfate forms of copper, zinc, manganese and cobalt, and (3) no additional trace minerals (Swenson et al., 1997). Samples were obtained prior to supplementation, within 24 hours of calving, seven days prior to start of the breeding season, 150 day post-supplementation and 30 days prior to calving the following year. Figure 9 illustrates the influence of mineral supplementation in the presence of antagonistic minerals (molybdenum, sulfur and iron) on accumulation of copper in the liver. Both the complexed and inorganic supplements increased liver copper storage following calving in the presence of the antagonistic minerals, molybdenum, sulfur and iron. Heifers supplemented with complexed minerals maintained higher liver copper concentration 150 days after supplementation ended at breeding. It was evident that the antagonistic minerals did affect accumulation of liver copper in the control supplemented heifers, because copper levels remained low following calving and did not increase until supplementation with antagonists ended at breeding when animals were consuming green forage.

Serum copper values ranged from 0.6 ppm to 0.7 ppm, which is in a physiological range considered adequate. Serum copper concentrations did not differ among treatments at any collection period. The differences observed in liver concentrations were not accompanied by similar changes in serum. Evaluating mineral status of the heifers based on serum alone would have been misleading. The control heifers had marginal liver copper levels; however, serum concentrations were consistently higher than those of cows offered the complexed or inorganic supplements.

When considering the use of liver biopsy values as a tool for assessing mineral status of a cowherd, the question often is asked as to how many samples are required to provide adequate information. During November 1996, liver biopsy samples were collected from 238 beef cows following weaning at six different ranches in North and South Dakota and Nebraska representing operations on typical northern mixed grass prairie. The objective of this study was to determine the minimum sampling number required within herd for diagnosing beef cattle mineral status. Breeds of cattle included Black Angus, Red Angus, Hereford and Angus x Hereford.

At four of the locations, cows and heifers were pregnant. Samples obtained at the other two locations were from open heifers and cows. Herd averages for liver copper concentrations ranged from a low of 7 ppm to a high of 115 ppm, with only one of six herds being adequate as indicated by a mean greater than the recommended level of 80 ppm copper. Four of the herds appeared to be copper deficient with means of 18 ppm or less. Liver zinc averages ranged from 114 to 163 ppm, with all herds similar to or greater than the recommended level of 120 ppm zinc. Standard deviations were utilized to determine the minimum number of samples needed within a herd to detect a deficiency within 5 units of recommended normal (95% confidence level). Based upon standard deviations from herds with marginal to deficient copper levels, the calculated minimum number of animals required for sampling within a herd was 23.

Liver biopsy samples from live animals may provide a more reliable indicator for diagnosing sub-clinical trace mineral deficiencies if adequate sample numbers are collected. Too few samples may be misleading and not a true representation of herd trace mineral status.

Grotelueschen et al., (1995) supplemented over 600 cows with either no trace mineral, complex trace minerals or twice this level with the sulfate form (Table 14). Consumption was similar and adequate for all treatments. Both the sulfate and complex sources increased the cow's zinc and copper liver status while a slight reduction was seen in liver manganese status.

Source exhibited a much greater influence in the calf (Table 15). Liver zinc was adequate for all calves yet the complex source increased more than 50% from the control and sulfate form.

Source exhibited even a greater effect on calf liver copper status (Table 16). While forage by itself (control) provided a marginal liver status, sulfate form increased this level only slightly. The complex form more than doubled the sulfate form as measured by calf liver copper status. Increasing bioavailability of trace minerals during times of stress, i.e., calf, repeatedly increases the response and their presumed function.

At weaning, these calves were followed to the feedlot and health was monitored. Sick incidents over the total feeding period were significantly reduced in the calves on the complex pasture supplementation (Table 17). The question of "Is it zinc, copper, manganese, cobalt or the combination?" remains speculative yet practical management of level and source remains clear.

Determining the trace mineral status of the beef herd is complex due to the variety of factors that can influence mineral bioavailability, absorption and utilization. Forage and water mineral profiles provide information that can be utilized to evaluate potential mineral intake and possible problem areas (Table 18). It is important to identify high levels of antagonistic trace elements (molybdenum, sulfur and iron) as well as imbalances between other trace minerals. However, forage and water mineral analysis reports give no indication of bioavailability to the animal.

Table 18 demonstrates how forage values can vary within a ranch. All pastures would appear to be either adequate or marginal in copper. However, pasture C would cause further evaluation because of the antagonistic effect of molybdenum on marginal copper concentration in the forage. Ideally, the ratio of copper to molybdenum should be greater than 5:1. Additionally, the high sulfur levels in pastures B and C would also warrant additional evaluation because of the antagonistic effects of sulfur and molybdenum on copper metabolism. McDowell (1992) summarized the effects of a copper, molybdenum and sulfur relationship. Molybdenum in the presence of sulfur reduced the deposition of copper in organs and the synthesis of ceruloplasmin.

Serum mineral levels have been used for many years to determine if livestock require supplemental trace minerals. However, recent research indicates that serum mineral concentrations may not be an accurate measurement of mineral status for beef cattle because serum levels remain in physiological ranges even though the liver is deficient or depleted. McDowell (1992) summarized research data, which suggested that in rats, a high level of dietary molybdenum increased plasma, copper levels without relieving a copper deficiency.

Currently, liver biopsy samples collected from live animals may provide the best indication of trace mineral status (Table 19). Liver values reflect absorption and utilization of trace elements, and allow for the diagnosis of deficiencies. Once a deficiency has been identified, one must be cautious of supplementing with a single trace mineral, as it may be antagonistic to other trace minerals in the diet causing other deficiencies.

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