Nutritional Consideration of the Immune System

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Abstract

The immune response is mediated by both specific and nonspecific effector mechanisms interacting with invading agents or antigens. Nonspecific conponents include phagocytic cells such as neutrophils, monocytes, and macrophages. In contrast to the nonspecific elements of the immune system, which are capable of interacting with a broad array of antigens, some components, such as T cells, are specific in their recognition of antigens. The concept of vaccination against infectious diseases is based on these principles of immunological specificity and memory.

Cattle are exposed to a variety of stressors that stimulate non-specific and specific responses that develop either a natural resistance or an acquired resistance.

Many factors affect the responsiveness of the immune system. It has been well established that protein and energy malnutrition severely depresses the immune system. However, in recent years, the effects of trace minerals on the immune system has been documented. The trace minerals, zinc (Zn), copper (Cu), selenium (Se) and iron (Fe), have been demonstrated to be involved in immunocopetence. Vitamin E has been documented to effect the immune system.

The exact mechanism of immune depression with Zn deficiency is not know. However, many factors during BRD could lead to Zn deficiency and decreased immune response.

Serum Cu increases during infection. However, if Cu deficiency exists and inadequate liver storage exists, an impaired immune response can result.

Other trace minerals such as Fe and Se are involved in immunity responses in cattle. Iron deficiency anemia is associated with impaired cell-mediated immunity.

Trace minerals in deficiencies and in excesses can affect the immune system of cattle. The importance of trace minerals in nutrition of cattle is well known. The effects of trace minerals on immunity has been established, but specific levels and action have not been completely documented.

A discussion of the interaction of nutrients and the immune system with recommendation of nutrient levels to aid the immune system during receiving and processing is discussed.

Immunity is resistance to infectious agents, foreign particles and cells. The survival of the host is absolutely dependent upon a functional immune system. The treatment of disease frequently involves measures to diagnose and reverse these functional deficiencies. In other instances, such as auto-immunity and immune hyperactivity, a misdirected immune response can have a deleterious effect on the host, leading to interesting and challenging clinical problems. Thus, an understanding of basic immunology is necessary to successfully diagnose and treat a vast number of disorders.

The immune response is mediated by both specific and nonspecific effector mechanisms interacting with invading agents or antigens. Nonspecific components include phagocytic cells such as neutrophils, monocytes, and macrophages. In contrast to the nonspecific elements of the immune system, which are capable of interacting with a board array of antigens, some components, such as T cells, are specific in their recognition of antigens. For example, B cells from cattle immunized with infectious bovine rhinotracheitis (IBR) virus will produce antibodies that bind to IBR but not to unrelated viruses. Similarly, T cells, once committed to a particular antigen, will recognize and respond only to that antigen upon subsequent exposure. The concept of vaccination against infectious diseases is based on these principles of immunological specificity and memory.

Cattle are exposed to a variety of stressors that stimulate non-specific and specific responses that develop either a natural resistance or an acquired resistance. Infectious diseases normally develop specific immunity. Table 1 illustrates the observed antibody titers for selected viruses from cattle shipped from the southeast to the Texas Agricultural Experiment Station in Amarillo, Texas.

Table 1. Calves Without Antibody Titers to Selected Viruses.

Virus	No. Tested	Without Antibody Titer, %
PI3	903	45
BVD	904	74
BRSV	810	65
IBR	904	75

Calves may not have been exposed to a virus, or did not respond with antibody production when exposure to the virus occurred.

Many factors affect the responsiveness of the immune system. It has been well established that depressed intake of protein and energy severely depresses the immune system. However, in recent years, the effects of trace minerals on the immune system has been documented. The trace minerals, zinc (Zn), copper (Cu), selenium (Se) and iron (Fe), have been demonstrated to be involved in immunocompetence.

Stress has been shown to decrease the responsiveness of the immune system. Stress is defined as a nonspecific response of the body to any demand (Selye, 1976), and is the environment in which the animal resides (Frazer, *et al*, 1975). Stress alters the steady state of the body, or challenges the adaptive processes of cattle. Management of stress in feedlot cattle has two major components: 1) management of the environment, the stressor, and 2) management of the effects of stress, the quantified changes seen in animals. Nutrition and stress interact in at least two different ways: 1) stress can produce, or aggravate, nutrient deficiencies, and 2) nutritional deficiencies can produce a stress response. The management of feeder cattle from farms and ranches through the livestock marketing systems currently employed creates many stresses for cattle. The major stresses created are deprivation of feed and water, weaning, crowding and exposure to disease. Other stresses encountered either prior to or on arrival at the feedlot include weather changes, castration, dehorning, vaccination, dipping, deworming, and other processing. All of these stresses may be involved in altering the optimum nutrient requirements and responsiveness of the immune system.

One of the first stresses a calf encounters after leaving the farm of origin is weaning, then during the marketing system, feed and water deprivation. Weaning is a physical stress which is generally impossible to alleviate; however, management techniques such as preweaning and preconditioning have been used to reduce this stress. These techniques have been shown to be effective, but many times cannot be implemented due to cost and/or facilities. Feed and water deprivation during the marketing system is an important stress which has nutritional consequences. The rumen fermentation activity and capacity is significantly reduced during feed and water deprivation and remains depressed five days after refeeding. Other changes that occur are increases in rumen pH, serum osmolality, glucose and urea nitrogen; however, these variables return to predeprivation levels within 24 hours. Rumen protozoa and bacteria counts are lower in fast-transited steers than controls (Cole and Hutcheson, 1981 and Galyean, *et al*, 1980). These microbial numbers tend to recover slower when feed deprivation and transportation occurs than with feed deprivation only.

A study partitioning the weight losses during transportation when either a hay or a 50% concentrate diet was fed 72 hours prior to transportation was conducted and the hay diet resulted in a significantly higher weight loss than the 50% concentrate diet (Phillips, *et al*, 1985). Another study indicated that cattle transported either 1, 12, or 24 hours had 5.1, 7.0, and 7.6% shrinkage (Cole, *et al*, 1988).

Appetite or willingness to eat is low during the first few weeks after arrival. Table 2 illustrates the intake of healthy and morbid calves for a seven year period at the TAES research beef cattle facility. These data are from 17 experiments from control cattle that all received a similar diet (Hutcheson, *et al*, 1986).

Table 2. Feed Intake of Newly Arrived Calves (% of Body Weight).

Days After Arrival	Healthy Lbs/Hd/Day	Morbid Lbs/Hd/Day
1 - 7	1.55 (.51)[a]	.90 (.75)
1 - 28	2.71 (.50)	1.84 (.66)
1 - 56	3.03 (.43)	2.68 (.68)

[a]Standard Deviation.

Table 3 illustrates the average daily gains from the calves in Table 2. All weights were calculated from pay weights at purchase and a full weight at the day of weighing.

Table 3. Average Daily Gain of Newly Arrived Calves.

Days After Arrival	Healthy	Morbid
1 - 7	-2.13 (2.53)[a]	-5.70 (2.95)
1 - 28	1.30 (.79)	.01 (1.30)
1 - 56	1.96 (.26)	1.39 (.42)

[a]Standard Deviation.

Intake is reduced significantly during virus infection. Figure 1 illustrates the intake of calves prior to a virus infection, during a virus infection and recovery after the infection. The calves were tested prior to the virus infection and no antibody titer to infectious bovine rhinotracheitis virus (IBRV) was found. The cattle were infected with live virus and rectal temperature and feed intake was measured for 28 days.

Cattle energy requirements for a responsive immune system is difficult to determine. However, different energy concentrations has been fed to yearling cattle and IBRV given to them. Figure 3 illustrates the results.

The intake is better illustrated by comparing the energy intake rather than dry matter. Figure 3 shows the metabolizable energy intake for calves fed 3 levels of cottonseed hulls.

While in transit, plasma urea nitrogen of calves increases suggesting a net catabolism of body tissue nitrogen. Disease stress effects the nitrogen kinetics of

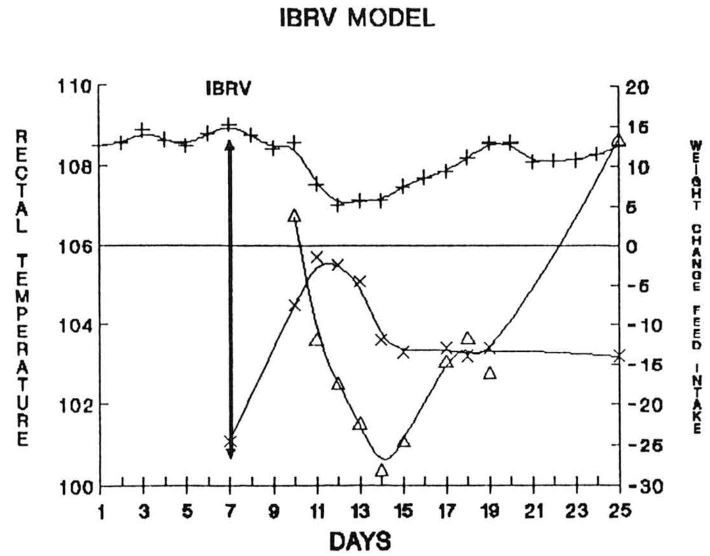

Figure 1

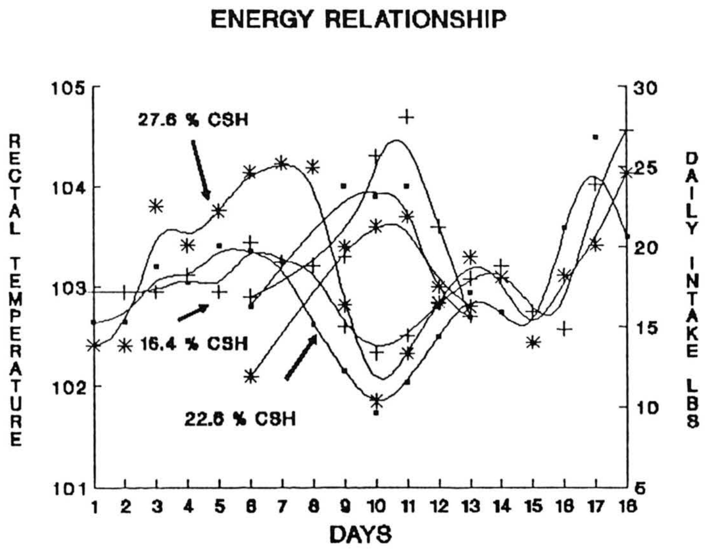

Figure 2

virus infected calves by shifting the rates of protein metabolism (Orr, *et al,* 1989). Figure 4 represents the changes in rate constants for virus infected calves.

Cattle subjected to the stresses of marketing and shipping encounter many metabolic changes, one of which is weight loss, primarily due to losses of body and digestive tract water. In the case of water losses due to transit shrink, water is lost from the digestive tract and then from the cells of the body. When water is lost from within the cells of the body, a cellular deficiency of K and sodium (Na) can occur (Hutcheson, 1980). Studies were conducted to determine the influence and level of additional K in the receiving diets of newly arrived feeder cattle on performance, morbidity, and mortality

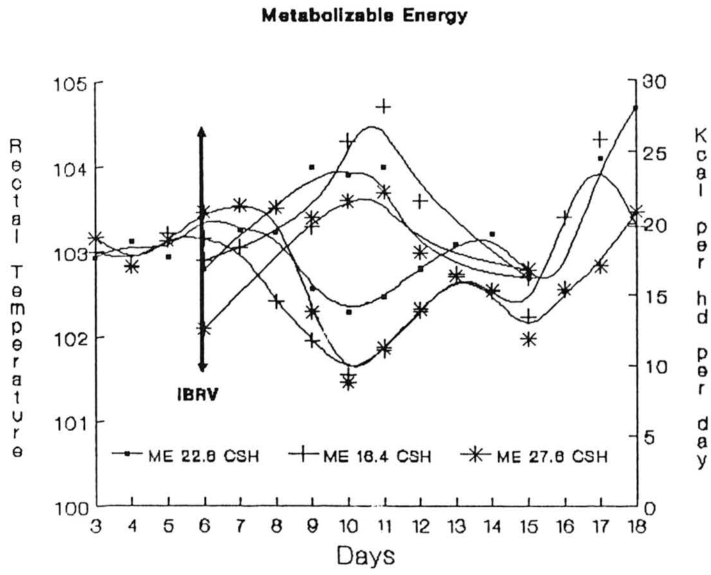

Figure 3

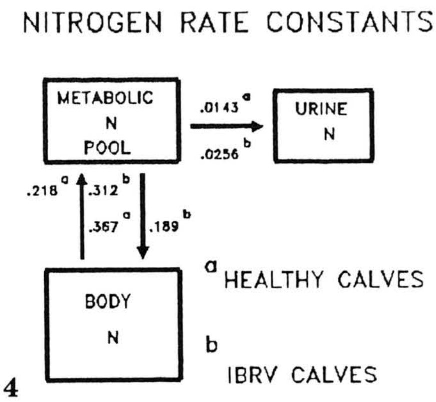

Figure 4

(Hutcheson, *et al,* 1984). Table 4 illustrates the data from 2 studies to determine the optimum level of K for receiving diets. Additional potassium was included in the diet for 2 weeks.

Table 4. Potassium Levels for Received Calves.

Level of Potassium Fed % of Dry Matter	Grams of Potassium per 100 lbs. of Body Weight 0-14 Days	0-28 Days	Average Daily Gain
.71	7.9	9.1	1.21
.86	8.6	10.3	1.50
1.27	11.5	11.6	1.70
1.41	14.6	12.9	1.76
2.15	21.1	15.5	1.36
3.11	29.3	19.1	1.25

This data suggests that 1.2 to 1.4 percent potassium in the diet is the most optimum level for newly received calves. It is important to note that potassium will give the largest response when the cattle shrink the most. If cattle shrink 2 to 4 percent, additional potassium may not result in a gain response, but with 7 or more percent shrink, a significant effect may be observed when additional potassium is added.

Summarizing the data from several experiments (Table 5), a significant reduction in death loss resulted with an increase in average daily gain and a decrease in feed to gain ratios when with additional K was added to the diet indicates the potential effect with of water balance on the immune system.

Table 5. Effects of Added Potassium.

	Potassium Level .8%	1.3%
Pay weight, lbs	455	443
Death loss, %	7.5	1.1
Calves treated, %	34.4	30.8
Average days treated	5.9	6.2
Daily feed intakes	11.6	11.4
Average daily gain	1.36	1.64
Feed/lb of gain	8.53	6.95

Niacin has been studied in receiving diets and Table 6 illustrates the average daily gains (Hutcheson and Cummins, 1984). Niacin added at 125 ppm seems to improve average daily gain of calves that were healthy. However, when calves were morbid, 250 ppm of niacin seemed to result in the best average daily gain. The best gains were observed when the cattle received 262 mg/cwt per hd per day.

Table 6. Average Daily Gains for Cattle Fed Niacin at Arrival.

	Days	
	0-28	29-56
Control		
Healthy	1.79	3.08
Morbid	.74	3.28
Niacin 125 ppm		
Healthy	2.16	2.93
Morbid	-.04	2.58
Niacin 250 ppm		
Healthy	.96	2.62
Morbid	.79	2.83

Figure 5 illustrates a study where vitamin E was fed for 28 days prior to IBRV infection, vitamin E injectable, and no vitamin E. The vitamin E in the feed seemed to give a more constitent response during IBRV infection.

Vitamin E Response

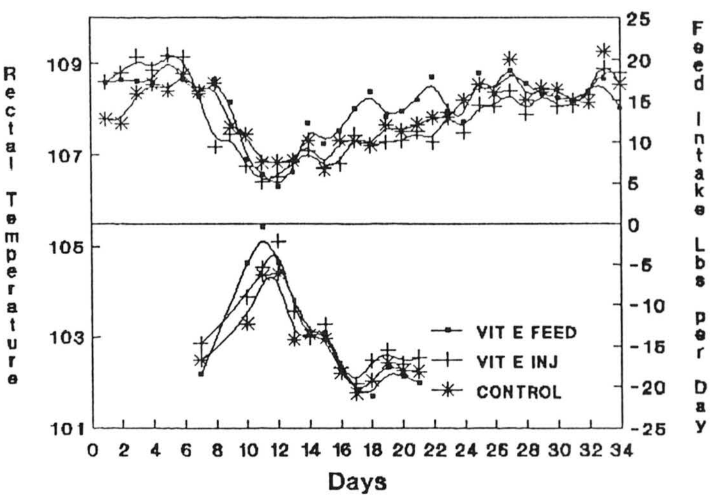

Figure 5

Vitamin E and selenium additions to receiving diets have resulted in a gain response (Hutcheson and Cole, 1985). Yearling cattle were backgrounded on a vitamin E deficient diet for 84 days and then fed varying levels of vitamin E and .1 ppm selenium (Table 7).

Table 7. Average Daily Gains for Yearling Cattle Receiving Vitamin E and Selenium.

Vitamin E IU/hd/day	Selenium Added	28 Day	56 Day
0	0	3.42^{c}	3.14
50	0	$3.71^{b,c}$	3.34
100	0	3.50^{c}	3.28
300	0	$3.90^{a,b,c}$	3.43
0	.1 ppm	$3.81^{a,b,c}$	3.35
50	.1 ppm	$3.89^{a,b,c}$	3.40
100	.1 ppm	4.38^{a}	3.47
300	.1 ppm	$4.35^{a,b}$	3.47

^{a}Significantly different P<.05.

One tenth (.1) ppm added selenium and 100 IU/hd/day of vitamin E resulted in maximum response for yearling cattle. Nutrient needs of diseased stressed cattle investigations have shown that additional Se can produce stimulatory effects on immunity. These same reports illustrate that deficiency of vitamin E and Se may depress immunity.

Serum zinc levels decrease dramatically immediately after virus infection (Figure 6). This study involved 8 calves that did not have antibody titers to IBR virus. The calves were challenged with virulent IBR virus and maintained in metabolism crates during the sampling period. Serum zinc is dynamic in the animal system. Serum zinc may respond to the lower fed intake of zinc which occurs during disease, or may be responding to the immune system. In contrast to declining serum Zn levels, excretion of urinary zinc increased significantly and in large amounts (Figure 7).

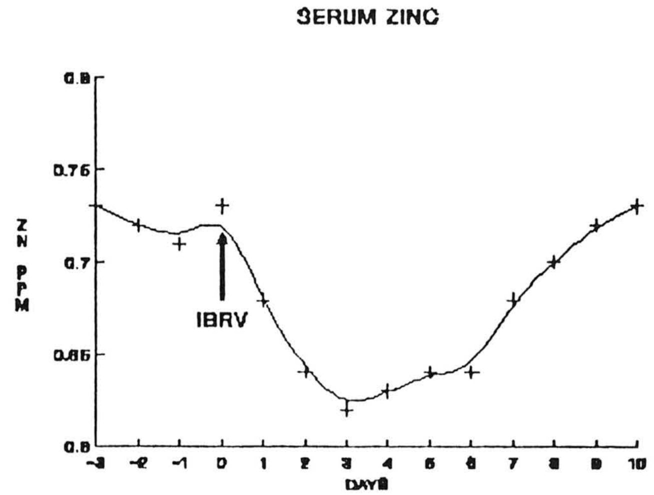

Figure 6

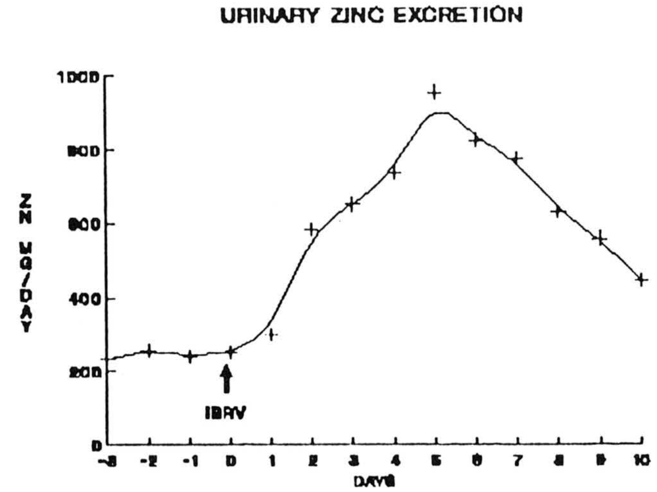

Figure 7

Therefore, the reduction in serum Zn may be partially accounted for by renal clearance. Serum and urinary Zn changes are a reflection of the body defenses to an infection.

Cell mediated immunity is decreased during conditions of Zn deficiency (Gross, *et al.*, 1979, Fernandes, *et al.*, 1979, Chandra, and Au, 1980). A deficiency of nucleoside phosphorylase is associated with severe T cell immune deficiency. This is indicative that zinc deficiency exerts a specific effect on the thymus, thymocytes, and cellular immune functions (Prasad, 1984). The cellular immune system depends on rapid cell proliferation and efficacy when functioning properly.

Table 8 illustrates the responsiveness of serum zinc during a natural outbreak of bovine respiratory disease (BRD). Peak morbidity occurred on day 7 of this study and serum Zn concentrations were significantly lower at peak morbidity than at the farm of origin, auction barn or in healthy pen mates. Therefore, the stress of marketing significantly reduced serum Zn.

Table 8. Mean Serum Zinc Levels for Calves During BRD.

	Healthy	Morbid
Day	PPM	PPM
Farm of Origin	1.66	1.60
Auction Barn	1.53	1.53
Peak Morbidity[a]	.97	.69
28 Day	.95	.93
No. of Calves	.33	67

[a] Means differ between morbid and healthy ($P<.05$).

A series of 3 experiments were conducted to determine the effect of source and level of zinc response when the animals were challenged with IBRV. Zinc methionine was used in all three studies. Table 9 illustrates the dietary concentration of zinc for the three studies (Charise, *et al*, 1991).

Table 9. Dietary Zinc for the Three Studies.

Experiment	Control	Zinc Oxide	Zinc Methionine
1	31.0	---	90
2	35.0	---	89
3	95.7	163	170.7

Figures 8 and 9 represent the first two studies. The studies were confounded with zinc source and level. The added zinc improved feed intake and reduced rectal temperature.

The third experiment was conducted with high levels of zinc using either zinc methionine (organic source), or zinc oxide (inorganic source). The study determined that added high levels of inorganic source was not well tolerated as evident by feed intake depression for 20 days after IBRV challenge Figures 10 and 11.

A fourth study was completed to determine the effect of source and level of zinc when animals were challenged with IBRV. Table 10 illustrates the levels and sources of zinc fed to cattle during the IBRV challenge.

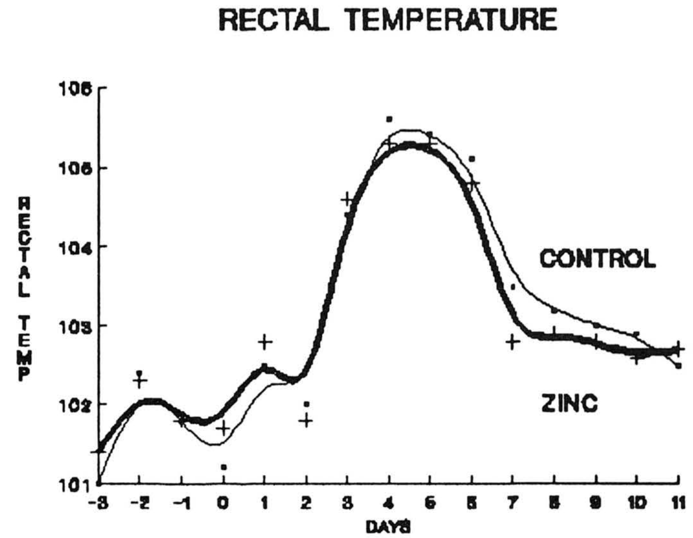

Figure 8.

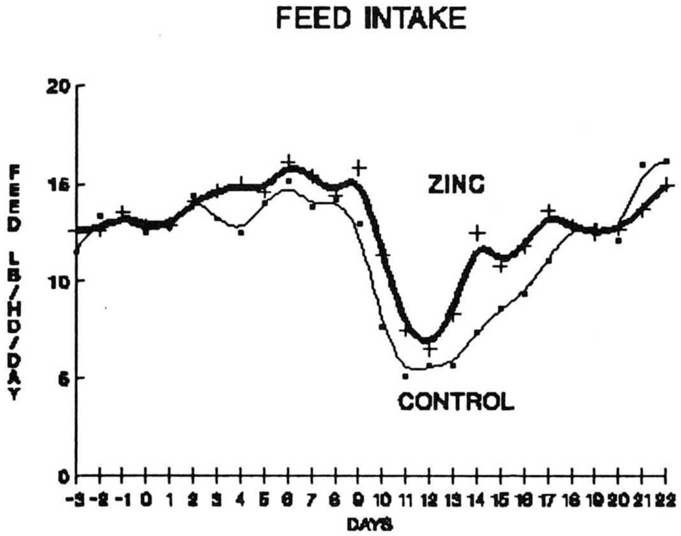

Figure 9.

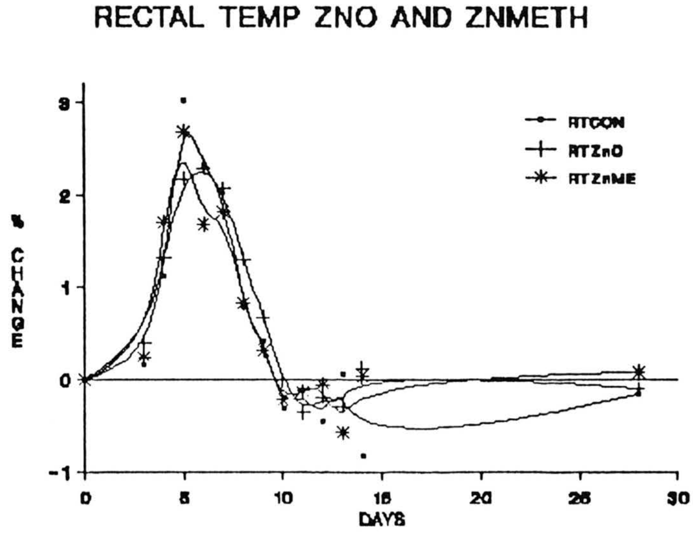

Figure 10.

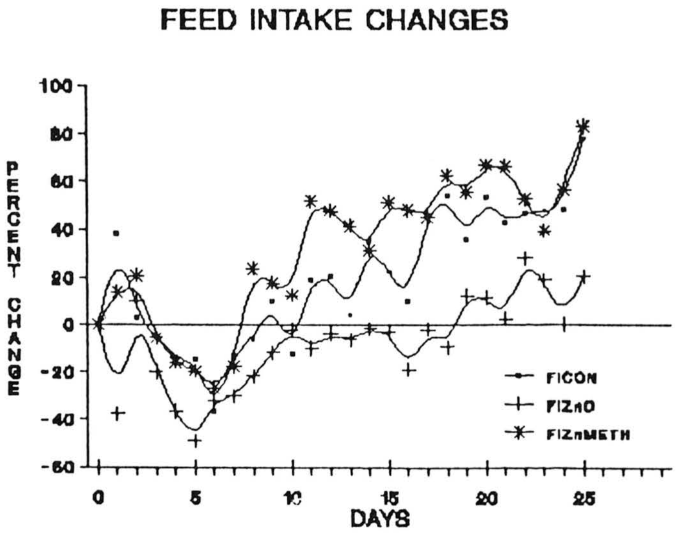

Figure 11.

Table 10. Source and Level of Zinc.

	PPM Zn
Control	42.4
Zinc Sulfate	75.0
Zinc Methionine	71.1
Zinc Proteinate	72.0

The control dietary zinc was from feedstuffs and 25 ppm zinc oxide. The other sources were added to the control diet to increase the level to 75 ppm zinc. Figures 12 and 13 are the rectal temperature and feed intake changes with the three sources of zinc(Blezinger, 1991). Rectal temperature provides an indicator of body core temperature. The mean rectal temperature for control (103.7) cattle was significantly (P<.05) higher than the zinc methionine (103.2) fed cattle with the zinc proteinate (103.6) and zinc sulfate (103.6) fed cattle not different from control or zinc methionine fed cattle. Rectal temperatures peaked on day 4 for control, zinc methionine and zinc proteinate, while zinc sulfate peaked day 5 after virus challenge.

Table 11 represents the average feed intake for 21 days after virus challenge.

Table 11. Feed Intake During Virus Challenge.

	lbs/hd/day
Control	9.0^{c}
Zinc Sulfate	10.5^{b,c}
Zinc Proteinate	9.6^{c}
Zinc Methionine	12.4^{a}

^{a,b,c}Superscripts differ. Means are significantly different, (P<.05).

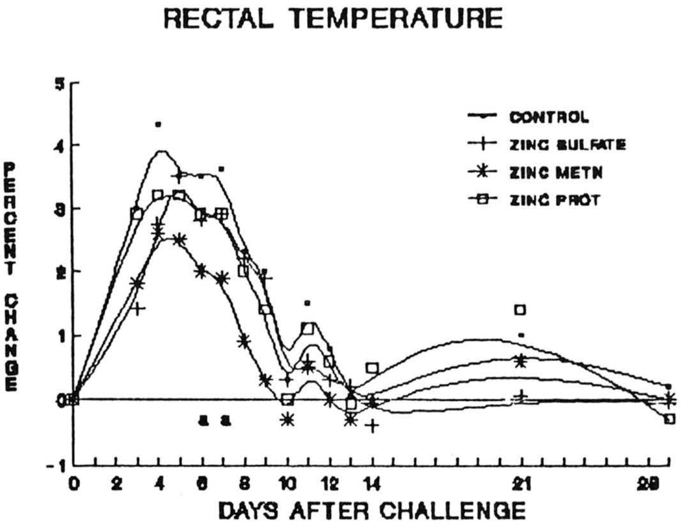

Figure 12.

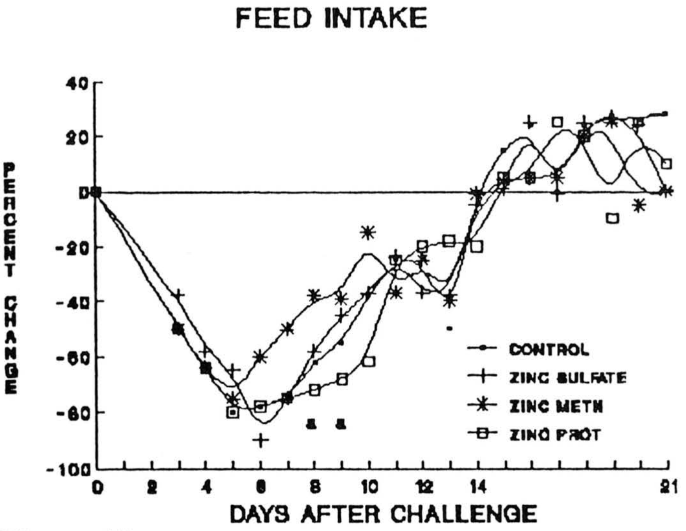

Figure 13.

Studies have been completed where cattle received zinc methionine prior to shipment during the cow/calf phase and the same levels during the feedlot phase. The data illustrated a benefit to added zinc from zinc methionine (Chirase, et al., 1991, Hutcheson, *et al.,* 1991, Spears, *et al.,* 1991) than zinc oxide. Less morbidity and better gains were observed with zinc methionine fed calves compared to zinc oxide fed calves.

These data would support that the organic forms of zinc methionine would have greater biological availability for the immune system than zinc sulfate, or zinc oxide.

Serum Cu increases during infection. Figure 14 illustrates the effects of serum Cu after IBR virus infection.

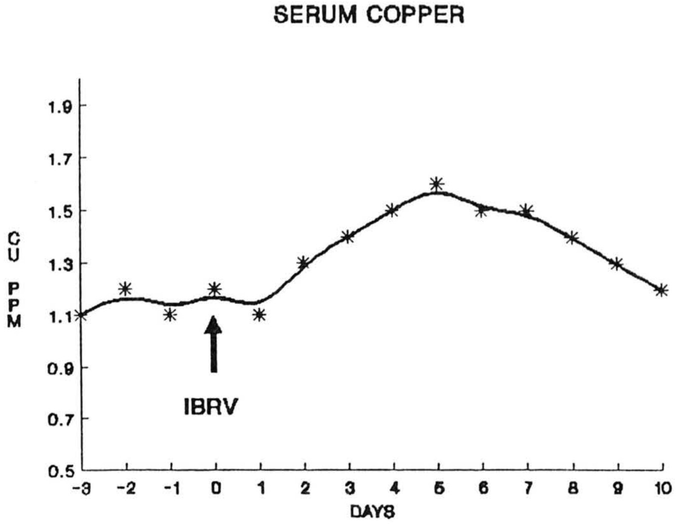

Figure 14.

The serum Cu had not returned to pre-infection levels after 14 days. The urinary Cu increases during infection; therefore, serum Cu increases are probably due to mobilization of Cu from the liver. However, if Cu deficiency exists and inadequate liver storage exists, an impaired immune response can result.

Table 12 illustrates serum Cu during a natural outbreak of BRD. Cu was significantly higher on the farm of origin compared to auction barn levels. The stress of marketing increased serum Cu, thereby mobilizing Cu. Copper deficiency has been associated with depressed immune response and an acute Cu deficiency may occur during BRD.

Table 12. Mean Serum Copper Levels for Calves During BRD.

Day	Healthy PPM	Morbid
Farm of Origin	1.03	.98
Auction Barn	1.17	1.15
Peak Morbidity	1.25	1.30
Day 28[a]	1.15	1.27
No. of Calves	33	67

[a]Means differ between morbid and healthy ($P<.05$).

Other trace minerals such as Fe and Se are involved in immunity responses in cattle. Iron deficiency anemia is associated with impaired cell-mediated immunity.

Trace minerals deficiencies and in excesses can affect the immune system of cattle. The importance of trace minerals in nutrition of cattle is well known. The effects of trace minerals on immunity has been established, but specific levels and action have not been completely documented.

Many changes, metabolic and biochemical, occur during different types of stress. The common most observed variable is a decreased feed intake. Since most diets are formulated in percentage, then care should be taken in formulation of diets for stressed cattle. Feed intake for newly arrived cattle is a major problem in ration formulation. The nutrients protein, potassium, selenium, copper, zinc, and vitamin E need to be considered for newly arrived feeder cattle. The immune system functions optimally when trace minerals are present in the rations for cattle. Critical nutrients must be prioritized for specific situations to ensure optimum performance during stress.

Table 13 illustrates the recommended nutrient levels for receiving diets. Many of the nutrients have been calculated, however, some have research data to support the recommended level. Cattle should be given free choice good quality hay on arrival. Each receiving program should be determined for each kind of cattle operation.

Table 13. Nutrient Recommendation for Receiving Calves.

Nutrient	Suggested Range
Dry Matter, %	80 - 85
Crude Protein, %	12.5 - 14.5[a]
Net Energy of Maintenance Mcal/cwt	70 - 75
Net Energy of Gain Mcal/cwt	37 - 40
Calcium, %	.6 - .8
Phosphorus, %	.4 - .6
Potassium, %	1.2 - 1.4[a]
Magnesium, %	.2 - .3[a]
Sodium, %	.2 - .3
Copper, ppm	10 - 15
Iron, ppm	100 - 200
Manganese, ppm	20 - 30
Zinc, ppm	75 - 100
Cobalt, ppm	.1 - .2
Selenium, ppm	.1 - .2[a]
Vitamin A IU/lb	2000 - 3000
Vitamin E IU/lb	50 - 100[a]

[a] Research at the TAES beef cattle facility has verified these nutrients, others are calculated.

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