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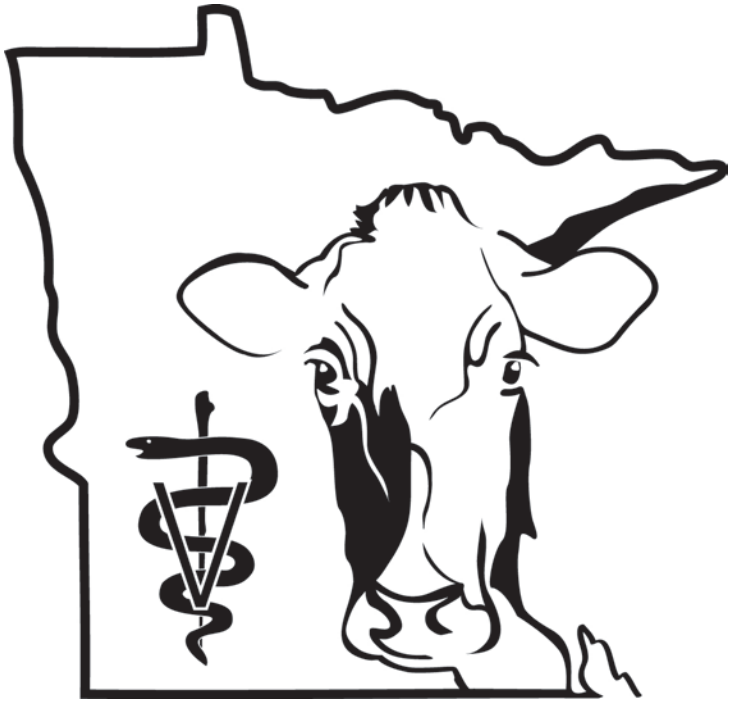

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Optimal Vitamin Nutrition for Functional Immunity in Cattle

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Introduction

The optimal vitamin nutrition concept seeks to establish levels of vitamin supplementation for a given species and physiological state that will produce milk, meat or fiber from livestock with maximal efficiency. Cattle in confinement production systems are subjected to levels of stress that challenge and can impair immune function (1). Mortality data from the 1996 NAHMS survey gives insight into the prevalence of disease in the dairy industry (2). Dairy producer and veterinarian alike are faced with the task of managing the ratio of disease exposure to disease resistance within limits that allow livestock to be profitable. Nutrition has long been known to influence disease resistance. Therefore the role of the vitamins in the immune system is a relevant topic to the dairy and beef cattle industries.

Functional Components of the Immune System

To those seeking to understand its function, the mammalian immune system presents an ever-growing array of biological complexity. For the purposes of this discussion a simplified version of the immune system is presented (3-5).

The immune system, being a primarily a defense system, is by necessity disseminated throughout the tissues and organs of the body. The immune system can be grouped into three main branches:

1.) skin and epithelial linings - forming physical barriers to invasion.

2.) innate immunity - a class of white blood cells (neutrophils, macrophages etc.) programmed to attack and destroy foreign cells or molecules.

3.) acquired immunity - mediated by a second class of white blood cells (T and B lymphocytes) which identify and "memorize" antigens (foreign organisms and compounds), enabling the body to mount a much more rapid and effective attack on the invaders the next time they may appear.

The skin and its derivatives, hair, hooves, horn, and the epithelial linings of the body, provide a physical barrier against microbial and foreign body penetration while allowing

the exchange of gases and water, the absorption of nutrients, and the secretory, excretory and reproductive functions vital for life. Members of innate and acquired immunity also occupy positions in these tissue layers acting as sentries against invasion. Peyers patches of the intestinal mucosa are an example.

The innate immune system consists primarily of the the neutrophils, basophils, eosinophils, mast cells, monocytes and macrophages. This class of immune cell are referred to as myelocytes (active origin in bone marrow). Each cell type has a unique jurisdiction. Neutrophils are the primary phagocytic cells of the blood and milk. Monocytes are precursors to tissue macrophages. Eosinophils attack parasitic organisms. Basophils are involved in allergic reactions. Mast cells are part of the "alarm system" of the skin, lung and gut epithelia. The cells of the innate immune system interact with the cells and organs of the acquired immune system, signaling the B and T lymphocytes to the presence of invaders.

The acquired immune system includes the B and T lymphocytes, the thymus, spleen and lymph nodes. This branch of the immune system produces antibodies and memory cells coding for specific antigens. The B lymphocytes produce antibodies and the T cells produce memory cells against microbial and other antigens. Each major antibody class has specific properties and functions. Likewise there are several types of memory cells, some of which destroy invading microorganisms and others which activate other components of the immune system. When a second invasion occurs the antibodies and memory cells signal the members of the innate immune system to the presence of intruders and then aid in their destruction.

Lymphocytes are categorized as T or B based on their origins. Although both cell types ultimately originate in bone marrow, T cells must undergo differentiation in the thymus gland while the B cells are further processed in the bone marrow prior to maturity. The term B cell is derived from the Bursa of Fabricius, their site of origin in birds.

Immune cells and organs communicate using a complex chemical language consisting of specialized molecules. Interleukins, cytokines, leukotrienes and interferons are some of the better known compounds. Directly or indirectly these compounds aid in the destruction of foreign bodies. This component of the immune system is the subject of much research today. The molecular details of immune system are beyond the scope of this paper.

The complement is an enzyme cascade within the immune system that is triggered by the presence of an antigen-antibody complex (3). Enzymes of the complement perform such tasks as lysis, opsonization, chemotactic signaling, agglutination and inactivation of foreign organisms and proteins. The immune system also contains general and widespread anti-bacterial and anti-viral enzymes and proteins such as lysozyme and the interferons (4).

Cellular Functions Required for Immune Defense

Immune cells and tissues must perform certain vital activities in order to mount an effective defense. The competence of the skin and mucosal linings depends on the normal production of collagen, keratin, elastin, glycoproteins and complex lipids. When these synthetic processes are disrupted by a lack of essential nutrients or impaired blood circulation, the integrity of the body's physical barriers deteriorates and begins to fail.

The effectiveness of the innate immune system depends on the production and differentiation of the neutrophils, monocytes and related leukocytes and the ability of these cells to migrate to the site of infection, engulf foreign microorganisms and destroy the organisms using oxygen radicals, enzymes and other compounds (5). Protozoans and other parasites are too large to be engulfed but are inactivated and destroyed by other mechanisms.

In acquired immunity T and B lymphocytes must undergo complete differentiation and maturation in order for these cells to be capable of producing a sustained molecular record or "fingerprint" of antigens in the form of antibodies and memory cells (3).

Applied Immunity of Cattle

In practical terms disease resistance in cattle depends on vaccination of otherwise healthy and well-nourished cattle at optimal times during development and adulthood, the strengthening of the immune system through optimal nutrition and management of stress levels. Optimal nutrition is an important factor in immunity as is true for all body systems. Stress in its many forms, both natural and man-made, is clearly an immune suppresser, although research shows that an optimal stress level exists at which point efficiency of production is maximal (1). In cattle parturition is a point at which the effects of stress, disease exposure, nutrition and management combine to determine the health and productivity of the cow and calf. Furthermore, immune function is depressed in the periparturient period (6-9), in part by adrenal steroid hormones (10). Not surprisingly, the greatest incidence of disease occurs at and around the time of calving (12). Much of the remaining disease occurs in the young calf or during periods of severe stress and heavy disease exposure such as the co-mingling of young cattle.

A critical event in the reproductive cycle of cattle is the success or failure of the dam in maintaining her own disease resistance while transferring sufficient immunity and nutrition to her calf via the colostrum. The success of this immune transfer depends on the care and nutrition of the cow prior to calving, as well as the care of cow and calf at birth. The transfer of immunity between cow and calf is made more precarious by the well-documented suppression of immunity that occurs around the time of calving (6-8). Estrogen and corticosteroids dominate the hormonal milieu during parturition and appear to cause the suppression of several components of the immune system, especially during the last 21 days prior to and the first 21 days following calving (8).

Immune suppression at parturition presumably serves a biological function, such as protecting the calf from the dam's immune system. Stress has long been known to depress immunity, primarily through secretion of adrenal corticosteroids (1,10,16). While calving is clearly a naturally stressful event, additional stress arising from the farm environment increases the likelihood of disease.

Other factors contribute to immune suppression. Certain intramammary antibiotics suppress neutrophil respiratory bursts (11). Coliform bacteria suppress the activity of milk neutrophils and disrupt the maturation of blood neutrophils (PMN) (11). Obesity reduces antioxidant defenses, impairing immunity (4). This may explain the observation of reduced disease resistance in the fat-cow syndrome.

During the parturient period, when the immune system is at low ebb, there is a concurrent nadir in the plasma concentration of vitamins E, A and beta carotene as well as several important microminerals including zinc and copper, which are co-factors for antioxidant enzymes (14,15,20,29). This suggests that nutrition may be used to offset some of the effects of parturient immune suppression.

Interrelationship of parturient disorders in cattle and the relationship with antioxidant status

Parturient disorders occur in conjunction with each other (12). The occurrence of a particular disorder can increase the risk of a cow developing a second disorder. For example, retained placenta significantly increases the risk of metritis (12). Although these relationships are at this point only statistical associations, scientists are searching for biological links between parturient diseases/disorders and the reduced activity of the immune system at parturition.

One potential effector of immune suppression may be the depletion of antioxidant capacity in the body (14,16). Plasma antioxidant status has a significant relationship to retained placenta, udder edema and mastitis. Plasma antioxidant status is in turn related to the dietary intake of antioxidant nutrients such as vitamin E. The final component of the equation is the oxidant load imposed on the body by external and internal sources. Pro-oxidants such as ferrous or ferric iron, mycotoxins and polyunsaturated fatty acids may be present in the diet. The cells of the immune system generate oxygen radicals during destruction of microorganisms. Therefore an increase in exposure to pathogenic bacteria will increase the demand for antioxidants in the immune system. Aerobic metabolism produces a constant load of oxygen radicals which must be quenched by the antioxidant vitamins and enzymes such as glutathione peroxidase, a selenium enzyme, and superoxide dismutase (SOD) which exists in two forms in mammals; a zinc-copper SOD and a manganese SOD (29). If the burden of oxidants depletes the antioxidant reservoir below a critical level, the body must reduce the activity of one or more of the systems giving rise to oxygen free-radicals. In the case of cattle the immune system appears to be affected (14).

Function of Vitamins in the Immune System

Vitamins are essential for the normal functioning of cells, tissues, organs and systems of the body, including the immune system. These functions will be discussed briefly in the context of the immune system components discussed earlier.

Skin and mucosal function

Skin integrity and mucosal function are dependent on vitamins A, D, E, C, riboflavin, niacin, biotin and pantothenate (15). Vitamin A is required for normal epithelial cell differentiation and maintenance. Vitamin A deficiency is marked by a deterioration and excess keratinization of epithelial and mucosal tissues (15,27). Incomplete cell differentiation and hyperkeratinization of mucosal tissues and glands causes the deterioration of the eyes (xerophthalmia) and taste buds, rough haircoat and reduced disease resistance of epithelial linings of the G.I. tract, respiratory tract and genito-urinary tracts with the related symptoms of diarrhea, edema and increased respiratory and ocular infections, characteristic of vitamin A deficiency (15,22,27).

Vitamin D and biotin are required for epidermal cell differentiation (22). Vitamin E affects capillary wall integrity and vitamin C is essential for synthesis of collagen (18,22,28).

Riboflavin, niacin, folate and pantothenate are required for normal skin integrity and secretions (22, 28). Topical pantothenate speeds healing of skin lesions. Deficiency of these vitamins cause characteristic skin lesions. Riboflavin, folic acid and niacin deficiency produce reddening and swelling of the tongue and oral cavity (28). Riboflavin and niacin deficiency cause deterioration of the mucous membranes and seborrheic dermatitis, particularly in areas of skin exposed to direct sunlight (22,28). Pantothenic acid deficiency is extremely rare except in cases of severe malnourishment. Biotin is required for production of keratin and the intracellular cementing substance of hoof horn, a complex of glycoproteins and essential fatty acids(22).

Cellular immunity: myelocyte and lymphocyte functions

The myelocytes (neutrophils, macrophages, etc) and the lymphocytes (T cells and B cells) are ultimately derived from bone marrow. Vitamins A and D are required for normal cell division and differentiation of these cells (5). There is an increase in the urinary excretion of vitamin A metabolites in a number of disease states (28). Vitamin D is involved in phagocytosis, possibly by regulating the contraction of the microtubule system (28). Vitamin E performs a crucial role as antioxidant within the white blood cells, protecting cell membranes intracellular oxygen radicals generated to destroy captive bacteria (24). Vitamin E and beta carotene also concentrate in the alveoli of the lungs where they perform antioxidant functions (22,24). Vitamin C is an antioxidant and regenerates

vitamin E after the latter has been oxidized (28). Consistent with this role, vitamin C is concentrated in the neutrophils (25). The B vitamins are required for normal production of antibodies by B lymphocytes (22).

Diet, Drug and Disease Interactions

This topic can only be addressed superficially in this paper. Some of the more important interactions that may reduce vitamin status are discussed.

The fat-soluble vitamins A, D, E and K absorbed by a common vehicle, primarily in the chylomicrons formed during fat digestion (22). The process is dependent on normal liver and pancreatic function. A minimal level of dietary fat is required for their absorption but the level has not been clearly established in ruminants. However the NRC minimum of 3% crude fat in ration dry matter is a reasonable minimum. Increased dietary fat levels increase absorption of vitamins A, E and beta carotene (22). However polyunsaturated fatty acids increase the requirement for vitamin E and biotin (21,22). High grain diets increase ruminal destruction of vitamin A and reduce biotin synthesis (22). Vitamin D activity is dependent upon adequate amounts of dietary calcium, phosphorus and magnesium (17,22). Vitamin E and selenium are interrelated in the biological antioxidant systems and immune function (34).

Although the mechanisms of transport and storage of the fat soluble vitamins vary, they interact with each other at the level of absorption. Therefore the dietary levels of these vitamins should be maintained within rational guidelines, avoiding both marginal levels and gross excess (22,32).

Vitamin A absorption is reduced by enteric disease such as coccidosis (30).
Liver or kidney disease or dysfunction would be expected to impair the metabolism of all the fat-soluble vitamins. Retinol binding protein is transported in plasma complexed with transthyretin, a thyroid hormone carrier (26). Thus vitamin A metabolism is related to thyroid function and iodine status (22). Displaced abomasum has been correlated to low vitamin A status (33). Interestingly, displaced abomasum and milk fever have been linked to O. Ostertagia infection (51).

Little is known about vitamin K metabolism in ruminants, although there is ruminal synthesis of menadione (22). Vitamin K is known to influence bone metabolism in non-ruminants (22). Therefore the roles of vitamin K and D are related. This may be a topic of future research in dairy cattle in relation to milk fever.

Thiamin status is reduced by feeding diets very high in soluble carbohydrate, in combination with high levels of sulfate, marginal copper levels and/or molybdenum concentrations of 2 ppm or greater (22,31). Diets of this type have been used experimentally to produce the thiamin-responsive polioencephalomalacia (PEM) sometimes seen in feedlots or in rapidly growing calves fed low forage rations. The relative contributions of thiaminases, anti-thiamin compounds, reduced thiamin synthesis

and hydrogen sulfide toxicity to this disorder are unclear. PEM is likely a multiple rather than a single disorder. Amprolium, which is anti-thiamin, is an additional confounding factor in calves being treated for severe coccidiosis. Vitamin B-12 status is affected by dietary cobalt (22).

Several pharmaceutical compounds affect vitamin status. Neomycin sulfate reduces vitamin A absorption (28). Prolonged use of corticosteroids depletes vitamin D and possibly vitamin C and E (28). Folic acid is depleted by some anti-protozoals (5).

Effects of Supplemental Vitamins on Immune Response

General:
Data from rats clearly shows the essentially of B-vitamins for antibody production. Individual deficiencies of thiamin, riboflavin, biotin or folic acid drastically reduce antibody production and growth rate (5). The requirement of vitamin A for T-cell proliferation is illustrated by data from chicks (5). An interesting finding from human clinical research in Australia is that children with a history of frequent respiratory infections respond to vitamin A supplementation with a 25% reduction in the incidence of respiratory disease (25). Young pigs respond to B- vitamin supplementation well above NRC levels with increased growth rate (5). The response occurred with both moderate and high antigen exposure.

Ruminants: stocker and feedlot animals
Vitamin E supplementation increases the antibody titer response to Clostridium Perfringens vaccination in lambs (5). Inclusion of vitamin E as an adjuvant in vaccines has been shown to increase antibody titer duration in cows and sheep (36).

Stressed beef calves (6 mo. old; 337 lb bwt) were injected with water soluble vitamins every 48 hours for 28 days starting 14 days prior to an inoculation with Bovine Herpesvirus-1 virus (1.1 M pfu intranasal) (51). The vitamin injection contained thiamin, riboflavin, niacin, folic acid, pantothenic acid, B-6, B-12 and 1000 mg vitamin C. The B-vitamins were in amounts of 2 to 30 times the estimated daily requirement per unit metabolic body weight.
Antibody titers of IgG were higher for vitamin treated calves on day 14 and 28 post infection, this despite the limited animal numbers of 6 per treatment group. Previous studies have shown reduce morbidity in feedlot receiving cattle supplemented with B-vitamins in the ration.

Vitamin C has been shown to be immunostimulatory in some species (23,25), including dairy calves (42), but its low rumen stability has been an obstacle to feeding. Recent data indicates that the 2-polyphosphate form of ascorbic acid is effective in increasing plasma ascorbic acid concentrations in dairy heifers (52). Researchers have reported that supplemental vitamin C is immunostimulatory in dairy calves, while some studies have found no effect (42, 45). Stability of vitamin C may have been a factor in these studies.

Vitamin C has been investigated as an anti-stress factor in cattle. In one study vitamin C had a beneficial effect on neutrophil function cattle treated with dexamethasone to simulate stress (38).

Supplemental vitamin E increased the response of lymphocytes to mitogen stimulation in dairy steers (22). Levels of 0, 500, 1000, 2000 IU/head/day were fed. Lymphocyte response was maximal at 1000 IU/h/day. Consistent with these results, performance of both receiving cattle and finishing cattle has been significantly improved by feeding 500 to 1600 IU/day supplemental vitamin E (53). Response to supplemental vitamin E will be influenced by forage vitamin E levels, stress, disease challenge, length of feeding, dietary oxidants and other factors (14).

Dairy cattle: reproduction, mastitis

There are relationships between reproduction and immunity in cattle. Supplementation with vitamin E has reduced the incidence of retained placenta and improved rate of conception in dairy cattle. An injection of selenium and vitamin E, 14 days prior to expected calving significantly reduced retained placenta and days open in a Florida study (37). All cows were fed 500 IU/day vitamin E and a diet containing .3 ppm selenium. The injection provided additional selenium and vitamin E coincident with the nadir in plasma concentrations which occur at calving.

A summary of 7 years of research involving 593 dairy cows at the University of Tennessee showed that cows fed 1000 IU/day supplemental vitamin E have significantly lower risk of having a retained placenta, udder edema and mastitis (14). Vitamin E status was also positively related to plasma antioxidant capacity, which was increased by feeding vitamin E.

Numerous studies at Ohio State University have found that supplemental vitamin E in the presence of adequate selenium in the diet significantly reduces intramammary infections and somatic cell count. Most recently (54) a regimen of 4000 IU/day during the last 2 weeks prior to calving and 2000 IU/day for 30 days after calving was shown to reduce clinical mastitis by 80% compared to controls (100 IU/day added vitamin E) and by 50% compared to the 1000 IU/500 IU regimen previously investigated. The higher level could be used effectively to target the parturient period in groups of cows with a high mastitis challenge. The economic return was 3:1 for the 4000/2000 IU treatment and 2:1 with the 1000/500 IU treatment compared to control. All diets contained .1 ppm selenium.

Research at the University of Vermont (40,41), using similar levels of vitamin E supplementation; (3000 IU/head/day for 56 days beginning 28 days prior to expected calving, plus an injection of 5000 IU vitamin E, 7 days prior to calving); has provided data on the effect of vitamin E on leukocyte function. Neutrophil superoxide production, neutrophil chemotaxis and plasminogen activity (an index of diapedesis) were all increased by vitamin E supplementation. The base diet contained .3 ppm selenium. During the 1980's several papers were published showing beneficial effects of supplemental beta carotene on intramammary infection rates. Feeding 300 mg/day of

beta carotene (500,000 IU of vitamin A activity) with a base diet of 53,000 IU vitamin A per day reduced somatic cell count compared to the base diet alone. Feeding 173,000 IU vitamin A gave statistically similar results to 300 mg beta carotene although numerically less effective (5,22). Other studies did not find this effect. A recent experiment reported some improvement in reproduction and a significant increase in milk production in response to feeding 400 mg/day beta carotene, although the vitamin A content of the base diets was not reported (55). There is an interaction between vitamin A status of the animal, forage carotene content, efficiency of absorption of beta carotene, season and breed of cattle which affects the response to supplemental beta carotene (22). Low forage carotene content and high stress levels would be conditions expected to elicit a beneficial response from supplemental beta carotene.

Beef and Dairy Calf Performance

Feeding 1000 IU per head per day supplemental vitamin E to beef brood cows starting 60 to 90 days before expected calving and for 60 to 90 days after calving can significantly improve calf performance (47,49). Plasma or serum vitamin E concentrations are increased in both cows and calves by vitamin E supplementation of the cow. Calf scours were reduced and plasma Ig levels and average daily gain were increased in calves from cows fed 1000 IU/day supplemental vitamin E. The response was greatest in spring-calving cows, probably due to forage quality of the winter ration.

Several studies have shown improved immunity and performance in dairy calves fed 200 to 400 IU/day supplemental vitamin E (43-46). Vitamin A levels can also affect performance of young calves (46). Many milk replacers now supply 100 to 150 IU vitamin E per pound of powder, and should contain 20,000 to 30,000 IU of vitamin A and 1400 to 1800 IU/lb vitamin D.

Dairy and Beef Cattle: hoof health

Vitamins affect the integrity of skin and its derivatives including the hoof. Results of 7 controlled clinical studies show that 20 mg/day supplemental biotin significantly reduced the incidence of several common hoof disorders (50). The reduction in the incidence of hoof disorders was accompanied by an increase in hoof hardness and tensile strength, as well as improvements in the intracellular cementing of hoof horn cells at the microscopic level. Ancillary studies found that rumen biotin synthesis is reduced by higher grain levels in the ration. Biotin is required for normal differentiation of the hoof epidermis and production of keratinized, cemented hoof horn and has been shown to reduce hoof disorders in swine and horses (22). Biotin is a prosthetic group for several key enzymes involved in gluconeogenesis, fat and protein metabolism in mammals (22,28). Biotin status is may be marginal in high producing cows fed higher concentrate rations. These animals would have the greatest metabolic demand for biotin combined with reduced ruminal biotin synthesis.

Diet Supplementation Guidelines for Cattle

Research to date supports feeding 1000/500 IU per day supplemental vitamin E in dairy cows during the dry period and lactation, respectively. The higher level of 4000/2000 IU during the last 14 days prepartum and first 30 days postpartum is warranted for herds with a high mastitis challenge (25 to 30 % clinical cases or more). Vitamin A levels should be maintained at 100,000 to 125,000 IU/day year round with higher levels (150,000 IU/d) used during periods of high stress, such as exposure of the herd to respiratory disease or when ration fiber levels are marginal. Vitamin D guidelines are 30,000 and 40,000 IU/day for dry and lactating cows, respectively. The levels may be increased to 35,000 and 50,000 IU/day under some conditions, for example an increase in the incidence of hypocalcemia following prolonged periods of low exposure to sunlight.

Feeding beta carotene at 200 to 300 mg/day fed for 90 days, beginning 14 days prepartum, may improve breeding performance of cows fed low-carotene forages for prolonged periods (56). Biotin supplementation at 20 mg per cow per day has been shown to reduce the incidence of several common hoof disorders in dairy and beef cattle. This supplementation should be targeted on herds with chronic hoof problems where other management steps are also being taken to control the problem. Cows fed high grain rations and high producing cows would be most likely to have marginal biotin status.

Final Thoughts

1. Cost-effective nutrition is balanced nutrition. Nutrients, when consumed in proper quantities, work in concert to maintain and optimize the function of body systems. The role of vitamins in immunity is a good example.

2. Avoid the common pitfall of viewing nutrients in isolation. The latter viewpoint can lead to the nutritional fallacy of "if a little bit is good, then a lot would be better", which is wasteful and can endanger the welfare of animals and people.

3. The most noble efforts at supplying livestock with optimal nutrition are largely wasted in situations where animal husbandry and farm management are in a state of neglect, benign or otherwise. The nutritional program must fit the management of the farm business.

4. Optimal nutrition supports optimal animal health and productivity. Optimal nutrition itself is not a treatment or therapy for disease. However optimal nutrition and preventative medicine are highly synergistic. Therefore it follows that together, professional nutritionists and veterinarians can have synergistic effects on farm productivity and profitability.

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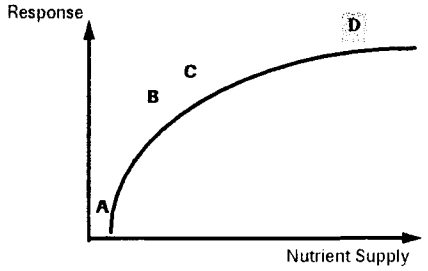
Vitamins and Immunity

Optimum Vitamin Nutrition for Immune Function in Cattle

Optimum Vitamin Nutrition Concept



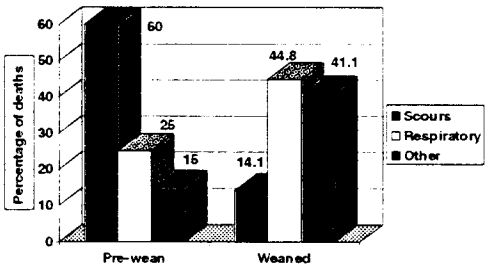
Non-culling deaths of U.S. dairy cows and calves: 1996 NAHMS

- Pre-weaned calves: 10.8%
- Weaned calves and heifers: 2.4%
- Cows: 3.8%

Causes of Death in U.S. Dairy Cows: 1996 (%of deaths)

• Calving	18.3%
• Other known	17.0%
• Mastitis	16.3%
• Unknown	14.8%
• Lameness	12.7%
• Respiratory	9.6%
• Digestive	9.0%

Causes of death in calves and heifers: 1996 NAHMS

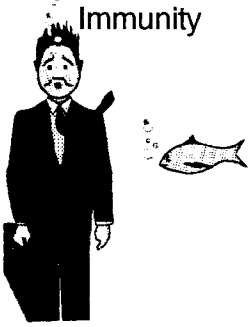


Manage:

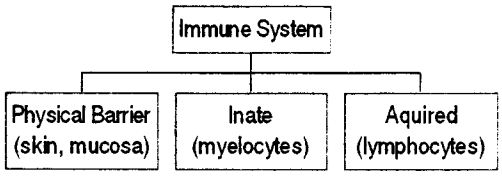
Disease Exposure

Disease Resistance

Functional Components of Immunity



Organization of Immune System



Immune System-Components

1.Physical barrier - skin, mucosa

2."Inate" or "Non-specific" - mast cells, neutrophils, basophil, eosinophil, monocytes.

3."Acquired", "Specific" - T-cell and B-cell mediated response to antigens; memory cells, antibodies.

Immune System Components and Functions

- Skin and mucosa - physical barriers to invasion.
- Myelocytes - destroy invaders.
- Lymphocytes - identify and "memorize" invaders.

Organs and tissues of immune system

- Lining respiratory, G.I., genito-urinary tracts; mammary and salivary glands - skin, mucosa.
- Bone marrow - myelocytes.
- Thymus, spleen, lymph nodes, Peyer's patches - lymphocytes.

Immunoglobulin Classes

- Ig M - acute infection; 10 binding sites.
- Ig G - bind antigens and macrophages.
- Ig A - lung bronchi and small intestine.
- Ig D - bind antigens to B cells in plasma.
- Ig E - parasitic infections and allergies; interact with eosinophils and basophils.

Cell Type Distribution - Leukocytes

Cell Type	Cow	Pig	Horse	Dog
Neutrophil	30	40	55	60
Lympho-	60	50	30	25
Mono-	5	8	10	8
E & B	6	3	5	6

Immune System Molecules

Interleukins -talk between WBC
Interferons - fever, antiviral
Platelet activating factor
Fibroblast growth factor
alpha-2-Macroglobulin
Leucotrienes
Cytokines
Granulocyte stimulating factors

Additional Immune Functions

- Complement system: enzyme cascade; responds to antigen-antibody complex. Lysis, opsonization, chemotaxis, agglutination and viral inactivation.
- Lysozyme, basic polypeptides, properdin, interferons.

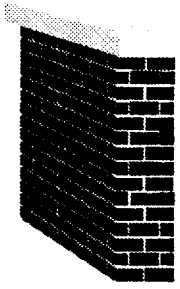
Skin and mucosa: barriers to invasion

1. Epidermis:
   Str. germinativum: cell division.
   Str. corneum: dry, hardened surface layer (keratinized, cornified layer).

2. Dermis (corium):
   blood, lymph, nerve supplies.

Skin and mucosa: compounds

1. Collagen
2. Keratin
3. Elastin
4. Glycoproteins and complex lipids



Myelocytes - Inate

Neutrophils	**-attack blood borne invaders**
Monocytes	**- migrate to tissue beds; become macrophages.**
Macrophages -circulating -stationary	**-derived from monocytes** **-skin, liver, lungs, spleen, lymph nodes, bone marrow.**

Myelocyte functions (neutrophils, monocytes, macrophages)

Diapedesis - squeeze through capillary walls.

Chemotaxis - migration to infection site based on chemical signals.

Phagocytosis - engulfment of microbes (followed by destruction by enzymes and oxygen radicals).

Lymphocytes

- Lymphocytes produce specific (acquired) immunity.
- Maturation in lymphoid tissues.
- B -Cells from bursa of Fabricius in birds or bone marrow(?); produce antibodies.
- T-Cells from Thymus gland; produce memory cells.

Applied Immunity in Cattle

Passive Transfer of Immunity

- Sanitation
- Colostral Ig concentration: >50 mg/ml (90% IgG, 5% IgA and 5% IgM).
- Colostral intake: 6-8 lbs.
- Time after birth: 12 - 24 hours.
- Vitamins A and E in colostrum.

Immune Suppression at Parturition

- Reduction in neutrophil and lymphocyte function days -21 to +21 peripartum.
- Hormonal effects: estrogen, adrenal corticosteroids dominate.
- Transfer of Ig and vitamins to calf.
- Disease exposure vs resistance.
- Optimum stress level

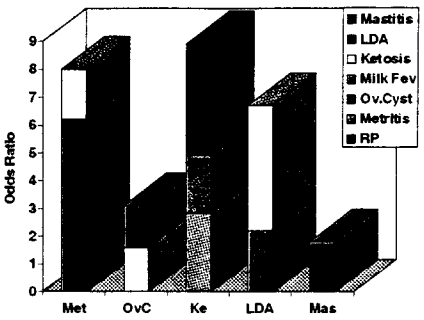
Immune Suppression at Parturition

- Vitamins E, A, beta-carotene. 9,13 di-cis retinoic acid(?). Vitamin C?
- Antibiotics can reduce PMN respiratory burst.
- E.Coli suppress milk PMN and disrupt maturation of blood PMN.

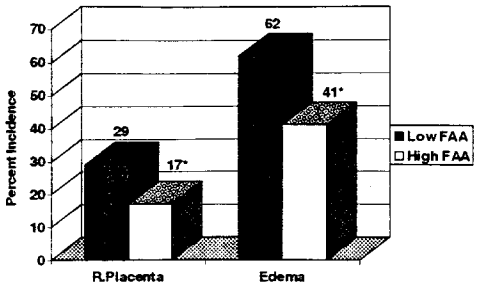
Parturient Disorders

- Relationship to immune suppression and nutritional history.
- Relationship of PMN respiratory burst to susceptability to mastitis.
- Relationships to plasma anti-oxidant concentrations and antioxidant vitamins.
- Disease interrelationships.

Disease Interrelationships (Grohn, 1997)

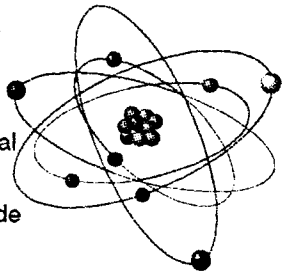


Plasma Antioxidant Status and Parturient Disease in Dairy Cows



Free Radicals

- Jerry Rubin
- Eldridge Cleaver
- Susan Sonnstag
- Bobby Seals
- superoxide radical
- hydroxy radical
- hydrogen peroxide



Role of Vitamins in Immune Functions

1. Skin and Mucosal Integrity

Vitamin A - epithelial differentiation, keratin production.

Vitamin D - epidermal (keratinocyte) differentiation.

Vitamin E - capillary wall integrity.

Role of Vitamins in Immune Functions

1. Skin and Mucosal Integrity

Vitamin C- collagen synthesis (PQQ).

Riboflavin, Niacin, Biotin, Pantothenate skin integrity, keratin synthesis, keratinocyte differentiation, hair coat, mucosal secretions.

Role of Vitamins in Immune Functions

2. Cellular Immunity (myelocyte and lymphocyte functions)

Vitamin A - transcription, cell division.

Vitamin D - transcription, phagocytosis, myelocyte differentiation.

Vitamin E - antioxidant / membranes, bactericidal activity of PMN.

Role of Vitamins in Immune Functions

2. Cellular Immunity(Myelocyte and lymphocyte functions).

B - carotene - antioxidant (alveoli); localized in lymphocytes, neutrophil killing ability enhanced.

Thiamine, Riboflavin, B-6, Pantothenate, and Biotin - antibody production.

Role of Vitamins in Immune Functions

2. Cellular Immunity (myelocytes, lymphocytes)

Folic Acid, B-12 - cell division, antibody production.

Vitamin C - antibody production, phagocytosis, antioxidant regeneration of tocopherol, PMN function. Anti-stress vitamin?

Vitamin A

Diet: vitamin E, D, beta carotene, zinc, iodine, phosphorus.

Drug: Neomycin sulfate, halogenated hydrocarbons, estrogen, progesterone.

Disease: fever, enteric disease (cocci, crypto), fatty liver, hypothyroidism, bilary disease, toxins, LDA?.

Vitamin D

Diet: vitamins A, E, C, calcium, phosphorus, magnesium.

Drug: corticosteroids, anticonvulsants.

Disease: skin, liver, parathyroid, renal, intestinal, bone, bone marrow disease.

Vitamin E

Diet: vitamin A,D,K,C,B-12, selenium, PUFA, iron, zinc, sulfur amino acid.

Drug: nitrofurans, acetaminophen, estrogen, anticonvulsants.

Disease: liver, intestinal, hemolytic, toxicosis, mastitis, metritis.

B-Vitamins

Diet: high grain, high sulfates, low copper, high molybdenum, cobalt, PQQ.

Drug: amprolium, some other antiprotozoals, some tetracyclines?

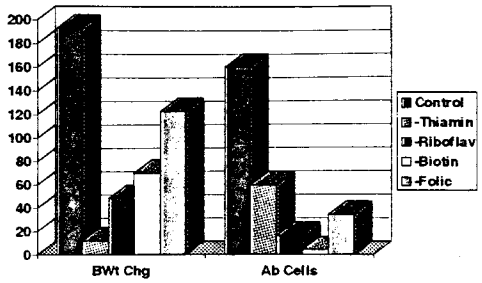
Disease: ketosis, diabetes, polioencephelomalacia, fatty liver, thyroid disease.

Vitamin Effects on Immunity

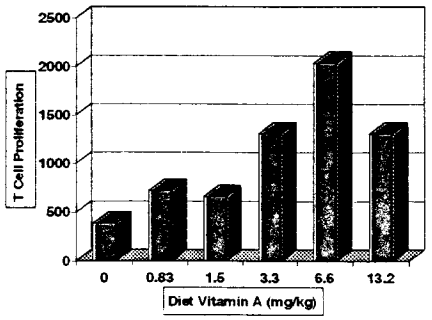
1. Examples from non-ruminant research.

2. Examples from ruminants.

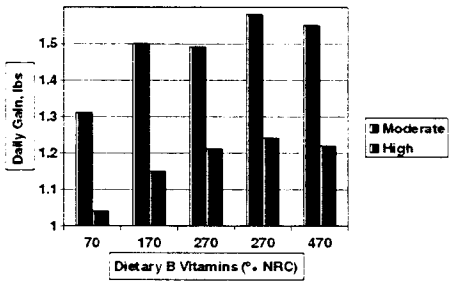
B-Vitamin Deficiency on Body Weight Gain and Antibody Forming Cells (rats)



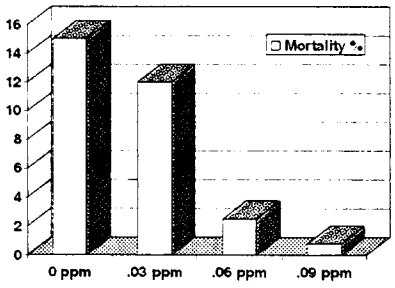
Vitamin A on T-Cell Proliferation (chicks)



Response of Piglets to Diet B Vitamins with High or Moderate Antigen Exposure

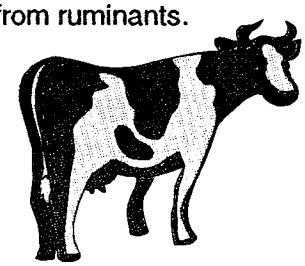


Effect of dietary biotin on FLKS mortality in broilers at 5 weeks of age (Whitehead et al. 1975)

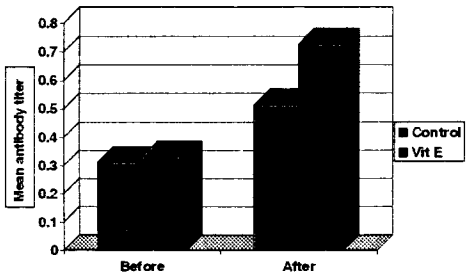


Vitamin Effects on Immunity

2. Examples from ruminants.



Vitamin E supplement on antibody titers in lambs before and after C. Perfringens vaccination



Vitamin Effects on Immunity

Inclusion of Vitamin E (DL-alpha tocopherol acetate) in vaccine adjutants increases immune response (Ig titer duration) in cows, sheep, poultry and mice.

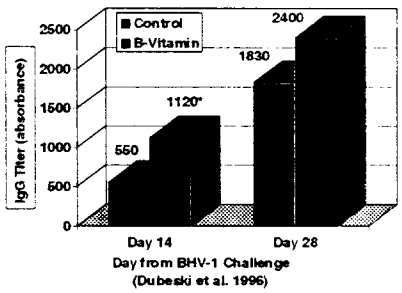
Effect of Supplemental Vitamin E on Mitogen-Stimulated Proliferation of Lymphocytes from Dairy Steers

Supplemental Vitamin E (IU/H/D)	Lymphocyte Proliferation, 56 D
0	114.2[a]
500	147.0[a]
1000	638.6[b]
2000	353.6[ab]

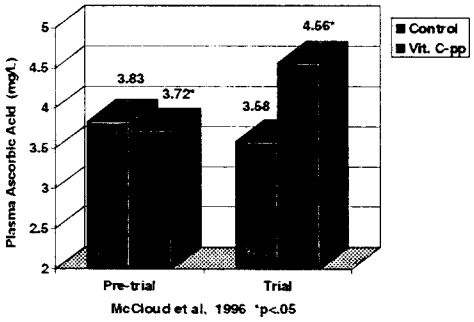
[a,b] means followed by different letters within columns are different

Garber et al, 1995

Effect of Vitamins B,C on IgG Response to Bovine Herpesvirus-1 in Beef Calves



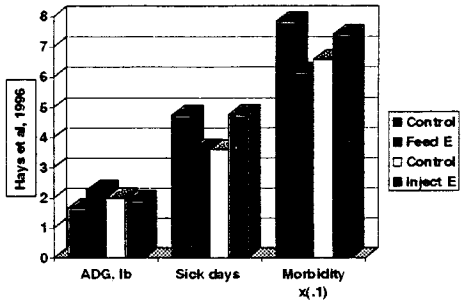
Effect of feeding ascorbyl-2-polyphosphate on plasma ascorbic acid in dairy heifers



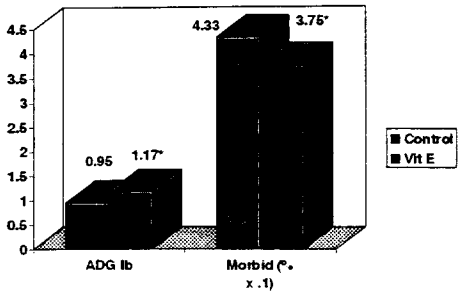
McCloud et al, 1996 *p<.05

Vitamin E and Stocker and Feedlot Cattle

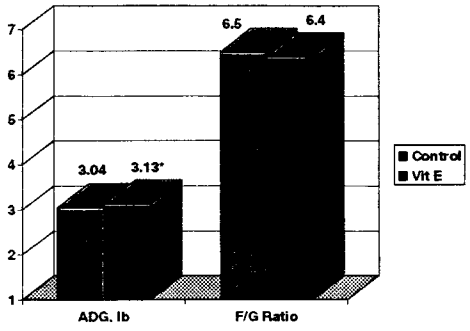
Effect of feeding 800 IU/d or injecting vitamin E on performance of stocker cattle



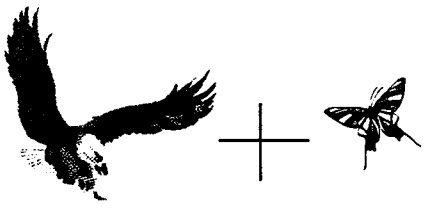
Effects of feeding 1600 IU/d vitamin E on performance of stocker cattle(Gill et al)



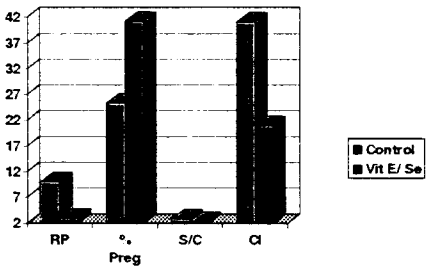
Feedlot data summary: Vitamin E (Secrist et al, 1996)



Vitamin E-Reproduction

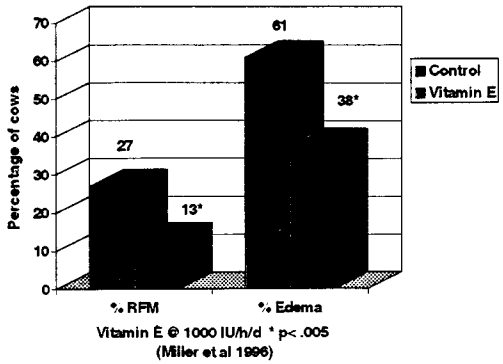


Vitamin E/ selenium injection on reproduction in dairy cows

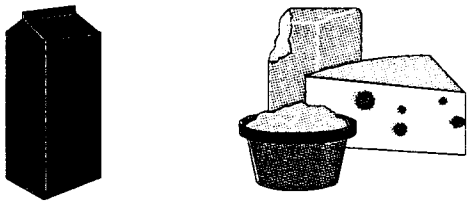


Arechiga et al. 1994 (all cows fed 500 IU vitamin E and .3 ppm Se)

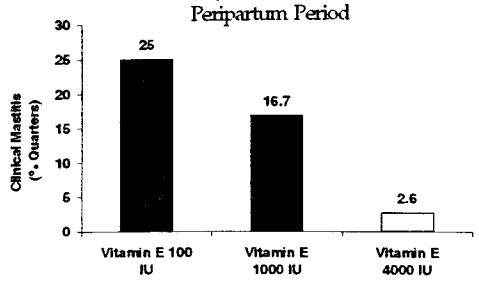
Effect of Vitamin E on retained fetal membranes and udder edema. (7 year data summary; 593 cows)



Vitamin E-Mastitis

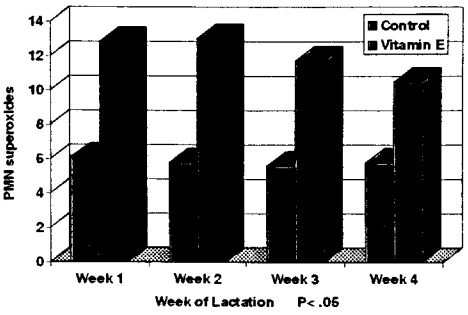


Effect of Vitamin E Supplementation on Clinical Mastitis of Dairy Cows and Heifers During Peripartum Period

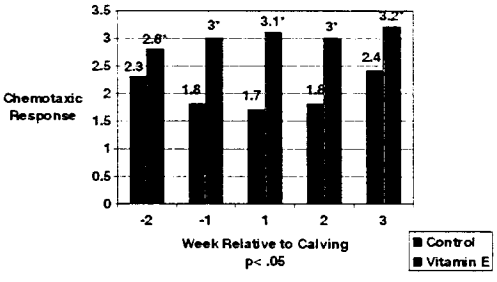


Weiss et al., 1996

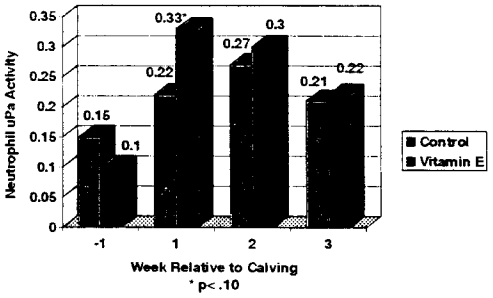
Effect of Vitamin E on Neutrophil Superoxide Production (Politis et al. 1995)



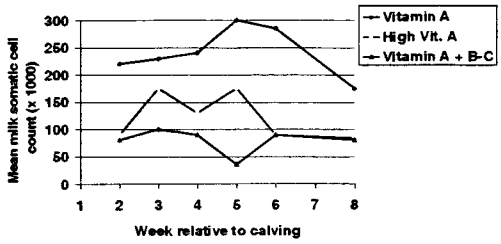
Effect of Vitamin E on Blood Neutrophil Chemotaxis. (Politis et al., 1995)



Effect of vitamin E on neutrophil plasminogen activity (Politis et al., 1995)



Effect of Vitamin A and Beta-Carotene on Milk Somatic Cell Count



Chew and Johnson, 1985

Tmts: Vit A-53,000, High Vit A-173,000, B-C 300 mg per day

Connection Between....

Antioxidant vitamins

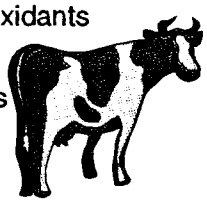
Plasma fast-acting antioxidants

PMN respiratory burst

Susceptability to mastitis

Retained placenta

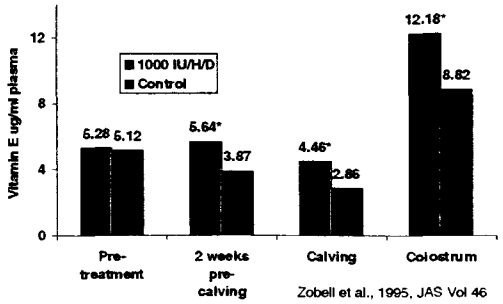
Udder edema



(based on Miller, Politis, Heyneman,Weiss)

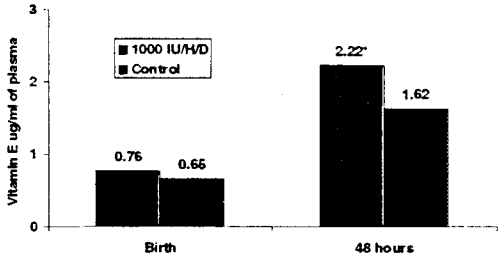
Vitamin E in Cow/Calf Nutrition

Beef Cow Vitamin E Status



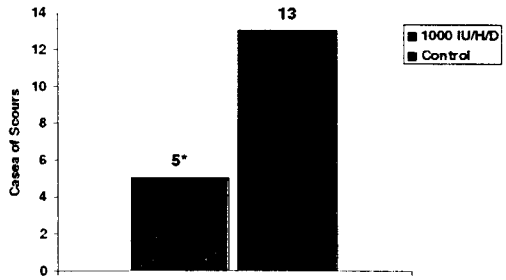
Zobell et al., 1995, JAS Vol 46

Beef Calf Vitamin E Status



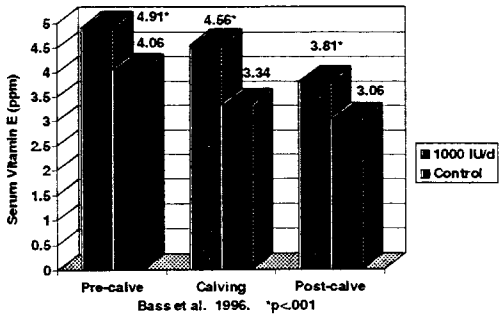
Zobell et al., 1995, Proceedings Western Section ANSC vol. 46

Scours Incidence - Beef Calves



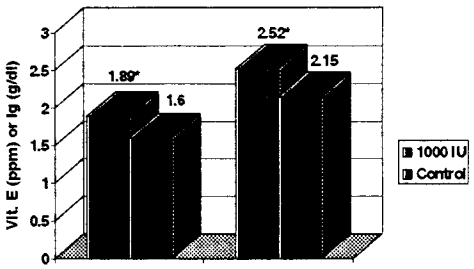
Zobell et al., 1995, Proceedings Western Section ANSC vol. 46

Vitamin E Status - Beef Cows



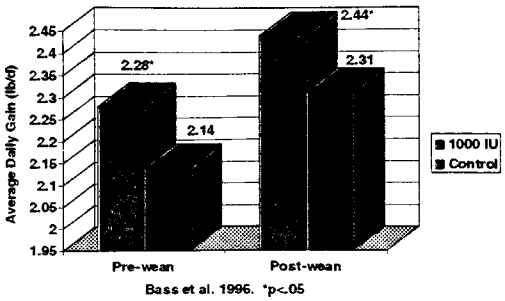
Bass et al. 1996. *p<.001

Serum Vitamin E and Ig of Calves



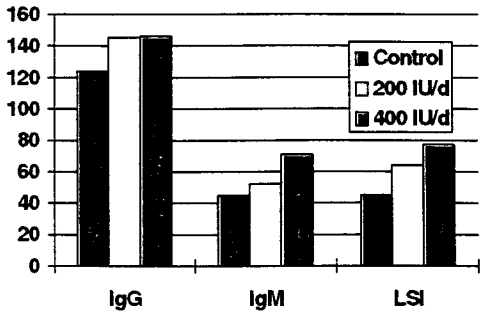
Bass et al. 1996. *p<.05

Effect of Vitamin E on Beef Calf ADG

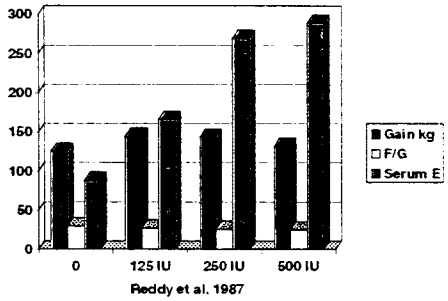


Bass et al. 1996. *p<.05

Effect of Vitamin E intake on Immune Response of Dairy Calves (Reddy et al 1987)



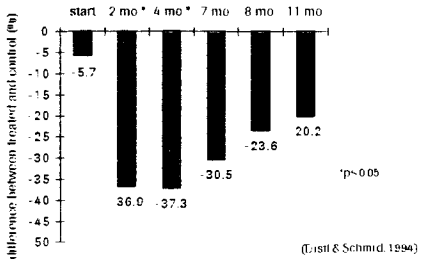
Effect of dietary vitamin E on performance and serum vitamin E in dairy calves



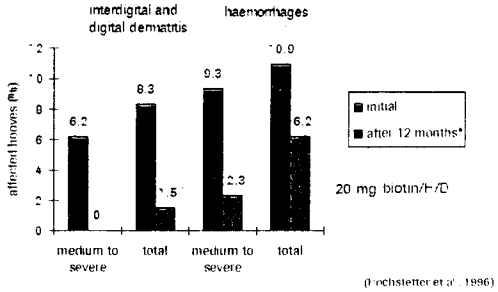
Reddy et al. 1987

Effect of Supplemental Biotin on Cattle Hoof Health

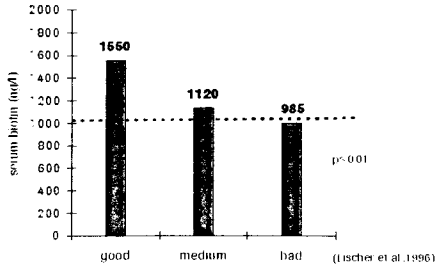
Incidence of Interdigital Dermatitis in Dairy Cows in Relation to Dietary Biotin Supplementation



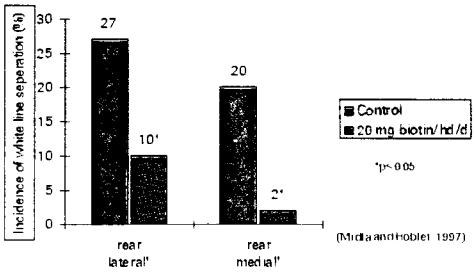
Incidence of Hoof Lesions in Dairy Cows in Relation to Dietary Biotin Supplementation



Serum Biotin in Relation Short Term Healing in Dairy Cows



Biotin Supplementation and White Line Separation in First-Lactation Holstein Cows



Vitamin Effects on Immunity
Vitamin Recommendations

Dairy Cow:

Vitamin E - 1000/500 IU/d regimen;
4000/2000 IU/d for challenge.

Vitamin A - 100,000 to 125,000 IU/d;
150,000 for challenge.

Vitamin D - 30,000 to 40,000 IU/d

Biotin - 10 - 20 mg/d

Vitamin Effects on Immunity
Vitamin Recommendations

Beef Cattle:

Vitamin E - 1000 IU/d beef cows
- 800 IU/d stocker cattle
- 500 IU/d feedlot cattle

Biotin - 10 mg/d

Final Considerations

- Balanced nutrition - do not view nutrients in isolation.
- Management / husbandry factors.
- Optimal nutrition supports optimal function of body systems, it is not a treatment or a therapy.
- Preventative medicine and optimal nutrition are synergistic.