

Immune Support for Your Horse

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Immunity, or protection against invading microorganisms, is critical in all living organisms, plants and animals alike. This defense can be as simple as a physical barrier, such as skin, or as intricately complex as cell-to-cell communications that lead to adaptive responses to protect the host against future attacks. The horse's immune system is challenged constantly without resulting in any overt signs. If, however, the attack is severe or the horse's defense system is compromised, infection and disease can ensue. Consequently, the best practice is to keep the horse "prepared" at all times by feeding particular immunonutrients, such as certain amino acids, omega-3 fatty acids, and antioxidants. For times when stressors may be present or the system is particularly susceptible –such as times of viral outbreak, trailering, or heavy competition –additional dietary modifications can be made to further bolster the horse's immune system.

Amino Acids

Commonly, amino acids are viewed as critical for their role as building blocks for proteins. More recently, "functional amino acids," such as arginine, glutamine, cysteine, methionine, tryptophan and phenylalanine, have been identified that play a direct part in processes such as growth, reproduction, and immunity.¹ For example, arginine serves as the primary precursor for nitric oxide, a cellular product that is responsible for cytotoxic activity against invading microorganisms.² As a result, supplemental intake of arginine may enhance both humoral and cell-mediated immune responses in animals^{3,4} and humans.^{5,6} Interestingly, pathogens express an "anti-arginine" activity by reducing the availability of arginine to the host system,⁷ suggesting an evolutionary attempt at "immune evasion." Glutamine, a non-essential amino acid, is now recognized as being conditionally essential with a dietary requirement existing during times of stress.⁸ As a precursor to glutathione, glutamine helps maintain levels of the antioxidant glutathione peroxidase, which can modulate excessive inflammatory responses and oxidative damage to cells.⁹ Glutamine is a primary source of energy for cells that turn over rapidly, including those in the intestine and immune system.^{10,11} Glutamine also helps maintain gut barrier function by reducing intestinal permeability and preventing translocation of enteric microbes into the general circulation.¹² Similarly, the sulfur-containing amino acids, cysteine and methionine, support intestinal mucosal growth and gut function,¹³ and roles for tryptophan and phenylalanine in immune-modulation have recently emerged.¹⁴

Omega-3 Fatty Acids

Proper immune reactions are characterized by traditional inflammatory responses. Therefore, it

may appear counterintuitive to learn that the anti-inflammatory omega-3 fatty acids aid in immune support. In reality, omega-6 fatty acids and their resultant pro-inflammatory metabolites induce immunosuppressive reactions.^{15,16} Omega-3 fatty acids, on the contrary, enhance immune responses. For example, horses supplemented with omega-3 fatty acids (from either flax or fish oil) have a more rapid immune response to intradermal injection of phytohemagglutinin than control horses.¹⁷ Enhanced humoral immune response has also been detected in other animals supplemented with flaxseed.¹⁸ One of the most important roles for omega-3 fatty acids in immune-modulation may be their potential to regulate inappropriately-activated immune responses and states of "hyperinflammation" that

Injury, illness and complications of infections are linked to immunosuppressive states in patients. Many physicians now use immunonutrition to reduce complications associated with infections. Omega-3 fatty acids and antioxidants are prime candidates for immunonutritive therapy and may be used pre- and post-operatively, as well in critically ill or injured patients.

compromise disease resistance. Indeed, excessive, chronic inflammation or repeated, acute inflammatory responses hinder immune function.^{19,20} To counteract these effects, omega-3 fatty acids are now being utilized as key immunonutrients. For example, the post-surgical state that is characterized by inflammation and impaired immune function²¹ has been reduced by presurgical supplementation with omega-3 fatty acids, an intervention that has reduced post-surgical

complications, such as infections and the need for antibiotics.²² Similarly, critically ill patients are often supplemented with omega-3 fatty acids with very favorable results, such as a decrease in mortality and length of stay in the ICU.²³

Micronutrients: Vitamins and Trace Minerals

Effective immune cell function depends on the production of reactive oxygen species.²⁴ However, excessive free radical activity without an adequate defense through antioxidant enzymes or compounds results in cellular oxidative damage, which can impair immune function.²⁵ Poor diet, injury or illness, as well as heightened immune cell activity itself all may induce cellular oxidative damage. Strategies to remedy imbalances between endogenous oxidants and antioxidants often include dietary intervention, including antioxidant supplementation. In this regard, the results of several studies suggest that adequate availability of various antioxidants is essential to improving or restoring normal immune function.

Zinc is an essential trace element that supports mammalian immune system function, in part by regulating certain white blood cell development and activity. In the horse, low serum zinc has been associated with infections such as cellulitis, shipping fever, and fever in racehorses,²⁶ as well as with certain viral and parasitic infections.^{27,28} A body of evidence supports the utility of zinc supplementation in augmenting a person's immune system.²⁹ In the horse, it was recently reported that zinc supplementation may reduce the risk of equine herpesvirus myeloencephalopathy, which is the devastating neurologic form of EHV-1.³⁰ **Selenium** is a trace mineral that also has immune-modulating benefits.³¹ Not only does selenium deficiency increase the risk of viral infections because of impaired immune function, but insufficient concentrations of selenium also enhance the virulence of certain infecting agents.³² Low selenium status may impair white blood cell cytokine production in the horse.³³ Furthermore, improvements in both the cellular and humoral immune response may be noted in horses supplemented with selenium alone or in combination with **vitamin E**.^{34,35} Although the horse can naturally synthesize **vitamin C**, consideration of research in other species showing that concentrations of vitamin C decline rapidly in white blood cells and plasma during times of stress³⁶⁻³⁸ and that vitamin C supplementation can increase certain white blood

cell numbers and activity,^{39,36,40,41} supplementation in the horse may prove to be beneficial.

Times of Stress

Supplemental products containing high concentrations of immunoglobulins, thymic protein, and colostrum, as well as growth factors, key polypeptides, lactoferrin, transferrin, and immune-supporting cytokines can provide added pathogen protection for horses during times of excessive stress or outbreaks of infectious diseases. These products are often designed to provide extra support for the gut, the "first line of defense" against pathogenic microorganisms, by maintaining a protective barrier between the external surroundings and internal environment.

Bovine Colostrum

The benefits of providing bovine colostrum orally to animals occur at the level of the intestinal enterocyte, where the immunoglobulins recognize and neutralize potential pathogenic organisms. The rationale for this approach differs from that associated with the intravenous administration of plasma or serum rich in immunoglobulins. In addition to immunoglobulins, bovine colostrum contains other components with proven therapeutic effects, including growth factors, polypeptides, and proteins with antimicrobial properties.⁴² For example, some of the growth factors in colostrum aid cells responsible for growth and repair, proline rich polypeptides are involved in production of cytokines that defend against microbes, and lactoferrin has potent antimicrobial activities. Additional examples of benefits associated with oral ingestion of bovine colostrum by non-bovine species include:

- Protection against GI disorders.⁴³
- Aid in treatment of hemorrhagic diarrhea in infants.⁴⁴
- Reduce the occurrence and severity of diarrhea in adult HIV patients.⁴⁵
- Protection of the intestinal mucosa during chronic NSAID treatment.⁴⁶
- Improved resistance to abdominal surgery-induced endotoxemia.⁴⁷

In addition to gut-related benefits of oral supplementation with bovine colostrum, there is convincing evidence in the literature that this approach has "far-ranging" systemic effects. Examples of these include the following:

- In a trial performed in people, immune responses to exercise were determined after several weeks of ingestion of bovine colostrum. In this study, white blood cells were isolated from the people, stimulated in culture, and their responses examined. While the number of white blood cells in circulation did not change, their activity level was maintained after colostrum administration unlike the placebo treated subjects who demonstrated immunosuppressive changes.⁴⁸
- In a similar trial, people ingesting bovine colostrum did not have the exercise-induced decrease in serum immunoglobulins that occurred in people not ingesting the colostrum. The colostrum-supplemented people also had a moderate reduction in the development of upper respiratory tract infections.⁴⁹

Calf Thymic Protein

Thymic extract is purified from the calf thymus gland, an organ that plays a major role in activating the immune system. This bovine-derived extract promotes the maturation of T-lymphocytes as well as subsequent functioning of both T and B lymphocytes in humans and laboratory animals.⁵⁰⁻⁵² Orally-administered calf thymic extract improves the activity of thymic hormone in humans;⁵³ this hormone regulates the activity of immune cells, such as natural killer cells. Similar to bovine colostrums, thymic extract does not have to be species-specific as demonstrated by the following beneficial effects in non-bovine populations:

- Children with recurrent respiratory infections demonstrated a significant decrease in frequency following oral supplementation with a calf thymus extract.⁵⁴
- Symptoms of food allergies have been improved in children.^{55,56}
- Improved response to therapy for hepatitis B.⁵⁷
- Restoration of immune parameters in experimentally compromised lab animals.^{58,59}

Role of Diet

A well-balanced diet is the foundation for your horse's healthy immune system. Unfortunately, most equine feeding practices actually counteract the beneficial effects of omega-3 fatty acids, antioxidants, and other immune-supporting supplements. For example grain, a common feed

additive used to increase caloric intake, is high in the pro-inflammatory, immune-suppressive omega-6 fatty acids. There is considerable evidence in the literature regarding the ill effects of grain feeding, primarily in cattle. For example, consider the differences in "meat quality" in grass versus grain-fed cattle. In general, grass-fed cattle have better lipid and antioxidant profiles than grain-fed cattle, as noted by the higher levels of omega-3 fatty acids, vitamins A and E precursors, and antioxidant enzymes in grass-fed animals.⁶⁰ Similar to grain, corn oil—another often-used dressing on equine feed—is high in omega-6 fatty acids. These diets with high omega-6 to omega-3 ratios may result in poor immune response, similar to what has been demonstrated in rats.⁶¹ Therefore, providing a daily wellness formula that includes a blend of omega-3 fatty acids, antioxidants and immunonutrients should benefit the horse's immune system and increase resistance to illness and disease. Interestingly, even feeding what appears to be a more "ideal" diet consisting of hay could also predispose the horse to immune-compromised conditions. Over time, baled hay loses its nutritive value, predominantly at the expense of omega-3 fatty acids and key vitamins. For example, an independent laboratory analyzed fresh versus 10-week old cut and baled alfalfa hay and reported an 82% decrease in omega-3 fatty acids (Figure 1) as well as an increase in the omega-6 to omega-3 ratio. Similar deleterious effects were demonstrated for B-vitamins (Figure 2) and vitamin D, which was essentially non-existent after 10 weeks (data not shown). These findings suggest that horses on a hay-based diet could benefit from supplementation with omega-3, vitamins and minerals.

Figure 1. Total Omega-3 Content in Alfalfa from Different Times of Cut

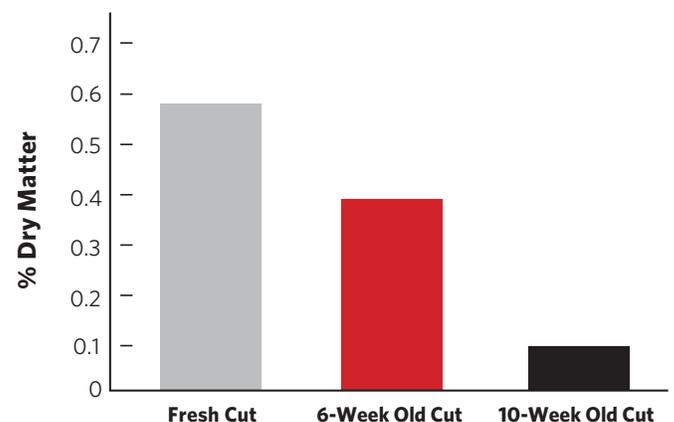
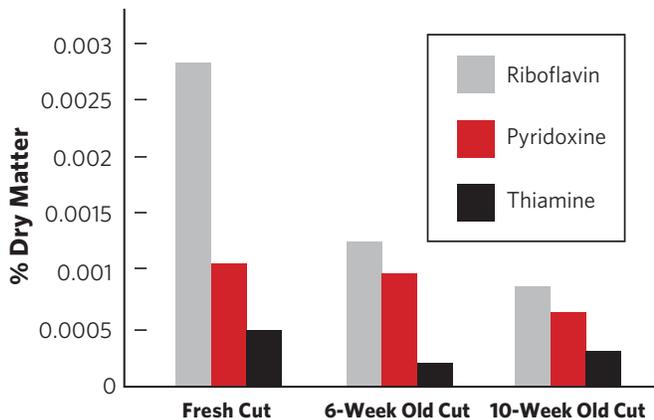


Figure 2. **B-Vitamins in Alfalfa from Different Times of Cut**



Summary

The immune system responds best to potential microbial pathogens when the levels of systemic inflammation and oxidative stress are low and there is sufficient availability of specific amino acids and other micronutrients. Inevitably, times of excessive stress will arise during which the immune system is not equipped to appropriately respond, whether due to surgery, injury, infectious outbreaks, or competition. During these times, additional immunonutrients, such as immunoglobulins, growth factors, thymic protein and immune-modulating cytokines, can provide the added protection to help preserve your horse's health.

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