



PERFORMANCE MINERALS®

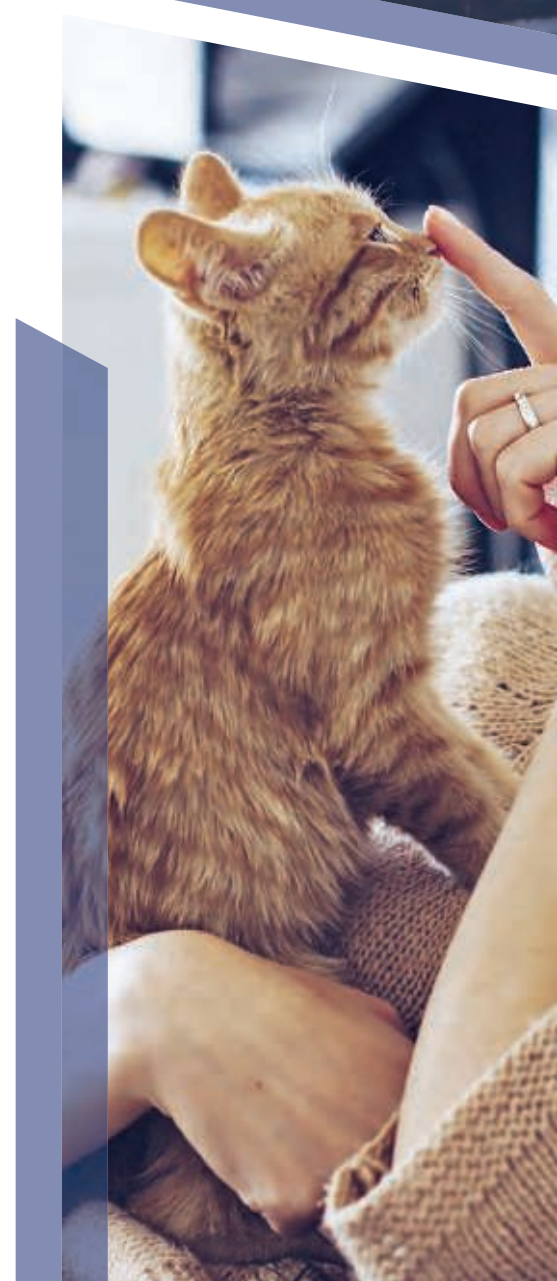


INFLAMMATION GOOD OR BAD?

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Companion animals are not just our pets. They are members of our family, and it's important as pet parents to ensure their happiness, health, activity and well-being.

Inflammation is a common factor affecting our companion's well-being, and they are often recognized as sick, unhealthy or unhappy. Chronic inflammation can have negative effects on health and well-being, growth and development, energy metabolism, skin and coat condition, reproduction, paw pad integrity and healing, joint and skeleton integrity, and immune response.



WHAT IS INFLAMMATION?

Inflammation is necessary for life, especially from a protection standpoint in companion animals. It is the process that helps the body fight off bacteria, pathogens and their toxins and that aids in repairing damaged tissue. If you've ever twisted your ankle, been stung by an insect or cut your finger, you may have experienced firsthand the familiar sensations of pain, redness, swelling and heat that results from an injury or infection. This is inflammation in action.

While an appropriate and robust inflammatory response is necessary, excessive or prolonged inflammatory responses may become detrimental if not controlled. Inflammation is divided into two categories: acute and chronic.

- **Acute inflammation** is the first defensive response to a pathogen or injury. It's a short-term process where the immune system sends white blood cells to the injury site or point of pathogen invasion to initiate the healing process. This response should be rapid and robust, appearing within minutes or hours following activation of an immune response.
- **Chronic inflammation** occurs when the immune response remains activated and may result from failure to eliminate the cause of the immune response or acute inflammation. Chronic inflammation may last for weeks, months or longer, and it often diverts nutrients away from growth and development in order to fuel the fight against an inflammatory response.

WHAT RISKS AND COSTS ARE ASSOCIATED WITH CHRONIC INFLAMMATION?

Pet parents should pay close attention to chronic inflammation. While inflammation is necessary for protection, there may be trade-offs in the comfort and well-being of our family companions. When our dog or cat gets sick, its food intake may decrease while the immune system redirects nutrients normally utilized for growth, reproduction or activity to maintain the inflammatory

Acute vs. Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: Minutes to hours, Innate immune system	Slow: Days, Adaptive immune system
Duration	Hours to days	Weeks to months or years
Cellular Infiltrate	Mainly neutrophils, followed by macrophages	Macrophages, plasma cells and lymphocytes
Vascular Changes	Prominent (vasodilation, increased permeability)	Not prominent, angiogenesis
Tissue Injury	Self-limited	Progressive
Fibrosis	Usually mild	Often severe
Local and Systemic Signs	Prominent	Less

response. When the inflammatory response persists and becomes chronic, nutrients are diverted away from functions that are needed for skin integrity, maintenance of a shiny, healthy coat, paw pad integrity and to maintain the animal's energy.

There are also financial costs to managing chronic inflammation in cats and dogs, including veterinary costs, purchasing medicine and shampoos, and buying specialty foods that may help relieve an allergic reaction that may be causing the inflammatory response.

IMMUNE SYSTEM IN ACTION

The immune system is comprised of a sophisticated network of cells, proteins and enzymes programmed to monitor animal wellness. This well-orchestrated network of cells and chemical signals detects and responds to bacteria and pathogens that may be on or in the body, as well as responds to injury, environmental challenges and stressors.

When a pathogen or bacteria crosses one of the body's barriers — such as skin, mucous membranes or blood vessel linings — the immune system will be alarmed to the invasion. In response, tissues at the site alert the immune system by sending chemical signals (cytokines) or pro-inflammatory proteins in a process called chemotaxis to indicate help or repair is needed. This process initiates movement of white blood cells to the site resulting in fluid accumulation, heat and swelling, all generally described as inflammation.

The first responders to the site are white blood cells (leukocytes) called phagocytes. These cells help protect the body by ingesting harmful foreign particles, bacteria, and dead or dying cells. There are two forms of phagocytes:

- Neutrophils, which are small, granular leukocytes that quickly appear at the site of a wound and ingest bacteria.
- Monocytes, which are larger leukocytes that appear about three days after infection and scavenge for bacteria, foreign particles and dead cellular material left behind by the neutrophils. These cells play a role in the adaptive immune response, thus giving the immune system memory.

The neutrophils appear at the site first and work to engulf and destroy pathogens or bacteria. They then display pieces of the pathogens on their surface to signal the monocytes to help continue the attack on the invading pathogens. This rush of immune cells, fluid accumulation and swelling is essential, but it must also be controlled or held in check.

Therefore, there is also a group of anti-inflammatory cytokines that help control the pro-inflammatory cytokine response. However, if the delicate balance between pro-inflammatory and anti-inflammatory proteins is not achieved, pro-inflammatory cytokines



may call too many monocytes (white blood cells) to the site damaging healthy cells and leading to chronic or prolonged inflammation. This is the point when an acute inflammatory response can potentially turn into a chronic inflammatory response.

POOR GUT INTEGRITY AS A POTENTIAL CAUSE OF CHRONIC INFLAMMATION

When a dog or a cat is suffering from itchiness or irritation of the skin, many pet parents will go in search of products to provide relief from the itching and irritation/redness, but few realize the problem may be rooted in poor gut integrity.

Epithelial tissues lining the gastrointestinal (GI) tract are key to nutrient absorption but also serve as an important barrier to prevent bacteria, pathogens and toxins from passing through the intestinal lining and into the bloodstream. When a breakdown in this epithelial barrier occurs, leukocytes are activated with localized inflammation resulting in a condition called leaky gut.

Digestive upsets or mild-to-moderate food allergies may also lead to leaky gut. Oftentimes these insults result in a loose or runny stool, which reflects damage within the GI tract and causes the immune system to focus there, which then draws immune cells away from their focus on keeping the skin healthy. When this happens, dogs and cats are more likely to suffer from canine atopic dermatitis (atopy), a hypersensitivity or skin allergy, that causes inflammation, irritation and itchiness.

Poor gut integrity can also be attributed to psychological stress. For example, some days feeding your dog on a regular schedule just doesn't happen and may lead to hunger, frustration and digestive irregularity. Similarly, there are days when pet parents leave for work a little earlier than usual and/or get home later than

normal creating physical distress and uneasiness which often leads to stress. Stressful events, both physical and psychological, can cause increases in cortisol (a stress hormone) which signals a reduction in blood flow to the gut reducing motility and immune protection thus increasing the potential for a leaky gut.

As these problems cascade, we may start to see breaks in the skin epithelial tissue resulting in increased shedding, a rough or dull hair coat, development of a bad smell, in addition to chronic or irritating itchiness.

CANINE ATOPIC DERMATITIS

Canine Atopic Dermatitis (atopy), an allergenic skin disease, is the second-most common problem in pets, second only to fleas. While atopy is more common in dogs, it also affects cats. Unfortunately, atopy can make life uncomfortable for your pet and you, and, in its worst case, can affect your pet's attitude and overall well-being.

Atopy can be caused by exposure to environmental allergens, like grass, weeds, mold spores, other animals, sawdust, house dust mites, bedding, soaps and shampoos, and other environmental irritants similar to humans. However, an allergic response may also result from an internal allergen, like food or medication.

The first sign of atopy is itchy skin, causing your pet to begin scratching. Just like humans, dogs have a normal diverse biome of bacteria, including *Staphylococcus* and *Streptococcus* bacteria on the skin surface. Excessive scratching can cause the skin to break, allowing these bacteria to enter and cause a bacterial infection.

Unfortunately, symptoms of atopy vary, making it hard to diagnose. Some animals may experience intermittent

Effects of Zinpro Performance Minerals® on Skin and Coat Health



Significant improvement to skin and coat health after 12 weeks

itchiness at first, which is not a problem, but it can progress to the point of becoming a severe skin irritation, causing constant discomfort with almost constant itching, biting or scratching of the skin. If not controlled and treated, this can lead to significant skin damage, hair loss, loss of sleep, possible infections or other complications.

OTHER ANIMAL WELL-BEING CHALLENGES RELATED TO INFLAMMATION



Joint and Skeleton

Inflammation can affect more than the soft tissues of skin, muscles, gut, respiratory, urogenital, reproductive tracts and organs, it may also affect the skeletal system. Inflammation can result in damage to bones and joints, dysplasia or nutritional imbalances and may lead to osteochondrosis in dogs and cats, primarily in large-breed dogs and over-weight cats. Another common inflammatory disorder in dogs and cats is hip and elbow dysplasia.

Pain, often associated with bone and joint inflammation, can also lead to lameness, which then causes locomotion problems, reduced mobility and lessens social activities. Lameness will reduce the desire for our pets to get out, walk and maintain personal health.



Integrity

Paw pad integrity is also an issue in companion animals. Chronic inflammation, even in a joint, can cause release of cytokines that may affect the keratinization process, thus potentially having negative effects on the skin and especially affecting heavily keratinized tissues like the nose, tongue and paw pads. Pet parents will tend to see breaks in the paw pads, causing their pets to lick the wound or crack, which may then become infected. This type of injury often requires veterinary treatment and care, in addition to isolating the root cause of the insult.



Respiratory Infections

Respiratory infections can damage or destroy epithelial lining of the upper respiratory system, allowing pathogens to access the circulatory system and result in systemic infection. When this occurs, it can result in a

prolonged inflammatory response requiring significant energy expenditure to activate immune cells (white blood cells) and may result in weight loss, increased sickness, depression, loss of thriftiness and poor animal well-being.



Vaccinations and Medications

Vaccinations are especially important to protect our pets from a number of diseases.

Unfortunately, chronic inflammation can depress immune function and lead to reduced or poor vaccination responses. Pet parents need to make sure their pet's immune system is strong through good nutrition and stress management, so they can respond to foreign organisms and routine vaccinations while remaining in optimal health.

THE ROLE OF PERFORMANCE TRACE MINERALS

Trace minerals like zinc, manganese, copper, iron, selenium, iodine and chromium play an essential role in the health and well-being of our pets and need to be supplemented as part of a well-balanced diet.

Zinc is the most influential trace mineral as it plays a role in over 300 enzyme systems and is a key component in over 3,000 proteins in the body. It is critical to the formation of the protective epithelial barrier and is a key component and building block in both the skin and immune system. Manganese plays critical roles in bone mineralization as well as production of glycosaminoglycans, a component key to cartilage integrity and joint health. Interestingly, chondroprotective products, such as glucosamine and chondroitin, need manganese to achieve optimal efficacy in their role as components in cartilage repair and replacement. While required in lesser amounts, copper is critical to crosslinking proteins, which is key to epithelial

tissue integrity and strength. Iron is second to zinc in required amount and is essential to red blood cell function. Red blood cells are critical to immune system activity as the immune cells kill bacteria with oxygen. Combined, zinc, manganese, copper and selenium join forces in removing inflammatory waste products also known as the antioxidant process.

Not all trace minerals are created equal. Peer-reviewed research demonstrates that Zinpro Performance Minerals® help fortify the immune system, when compared to supplementing companion animal diets with inorganic or organic trace minerals. This provides more protection to our pets.

Zinpro Performance Minerals can help manage the effects of chronic inflammation by ensuring a robust and balanced immune response. They help build healthy first-responder cells, as well as ensuring the pro-inflammatory proteins (cytokines) are in balance with the anti-inflammatory proteins.

Research has shown that ZINPRO® zinc methionine supplementation can be considered an adjunctive treatment for dogs with atopy or skin allergy issues. Dogs that were supplemented with ZINPRO zinc methionine saw a 44-percent reduction in Canine Atopic Dermatitis Lesion Index (CALDI) score while dogs supplemented with a placebo saw no change. Additionally, 69 percent of dogs on ciclosporin and 55 percent on glucocorticoids were able to decrease their medication dose to control atopy by half without incurring an allergy flare. Visual observations of dogs receiving the Zinpro zinc supplement revealed an improvement in skin and coat quality.

Including Zinpro Performance Minerals in your companion animals' nutritional program can help manage the well-being challenges associated with chronic inflammation and help your family members remain healthy and happy.

A Key Role in Companion Animal Diets

When incorporated as part of a well-balanced nutrition plan, essential trace minerals deliver important benefits:

Benefit	Trace Minerals	Benefit Description
Immune Response	Zinc, Manganese, Copper, Selenium and Iron	<ul style="list-style-type: none"> • Humoral immunity, antibody titers in response to vaccination • Cell-mediated immunity • Non-specific immunity • Antioxidant activity to remove free radicals and protect cell membranes
Joint and Skeleton	Manganese	<ul style="list-style-type: none"> • Chondroitin sulfate synthesis, which is important for formulation, maintenance and repair of joint cartilage • Bone matrix development and maintenance
	Zinc	<ul style="list-style-type: none"> • Cell division and protein synthesis for skeletal growth and repair
Pad Condition	Manganese	<ul style="list-style-type: none"> • Antioxidant activity to protect cell membranes
	Zinc and Copper	<ul style="list-style-type: none"> • Cell division to support paw pad growth and repair • Paw pad protein synthesis; collagen, keratins, cell envelope proteins and intercellular cementing substance
Reproduction	Iron and Copper	<ul style="list-style-type: none"> • Reproductive hormone synthesis: steroidogenesis • Helps avoid or reduce nutritional anemia
	Manganese	<ul style="list-style-type: none"> • Male libido • Fetal skeletal development
	Zinc	<ul style="list-style-type: none"> • Reproductive tract tissue integrity • Conception rates • Sperm maturation and quality
	Selenium	<ul style="list-style-type: none"> • Key to normal ovarian function • Reproductive tract repair and immune function
Skin and Coat	Zinc, Manganese and Iron	<ul style="list-style-type: none"> • Epidermal (skin) cell maintenance through cell division, protein synthesis and antioxidant activity to remove superoxide radicals • Facilitates wound healing • Helps avoid or reduce nutritional anemia • Development of a longer, fuller coat
Energy	Zinc, Manganese, Copper, Iron, Selenium and Iodine	<ul style="list-style-type: none"> • Improved health leaves more energy for activities • Well-being enhanced, as health problems are minimized or reduced in severity

Additional companion species info on trace minerals available upon request.

Product availability varies by country. Contact your Zinpro representative for product availability in your market.

To learn more about inflammation or about feeding Zinpro Performance Minerals to help manage inflammation, visit EssentialFeed.zinpro.com or contact a Zinpro representative today.