



Unlocking Solutions to Chronic Inflammation

Why Feeding Zinpro Performance Minerals® is Key For Success When Formulating Diets for Livestock, Poultry, Aquaculture, Equine and Companion Animals



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Inflammation is a natural and essential component of the immune response to infection, pathogens and/or tissue damage. While often considered a negative reaction, inflammation serves as a protective response to pathogens or tissue damage. It also promotes blood flow and immune cell recruitment to the insult site, which assists the animal in eliminating the initial cause of injury and promotes affected tissue recovery.

While an appropriate inflammatory response is necessary, excessive or prolonged inflammation can become

an inflammatory response can easily lose more than one kilogram of energy (glucose) to the immune system in a day. This energy could be used for performance and production. Based on this loss alone, it can be argued that ameliorating an inflammatory response when possible needs to be a top priority for animal agriculture.

Given the recent trend in many countries to move away from antibiotic use, methods to effectively manage and minimize inflammation are becoming increasingly important. Many potential

subsequent immune function, are vital to animal agriculture.

Trace minerals are essential to all living creatures, and production animals are no exception. Recent data has shown the benefit trace minerals provide to immune responses and associated inflammation (Chirase *et al.*, 1994; Percival *et al.*, 1998; Underwood and Suttle, 1999; Gaylean *et al.*, 1999; Hudson *et al.*, 2004; Kellogg *et al.*, 2004; Enjalbert *et al.*, 2006; Jahanian *et al.*, 2008; Siciliano-Jones *et al.*, 2008; Rabiee *et al.*, 2010). How well a diet meets an animal's trace mineral needs will vary by not only the amount of trace minerals consumed, but also by trace mineral source, level of antagonists in the diet and stress. Feeding Zinpro Performance Minerals® has been heavily researched in many production species. Extensive peer-reviewed research has shown this unique trace mineral category, known as Performance Trace Minerals, to significantly improve livestock and poultry wellness and performance by minimizing the effects from both antagonists and stress on trace mineral availability. This review will highlight the role Zinpro Performance Minerals plays in the immune response and mitigation of chronic inflammation.

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detrimental to the animal in many ways. Animals suffering from chronic, prolonged inflammation may be unable to mount a successful immune response in the future. Chronic inflammation also pulls nutrients and energy away from other key functions within the animal such as growth, reproduction, and meat, milk or egg production. An animal undergoing

dietary ingredients, including trace minerals, are now being promoted as alternatives to antibiotics in order to enhance animal wellness and performance in poultry, swine, and dairy and beef cattle. Since inflammation is intertwined with the immune response, conditions and feedstuffs or ingredients that help modulate the inflammatory response, and



Inflammation and the Innate Immune System

Inflammation and the Skin

The first line of defense against a threat to immunity is epithelial tissue. Commonly referred to as the largest immune organ, skin bears the constant burden of protecting a body's internal organs from damage and invading pathogens. In poultry, skin prevents infections and potential food-poisoning bacteria from entering carcasses. As classified by food inspectors, cellulitis is considered the second most important condemnation cause in poultry processing plants in the United States. From an animal wellness and commercial perspective, maintaining skin integrity is a critical means to prevent a number of abnormalities, such as cellulitis, that afflict poultry and other livestock.

Positive improvements to skin integrity and reduced skin abnormalities in response to supplementing poultry with an effective zinc source (such as Availa®Zn or ZINPRO® zinc methionine from Zinpro Performance Minerals) are commonly observed. This is no surprise, given the multitude of roles zinc plays in epithelial production, maintenance and repair (Mertz, 1986). Specifically, zinc is known to influence skin strength, elasticity, inflammatory response and healing.

Zinc from Zinpro Performance Minerals has been shown to heighten immunity (as reviewed by Kidd *et al.*, 1996; Moghaddam *et al.*, 2009, 2016) and reduce the incidence of cellulitis alone or in combination with vitamin E (Downs *et al.*, 2000; **Figure 1**). In a broiler study at Auburn University, skin lesions (sores, scabs and scratches) decreased from 42.7 percent to 9.6 percent when birds were fed zinc from Zinpro Performance Minerals (Saenmahayak, *et al.*, 2010; **Figure 2**). The severity and frequency of foot pad dermatitis was also reduced in broilers fed zinc from Zinpro Performance Minerals (Hess *et al.*, 2001; Saenmahayak *et al.*, 2010). The effect of zinc from Zinpro Performance Minerals on the epithelial inflammatory response is evident in chickens injected with phytohemagglutinin in the toe web (increased skin thickness and lymphocyte proliferation; Moghaddam and Jahanian, 2009) and wattle (enhanced

Figure 1. Effect of Vitamin E and Availa®Zn^a on the Incidence of Cellulitis^b

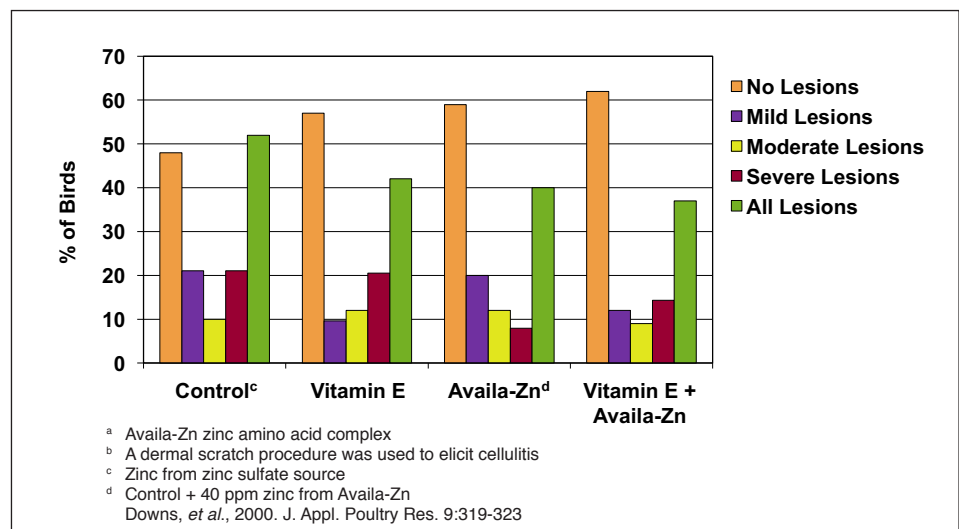
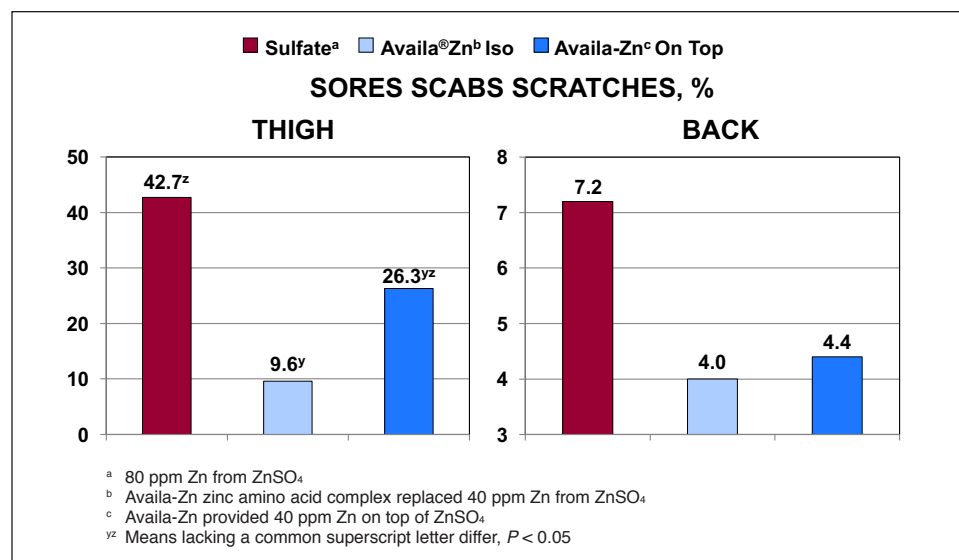


Figure 2. Effects of Availa®Zn on 49 Day Skin Integrity



cutaneous basophil hypersensitivity; Kidd, *et al.*, 1993).

In ruminants, the importance of skin integrity to overall health is also well documented. One such area susceptible to invading organisms is the skin region near the hoof horn. Of particular interest is the disorder known as digital dermatitis. Acute (M2) digital dermatitis typically appears as a bright-red, active lesion on the skin above the heel bulb, and is caused by a host of bacteria invading the area when skin integrity is compromised. In particular, anaerobic bacteria (Spirochetes), such as *Treponema* species may enter the compromised skin to cause excessive inflammatory response when conditions are not ideal (wet, poor hygiene, etc.). Multiple studies

have shown that feeding a combination of zinc, manganese and copper as amino acid complexes and cobalt as cobalt glucoheptonate from Zinpro Performance Minerals to dairy and beef cattle can limit the impact/occurrence of digital dermatitis, while also improving claw integrity and decreasing the incidence of lameness and other claw disorders (Gomez *et al.*, 2014; Kulow *et al.*, 2017).

The impact of trace minerals on hoof integrity extends beyond the skin. One primary initiator of the inflammatory pathway is via the toll-like receptors (TLR). The primary outcome of the TLR pathway is the synthesis of pro-inflammatory metabolites (De Nardo *et al.*, 2015). In a study conducted at the University of Illinois (Osorio *et al.*,

2016b), cows fed zinc, manganese and copper as amino acid complexes and cobalt as cobalt glucoheptonate from Zinpro Performance Minerals, in place of sulfate forms, had greater expression of one of the TLR genes. However, these animals also had decreased expression of genes coding for downstream metabolites in the hoof corium. This reduction in gene expression reflects less inflammation in the corium of cows fed Zinpro Performance Minerals, as well as potential readiness to respond to an acute insult if necessary. Cows fed Zinpro Performance Minerals also had greater expression of genes that regulate the antioxidant response, which can have obvious, positive impacts on an inflammatory response (Wang *et al.*, 2015).

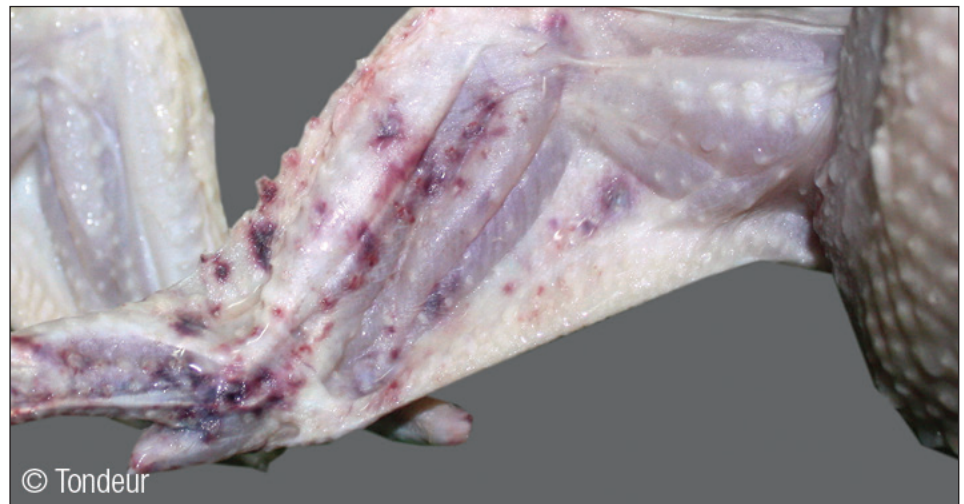
Taken as whole, one possible explanation for these observed results (i.e., reduction in claw disorders, such as digital dermatitis) is that cows fed Zinpro Performance Minerals more effectively initiate the beginning state of an inflammatory response without initiating the entire inflammation pathway. Instead, there is an observed decrease in expression of downstream metabolites in cows fed trace minerals from Zinpro Performance Minerals. This may be due to production of more structurally sound tissue in these animals, resulting in less tissue damage.

Inflammation and Vascular Fragility

Vascular systems often become fragile following periods of infection or various forms of stress – including metabolic stress. When handling birds either before or during live haul, a number of hemorrhagic lesions can be produced. Common carcass defects include bruises, blood splash, breast blisters, and red wing tips (Figure 3). In addition, vascular fragility issues can sometimes be linked to mycotoxins. Inflammation due to metabolic stress can play an important role in increasing the severity of hemorrhages.

Both acute and chronic inflammation, regardless of whether it is infectious or non-infectious, influence vascular integrity and function by creating endothelial dysfunction, compromising vascular tone, thrombosis and vascular remodeling. Oxidative stress associated with inflammation can dysregulate the

Figure 3. Example of Mild Hematoma (Score 1) Wing Bleeding

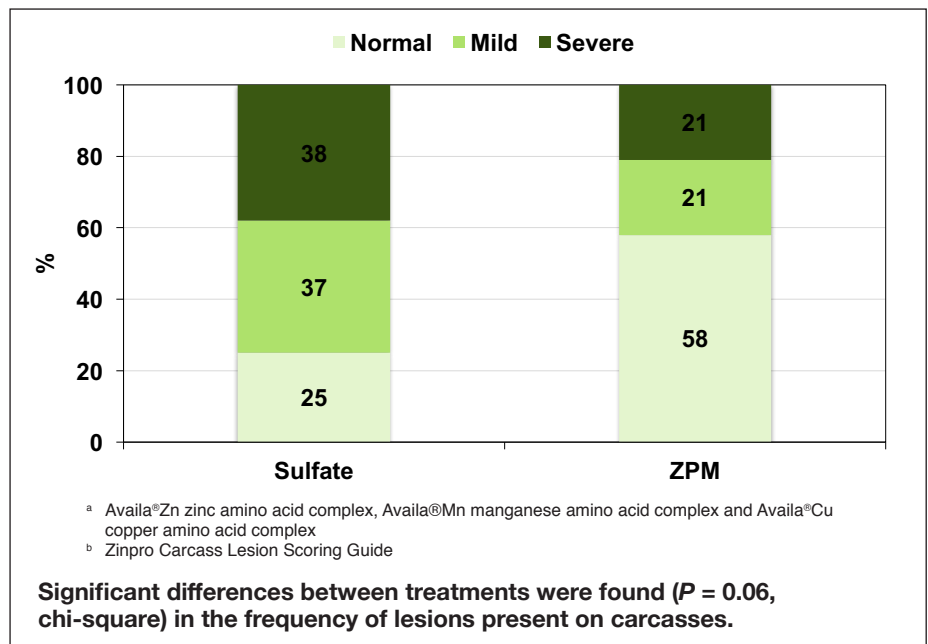


production of nitric oxide (NO), essential for the endothelial cells. This leads to the production of superoxide anions and peroxynitrite (ONOO⁻) which become very harmful for the blood vessels. Zinc plays important roles in the protection of these cells by increasing anti-oxidant status [zinc-mediated glutathione de novo synthesis, increasing superoxide dismutase (SOD) activity] and by down-regulating inducible nitric oxide synthase (iNOS) – derived NO formation. iNOS production is instrumental during the inflammatory response but it becomes harmful if it is not regulated – known as “aberrant” production of NO. Zinc-mediated

regulation of iNOS expression is affected by the regulation of NF-κβ transactivation. Researchers in Germany have been able to reproduce some of these pathways by exogenous added zinc.

In animal nutrition, a number of poultry studies using Availa-Zn zinc amino acid complex have shown a reduction in the appearance, severity and duration of hemorrhages in poultry carcasses. Researchers in Colorado, USA, found a reduction (38 percent, *P* < 0.11) in bruising area (in²) in carcasses coming from 53 d broilers supplemented with 100 ppm zinc (40 ppm from Availa-Zn and 60 ppm from

Figure 4. Effect of Availa®Mins^a on Incidence of Blood Splashes^b in Carcasses of 49-Day-Old Broilers



zinc sulfate), when compared to broilers fed only zinc sulfate at the same total level. In 2013, Khattak and colleagues from Scotland's Rural College reported a reduction in the severity and incidence (46 percent, $P < 0.05$) of hematoma in wings of carcasses from 35 d broilers fed Availa-Zn compared to those fed zinc sulfate. More recently in 2016, Petracci and colleagues at University of Bologna found a reduction in blood splashes (**Figure 4**; 45 percent, $P < 0.01$) in legs and thighs from 49 d broilers feeding a combination of zinc, manganese and copper amino acid complexes (Availa®ZMC). These findings confirm the role of zinc in protecting endothelial tissues and shows the advantage Availa-Zn zinc amino acid complex sources have over feeding an inorganic trace mineral source.

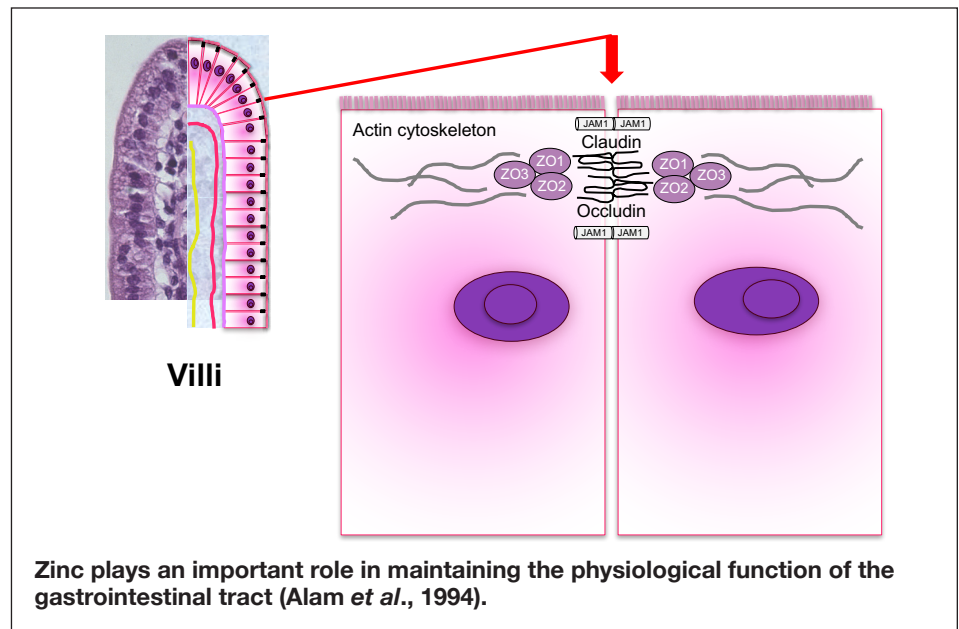
Inflammation and the Gastrointestinal Tract

The gastrointestinal tract (GIT) is one of the largest immune organs in the body. When pathogens are ingested and reach the lumen of the GIT, they have not yet been absorbed into the animal's body. Maintaining GIT epithelium integrity is of the utmost importance to prevent pathogens from invading the body, similar to that of the skin.

Several key anatomical features of the intestinal epithelium aid its ability to maintain the barrier between pathogens in the gut lumen and the internal body. The mucosal epithelial layer contains goblet cells, which secrete mucous and mucins that provide the initial protection layer over the enterocytes of the intestinal epithelium. In addition, these enterocytes are "stitched" together by tight junction complexes (**Figure 5**). This region is important for limiting the amount of harmful bacteria and contents of the intestinal lumen from entering the blood stream. Dehydration, malnutrition, cold stress, and oxidative free radicals can all cause the epithelial lining to be weakened, potentially leading to a pathogen invasion into the animal's body.

Heat stress and associated reduced feed intake can also decrease intestinal integrity and increase circulating endotoxins in production animals (Pearce *et al.*, 2013, 2014). Replacing inorganic zinc with zinc from Zinpro Performance Minerals

Figure 5. Protein "Stitching" of the Tight Junctions Between Two Enterocytes



has been shown to mitigate potential gut leakage in pigs associated with acute and chronic heat stress (Pearce *et al.*, 2015; Mayorga, *et al.*, 2017). Improved gut integrity resulted in decreased presence of TNF α in blood, suggesting that zinc from Zinpro Performance Minerals can help prevent some of the endotoxin's negative effects by reducing the amount of endotoxins that enter circulation. In addition, the gut morphology of pigs fed zinc from Zinpro Performance Minerals

was more similar to pigs housed under thermal-neutral conditions (**Figure 6**).

Similar to what was observed in heat-stressed pigs, feeding zinc from Zinpro Performance Minerals helped maintain intestinal morphology/integrity of heat-stressed steers in a manner similar to steers housed under thermal-neutral conditions (**Figure 6**; Abuajameh *et al.*, 2016). In this study, feeding zinc from Zinpro Performance Minerals in place of inorganic zinc improved heat tolerance

Figure 6. Comparison of Swine and Ruminant Intestinal Morphology

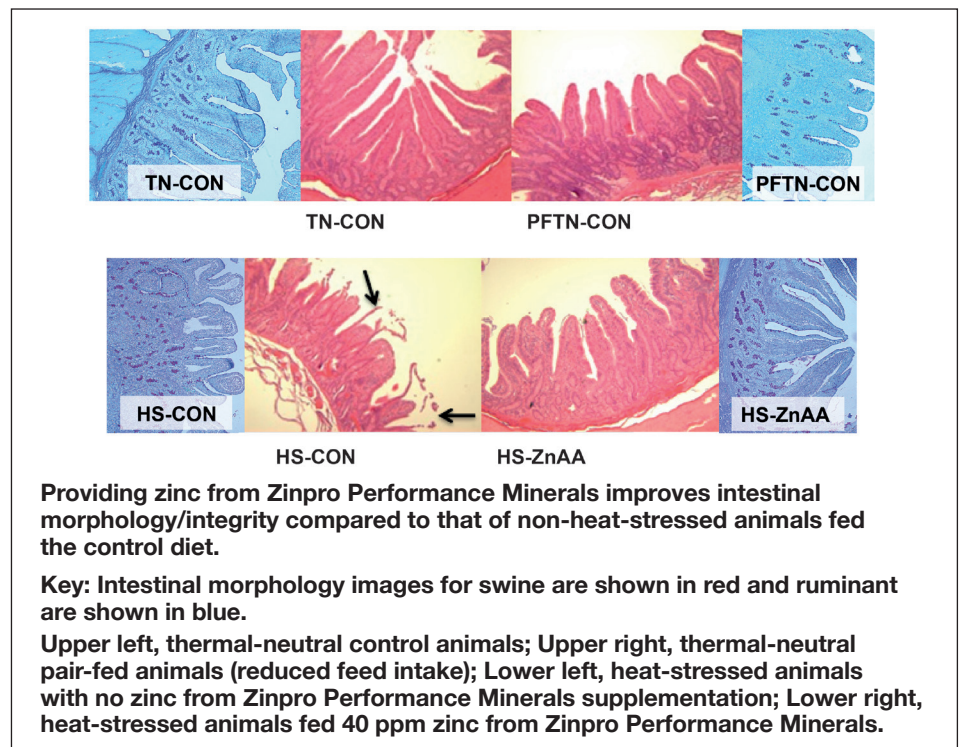


Figure 7. Prevalence of Conjunctivitis, Nasal Discharge and Coughing in Broilers Directly Infected with IBV^{ab}

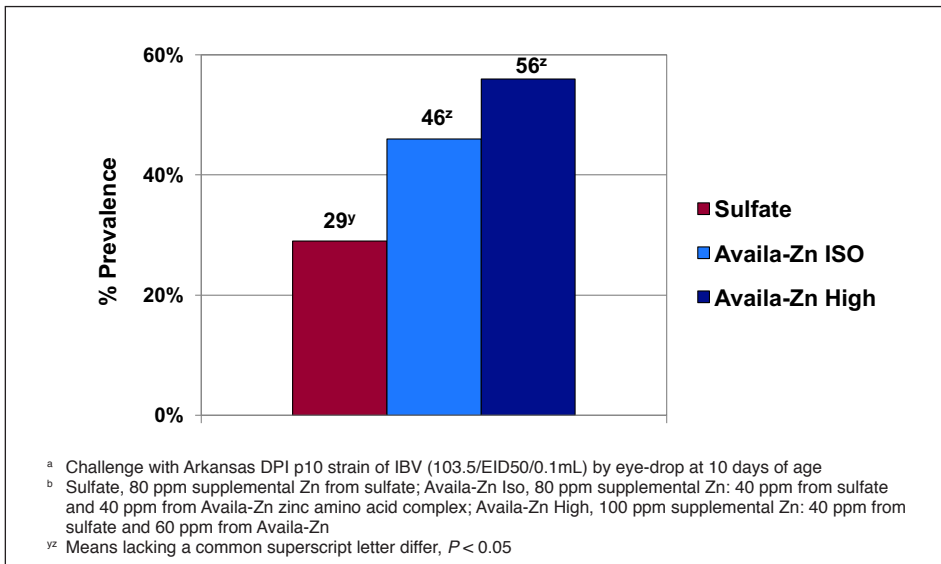
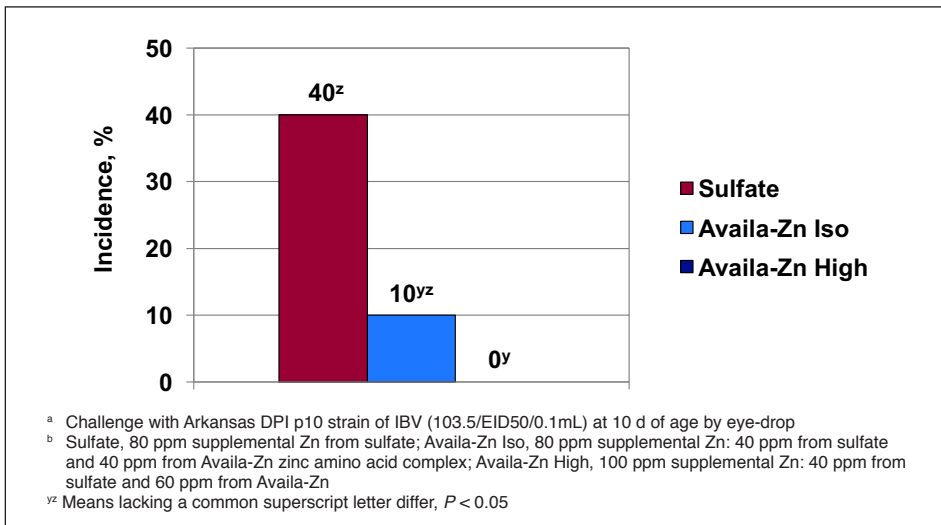


Figure 8. Incidence of airsacculitis in broilers directly infected with IBV^a at 10 days post-challenge^b



of steers, as evidenced by increased dry matter intake and decreased rectal temperatures. The ability to absorb nutrients from the gut may have been improved for steers fed zinc from Zinpro Performance Minerals, as these animals had decreased duodenal villi width and increased jejunum villi height and height: crypt depth, as compared with heat-stressed steers fed only inorganic zinc.

Weaning presents another potential stressor for almost every mammalian species. Data in piglets indicates that feeding Zinpro Performance Minerals has a positive impact on villi anatomy and increased number of goblet cells in pigs. Gastric nutrient-intubation of piglets

at birth, d 10, and d 21, with 40 mg of zinc from Zinpro Performance Minerals increased the number of epithelial goblet cells of the jejunal villi and tended to increase mucosal thickness (Metzler-Zebeli *et al.*, 2010).

Inflammation and the Respiratory Tract

Zinc appears to have an important role in the integrity and defense mechanisms of the respiratory epithelium (antioxidant, organelle stabilizer, anti-apoptotic agent, epithelial healing and renewal, anti-inflammatory; Truong-Tran *et al.*, 2000). A study in rabbits has shown that an antibacterial peptide with zinc as a cofactor is able to reduce *E. coli* colony

counts by 70 percent in the respiratory tract (LaForce *et al.*, 1984). A study measuring intracellular zinc in pulmonary arterial endothelial cells showed zinc was important in the reduction of LPS-induced apoptosis (Thambiayya, 2012).

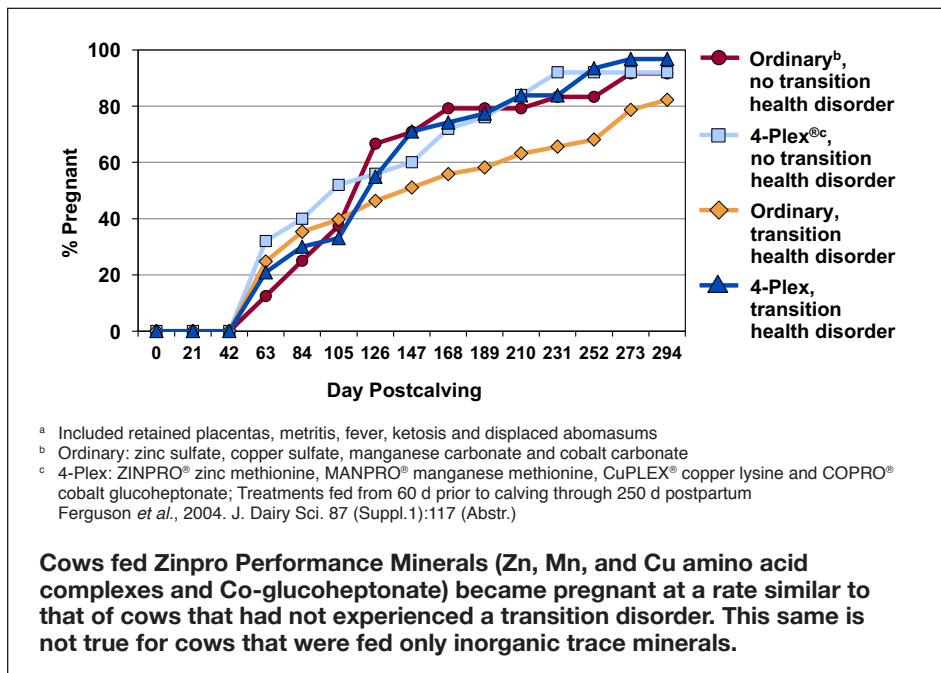
Respiratory tracts of birds are exposed to a number of irritants. Recent work in chickens challenged intraocularly with a pathogenic strain of *Infectious Bronchitis Virus* (Arkansas DPI p10) showed broilers fed zinc from Zinpro Performance Minerals had an increase in early clinical inflammatory manifestations (Figure 7), and significantly lower airsacculitis (Figure 8). Also observed were a decrease in virus shedding and birds that were able to maintain a better daily weight gain 10 days post-challenge, compared with zinc sulfate-fed birds (Rebollo, unpublished). According to these findings, improved zinc status may create a more consistent epithelial reaction in the upper respiratory tract, reducing the access of harmful agents to the air sacs, and in turn, decrease viral output.

While some data exists indicating the role Zinpro Performance Minerals play in the respiratory tract of poultry, data regarding its impact on the respiratory epithelium in mammals are limited. Analysis of beef data indicates that calves born to cows fed Zinpro Performance Minerals had a greater than 50 percent decrease in treatments for bovine respiratory disease during the growing phase, which contributed to a greater return on investment for those animals (Marques *et al.*, 2016). Research regarding the impact of Zinpro Performance Minerals on the respiratory epithelium of ruminants presents a great research opportunity.

Inflammation and the Reproductive Tract

Follow the birthing process, a dramatic physiological shift occurs in animals. One such shift occurs in the epithelium of the reproductive tract. It is critical for production animals to mount an effective immune response in order to effectively eliminate reproductive tract pathogens that enter during the birthing process and to repair tissues damaged during birthing. This helps prepare the animal for subsequent pregnancies. Analysis of endometrial gene expression indicates that

Figure 9. Impact of Zinpro Performance Minerals^a on Pregnancy Rate of Cows with or without a Transition Disease



cows fed Zinpro Performance Minerals attain a pro-inflammatory state earlier as compared to cows fed only inorganic minerals (Batistel *et al.*, 2017). This may indicate that cows fed Zinpro Performance Minerals were able to effectively eliminate pathogens from the reproductive tract and repair damaged tissue more quickly. This is further confirmed by the differential expression of other genes known to play a role in eliminating pathogenic bacteria that have invaded the epithelium. However, gene expression data alone does not necessarily correlate to a phenotypic response. A key finding related to feeding Zinpro Performance Minerals is the improvement in reproductive performance above that attained by feeding only inorganic mineral sources. This was clearly illustrated in a study conducted by Ferguson *et al.* (2004) where feeding Zinpro Performance Minerals to cows that experienced a transition health disorder, improved reproductive performance (i.e., pregnancy rates) to a level similar to that of cows that never experienced a transition disorder. The same results did not occur when only inorganic trace minerals sources were fed (Figure 9; Ferguson *et al.*, 2004).

The reproductive process is inherently different in poultry. In birds, egg production and quality depends mostly

on hens having a healthy oviduct. Egg white, shell membrane, shell structure, shell color and protective cuticle are produced as the egg moves down through the different portions of this organ. The oviduct is lined with highly specialized cells for each portion according to the egg formation process. Since zinc, manganese and copper are important components of the organic shell matrix and coordinate shell formation (Yves, 2001), adequate levels of these minerals need to be

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provided at all times in the feed. Mabe *et al.* (2003) found that supplementation with Zinpro Performance Minerals improved eggshell quality in aged laying hens. Guo *et al.* (2002) found an increase in shell gland carbonic anhydrase (zinc-dependent enzyme that produces the major component of the eggshell) and an increase in yolk zinc concentration of 59-week old layer hens fed 80 ppm zinc from Zinpro Performance Minerals, compared to feeding the same or higher levels of zinc from zinc sulfate. Additionally, the

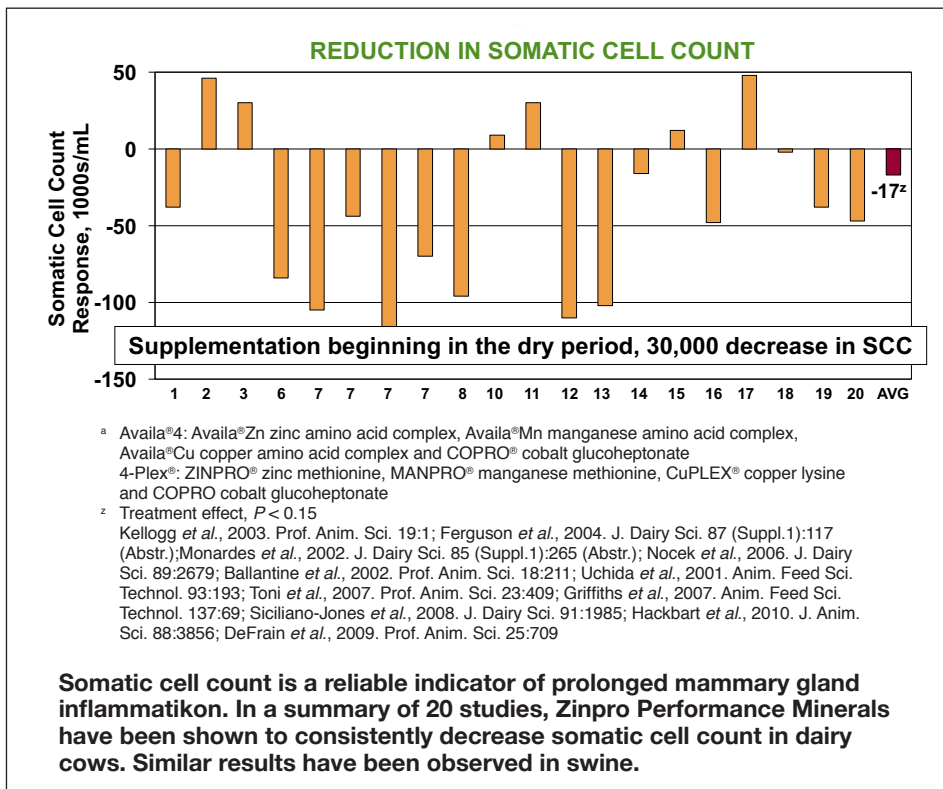
epithelium in the oviduct is very active and has a continuous turnover. Since some pathogens like *Infectious Bronchitis Virus* and *Mycoplasma spp.* commonly challenge these cells (Saif, 2011), the fortification of layer and breeder diets with zinc and manganese from Zinpro Performance Minerals could prove helpful due to their known role in immune and inflammatory responses. This benefit is an area that requires additional research.

Inflammation and the Mammary Gland

In the mammary gland, the keratin plug of the teat is one of the first lines of defense to protect the animal from a mammary infection (i.e., mastitis). Feeding zinc from Zinpro Performance Minerals has been shown to increase teat keratin production in cows, which may protect the cow from a mammary infection (Jones, 1995). Furthermore, elevated somatic cell counts (SCC) in milk are a key indicator of mammary gland inflammation (Pyörälä, 2003), and numerous studies have confirmed that feeding Zinpro Performance Minerals decreases SCC in lactating dairy cattle (Kellogg *et al.*, 2003, 2004; Sobhanirad *et al.*, 2010; Nayeri *et al.*, 2014). A 12-trial summary indicated that feeding cows zinc from Zinpro Performance Minerals reduced SCC on average by nearly 100 (1000/mL; Kellogg *et al.*, 2004; Figure 10).

Although the ruminant mammary gland is most commonly associated with mastitis, several studies in swine have shown that SCC decrease when sows are fed Zinpro Performance Minerals. A study from the University of Barcelona showed that feeding sows Zinpro Performance Minerals in place of inorganic trace minerals lowered SCC by roughly 400 (1000/mL). A second study had similar trends, showing an interesting parity response for sows fed zinc from Zinpro

Figure 10. The Impact of Zinpro Performance Minerals on Somatic Cell Count



Performance Minerals compared to feeding zinc sulfate. Log transformed SCC decreased 2.64 in first parity and 1.21 in second parity when sows were fed Zinpro Performance Minerals (Martineau *et al.*, 2017).

Although SCC is a reliable indicator of inflammation within the mammary gland, integrity of the mammary epithelium is also of paramount importance. Recent data indicates that zinc from Zinpro Performance Minerals may impact mammary gland epithelial integrity. In this study, mid-lactation cows subjected to either thermal-neutral environments or heat-stress conditions were fed 40 ppm zinc from either Zinpro Performance Minerals or zinc tetrabasic chloride (ZnCl). In both the thermal-neutral and heat-stress phases, plasma lactose increased in cows receiving only zinc from ZnCl, but remained unchanged in cows consuming zinc from Zinpro Performance Minerals. These results indicate that feeding zinc from Zinpro Performance Minerals in place of ZnCl better maintains mammary tight junction integrity, which is crucial for milk secretion and avoiding milk leakage from the lumen of alveoli (Weng *et al.*, 2016).

Inflammation and the Adaptive Immune System

The adaptive immune system differs from the innate immune system in the sense that it has the ability to recognize specific antigens and has a memory function. In contrast, the innate immune system does not have memory, includes anatomical features that prevent bacterial entry into the body and binds to general classes of bacterial or viral antigens. Components of the innate immune system include epithelial barriers, macrophages, granulocytes, mast cells and natural killer cells. Binding to specific peptide sequences would be reserved for the adaptive (acquired) immune system components and their memory-like function. Components of the adaptive immune system include B-lymphocytes (10 percent to 20 percent of circulating lymphocyte population) and T-lymphocytes (60 percent to 70 percent of circulating lymphocyte population). For simplicity sake, data from multiple cell classes will be discussed herein, although they may not be specific to the adaptive immune system, as many of these cell types work in concert to mount an inflammatory event and successful immune response.

A study at the University of Illinois indicated improved health when transition dairy cows were supplemented with Zinpro Performance Minerals (Osorio *et al.*, 2016a). In this study, feeding Zinpro Performance Minerals in place of sulfate forms of zinc, manganese, copper and cobalt, improved liver function, increased polymorphonuclear leukocyte (attract leukocytes to site of infection) phagocytosis (greater than 20 percent), and increased antioxidant capacity postpartum. Oxidative stress can activate a variety of transcription factors, which will eventually lead to inflammation (Reuter *et al.*, 2010). While blood total antioxidant capacity was lower precalving for cows supplemented with Zinpro Performance Minerals, postcalving these same cows had greater total antioxidant capacity in blood, indicating they were under less oxidative stress. This may partially explain why cows fed Zinpro Performance Minerals had a reduction in expression of genes for the pro-inflammatory cytokines, such as tumor necrosis factor and IL-6.

The response observed in the University of Illinois study mirrors work in finishing steers, where supplementation with zinc from Zinpro Performance Minerals positively impacts whole blood white blood cell counts, and blood eosinophil and basophil concentrations (Genther-Schroeder *et al.*, 2016).

Perhaps the most interesting aspect of the data presented from the University of Illinois is the impact of Zinpro Performance Minerals consumption by the dam on the calf (Jacometo *et al.*, 2015). Calves born to cows supplemented with Zinpro Performance Minerals during the last month of gestation had a decrease in liver damage and altered gene expression, suggestive of a more efficient immune system. In contrast, calves born to cows fed only inorganic trace minerals had an upregulation of a series of genes that ultimately suggested that those calves were in a pro-inflammatory state shortly after birth. This is supported by a decrease in rectal temperatures for the first two weeks postpartum in calves born to dams fed Zinpro Performance Minerals, potentially indicating a decrease in stress and inflammation following the birthing process.

Additional work in poultry has shown feeding Zinpro Performance Minerals to reduce oxidative stress by lowering MDA (malondialdehyde), increasing blood uric acid, regulating TLRs and anti-inflammatory cytokines, and increasing polymorphonucleated and mononuclear cell proliferation and activity (Guo *et al.*, 2004; Echeverry *et al.*, 2016; Reza *et al.*, 2016). As compared to inorganic sources, feeding Zinpro Performance Minerals have shown more consistent effects on the different steps of the inflammatory response. Zinc and manganese from Zinpro Performance Minerals have been shown to increase phagocytosis in both opsonized and unopsonized turkey blood macrophages when exposed to sheep red blood cells *in vitro* (Ferket *et al.*, 1992). This is consistent with studies in mice and other species where phagocytosis is impaired during zinc deficiency and restored with zinc supplementation (Darlynn *et al.*, 2011; Hammon *et al.*, 2014). Replacing inorganic zinc and manganese with zinc and manganese from Zinpro Performance Minerals increased tumoricidal activity of macrophages from 25 percent to 65 percent (Ferket *et al.*, 1992).

Zinc from Zinpro Performance Minerals has also shown evidence of elevating the sensitivity to LPS (lipopolysaccharides) from *Salmonella typhimurium* injected in layer hens, in fever and circulatory cytokine responses (Cheng *et al.*, 2004), meaning a shortened acute phase response. Redistribution of zinc due to inflammation was observed in LPS-challenged birds, with increased zinc sequestration in liver and spleen, and reduced level in the blood (Cheng *et al.*, 2004). This is part of the inflammatory response to systemic infections, designed to starve harmful microorganisms of zinc and iron that are essential nutrients for many bacteria (Klasing, 1984). Ceca IL-10 levels were higher in broilers fed zinc

from Zinpro Performance Minerals after being challenged with *E. acervulina*, *E. maxima* and *E. tenella* (Troche, 2015). Interleukin-10, an important anti-inflammatory cytokine, is produced during chronic infections. It inhibits Th1 cells, NK cells, and macrophages and helps transition to M2 phase, turning down excessive response and beginning tissue repair (Couper *et al.*, 2008). This regulatory response was observed in the previous study when fever and IL-1 β levels declined faster in birds fed zinc from zinc amino acid complex (Cheng *et al.*, 2004).

Conclusions

Trace minerals are involved in many enzymes and processes associated with immune system function. Ensuring that trace mineral requirements are met for production animals, including poultry, swine, dairy and beef cattle, is critical in order for the animal to mount an appropriate inflammatory response. This response begins with the innate immune system, where animals supplemented with Zinpro Performance Minerals experience improved skin integrity and wound healing, enhanced GIT morphology and integrity, better mammary gland integrity accompanied by a reduction in SCC, and improved pathogen clearing/inflammatory responses in the reproductive tract following parturition.

Moving deeper into the immune system and the cellular mechanisms responsible for an inflammatory response, when

production animals are fed Zinpro Performance Minerals, an increase in antioxidant capacity is observed. We also see an improvement in immune cell function within the blood, which may explain the ability of the animal to neutralize free radicals that cause oxidative damage. In addition, animals fed Zinpro Performance Minerals have decreased metabolites circulating in the blood, which are classic indicators of a pro-inflammatory state.

The impact of trace minerals on inflammation and the immune system are complex, and require more detailed analysis. However, the data shown here indicate that feeding Zinpro Performance Minerals helps improve the inflammatory state of production through multiple mechanisms, and it has been observed at the deepest cellular level, via the alteration of key genes associated with inflammation. The impact of trace minerals from Zinpro Performance Minerals on production animals is not limited to the current generation, but is also communicated to the next generation via a fetal programming mechanism that equips the immune system of the offspring to mount an inflammatory response when needed. Remember that inflammatory signaling is a means of communication within animals, and is critical to fighting off pathogens and infections. When Zinpro Performance Minerals are fed, that communication appears to be improved and the inflammatory response is made more efficient.

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