

CHRONIC OXIDATIVE STRESS: CLINICAL OBSERVATIONS SUGGEST A RELATIONSHIP BETWEEN OXIDATIVE STRESS, TRACE MINERAL IMBALANCES, AND AIP

BORN OF FRUSTRATION

AIP Background

Acute Interstitial Pneumonia (AIP) is a multifactorial respiratory disease that affects feedyard cattle. Cattle affected by the disease present dyspnea, panting, and death. At necropsy, lungs grossly display edema and emphysema. Histopathology reports detail hyaline membranes, type II pneumocyte hyperplasia, sterile necrosis, pro-inflammatory state and multifactorial in cause.

Loneragan reported AIP affected animals are in a ratio of 3:1 heifers to steers.

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Cellular Physiology and Chronic Oxidative Stress

There are specific inter-relationships between cellular physiology and the incidence of subclinical and clinical disease. Alterations in normal cellular functions can predispose animals to a wide variety of infectious and non-infectious situations. An understanding of the inherent protective mechanisms of the individual cell and how these alterations manifest themselves in various physical symptoms, the influence of environment, and the physiological impact of adequate nutrition, aids in the development of sound preventative medicine programs.

AIP's have increased steadily over the past decade, especially in high performing yards, and worse yet, treatment response has declined.

Veterinarians were trying a number of things, most frequently settling on antibiotics and steroids. And although they seemed to prolong life, in the end, we were losing the vast majority of AIP cattle.

Under the microscope, we were seeing sterile tissue destruction, that was becoming more widespread - which was baffling. This was not an infectious disease, but it seemed to be spreading.

We were frustrated and ready to try something new. After a number of false starts and disappointments, we found an academic paper that held out some hope.

Dr. Robert Coffey's paper suggested that metabolic meltdown due to depletion of enzymes in the blood could lead to sterile tissue destruction. It matched what we were seeing, so we reached out to industry partners and began working on several formulations to test.

It was a Friday morning "Hey the new stuff is working." The AIP's from yesterday are eating and only one is still "puffing." At first we used our best formulation with antibiotics and steroids, but when we tried it alone, we found it worked just as well.

Of course, it didn't work on all AIP's. But, instead of losing more than 80%, we were now saving many of them. And we found that acute AIP pulls that resumed normal breathing quickly (in less than 12 hours) did not appear to have developed permanent lung damage.

To get where we are today, we had to brush up on our physiology and read a bunch of academic papers. The rest of this document is dedicated to sharing that information with you.

Tissue Meltdown

During the production of energy, about 2% of oxygen escapes in the form of reactive oxygen species called free radicals. Free radicals are oxidants, which are very reactive molecules that bind to and break DNA chains, directly causing mutations. They can also bind to and destroy proteins and fats in cell membranes.

3 Red Blood Cell Enzymes

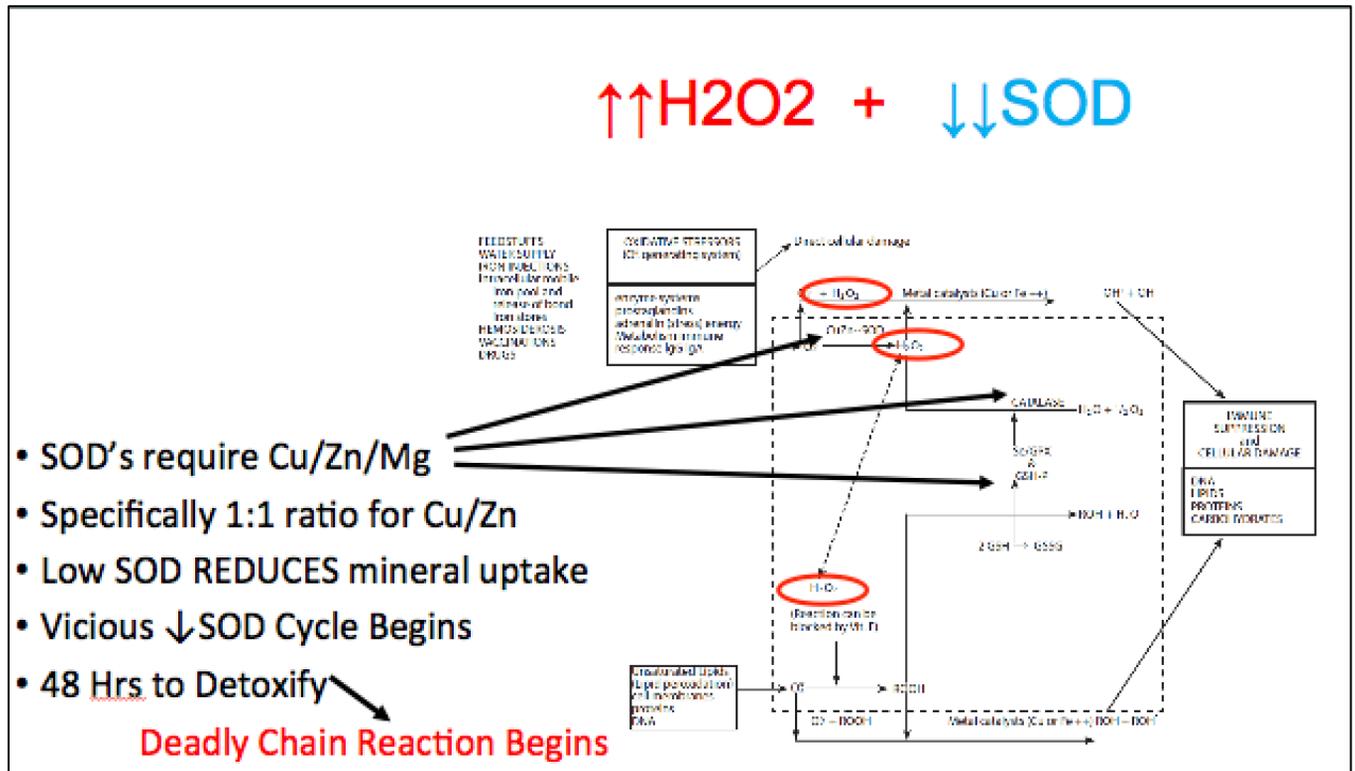
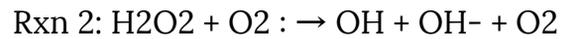
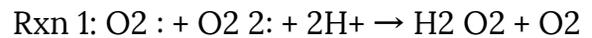
Under normal conditions cells are protected against free radicals. Catalase, Cu/Zn-Superoxide Dismutase, and Gutathione Peroxidase are three red blood cell enzymes that have a protective role in the animal and serve as a biological monitor of the physiological and nutritional state of the animal.

If the above oxidative enzyme systems are suppressed or do not function properly, the chemistry of the cells is altered due to buildup of free radicals and enzymes are either depleted or do not perform their tasks due to mineral deficiencies.

Oxygen Toxicity

The Superoxide radical, O_2^- , is formed during various metabolic processes, many of which are considered normal; Liver cells, muscle cells, leukocytes, erythrocytes, aerobic bacteria, any cell that undergoes oxidative cellular metabolism, all form oxygen radicals during normal metabolic processes.

These oxygen radicals are converted to hydrogen peroxide (Reaction 1) or the more deadly hydroxide radical (Reaction 2):



In a properly functioning system the hydrogen peroxide is then converted to oxygen and water by Catalase. If the hydrogen peroxide and the superoxide radical are allowed to combine, the more reactive and destructive hydroxide radical is formed. When the formation of one or more of radicals becomes uncontrolled or the organism loses the ability to regulate these reactions, changes in cellular physiology result that become detrimental to the individual cells, organ systems, or the entire host or animal.

Some of these changes include generalized tissue destruction, lameness and joint inflammation, DNA miscoding or degradation, lipid peroxidation, altered immune function and inactivation of important cellular enzymes.

Replenishing Enzymes with Amino Acid Chelates

One factor which may contribute to the inability of the body to control free radical accumulation within oxygen consuming cells is that ionic mineral absorption in the gut requires an integral protein carrier molecule embedded in and traversing the mucosal membrane.

Once absorbed into the mucosal cell, the transfer of the cation from the terminal web below the microvilli to the basement membrane requires the presence of carrier proteins. For iron, apoferritin is a suitable carrier. In the case of zinc, albumin is the carrier protein. For copper the carrier is ceruloplasmin and for manganese it is transmanganin. Both protein and albumin are necessary to transport mineral ions from the gut to the plasma.

Inorganic and metal amino acid chelated (AAC) minerals are primarily absorbed in the small intestine of animals. The small intestine is divided into three parts; the duodenum, jejunum and the ileum (respectively). Inorganic minerals are mainly absorbed in the duodenum. AAC minerals can be absorbed throughout the small intestine but are mainly absorbed in the jejunum of animal species.

The small intestine in cattle is generally 130-140 feet long. The duodenum is 6-7 feet, the jejunum is 36-40 feet and the ileum is roughly 80-90 feet. In ruminant animals, after the digesta leaves the rumen and enters the abomasum (stomach) the digestive system mostly follows the same process in the majority of other animal species.

↑↑H₂O₂ + ↓↓SOD

Cant Get Cu/Zn/Mg in fast enough

- Inorganic Minerals Absorbed in Duodenum
- The Rumen contents tie up much of minerals reducing availability
- Increased sulfur in water and distillers further ties up minerals
- 1000lb Steer in 95° weather will drink 150lbs of Water/Day (19 -30 gallons - UNL)
- Absorption from duodenum requires complex reactions that also depend on the depleted minerals.
- Reduced SOD's slows absorption further
- Vicious cycle further reducing SOD's

Note: Cattle infected with BVD have inflamed duodenums which restricts mineral absorption

Duodenum is the Bottleneck

1. Ruminates Only- When inorganic minerals mix with the fluid in the rumen contents, they become susceptible to the interfering and complexing inhibitory properties of certain metal groups (iron, sulfur and molybdenum) as well as plant phytates. This can result in the inorganic minerals becoming unavailable for absorption in the animal. AAC minerals are not as susceptible to these reactions.

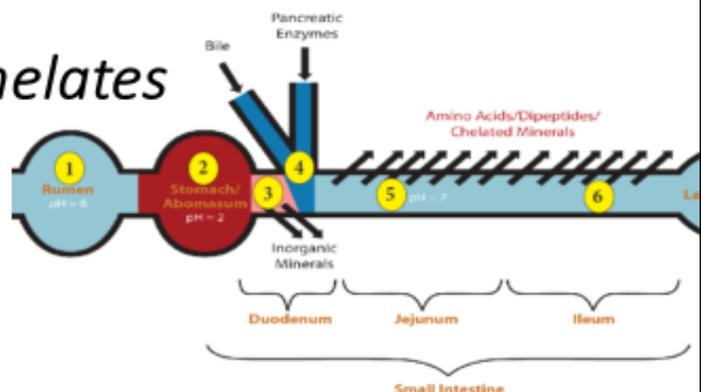
2. Digesta including inorganic mineral sources pass into the stomach where the low pH (of 2) causes the solubilization of the inorganic minerals. This environment keeps the inorganic minerals soluble until bile and pancreatic enzymes are introduced at the junction of the duodenum and jejunum. AAC minerals do not react in this low pH (chelated) environment and molecule remains intact.

3. The digesta moves from the stomach to the duodenum. The low pH (of 2) of the digesta allows the inorganic minerals to remain soluble thus allowing for absorption

As pancreatic juices and bile from the gallbladder enter the system, they act as buffers at the end of the duodenum which then in turn raises the pH of the digesta and the pH rises from approximately a pH of 2 to a pH of 7 resulting in the digesta becoming pH neutral before moving to the jejunum.

4. As the pH becomes more neutral, solubility and absorption of inorganic minerals decreases. Whatever inorganic minerals were not absorbed the duodenum are excreted as waste. Inorganic minerals are either rendered unabsorbable by antagonistic minerals (Fe, Mo and S) and plant compounds called phytates.

Metal Amino Acid Chelates



Advantages of Amino Acid Chelates

- Absorbed in Jejunum quickly as an amino acid
- Electronically neutral – less susceptible to antagonisms such as iron, sulfur, and mycotoxin binders.
- By-pass Rumen
- Independent of Rumen PH
- Independent of complex transport reactions
- Minimum 1:1 molar ratio.

ABSORPTION

Amino Acid Chelated Vs Inorganic Minerals

- Iron 490% greater
- Copper 580% greater
- Magnesium 410% greater
- Calcium 421% greater
- Manganese 340% greater

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The short length of the duodenum results in limited ability for mineral absorption. Amino Acid Chelated minerals are unaffected by these factors.

5. The jejunum is the main absorption site of amino acids, peptides and dipeptides. The length of the jejunum and how it recognizes the Amino Acid Chelated minerals (Amino Acid) make the jejunum the primary location for AAC mineral absorption.

6. The Amino Acid Chelated mineral's structure results in a unique recognition allowing for absorption in the ileum. After materials enter the large intestine, virtually no mineral will be absorbed. Amino Acid Chelated minerals have the advantage over inorganic minerals by:

- 1) remaining viable in the presence of antagonistic mineral complexing as well as phytates and other feed ingredients such as mycotoxin inhibiting
- 2) the ability to be absorbed in the jejunum and ileum
- 3) being recognized as an amino acid. Chelation of minerals is a very precise science.

Only the resulting specific amino acid chelate can resist digestion and maintain its integrity as it travels thru the digestive system and is ultimately absorbed through the gut.

Intact absorption is faster, easier, and requires less metabolic energy, provided the chelate is under 1000 Daltons in size.

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