Introduction

Lameness has long been recognized as a problem and has been associated with a decrease in sow fertility (Penny, 1980). A study conducted in Germany reported fewer litters for lame sows than nonlame sows (<3.0 litters vs. 4.5 litters; Grandjot, 2007). This author also reported higher piglet losses for lame sows than healthy sows (27% vs. 12.4%). These production losses along with early culling of young lame sows cause a financial burden to swine production estimated at $52/sow (Grandjot, 2007). Lameness and locomotion problems are major reasons for culling (Friendship et al., 1986; Jorgensen, 2000). Therefore, maintaining herd productivity through the removal and replacement of non-productive sows has proven crucial to the well-being and success of the business. The knowledge and understanding of lameness continues to grow as an increasing number of research groups work to collect and report new data on the issue. Lameness has been linked to a significant decrease in sow productivity and is known to increase the odds of early removal from the herd (Anil et al., 2008). Often times, the sows that are removed for this reason are culled at a younger age than those removed for any other reason. The early age of removal has a negative impact on litter size, piglet survival and may increase the disruption of herd health status (Dagorn and Aumaitre, 1979; D’Allaire et al., 1987; Patterson et al., 1997). Anil et al. (2009) conducted a cohort study to examine the relationship between lameness and its effects on reproductive performance and sow longevity. The results of the study showed that lame sows had litters of smaller sizes along with a smaller number of pigs born live (Table 1). With this, sows had a lower rate of survival 350 days after reports of lameness, and spent fewer days in the herd. Clearly, the study revealed the significant differences between lame and nonlame sows in survivability. The sow longevity also was affected by parity and farrowing performance (Anil et al., 2009a). Odds ratios have been reported for sows with elongated claws, claw cracks, heel erosion and heel overgrowth. These same studies have further concluded that uneven toes significantly impact the incidence of lameness (Vestergaard et al., 2006; Anil et al., 2008).

Many sows have claw lesions. Surveys have shown that greater than 88% of sows have at least one claw
lesion (Anil et al., 2007). These numbers can range and change due to environmental influences and aggressive behaviors depending on whether sows are housed in group pens or crates. Claw lesions may not be indicative of lameness. The lesions of greatest concern are those which penetrate the horn wall into the corium of the foot and cause an inflammatory response such as side wall cracks of the outer horn wall or white line lesions. The focus of this paper is the impact of lameness that causes pain and locomotor problems for sows. It is important for swine producers to measure and understand how and why claw lesions are occurring. This will help develop management strategies to decrease claw lesions, lameness and the risk of early removal of sows from the herd.

The objective of this paper is to build an understanding of how the metabolic and mechanistic pathways of inflammation due to lameness influence sow reproductive performance. An understanding of these mechanisms may help one to modify management practices, alter dietary formulations and implement new disease prevention strategies. These modifications should help decrease and/or prevent this possible inflammatory response as well as lead to more productive and healthier sows. This paper will mainly focus on the inflammatory response of lameness. However, the authors will use other inflammatory responses, such as starvation, mastitis and immune barrier dysfunction, to demonstrate how inflammation from lameness may cause reproductive problems.

**Table 1.** Effects of lameness on pigs produced per day and longevity\(^a\).

<table>
<thead>
<tr>
<th></th>
<th>Not Lame</th>
<th>Lame</th>
<th>(P) value</th>
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<tr>
<td>Pigs born/d</td>
<td>0.049 ± 0.002</td>
<td>0.028 ± 0.003</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Survival at 350 d, %</td>
<td>44.6</td>
<td>23.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total days in herd</td>
<td>215.7 ± 4.45</td>
<td>148.3 ± 10.67</td>
<td>&lt;0.001</td>
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Decreased Feed Intake and Nutrient Partitioning

Inflammation, often accompanied by pain, is one of the most apparent consequences of lameness. Many times lame sows are thin and have poor body condition. Often sows with chronic lameness have decreased feed intake. The adjustments in the sow eating habits will lead to further complications, as observed with changes in reproductive performance. Generally if a younger parity sow does not eat well, she will show a decrease in her reproductive capabilities. Younger first litter gilts are more sensitive to the negative effects of decreased feed intake during lactation than were older gilts or multiparous sows (Eissen et al., 2003). Australian researchers (King and Dunkin 1986) were some of the first to demonstrate the linear relationship between daily feed intake during lactation and increased time required for sows to express estrus after weaning. Lactation is one of the most energetically expensive and challenging activities that a female can undertake. Therefore, maintaining feed intake is crucial to sow well-being and overall performance. Feed intake, especially during certain stages in the reproductive cycle, influences many of the body's systems in significant ways. For instance, the decrease of energy and protein consumption during lactation may disrupt or even change the amount of signaling of gonadotropin-releasing hormone (GnRH) from the hypothalamus. This signal impacts the amount of LH and FSH released and subsequently affects steroidogenesis of the ovary. The reproductive effects of inadequate feed intake during lactation seem to be mediated, at least in part, through LH secretion and embryo mortality (King and Martin, 1989). Meeting sufficient levels of energy and protein through consumption of feed is crucial to the release of the hormones necessary for the proper functioning of the reproductive system.

Inflammation not only has the potential to impact feed consumption, but release of cytokines in response to inflammation will cause a change in how nutrients will be utilized and prioritized within in the body. When an inflammatory response is signaled the animal will shift where nutrients will be utilized. Processes and organs of the immune system will take priority over other production metabolism. In other words, increased energy will go to the intestinal tract, immune organs, liver, lungs and brain, while systems not as necessary for survival such as reproduction will receive decreased nutrient flow. Anabolic processes will be interrupted, and companion catabolic activities will be enhanced to help supply nutrient needs for the immune system (Spurlock, 1997). Stallmach et al. (1995) documented the presence of numerous cytokines in human amniotic fluid and several of the cytokines, such as IL-6, IL-8 and TNF, were found in
fetal blood. Interestingly, the presence of IL-6 and IL-8 has been associated with intrauterine growth retardation in humans. This may suggest a possible mechanism of growth retardation or compromised development in livestock species that deserves further investigation. In addition, the immune system demands and requires a different priority of amino acids compared to those that optimize lactation, growth and reproduction. The effects of inflammation on feed intake or nutrient partitioning negatively impacts sow body composition and condition during lactation.

**Body Condition**

The body condition of a sow is based on a scale from 1 to 5, with 1 signifying an under conditioned body and 5 representing an over conditioned state. Often the sows or gilts with low feed intakes during lactation have a body condition score of 1 (with scores ranging from 1-5, with 1 being thin). Those pigs with lower scores often showed signs of reproductive complications. To illustrate this point, it has been seen that sows with a body condition score (BCS) of 1 have a higher frequency of acyclic ovaries than sows with a BCS of 4 (Knauer et al., 2007). It is believed that for those sows with a lower BCS, changes in other body functions will likely result. A low feed intake during lactation can lead to an excessive loss of body weight, which will ultimately result in decreased sow longevity (Gaughan et al., 1995) and reproductive performance (Quesnel, 2005). It is important to keep in mind the factors that contribute to a decreased BCS in lame sows. It is reasonable to account for some of the weight loss as being due to the increase in protein loss. Loss of protein causes dramatic effects on body condition and function. Clowes *et al.* (2003) reported that a mass loss of body protein, losses greater than 9 to 12%, rapidly decreased ovarian function. Protein restriction throughout lactation alters the concentrations of circulating somatotrophic hormones and insulin at the conclusion of the lactation period. These low concentrations negatively impact post weaning ovulation rate (Mejia-Guadarrama *et al.*, 2002). It should be noted that limited follicular development and incomplete recovery of the reproductive axis at weaning seem to be the most likely causes of decreased embryonic survival in second parity sows with earlier weaning age (Willis *et al.*, 2003). For reasons similar to these, sows with inadequate feed intake during lactation increased their odds of removal from the breeding herd (Anil *et al.*, 2006). The prevention and early treatment of lameness and other claw injuries will help maintain feed consumption and appetite, leading to a decrease in reproductive complications due to lameness. It is important to note that not all sows with claw lesions will
show changes in appetite and feed consumption. The injury of the sow must be inflammatory to see many of the responses described above and yet to come.

Cytokine Release

Severe tissue injury induces a relatively stereotypical pathophysiologic response that is manifested by catabolism, fever and other behaviors observed with illness. When an animal has an insult, most of the adjustments that happen within the body are mediated by a cascade of polypeptide molecules called inflammatory cytokines. The release of possible toxins and/or other products from cell injury drives the activation of the inflammatory cytokines. This activation leads to a variety of metabolic and endocrine changes in the body. These changes are mediated by the direct action of cytokines on tissue function and by changes in pituitary-endocrine end-organ function. Cytokines are released from immune barrier functioning cells such as endothelial cells, monocytes, macrophages, specialized immune cells like lymphocytes and several other types of parenchymal cells. Some of the cytokines that are released are interleukins and come in the forms of IL-1, IL-2 and IL-6. Tumor necrosis factor-alpha (TNF-α), interferon-gamma (INF-γ) and several other cytokines with anti-inflammatory activity, such as IL-10 and IL-1, work in a synergistic reaction to regulate body metabolism and help the animal survive. In simplistic terms, cytokines are released to help the body in the fighting against possible toxins and other harmful byproducts of an injury. These cytokines, along with hormones, also have specific impact on the functioning of specific reproductive organs.

Cytokines and Reproduction

In the ovary, intrinsic cytokines IL-6, TNFα and IL-1 regulate steroidogenesis, maturation, atresia and apoptosis of ovarian cells. The release of cytokines causes a decrease in GnRH from the hypothalamus that decreases the amount of FSH and LH released from the pituitary. A severe inflammatory response from a wound may release large amounts of cytokines, such as TNFα, which will then influence the ovary. The effects on the ovary will cause a reduction in steroidogenesis and even apoptosis of the ovarian cells and ultimately can result in a lost pregnancy. The most common reproductive anomaly found in cull sows was acyclic ovaries (9%, Knauer et al., 2007). The occurrence of acyclic ovaries increased (P<0.05) as BCS of the sow decreased. Acyclic ovaries also were positively correlated (P<0.01) with
rear foot abscesses. There is a strong correlation between lameness and reproductive problems as just revealed with the increase of acyclic ovaries in sows with rear foot abscesses.

In relation, at the level of hypothalamus, IL-1 inhibits pulsatile secretion of GnRH, which leads to low gonadotropin secretion and low levels of sex steroids (Rivest and Rivier, 1995; Shalts et al., 1991). Severe inflammatory illness induced a dramatic decrease in circulating sex steroids (Dong et al., 1992) in the human male while studies with TNFα showed inhibited gonadotropin secretion in the mouse (van der Poll et al., 1993). The interrelationships between stress, hormones and basic ovarian functions in the ovary were tested in sows (Sirotkin, 2010). This study showed that involvement of hormones (IGF-1, leptin, FSH) controls proliferation, apoptosis and secretory activity of ovarian cells. More importantly the research showed that stressors (heat stress and malnutrition) impacted proliferation, apoptosis and secretory activities of granulose and ovarian follicular cells. Most of these responses probably are mediated at the hypothalamic level by the induction of corticotropic releasing hormone (CRH) and/or vasopressin (VP), which together act to increase the release of the adrenocorticotropic hormone (ACTH). The way the reproductive system responds to lack of nutrients is similar to the body’s inflammatory response due to cytokine release. When the body lacks in energy, due to a decrease in feed intake, the reproductive system will often not receive the proper amount of nutrients that is needed for a high or even normal level of performance. Similarly, when cytokines are released because of an injury, the inflammatory response is activated. This system uses more and more energy to fight inflammation or insult, taking energy that would have been distributed to the reproductive system. In that way, when cytokines are released, the reproductive system has a similar response as it does to lack of energy. The distribution of energy is controlled by the brain and in essence, the metabolic response to starvation and the response to severe inflammation essentially cause similar signals within the body and impact signals from the brain similarly.

**Inflammatory States**

Although the reproductive system is highlighted in this paper, one should also remember that all organ systems are altered by acute and chronic inflammatory states. There are dramatic shifts observed in liver function in livestock with an acute phase inflammatory response. Some of the changes in the liver include suppression of albumin, transferring of ceruloplasmin, and increased synthesis of proteins like fibrinogen and C-reactive protein (Dinarello and Wolf, 1993). Many of the claw lesions and injuries
similarly fall into these types of acute and chronic inflammatory wounds and show dramatic changes in the reproductive system. The release of cytokines that accompany foot injuries ultimately leads to complications in sow reproduction; just as acute inflammatory states can lead to alterations in the liver in different species of livestock. This link makes the impact of lameness and other foot injuries on reproduction seem much more plausible and also, leads to an understanding of why researchers report an increase in abortions, absorptions of embryos, a decrease in litter size and a lack of sows returning to estrus when sows are severely lame.

Other Inflammatory Responses

Inflammation due to lameness uses certain pathways and causes certain reactions in the body that mirror other inflammatory responses such as starvation, mastitis and immune barrier dysfunction. With the release of cytokines during an inflammatory disease, a profound change in the functioning of the neuroendocrine system is observed (Reichlin, 1993; Wilder, 1995). Inflammatory cytokine-driven responses of the neuroendocrine system are similar to and resemble those reactions seen in the body during starvation; decreased thyroid function, lower levels of GH-dependent peptides and suppression of gonadal function (Reichlin, 1999).

Not only does inflammation due to lameness share commonalities with starvation, but also with the certain reproductive complications observed with mastitis. In dairy cattle, 30% of the cows with an inflammatory response to chronic subclinical mastitis showed decreased levels of circulating estradiol, timing of ovulation, follicular steroidogenesis and oocyte competence. These symptoms help partially explain the lower fertility of mastitic cows (Wolfenson et al., 2009). The estradiol concentrations in control cows without mastitis, normal response cows with subclinical mastitis and chronic cows with subclinical mastitis showed differences that should be noted (870 ± 62, 815 ± 127 and 269 ± 71 ng/ml, respectively) (P<0.01) (Lavon et al., 2009). These numbers show the significant decrease in estradiol concentrations in mastitic cows. In addition, these researchers showed that the mRNA expression for the LH receptors, cytochrome P450 and P450 7α-hydroxlase were lower (P<0.05) in chronic mastitic cows. Along with these findings, it was discovered that blastocyst formation rate was significantly lower in embryos from mastitic cows (Wolfenson et al., 2009). This decrease in formation rate is similar to the inflammatory response of embryos that were obtained in laboratory from the cows during the hot summer months.

Immune barrier dysfunction is another inflammatory response that can
be studied to help in the understanding of claw inflammation. Studies showed an increase in barrier dysfunction with the impact of several factors including heat stress, water deprivation during strenuous workouts and the usage of aspirin and ibuprofen during intense exercise (Lambert et al., 2002, 2007 and 2008). These studies help to understand some of the different stressors which can create inflammatory response, by increasing the amount of endotoxin that passes through the immune barrier of the intestinal tract. These different kinds of stressors can also impact keratinocyte growth and differentiation of the claw horn tissue. Release of cytokines and growth factors such as IL-1 and keratin growth factor (KGF) due to a stressor may control keratinocyte growth and differentiation through a double paracrine loop of communication between fibroblasts in the dermis and keratinocytes in the epidermis (Werner, 2001). Changes in the architecture of the horn tissue may be affected when communication between the dermal and epidermal layers is interrupted causing changes in biomechanical properties like elasticity and hardness (Hinterhofer et al., 2006). Much more is known on the mechanisms of horn development in cattle than in swine at this time, but this information suggests that inflammatory responses may impact horn development in swine as well. In a small sow study, feet showing claw lesions were selected for a post mortem examination. Of the 100 feet chosen, 35 of claws were considered a lesion score 3. All feet were evaluated for the correlation between visible claw lesions and inflammation of the underlying corium, researchers found a high correlation, 90% of the lesions were associated with a pathology of the underlying corium and all of the 35 severe lesions had underlying pathology of the corium (Da Silva et al., 2010a). This study demonstrates that there is a potential pathogenesis of lameness and promotes that methods of ameliorating inflammation may be useful to the swine producer.

Impact of Nutrition

Tomlinson et al. (2004) wrote a valuable review on the impact of nutrition on claw health by focusing on the roles of protein, energy, macro minerals, trace minerals and vitamins on the maintenance of the claw. Trace mineral amino acid complexes from Zinpro have been shown to be more bioavailable (Wedekind et al., 1992). Research also shows that trace mineral amino acid complexes are better retained by the body (Nockels et al., 1993). Supplementation of trace mineral amino acid complexes has been shown to have multiple impacts on cattle performance and health. Feeding trace mineral amino acid complexes has shown improved claw integrity (Nocek et al., 2000), fertility, lactation performance (Ballantine et al., 2002; Siciliano-Jones
et al., 2008), immune function expressed as somatic cell counts, (Kellogg et al., 2004) and longevity (Siciliano-Jones et al., 2008) in dairy cattle.

The claw health of dairy cattle when trace mineral amino acid complexes replace inorganic sources has been more variable in response at improving claw integrity (Nocek et al., 2006). It has been suggested that the limited effects of trace mineral source on claw integrity may be attributed to a lower incidence of claw lesions in some studies (Nocek et al., 2006) as compared with the incidence of claw lesions observed in other studies (Ballantine et al. 2002; Nocek et al. 2000). This suggests that greater treatment responses are seen with herds with higher lesion scores. It should not be too surprising that the integrity of the claw may give us more variable responses since it has so many complex interactions with environment and metabolism. Interestingly, measurement of liver stores of the trace minerals doesn't seem to provide much of an answer either as several studies have shown the liver values are not different between inorganic treatments and trace mineral amino acid complexes (Table 2; Siciliano-Jones et al., 2008).

Table 2. Effect of trace mineral source on liver mineral concentration in dairy cows, 14 wk postpartum.¹

<table>
<thead>
<tr>
<th>Mineral, mg/kg of DM</th>
<th>Treatment</th>
<th>P=</th>
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<tbody>
<tr>
<td></td>
<td>Sulfates</td>
<td>Complex trace minerals</td>
</tr>
<tr>
<td>Cu</td>
<td>465.0 ±</td>
<td>492.0 ± 25</td>
</tr>
<tr>
<td>Fe</td>
<td>248.0 ±</td>
<td>227.0 ± 14</td>
</tr>
<tr>
<td>Mn</td>
<td>10.3 ±</td>
<td>10.2 ± 0.04</td>
</tr>
<tr>
<td>Mo</td>
<td>3.4 ±</td>
<td>3.4 ± 0.1</td>
</tr>
<tr>
<td>Zn</td>
<td>96.9 ±</td>
<td>105.0 ± 4.4</td>
</tr>
</tbody>
</table>

¹Liver biopsies were collected before trial initiation and at 14 wk postpartum. Data collected before trial initiation were used as a covariate. Least square means (±SEM) are presented.

The most important point to all this is that trace mineral amino acid complexes deliver animal performance in cattle in production and/or health. The responses may vary in magnitude depending on the specific influences of each herd, but improvement in one or more of the following parameters is commonly reported: claw lesions, somatic cell counts, reproductive performance, milk production and longevity.

Data is not near as abundant on the issue of lameness in swine. More work has been done in the last several
years as we are starting to see many of the same responses as we see in cattle. A recent study where Zn, Mn and Cu fed as amino acid complexes (Availa®-Sow) were supplemented to stall-housed sows in a controlled experiment, results showed a decrease in claw lesions of sows housed in gestation crates (Anil et al., 2009b). These sows were fed basal gestation and lactation diets that differed only in the source of Zn, Mn and Cu in the diet. Inorganic treatment diets supplied (Zn 125 ppm, 40 ppm Mn and 15 ppm of Cu) to the diet as sulfates. The other sows were fed diets with a partial substitution of the inorganic trace minerals with Availa-Sow (supplying 50 ppm of Zn, 20 ppm Mn, 10 ppm of Cu) with the remainder of total added levels being supplied by sulfates to make both diets iso for trace minerals added. Results showed that stall-housed sows fed Availa-Sow had fewer (P<0.05) lesions after measuring lesion numbers at two consecutive gestation periods on the hind limbs and soles (Figure 1). These sows had fewer (P<0.07) lesions on the lateral claws and total lesions. In this same study, lesion scores (severity of the lesions) were improved (P<0.05) for total lesions and for total lateral claw lesions when sows were fed diets containing Availa-Sow (Figure 2).

**Figure 1.** Association of supplementing Availa®-Sow with the number of claw lesions in stall- housed sows.
Research from another project reported similar results for improvement in lesion score or severity. This study was of two different herds that had begun feeding Availa-Sow in the diets and measured the number of sows that remained the same or improved the severity of lesions with observations being taken prior to the start of ZPM treatment. A second observation was recorded in the next farrowing after feeding Availa-Sow (Da Silva, et al., 2010b) and showed that all lesion scores were better or the same (P<0.05) in one farm, while in the second farm only long toes, heel sole cracks, side wall vertical cracks and side horizontal cracks were improved (P<0.05). If improvements were made to inflammatory lesions then one should see changes in the number of lame sows. Analysis on prevalence of lameness was lower (P<0.05) for the sows fed Availa-Sow (34% vs. 51%) over sows fed inorganic trace minerals (Anil et al., 2010a)(Figure 3).
Figure 3. Percent lameness$^a$ in sows when fed Availa-Sow verses inorganic trace minerals.

![Bar chart showing percent lameness in sows fed Availa-Sow versus inorganic trace minerals.](chart.png)

$^a$ Kruskal-Wallis test
$^b$ Reduction in lameness, $P < 0.001$


When reproductive performance was evaluated there were more (P<0.05) pigs born alive (11.07 ± 0.21 vs. 10.44 ± 0.22, Figure 4) and litter birth weight tended to be higher (P<0.07) (16.99 ± 0.31 vs. 16.16 ± 0.33, kg) (Anil et al., 2010b).

![Bar chart showing pigs born alive in sows fed Availa-Sow and inorganic trace minerals.](chart2.png)

$^a$ Sulfates provided 125 ppm Zn, 40 ppm Mn, 15 ppm Cu
$^b$ Availa-Sow, partial substitution with 50 ppm Zn as zinc amino acid complex, 20 ppm Mn as manganese amino acid complex, 10 ppm Cu as copper amino acid complex
$^y$ Means lacking a common superscript letter differ, $P < 0.05$

These researchers found that group-housed sows in this experiment had higher lesions scores in all claw areas (P<0.05). In the second examination of side wall cracks of group housed sows in the same experiment, results showed that the sows fed trace mineral amino acid complexes had a higher (P<0.05) proportion of sows with lesions that either improved or stayed the same than the controls (91% vs. 73%) (Anil et al., 2010c). These researchers also showed that sows fed diets containing only inorganic sulfate trace minerals were 40% more likely (P<0.05) to have ≤ 10 live born piglets compared to sows fed Availa-Sow (Anil et al., 2010d). Da Silva (2010c) showed that white line lesions and overgrown toes odds ratios of 1.151 and 1.154 respectively were positively associated (P<0.05 for both lesions) with the likelihood of having ≤ 10 pigs born alive.

Conclusion

Claw health is crucial to the overall well-being of the sow. If not properly treated, negative claw conditions can lead to lameness and may result in further complications. This causes a devastating loss to swine producers by decreasing reproductive performance and longevity. By improving our understanding of the factors that contribute to sow lameness and inflammation hopefully we can prevent these circumstances from occurring and avoid the many downfalls of lameness. The most important aspect of amino acid complex trace minerals is proven animal performance.

Research has shown that feeding Availa-Sow decreases the number and severity of claw lesions ultimately decreasing sow lameness. The purported mechanism of decreasing inflammatory mediators results in improved reproductive performance observed by in numbers of piglets born alive, increased litter weights, less potential for small litters, heavier weaning weights and increased feed consumption in lactation.

The economic implications for feeding Availa-Sow are a decrease in the net cost of pork production and improved profitability of the pork production enterprise.
References


Da Silva, A., S. S. Anil, J. Deen and R. B. Morrison. 2010b. Effect of the supplementation of trace mineral complexes on the healing of claw lesions in two sow


