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Lameness hurts sow reproduction

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Lameness has long been recognized as a problem in the reproductive herd. Removal of non-productive sows along with introduction of replacements is an essential part of maintaining herd productivity at a constant level. There are economic and welfare impacts of a lower sow retention rate due to lameness.

Knowledge and understanding of lameness in swine is increasing as more research groups are reporting data. Odds ratios have been reported for sows with elongated claws, claw cracks, heel erosion and overgrowth and uneven toes has been shown to significantly impact the incidence of lameness (Vestergaard *et al*., 2006; Anil *et al*., 2008). Lameness increases odds ratios of early removal and has shown a highly significant decrease in sow productivity due to lameness (Anil *et al*, 2008). The objective of this paper is to understand the metabolic and mechanistic pathways of how inflammation due to lameness potentially directly and/or indirectly impacts reproductive performance of the sow herd. To further demonstrate the lameness model of inflammatory response, this paper will utilize other inflammatory responses such as mastitis, starvation, immune barrier dysfunction, and heat stress to help demonstrate the commonality of the pathways involved. With an understanding of these mechanisms one can implement management practices, nutrition and selective disease prevention strategies to reduce or prevent inflammatory responses due to lameness.

One of the obvious consequences of lameness is pain and inflammation causing a reduction of feed intake. If a younger parity sow does not eat well they generally have reduced reproductive performance. The reduction in energy and protein consumption during lactation may disrupt or change in the amount of signal from the hypothalamus of GnRH which impacts amount of release of LH and FSH and subsequently impacts steriodogenesis of the ovary. Often sows or gilts with low intakes in lactation are under conditioned with a body condition score of 1 on a 1-5 scale, with 5 being over conditioned. Sows with inadequate feed intake during lactation increased their odds of removal from the breeding herd (Anil *et al*., 2006). Inflammatory cytokine-driven responses of the neuroendocrine system are similar and resemble those seen in starvation: reduced thyroid function, reduced levels of GH-dependent peptides, and suppression of gonadal function (Reichlin, 1999). Metabolic response to starvation and severe inflammation essentially cause similar brain signaling and responses to metabolism within the animal.

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. Younger first litter gilts were more sensitive to negative effects of reduced feed intake during lactation than older gilts and multiparous sows (Eissen *et al*., 2003). Lactation is one of the most energetically expensive and challenging activities that a female can undertake. The reproductive effects of inadequate lactation feed intake seems to be mediated, at least in part, through LH secretion, and embryo mortality (King and Martin, 1989). Sows with a body condition score (BCS) of 1 have a higher frequency of acyclic ovaries than sows with a BCS of 4. It is reasonable that some of the body weight loss was due to increased protein loss from these sows. Clowes *et al.* (2003) reported body protein mass loss greater than 9 to 12% rapidly reduced ovarian function. Protein restriction throughout lactation alters circulating concentrations of somatotrophic hormones and insulin at the end of lactation and negatively impacts post weaning ovulation rate (Mejia-Guadarrama *et al*., 2002). 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). A low feed intake during lactation involves mobilization of body tissues and can lead to an excessive loss of body weight, reducing sow longevity (Gaughan *et al*., 1995) and reproductive performance (Quesnel, 2005). Prevention and early treatment of lameness and claw injuries will help maintain feed consumption and appetite.

Severe tissue injury induced a relatively stereotypical, pathophysiologic response manifested by fever, catabolism and sickness behavior. All organ systems are altered by acute and chronic inflammatory states. Activation of inflammatory cytokines by toxins or products of cell injury leads to a variety of metabolic and endocrine changes, mediated in part by the direct action of cytokines on tissue function and by changes in pituitary-endocrine end

organ function (Reichlin, 1999). Many of the claw lesions and injuries fall into these inflammatory type wounds. Investigating the possible mechanisms for these lameness and foot injuries impacting reproduction becomes quite plausible when one sees how similar lack of nutrients causes some of the same responses as an inflammatory response due to cytokine release. Is it any wonder that we see more sows abort or absorb embyros, decreased litter sizes born, and a lack of return to estrus when sows are severely lame? Organ systems are altered by acute and chronic inflammatory states. In livestock production most recognize the dramatic changes to acute phase responses where dramatic changes occur in liver function such as suppression of albumin, transferrin and ceruloplasmin and increased synthesis of proteins such as fibrinogen, C-reactive protein (Dinarello and Wolf, 1993). When an animal gets an insult or injury most of the changes that happen in the body are mediated by a cascade of polypeptide molecules called inflammatory cytokines. These cytokines are released from immune barrier functioning cells such as endothelial cells, specialized immune cells such as lymphocytes, monocytes, macrophages and several other types of parenchymal cells. Examples of some of these cytokines that are released are interleukin (IL)-1, IL-2, IL-6 just to name some of the first ones identified. In addition, tumor necrosis factor-alpha (TNF-α), interferon-gamma (INF-γ) and several other cytokines with anti-inflammatory activity such as IL-10, IL-1 receptor antagonist, transforming growth factor-B all work in a synergistic reaction to regulate body metabolism to get the animal to survive. One of the major impacts of cytokines is a profound change in neuroendocrine function during inflammatory disease (Reichlin, 1993; Wilder 1995).

Severe inflammatory illness induced a dramatic fall in sex steroids (Dong *et al*., 1992) in the human male. TNFα also inhibits gonadal secretion in the mouse (van der Poll *et al*., 1993). In the ovary, intrinsic cytokines, IL-6, TNFα, and IL-1 regulate steroidogenesis, maturation, atresia, and apoptosis of ovarian cells. At the level of the hypothalamus, IL-1 inhibits pulsatile secretion of gonadotropin-releasing hormone (GnRH), which leads to low gonadotropin secretion and low levels of sex steroids (Rivest and Rivier, 1995; Shalts *et al*., 1991). Most of these responses are probably mediated at the hypothalamic level by the induction of corticotropic releasing hormone (CRH) and/or vasopressin (VP) which act together to increase the release of adrenocorticotropic hormone (ACTH).

The release of cytokines causes a decrease in GnRH which reduces 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 TNFa which cause a direct effect on the ovary. The effect on the ovary will cause a reduction in steroidogenesis and even apoptosis of the ovarian cells and the pregnancy will be lost. The most common reproductive anomaly found (9%) when harvesting reproductive tracts from cull sows was acyclic ovaries (Knauer *et al*., 2007). The occurrence of acyclic ovaries increased ($P < 0.05$) as Body Condition Score (BCS) of the sow decreased. Acyclic ovaries were also positively correlated ($P < 0.01$) with rear foot abscesses. Again we see a correlation between lameness and reproductive problems as acyclic ovaries increase in sows with rear foot abscesses. Not all sows with claw lesions will see changes in appetite and feed consumption. The injury must be inflammatory to see the responses described above.

Other inflammatory responses have been shown to have very similar modes of action and pathways in which the animal responds. In dairy cattle, the inflammatory response from chronic subclinical mastitis showed that 30% of these cows showed reduced levels of circulating estradiol, timing of ovulation, follicular steroidogenesis, oocyte competence which partially explain the lower fertility of mastitic cows (Wolfsenson *et al*., 2009). Estradiol concentrations in control cows (no mastitis), normal response cows from subclinical mastitis and chronic cows with subclinical mastitis showed differences (870 ± 62, 815 ± 127, and 269 ± 71 ng/ml) ($P < 0.01$) (Lavon *et al*., 2009). In addition these researchers showed that mRNA expression for the LH receptors (cytochrome P 450 and P450, 7 α-hydroxylase) was lower ($P < 0.05$) in the chronic mastitic cows. Blastocyst formation rate was significantly lower in embryos from mastitic cows (Wolfsenson et al., 2009) which are similar to the response of embyros inflammatory response of embryos from laboratory results obtained from cows during the hot summer months. Scientists have created a model for testing the inflammatory response for binge alcohol consumption using MT-KO mice. Lambert, J.C. *et al*., (2004) showed that the addition of zinc sulfate could reduce the entrance of alcohol into the intestines, reduced the liver TNFα concentrations, and reduced the serum alanine transaminase which is indicative of hepatocyte necrosis. Further studies on immune barrier dysfunction showed impact of heat stress, a water deprivation in strenuous works outs, and impact of aspirin and ibuprofen during intense exercise increase barrier dysfunction (Lambert *et al*., 2002, 2007 and 2008). These studies help us 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.

Tomlinson *et al*., (2004) has written an excellent review of how the impact of nutrition, protein, energy, macro minerals, trace minerals and vitamins have been implicated in maintaining claw health. An eight trial summary shows an improvement in feet lesion scores, improved milk production and improved reproductive performance in dairy cattle (Siciliano-Jones *et al*., 2008) with the addition

of complexed organic minerals from Zinpro Corporation. Claw health is improved in the dairy cow by feeding complexed Zinpro minerals (Nocek *et al*., 2000, Nocek *et al*., 2006). Although further research is needed in sows, these examples suggest that nutrition may play an important role in supporting the immune system and improving lameness and reproductive performance.

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