

# Growth and Development Symposium: Understanding and Mitigating the Impacts of Inflammation on Animal Growth and Development

**516 Containing inflammation is essential for animal growth and health.** T. A. Niewold\*, *Nutrition and Health Unit, Department of Biosystems, Faculty of Bioscience Engineering, Katholieke Universiteit Leuven, Heverlee, Belgium.*

It is well established that infection leads to inflammation and release of pro-inflammatory cytokines. Cytokines activate immune cells and have a profound effect on growth by reducing intake and increasing catabolism of muscle tissue. Less is known about the postprandial (low-grade) inflammatory response in the intestines, a normal physiological response, called metabolic inflammation (MI). The extent of MI is related to energy value and glycemic index of feed as well as specific (e.g., fatty acid) constituents in the feed. To maintain integrity in the body, MI is tightly regulated. The host benefits from downregulation of inflammatory responses directly (e.g., tissue integrity, nutrient transport, and energetically) and indirectly (e.g., Lawsonia and Clostridium benefit from inflammatory responses). Tight control of MI is often disrupted due to the regulatory mechanisms being overwhelmed by high-energy feed intakes fed in production settings. Moreover, feed may also contain pro- and anti-inflammatory components. Prime examples of the latter are the antimicrobial growth promoters (AGP). Initially, beneficial effects of AGP were attributed to their antibiotic characteristics; however this is highly unlikely for a variety of reasons. A prime reason is the sub-therapeutic concentrations in commercial rations. Thus, AGP are much more likely to work as growth permitters as direct inhibitors of intestinal inflammatory responses. This theory is corroborated by the good correlation between the (in vitro) direct anti-inflammatory effect of certain antibiotics, and their effectiveness as AGP. It also explains why non-antibiotic anti-inflammatory compounds like acetylsalicylic acid have a similar effect. It is concluded that effective growth promoters are inhibitors of the intestinal inflammatory response. Their proximal intestinal uptake should be low to maintain effective concentrations in the distal small intestine. Inflammation, whether it results from feed or disease, is inversely related to growth and health. Therefore, research should focus on anti-inflammatory compounds and anti-inflammatory feed composition.

**Key words:** inflammation, anti-inflammatory, antimicrobial growth promoter

**517 Impacts of inflammation on cattle growth and carcass merit.** C. R. Krehbiel\*, C. L. Maxwell, C. A. Gifford, and R. L. Mills, *Oklahoma State University, Stillwater.*

Inflammation caused by bovine respiratory disease (BRD) continues to be one of the greatest challenges facing beef cattle producers and feedlot managers. Inflammation decreases DMI, ADG, and G:F in feedlot calves decreasing rate of growth and increasing days on feed which results in performance based economic losses during the feeding period. In the past decade, marketing of feedlot animals has drastically switched from selling cattle on a live basis to a grid-based marketing system. When cattle are marketed on a live basis, the economic effects of BRD stop at decreased feedlot performance, carcass weight and death loss. However, when cattle are marketed in a grid-based system, inflammation has the potential to also affect carcass cutability, quality, and consumer acceptability. The effects of inflammation on feedlot cattle in regards to performance are well understood; however, effects on cattle growth and ultimately carcass merit are not as well

described. Recent studies in feedlot cattle have suggested that the incidence of BRD decreases both HCW and marbling. Research in other species has demonstrated that during the acute phase response, pro-inflammatory cytokines promote skeletal muscle catabolism to supply amino acids and energy substrates for immune tissues. Further, during this early immune response, the liver changes its metabolic priorities to the production of acute phase proteins for use in host defense. Together these dramatic shifts in systemic metabolism may explain the detrimental effects on performance and carcass traits commonly associated with BRD in feedlot calves. Moreover, recent studies relative to human health have revealed complex multilevel interactions between the metabolic and immune systems and highlighted inflammation as being a significant contributor to major metabolic diseases. The objective of this paper is to gather recent data to help explain the economical and physiological effects of inflammation on cattle growth and carcass merit.

**Key words:** bovine respiratory disease, carcass merit, cattle growth

**518 Endotoxin, inflammation, and intestinal function in swine.** N. K. Gabler\*, L. H. Baumgard, and V. Mani, *Iowa State University, Ames.*

Circulating endotoxin or lipopolysaccharide (LPS) can stimulate localized or systemic inflammation via activation of toll-like receptors (TLR) and the immune system. This may partition energy away from growth and toward immune system requirements. Furthermore, inflammation can regulate intestinal epithelial function by altering intestinal integrity and nutrient transport. The gastrointestinal tract is a large reservoir of both gram-positive and negative bacteria in which bacterial populations gradually increase from approximately 0 to 10<sup>3</sup>/mL of luminal contents in the duodenum to 10<sup>11</sup>/mL in the colon. Thus, gram-negative bacteria serve as a source of endotoxin in the intestine, which can enter the systemic circulation, resulting in localized or systemic inflammation. Inflammation can alter feed intake, small intestinal nutrient transport, and growth. Furthermore, environmental factors can modulate intestinal endotoxin transport via altering either: 1) non-specific paracellular transport through the tight junctions or 2) transcellular transport, potentially through lipid raft membrane domains via TLR4-mediated endocytosis. Paracellular endotoxin transport occurs through reduced tight junction integrity, which may be a result of enteric disease, inflammation, or stress, causing a dissociation of tight junction protein complexes. Lipid rafts involved in transcellular transport are specialized membrane regions rich in glycolipids, sphingolipids, cholesterol, and saturated fatty acids. Endotoxin-related signaling proteins such as TLR4, CD14, and MD2 assemble in the lipid raft, which permits endotoxin signaling or endocytosis. Either transport pathway may be altered by dietary and membrane fatty acid composition or environmental stresses and inflammation. This presentation will discuss the role of endotoxin and inflammation in regulating intestinal function as it relates to pig growth performance.

**Key words:** endotoxin, lipid raft, intestine

**519 The role inflammation plays during clinical mastitis on the performance and health of dairy cows.** M. A. Ballou\*, *Department of Animal and Food Sciences, Texas Tech University, Lubbock.*

Genetic selection for increased milk production in dairy cattle over the past half a century was not associated with an attenuated inflammatory response. The systemic and local inflammatory responses contribute to the altered metabolism, reduced production performance, and high cull rate of lactating dairy cows with clinical mastitis. More aggressive inflammatory responses were observed in early lactation when compared with late lactation following an intramammary challenge with purified endotoxin. The epidemiology of clinical mastitis indicates the highest incidence is observed during the peripartum period; therefore, an enhanced inflammatory response may be involved in the etiology and severity of the clinical mastitis observed during the peripartum period. Milk production losses and compositional changes are observed among all mammary quarters from a cow with clinical mastitis, but the responses are more severe and sustained among culture-positive quarters. The culture-positive mammary quarters reflect both the systemic and local reactions; whereas culture-negative quarters only represent the systemic response. The systemic effects of the inflammatory response include: reduced dry matter intake, hyperthermia, and changes in whole-body nutrient partitioning affecting mammary epithelial substrate availability; whereas the local inflammatory effects include: the energetic requirements of the increased inflammatory leukocyte pool, decreased synthetic capacity of mammary epithelium independent of substrate availability, and paracellular leakage of milk components from the alveolar lumen into the extracellular fluid. Research has focused on either improving other host immunological defenses or attenuating the inflammatory response to limit the deleterious effects during peripartum mastitis. This paper will highlight recent research on the production losses associated with the inflammatory response during mastitis as well as potential management strategies to reduce or prevent those losses.

**Key words:** dairy, inflammation, performance

**520 Nutritional costs of inflammation and consequences for animal growth and production.** K. C. Klasing\*, *University of California at Davis, Davis.*

The pro-inflammatory response to microbes or trauma results in decreased growth, impaired efficiency of nutrient use, altered nutrient requirements, and a clear stress response. Pro-inflammatory cytokines (IL-1 and IL-6 in chickens and IL-1, IL-6, and tumor necrosis factor in mammals) mediate many of these changes, either by direct effects on cells or by altering the endocrine milieu (e.g., corticosteroids). Other cytokines, including interferon gamma and IL-18 may also contribute. Growth and efficiency of nutrient use are diminished by changes in food intake, nutrient absorption, metabolism, and tissue accretion. Decreases in intestinal absorption of nutrients are also important and are greatest for lipids (including fat-soluble vitamins) and some trace minerals. Metabolic inefficiencies caused by inflammation are due to increased turnover of muscle and bone. Skeletal muscle and bone accretion are impaired, but liver accretion is increased due to increased production of lipids and acute-phase proteins. In aggregate, these alterations change the requirements for many amino acids and trace nutrients. Although accommodating these proportional changes in nutrient needs via dietary adjustments improves feed efficiency, growth cannot be completely normalized by nutritional means. Dampening the acute-phase response to inflammation by nutrients with regulatory properties (e.g., n-3 PUFA) has some utility, but diminishing the frequency and intensity of inflammatory challenges is the most useful strategy. This can be accomplished by sanitation, vaccination, and feeding prophylactic antibiotics or other antimicrobials.

**Key words:** inflammation, acute-phase response, growth