



Inflammatory Cytokines Sequester Protein from Animal Growth During Infections – A Short Communication

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Abstract

It is now a known fact that in the modern high-density production systems reared animals' environment need to be highly sanitized to avoid being invaded by pathogens or disease-causing organisms, such as bacteria. Domesticated animals, particularly non-ruminants, such as the pig and poultry have inherent immune system that is primarily concerned with the protection of the animals, in terms of their welfare and well-being. However, protecting the animals immune system can be very expensive economically. To this therefore, a number of studies have provided empirical evidences that animals reared in unsanitary environments usually lead to a high level of host-pathogen interactions. This results in such animals growing more slowly and consume less feed than animals reared in more sanitary conditions. This is primarily due to the fact that nutrients that ought to be used to supporting growth and skeletal muscle development are redirected or sequestered to support the host's defenses against pathogenic microorganisms. The overall effect of this result is poor animal growth, performance indices, and profit the margin is significantly reduced.

Key words: Cytokines, Sequester of Protein Metabolism, Health, Growth and Monogastrics

INTRODUCTION

The major objective and aim of the pig/poultry farmer is to make profit from his or her ventures. One of the major means the farmer can achieve this is to improve efficiency of feed utilizations by his animals principally for the fact that feed costs alone accounts for the largest economic input in the animal enterprises. This is particularly true for proteins because they account for a major portion of total feed costs (NRC, 2012). Therefore, wasteful usage of protein sources no



doubt would significantly lead to increase in the cost of production in the animal enterprise (Patience *et al.*, 1995; NRC, 2012). Conversely, feeding of excess protein to pigs or poultry can result to severe adverse effects on the environment (Sutton *et al.*, 1999). To this point therefore, the management of wastes and odors have become major challenges to the swine and poultry industries. It is important to note that large amounts of nitrogen excreted in animal wastes often lead to contamination of water and odorous emissions because principally many odorous compounds originate from undigested dietary protein and other nitrogenous compounds.

Again, it is also now well-established that animals reared in environments where they are exposed to a high number of pathogens neither eat well nor grow well, even when no clinically identifiable disease is found or present. The early study by Coates *et al.* (1963) showed that chicks reared in a germ-free environment grew faster and consumed more feed compared to chicks reared in a conventional environment. At that time, it was thought that a bacterial or viral contaminant was directly responsible for decreasing the performance of the host. At present, it has been proposed that an immunological mechanism is at least partly, if not totally responsible for the decreased performance of the immune-challenged animals (Johnson, 1997) suggesting the implication of cytokines that were confirmed by the findings of independent studies such as those of Finck *et al.* (1998).

Many cytokines are involved in metabolic regulations. However, the major ones are the inflammatory cytokines, mainly interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) (Duitman *et al.*, 2011). The objectives of this paper therefore, are to briefly discuss the mechanisms via which the above stated inflammatory cytokines sequester dietary protein from protein accretion and growth in the monogastrics leading to poor animal growth and performance.

Effects of Inflammatory Cytokines on Nitrogen Metabolism

The metabolic changes caused by these cytokines are homeostatic in nature therefore nutrients that would have been used for growth and skeletal muscle accretion are usually sequestered to supporting host defense systems which is of more importance to the animal at such times. As rapid efficient protein accretion is the goal of the animal farmer, inflammatory cytokines thus



have profound impacts on protein accretion (NRC, 2012). To this point therefore, the net impact of cytokine synthesis and subsequent release is a significant decrease in whole-body protein accretion. The overall effect of this entire process is the alteration in whole-body protein and skeletal muscle metabolism leading to a decrease in protein synthesis and an increase in protein degradation and protein wastage; this is at the core of poor animal performances involving inflammatory cytokines (Scheller *et al.*, 2011). The combination of these processes culminate in the decrease in protein accretion and an increase in nitrogen excretion. This act has also been implicated in environmental pollution (Sutton *et al.*, 1999; NRC, 2012). Table 1, further aids in identifying and shedding more light on the specific roles each of the cytokines play in the sequestration of nitrogen from protein accretion and skeletal muscle growth in their immunologic and metabolic functions in protein metabolism.

Table 1. Immunologic and Metabolic Effects of Cytokines

Immunologic and Metabolic Roles of Cytokine in Protein Metabolism		
Interleukin-1	Interleukin-6	Tumor Necrosis Factor-α
	Major Immunological Effects	
Activates lymphocytes	Activates lymphocytes	Inflammation
	Antibody production	
	Acute-phase protein synthesis	
	Major Metabolic Effects	
Muscle protein degradation	Muscle protein degradation	Muscle protein degradation
Reduced muscle protein synthesis	Reduced muscle protein synthesis	Reduced muscle protein synthesis
Fever	Fever	Fever
Anorexia	Acute-phase protein synthesis	Anorexia
Hypoferremia		Lipolysis
Hypozincemia		
Hypercuppremia		

Negative Nitrogen Balance



The information provided in Table 1 had been demonstrated by previous workers that exogenous IL-1 and TNF- α elicit a negative nitrogen balance that is accompanied by a decrease in whole-body protein synthesis and an increase in skeletal muscle protein degradation. Consistent with these findings, peak plasma concentrations of IL-6, TNF- α and urea nitrogen were evident in pigs that were fasted and then challenged with lipopolysaccharide (Webel *et al.*, 1997; Escobar *et al.*, 2004).

The influence of cytokines on protein synthesis and degradation is dependent on the tissue and skeletal-muscle fiber type. In general principle, protein synthesis is decreased in skeletal muscle and increased in liver, lung and heart (Duitman *et al.*, 2011). Therefore, the effects of cytokines on protein turnover or kinetics are quite different from those induced by fasting wherein peripheral proteins are spared and visceral proteins are broken down. To this point, the increase in protein synthesis in the liver is most likely due to the increase in the synthesis of the acute-phase proteins. Different independent *in vivo* and *in vitro* studies have demonstrated that synthesis of the positive acute-phase proteins is mediated by the direct action of cytokines upon the hepatocyte and indirectly as a result of hormonal changes induced by cytokines (Josefowicz *et al.*, 2012).

The inflammatory cytokines IL-1, IL-6 and TNF- α are well known to increase the rate of hepatic amino acid uptake and protein synthesis. The increase in hepatic protein synthesis results in a net increase in hepatic protein accretion and an increase in protein release into the circulation (Josefowicz *et al.*, 2012). It is also generally accepted that the increase in acute-phase protein production is of fundamental significance as is an adaptive physiological response essential for the survival of the animal (Escobar *et al.*, 2004). Proteins released by the hepatocyte have a wide range of functions. Acute-phase proteins enhance macrophage phagocytosis and lysis ability, inhibit serum protease activity and alter plasma mineral concentrations amongst other important functions (Duitman *et al.*, 2011; Josefowicz *et al.*, 2012).

Conclusion

Inflammatory cytokines are capable of sequestering protein from protein accretion and skeletal muscle growth during an immune system challenge of the animal thereby negatively affecting animal growth and performance indices. Furthermore, immune system challenge causes the



immune system to trigger acute-phase protein synthesis, especially in the liver majorly for the survival of the animal.

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